" STUDIES IN

# THE LIFE-CYCLE OF HUMAN AMOEBIASIS:

FROM ITS

PROTOZOOLOGICAL, MORBID, & CLINICAL

ASPECTS."

(Illustrated)

BEING A

THESIS

FOR THE M.D. DEGREE OF THE

UNIVERSITY OF EDINBURGH,

1917.

BY

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I.M.S.

Holder of the Sir James Ranald Martin Gold Medal

Tropical Medicine, April 1914, presented at the

Royal Army Medical School, Millbank, London.

## INTRODUCTORY & EXPLANATORY NOTES ON THE THESIS.

The Scope and nature of the Thesis is explained by its TITLE. It has been studied in its most recent advances and from accepted established Principles. It is a Disease of great antiquity and of great importance. Dysentery goes back to the time of Hippocrates - although its exact differentiation into recognised Types dates practically only from the closing decade of the XIX Century. In fact, although Löesch discovered Amoebae in 1875, Lambl described the same organism in 1859, but regarded it as a "Monad" - the term in use. It was only after Kartulis' Researches in 1885, and the further verification of this by Osler, Councilman & Lafleur in 1890-1891 that the Disease was established on a firm & scientific basis.

The term 'Tropical' used in the Thesis solely applies to Amoebic Dysentery; although perhaps it is a misnomer, as Amoebic Dysentery occurs in many sub-Tropical Countries and Autochthonous cases have been described in England, including Liver-abscess, by Norman Moore & Dickinson in 1880, and Marshall in Edinburgh in 1912.

Nomenclature is complicated with the introduction of alternate terms. "Amoebic Dysentery" - introduced by Councilman & Lafleur; "Amoebic Colitis" by those who find a distinction between Colitis & Dysentery; "Dysenterie Amibienne" or "Dysenterie À Amibes" of French Writers; "Amöbenruhr" or "Amöbenkrankheit" of German Writers. Recently there has come into general usage, the term "AMOEBIASIS", introduced to cover the whole subject of Amoebic Infection as ONE Disease. Brown has taken exception to the term, as it does not express

express the dysenteric state, whereas the title Amoebic Dysentery conveys a distinctive & practical state and excludes all Other Protozoa of NON-Pathogenic Type. As in the Thesis it has been found necessary to cover the whole ground before Pathogenicity can be established, the title AMOEBIASIS has been selected.

In the matter of REFERENCES, those which were out of hand & which I could not possibly verify personally, but which are quoted by AUTHORITIES are asterisked * ; and marginally noted in red. Those I have been able to verify personally or select from current Journals, are typed in blue, or asterisked *. Additional Notes are marginally noted in blue.

The following Works have been referred to during the work of compilation of the Thesis, (excluding Journals of the British Medical Journal; Lancet &c)


CASTELLANI & CHALMERS "MANUAL OF TROPICAL MEDICINE", 2nd.End. 1913.

Sir PATRICK MANSON "TROPICAL DISEASES", 5th. edn. 1914.

L.POWELL PHILLIPS "AMOEBIASIS & THE DYSENTERIES", 1915.

Sir LEONARD ROGERS "DYSENTERIES - THEIR DIFFERENTIATION & TREATMENT", 1913

W.CARNEGIE BROWN "AMOEBIC DYSENTERY", 1910.

Sir WILLIAM OSLER "THE PRINCIPLES & PRACTICE OF MEDICINE", 7th.Edn.1910.

T.DIXON SAVILL "A SYSTEM OF CLINICAL MEDICINE", 3rd. Edn. 1912.

HERBERT FRENCH (Editor) "INDEX OF DIFFERENTIAL DIAGNOSIS OF MAIN SYMPTOMS" 1912.

KEEN & DACOSTA (Edited) "KEEN'S SURGERY, Vol.IV, 1908 Vol.VI, 1913.

## STANDARD WORKS & REFERENCES IN COMPILATION.

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| BEATTIE & DICKSON | " TEXT BOOK OF SPECIAL PATHOLOGY", 1909. |
| F.W.E.BURNHAM | " HAEMOCYTES & HAEMIC INFECTIONS", 1st.Edn.1913. |
| W.D'ESTE EMERY | " IMMUNITY & SPECIFIC THERAPY" (ILLUSTRATED). 1909. |

"The Medical Annual"of 1915 & 1916 - Sir.L.Rogers.

"MEMORANDA ON SOME MEDICAL DISEASES IN THE WAR MEDITERRANEAN AREA, WITH SOME SANITARY NOTES".*
1916; H.M.STATIONERY OFFICE,LONDON.

* Military Books.

The Thesis has been divided into Sections, so as to facilitate reading. The Section on Liver-Infection has been further divided into parts, Parts 1-12. This keeps the subject together.
A TYPED PAGE with a brief RESUMÉ of the contents of each Section will be found dividing off the Sections from each other; and a similar plan has been adopted in the PARTS. By these means it is hoped to simplify the work of the EXAMINER.

Lastly, there is a RESUMÉ given after all Sections and Parts so as to bring out the salient points, wherever this has been deemed practical.
A SUMMARY & CONCLUSIONS will be found at the end of the WORK, embodying the Main Points from the Thesis as a WHOLE.
In conclusion, that the material has been gathered together during the War. The Cases have been selected from amongst the FORCES of the Empire - a unique opportunity afforded by active service in the MEDITERRANEAN WAR AREA; from the DARDANELLES and from MESOPOTAMIA & PERSIA. Liver-Abscess has so far not occurred during these experiences. I have had therefore to rely on the presentation of clinical & Pathological data from the Work of OTHER Writers & Observers.

## INTRODUCTORY & EXPLANATORY NOTES ON THE THESIS.

Being in charge of the Laboratory in I.Indian Genrl. Hospital, Karachi, for a time ; and now in charge of the Laboratory at the "Annexe Hospital" Karachi I have been personally able to carry out the investigation of stools forwarded in cases of Dysentery.

The Thesis has been typed out for me by my wife, without whose help in this matter such a complicated and difficult subject could hardly have been done & checked throughout.

I have been able to make a few original observations on Spleen cases treated with EMETIN. These will be found in the Section of SPLENITIS.

Stress throughout has been laid on Clinical Pathology; Differential Diagnosis & Treatment.

Historical References are also given where these are of use in the reasoning out of Theories & the Practice of Medicine, as applied to AMOEBIASIS, in all its protean aspects.

# E T I O L O G Y

## The Case for the Pathogenicity of Ent. Histolytica.

The vexed question of what indeed is the real cause of Amoebic Dysentery was furiously debated in the past, and indeed beyond accepting the Ent. Histolytica as the specific agent in Dysentery, we have still to consider whether many of the numerous Species found in stagnant water, habituated to a parasitic existence and cause Dysentery. The following case has been cited by Axtell in "Northwest Medicine, Alaska, 1911, iii, 51."
A Patient who had been for years in the country and never in the South, suddenly developed Acute Dysentery after the Spring Floods of the Yukon River had left pools of stagnant water from which he had drunk. Contamination of the water by Dysenteric discharges seems to have been excluded. Whether this man was really a Latent Carrier of Ent. Histolytica and his disease was lit up by irritation caused by putrefactive substances in the Stagnant water, has however not been answered. Musgrave & Clegg of Manila*, considered all Intestinal Amoebae potentially pathogenic, and believed that there are several varieties. Amoebae are successfully cultivated in the laboratory only in Symbiosis with various Bacteria. This leads to the interesting question as to just what effect association with Bacteria of the Intestines may have on the Amoebae. This has been noted by Musgrave.
A very good account is given by Dr. F.M. Sandwith of the Historical portions of the Dysenteric problem was read before the Medical Society of London in 1914, and published in the Lancet, Sept. 5, 1914, pp 637 -642. The best general account is in Manson's Amoebic Dysentery, pp 7 - 22.

* Musgrave & Clegg, Amoebae: Their Cultivation & Etiological Significance- Pt. I, Bull: No. 18, Bureau Govt. Labs. Dept. Int. Manila, 1904.

## SECTION I. THE ETIOLOGY OF AMOEBIC DYSENTERY -

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## THE EPIDEMIOLOGY & GEOGRAPHICAL DISTRIBUTION.

HISTORICAL. - The history of Amoebic Dysentery definitely begins with the discovery by Lambl of a Rhizopod in Intestinal mucus of a Jewish child who died of Infantile Diarrhoea at the Kinder Spitale in Prague in 1859. In his original paper *, he definitely drew attention to its pathological significance and states, " It is an established fact that Minute organisms, which appear to be closely related to the Rhizopods, are present in the Human Intestinal canal, and their importance in regard to the concomitant pathological processes in children should certainly not be under-rated."

*Lambl - Beobachtungen und Studien aus dem Gebiete der pathologischen Anatomie and Histolgie, Prague, 1860 - quoted by Brown.

Five years later Losch, isolated Amoebae from the Intestinal mucus of a young peasant suffering from Chronic Dysentery at Archangel, and at the post-mortem they were shewn to be in enormous numbers in numerous ulcers on the mucus membrane of Colon and Sigmoid Flexure. He injected the mucus into the Rectum of 4 dogs, one of which became infected and when killed showed extensive ulceration of the lower part of the Colon.

Grassi in 1879 discovered the Cystic stage.
In 1883, Koch while engaged on Cholera investigation in Cairo, discovered a species of Amoeba embedded in the Intestinal tissues, which he regarded as possibly pathogenic, and asked Dr. Kartulis to investigate whether the organism had any

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definite relation to a morbid process.
The ultimate establishment of Amoebic Dysentery as a distinctive disease is largely due to Kartulis pioneer work in Egypt. His papers are numerous, and a complete list of his works is given by Brown, p.11-12 (footnotes). But the nomenclature adopted is confusing in the light of modern advance, for he describes the pathogenic organism as "Amoeba Coli".

In 1890 Osler at Baltimore, corroborated Kartulis' work by finding Amoebae in a case of Dysentery with Liver Abscess, which had originated in Panama. A series of such cases occurring in the wards of the John Hopkins Hospital, were investigated by Councilman & Lafleur, who introduced the term "Amoebic Dysentery". Not the least important of these researches was the observation of two distinct types differing in appearances and pathogenic virulence, and these they named A.Dysenteriae and A.Coli.
Quincke & Roos, in 1893, threw still more light upon the problem, for they differentiated the different phases of A.Dysenteriae & A.Coli, and noticed their variations and differences in appearance, and they re-classified the two varieties of Pathogenic Amoebae "one of which - the Tropical or Egyptian - was more virulent to the other " - an argument they supported by experimental introduction into the Rectum of cats, observing that their first organism was highly pathogenic, but their 2nd. & 3rd. varieties failed to cause Dysentery. Kruse & Pasquale repeated these observations, but used amoeba-containing pus from a hepatic abscess.

Celli & Fiocca maintained that as they had observed the close symbiosis of Bac.Coli & Amoeba Coli, they suggested that in the development of Amoebae, a metamorphosis of Bac.Coli into Bac. Dysenteriae occurred, and hence all dysentery was bacterial.
It is however, Schandinn's great work on the shores of the Adriatic that has placed our knowledge upon its present basis.
In his Memoir " Die parasitaren Amöben des menschlichen Darmkanals" in 1903, he drew attention to his theories. It was at Rovigno that he extended his series of researches into the life-history & biological relations of the parasites of Malaria & Dysentery, and the material was obtained in the endemic areas of neighbouring Villages. One of the organisms he found harmless & named it the Ent.Coli the other he stated was the definite cause of Amoebic Dysentery and named it Ent.Histolytica. In the course of one of his investigations, he himself swallowed developmental Cysts of the organisms, and had in consequence two serious attacks of Dysentery and later by dysenteric attacks which probably caused his death 4 years later by deep suppuration round the Sigmoid Flexure. Schandinn's great work has become the foundations of our knowledge.

# E T I O L O G Y

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In a masterly paper by C.M.Wenyon, Protozoologist to the London School of Tropical Medicine, and published in the B.M.J of Nov.15/1913, pp.1287 - 1288, shows how complex is the problem of the clear separation of the various Amoebae and Entamoebae from one another, and he says " that until some satisfactory method of cultivation has been discovered, it will be impossible at times to distinguish between these various Entamoebae". The following is a Shyopsis:-

i. In the free-living fresh-water Amoebae, it is possible to produce marked changes in any individual amoeba, by altering the quality of the water. Similarly Intestinal Amoebae will alter as the Intestinal contents change in density, composition, alkalimity, etc.

ii. Darling has drawn attention to the fact that Entamoebae are not uniform in appearance at every stage of their life-history, and that in the case of Pathogenic Entamoebae of Man, there is a life-cycle in which an active multiplication stage alternates with a stage of Encystment, and that as Encystment approaches the Entamoebae gradually assume a type which may be very different from that of the actively multiplying Entamoebae; so much so that Elmassian has mistaken this for a new species he includes as Entamoeba Minuta.

iii. Many of the Entamoebae escaping from a human Intestine, are in a degenerative condition or are actually dead. Hartmann draws attention to "Schandinn's extraordinary error of regarding the degenerating forms of the pathogenic Entamoebae as belonging to a species distinct from others which were not degenerating in the same preparations;" and another illustration is Ent.Undulans, Castellani, which were practically changed Trichomonas losing their three anterior flagellae, and the large one attached to the border of the undulating membrane is detached and finally cast off, leaving merely a mass of protoplasm performing Amoeboid movements.

iv. Sometimes the Ent.Coli or what is presumably this Entamoeba, occurring in the healthy Intestine, may sometimes have a very definite ectoplasm and simulate very closely the typical pathogenic form. In such cases are we really dealing with a Mixed Infection of the Pathogenic and Non-pathogenic Entamoebae in the healthy Intestine ? - a question of importance in view of Musgrave & Clegg's work and belief that all amoebae are potentially pathogenic. "Till we know more about the appearances of the pathogenic entamoebae in the healthy Gut, and of the non-pathogenic entamoebae in the ulcerated dysenteric Intestine, it will be impossible to answer this question with any degree of certainty".(Wenyon).

v. Very rarely Wenyon has met with cases in which a rapid encystment of the Entamoebae occurred with the result that Cysts of all sizes are produced, from large ones 18 μ in diameter, to

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small ones 9 μ; and these small Cysts contain 1, 2, 4, or 8 nucleii, as the large ones, but usually the nuclear multiplication ceases at 4. In such cases it may be impossible to distinguish some of these smaller Cysts from those of the pathogenic entamoebae which have a maximum of 4 nucleii (hence their name Tetragena), and are generally smaller than the Cysts of the Non-pathogenic types. The various gradations in size exclude possibility of Mixed-Infection. There is no known method of differentiating between the smaller Cysts of Ent.Coli, from a Cyst of the pathogenic entamoebae. Fortunately the Cysts of the pathogenic entamoebae are not subjected to the same extent of variation as the non-pathogenic types.

vi. Lastly some very small amoeboid organisms of the free-living non-pathogenic Amoeba Limax Type, are met with. "Are these small Amoebae necessarily distinct from the Entamoebae"? and in some of the minute graded forms of an undoubted Ent.Coli, the smallest take on this Limax Type of nucleus. If therefore this Limax-Type-nucleus are in reality E.Coli, then are those numerous small amoebae met with in the Intestine, a stage in the life history of Ent.Coli and not a distinct Amoeba ?

All these questions have an important bearing on the question of the interdependance of the Entamoebae on one another, and to what extent we must be prepared to go to exclude Mixed Entamoebic Infection, to fix the Specific Dysenteric action on E.Histolytica alone.
The question of species therefore, is narrowed down. Recently Castellani* has described new forms of Amoebae he has met with in three Dysenteric stools in Ceylon, producing clinically a mild type of Dysentery with abrupt onset and slight fever. Large oval active parasites were found, without flagella or cilia, but presenting a rapid peculiar vibrating movement, no differentiating ento- or ecto-plasm and no nucleus. These may be the altered Trichomans described by Wenyon. There are two other types isolated by him, distinguished as "notes on 2 Protozoa - Castellania Castellani"- "Entoplasma & Toxoplasma" - producing mild Dysentery. There were no distinct nucleus, no flagella or cilia. (cf.Trpl.Diseases Bulletin, Vol.5, 1915, p.293). The Morphology of the Intestinal Amoebae of man is therefore an important factor in the question. Recently,however, the important work of E.L.Walker and A.W.Sellards * places the Etiology of Amoebiasis on a firmer basis, and will be alluded to later.

* Castellani, Jrnl.Trop,Med. & Hyg. 1914, 65.

*Walker & Sellards, Phillipine Jrnl.Sci B.Trop.Med,1913,253.

The Case against pathogenicity has been urged by previous writers and their standpoint throughout has been the failure of growing Pathogenic strains and the nature of the Experimental investigations. Their view may then be narrowed down to the following:-

1. Entamoebae are often found in the dejecta of healthy persons, and in those suffering from diseases other than Intestinal and other than Dysenteric. This view, therefore, does not accept the Latent view; or at any rate was a point before the true nature of this condition had been recognised. If true, this view would reduce to nought the carefully-weighted Statistics and arguments of the Carrier-Problem, and would further militate against the actual finding of true lesions in healthy subjects, showing no evidence of disease during life, but with well-marked signs discovered on post-mortem. Moreover, we do not yet fully know of the life-history and morphological variations of Amoebae. "Infection" by harmless Entamoebae are recognised all over the world; and there is a remarkable variation in the percentage of persons thus affected. In Manila, Strong & Musgrave found Non-pathogenic Entamoebae in no more than 4% of cases; and in Malaya, Brown met with them in about 10% of all instances of non-Malarial febricula occurring in Europeans and Natives. There is no disputing the fact that there are two broad groups essentially distinct from each other - differentiated by Schaudinn, and accepted by the whole Medical World. If at times gradations take place, and simularities arise amongst the least-developed members, that in itself is no argument against the main finding but perhaps some developmental feature not understood and may be of "atavistic" origin. Musgrave, however, further asserted, as a result of investigations on 300 prisoners in Manila Jail in 101 of whom Entamoebae were found, that not only is there a distinct relationship between non-pathogenic and pathogenic entamoebae infections, but that they are in fact the same; and it may be that harmless Entamoebae probably by environment and lengthened residence in Alimentary Canal, acquire new Morphological characters and definite pathological functions. In Musgrave's 101 cases, 61 were actually suffering from Dysentery, but the other 40 were quite well. Of the latter, 8 died within 2 months, and amoebic infections were found in them all, and in 30, amoebic Dysentery developed within 3½ months. Here then is a perfect picture of Ambulatory or Latent Dysentery; but it is impossible to say whether this combination of intrinsically Pathogenic and Non-Pathogenic type produced the disease. The evidence of permutation is singularly wanting; the evidence of immediate or inherent pathogenic properties is fully proved by Experimental investigation. Finally, there does not appear to be any proportional relation between the Endemic Index of non-pathogenic amoebic infection, and the case-incidence of Amoebic Disease, for in Temperate climates the Endemic Index of non-pathogenic amoebae is often as high, or higher, than in the Tropics, and the case-incidence on this evidence is in inverse-ratio -leading to the only possible conclusion that strictly Tropical Dysentery is caused by definite strictly Tropical Amoebae or Ent. Histolytica.

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2. That Ent.Histolytica has not been grown in pure culture, and that there is therefore no direct or conclusive evidence of pathogenicity.
So far efforts to grow the Pathogenic Amoebae have not been followed by success. In the Jrnl. of Experimental Medicine, Couret & Walker, Vol.xviii, p. 252-258, give a good account of the progress made in Cultivation of Amoebae -"The Cultivation of Amoebae in Pure Culture upon Autolyzed Tissues." Cf.also,Musgrave & Clegg, No.18,Bureau of Govt. Labs.Manila -"Amoebas: their Cultivation & Etiologl significance".
Specific function has therefore been established on the ground of constant association of an organism with the Clinical condition, and with a definite pathological effect, and the behaviour to certain Specific substances, Emetin, which destroys the pathogenic Entamoebae, but leaves the E.Coli unharmed, although these may disappear during its use, to reappear on stopping the drug. This is not in the nature of a Relapse on account of the short space of time afterwards, and the non-production of any of the symptoms Associated with the dysenteric process. The Symbiosis of Amoebae and Bacteria has been well-understood and fully investigated - all the symbiotic bacteria have failed to produce the disease, but Strong suggested that they may act by preparing the Intestinal Mucosa to direct attack by the Amoebae. It is doubtful whether a genuine infection can be reproduced by a culture of Ent.Histolytica in symbiosis with another organism. "Ent.Coli moreover has never been artificially cultivated, either pure or in symbiosis, and until this can be done, and the results compared with the effects of cultures of Ent.Histolytica on susceptible animals, an important link in the chain of evidence is missing." (Brown).
Frösch's law still holds good. It is "that all varieties of Amoebae, free-living as well as parasitic, require for their development, natural or artificial, a special form of nutriment, which must be supplied either by the medium on which they grow, or by a concomitant culture of bacteria."
E.L.Walker* has confirmed the results of previous observers, and summarises his own culture experiments as follows:-

"1. Parasitic Amoebae grow only on the surface of a solid medium.

2. They multiply only on a neutral or Alkaline medium, not on one that is acid.

3. The presence of living Bacteria, on which the Amoeba probably feed, is an essential factor in cultivation.

4. A free supply of moisture and free $O_2$ is necessary.

5. The most suitable temperature is $20^{\circ}$ -$25^{\circ}$ C.

* E.L.Walker, "The Parasitic Amoebae of the Intestinal Tract of Man & other Animals" -The Jrnl. of Medl:Research, Feb.1908.

6. If these Conditions be satisfied, the nutrient content and general composition of the medium have little or any influence on development - (directly opposite to what Wenyon has shewn).

7. It was not found possible to cultivate Amoebae from dysenteric mucus direct; and the only type of pathogenic Amoeba was a specimen of E.Histolytica, isolated by Musgrave from dysenteric material, and passed through several sub-cultures."

Craig, in his "Studies upon the Amoebae in the Intestine of Man", Chicago, 1908, has thrown serious doubt upon Walker's work, as the probability of contamination seriously depreciates the value of these observations.

Lesage, in 1905 * stated that he was convinced E.Coli had never been successfully cultivated either pure or in symbiosis; but that in 7 out of 30 attempts he had succeeded at Saigon & Toulon, in growing a parasitic Amoeba from mucous matter of patients suffering from Tropical Dysentery, which was undoubtedly Ent.Histolytica. He further states that during a period of 2 years, he carried a growth of E.Histolytica through a series of no less than 66 subcultures, but always in symbiosis with a bacterium. Unfortunately no attempts were made to communicate Amoebic Dysentery so cultivated to animals - a violation of Koch's postulate which renders all cultivation experiments valueless.

*Lesage, "Culture de l'amibe de la Dysenterie des pays chauds" -Annls. de l'Institute Pasteur, 1905.

In 1909, Gauducheau grew pathogenic Intestinal Amoebae in association with Bacillus of Rat-Typhus, and was able to observe by Schaudinn's Fixation with Corrosive Sublimate and Alcohol & staining with Heidenhain's Iron-Haemotoxylin Method, he was able to trace at least two distinct stages of development - one of active reproduction and the other of degeneration. One further observation was of importance -viz, the production of artificial immunity by intraperitoneal injection of cultures which immunised against Experimental Amoebic Infection.

Lastly reference must be made to Musgrave & Clegg's work in connection with Cultivation experiments. They gave a formula for Medium for the growth of Amoebae as follows:-

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| Agar-Agar ..... | 2.5 grms |
| Sod.Chloride ..... | 0.05 " |
| Liebig's Extract of Beef ..... | 0.05 " |
| Normal Sod.Hydrox. ..... | 2.0 c.c. |
| Distilled water ..... | 100.0 c.c |

without clarifying, sterilised at 7 Kilograms pressure per square c.m. for 45 mins. It should be neutral to Phenolphthalein -though it may be made 1% Alkaline.
This then, is the Universally accepted medium for plating cultures on; though,
Couret & James Walker (cf.Jnl.Exptl.Med. 1913, vol.xviii, No.3, pp.252-258) claim that they have cultivated 5 varieties of Intestinal Amoebae by

the use of a Special medium to which sterile autolysed tissue fluid has been added (obtained by exposing Sterile brain, liver & other tissues in a sterile thermostat for from 10-20 days at 40° C); the acidity of the media should not be more than 1.5%; and the surface of the Agar should be broken up before use. They state that it is the want of autolyzed tissues which Entamoebae require for their growth which explains previous negative experiments, as the role of the symbiotic bacteria in the body is the autolization of tissues which aid Amoebic growth.
These results have neither been confirmed, nor, what is more important, have their pathogenicity been proved.

Whitmore & Hartmann, have concluded that all cultures of Amoebae obtained from Manila from dysenteric patients' stools and Liver pus, as well as Water-cultures were found to contain free-living Amoebae of no practical Aetiological Significance. Rogers, moreover has been struck by the fact that in his own Laboratory in Calcutta, he has failed to grow any Amoebae on Musgrave & Clegg's media from stools swarming with Ent.Histolytica.

I have gone into this question rather fully, because the crux of the matter appears to lie in this Artificial cultivation & propagation of Disease. Were this possible, the last claims upon Symbiotic Bacteria & Non-pathogenic strains of Amoebae would be definitely negatived. As the matter stands, there is ample clinical evidence which places the Ent.Histolytica as the Active Causal Organism, and practical therapeutics successfully prove that with the cell-death of Ent.Histolytica, the ravages of the disease are controlled, and the Dysenteric process and pathological-cycle completely arrested.

Balantidium, on the other hand, is seldom found in association with other Intestinal parasites, and the almost invariable absence of Entamoebae and other Phizopoda when Balantidium is present in the Alimentary Canal is one of the most remarkable features of the infection.

3. That deductions based on infection-experiments on cats and other domestic animals are unreliable, on account of their natural predisposition to dysenteric affections. The experiments of Grasser, who injected Garden mould into the Rectum of cats and induced an Acute Colitis from which Amoebae was identified similar with those of Losch & Kartulis; Quincke & Roos, Kruse & Pasquale Zancarol, Schaudinn, Musgrave & Strong, and others, have shown that the artificial transplantation of Ent.Histolytica, either from Liver-pus or dysenteric discharges into the Rectum of Cats, dogs or monkeys, is followed by typical dysenteric lesions; whilst with the Ent.Coli, there never is produced any symptoms of the disease. Feeding experiments have been often negative when Ent. Histolytica in its active cell-stage has been given, because of the deleterious action of the Gastric Juice, but if Cystic forms are also present

the disease is readily induced. No such positive reaction can be produced by Ent.Coli, either in its active form or Encysted stage.
But these experiments have been objected to for the following reasons:-

1. Innoculation Results are not always successful, and depends upon natural susceptibility, suitable conditions, viability of the organism, & age. Thus in the very young cat, the introduction of any irritant is often followed by a reactive inflammation, whilst this susceptibility decreases with age - thus the older cat and old cats are often extremely resistant.
Richet in his Monograph on "Anaphylaxis", 1912, has shown that Acute dysenteric seizures, collapse, passing of pure blood by the Rectum, has been induced experimentally in dogs, cats, etc, by the introduction of any Albuminous substance - Alkaloid or food - either by subcutaneous innoculation or by feeding. This anaphylactic reaction is sometimes manifested by severe vomiting, restlessness, paresis, diarrhoea, or it may be of the Acute type described. For this reason therefore, it has been urged that this experimentation may be Anaphylactic in the case of Amoebae.

2. The type of disease experimentally induced by Rectal injections in cats is generally of greater intensity than the clinical condition in man; for in these animals not only is the reaction to mechanical effect excessive, but the toxaemia caused by Amoebae produce Paralysis & Collapse before even the dysenteric process has been established. This may in part be the Anaphylactic syndrome-complex, described above. Feeding experiments, although producing less acute symptoms than direct intrarectal transplantation, agree in the type of reaction induced by the direct method and the resulting disease is always of a more acute type than in man.

3. There is the possible fallacy that in the above pathological tests, pathogenic bacteria may have been introduced at the same time, e.g -Shiga's Bacillus, & if the specific nature of Ent.Histolytica is to be established, the absence of Ent.Coli must also be demonstrated.
Harris & Craig have endeavoured to meet this objection by careful isolation of all pathogenic bacteria, and separately proving by experiment that they were not capable of producing dysenteric symptoms or lesions in cats, preferably in half-grown kittens.

4. Often when undoubted Ent.Histolytica has been given to cats, the constitutional symptoms have been so severe as to cause their death, but no ulceration has been discovered.
This has been successfully shown to be exactly a plea for & not against E.Histolytica, for the excessive toxaemia has proved fatal before time has been given for dysenteric lesions to appear; and in animals surviving, typical ulcers are found.

## E T I O L O G Y

-continued-

This is so far as the symptomatic evidence goes in feeding-experiments and the observation on such gross lesions as ulcer-production and naked-eye changes. The finer microscopical changes induced have not been described. Even in the earliest period, there is characterictic infiltration of the submucosa and lymph follicles. After Rectal innoculation in the three first days, there is always infiltration of the Colon & submucous haemorrhages. From the 4-6th day, the points of necrosis appear exactly as in Human Amoebiasis, and as the ulcers increase their characteristic irregularity and deep-undermined nature are apparent, and if the necrosis turns general and areas coalesce, large ulcerated patches are left, extending down to the muscularis, which may become denuded or covered only by ragged fringes of disintegrated mucous membrane. This widespread destruction is generally limited to the Sigmoid and lower Bowel, but in some instances the Caecum has become involved, but the disease has not spread beyond the Ileo-Caecal valve. The initial process is always in the submucosa, and as in man, the route of Invasion is by Liberkühn's Glands, and in the earliest stages the Entamoebae may be seen lying free in the lumen of the tubes, the epithelium of which is as yet intact and unchanged. The organisms enter the deeper layers by pushing aside with their sharp pseudopodia the epithelial cells at the fundus of the gland. From the base of the gland, they wedge themselves into the meshes of the Connective-tissue, and tear asunder the bundles of fibres. Dense infiltration of the Submucosa results, and necrotic areas form along the tracks where the infiltration is most marked. These points are often at a considerable distance from the base of the Glands, and the mucosa overlying them is at first quite healthy. Dense infiltration of the submucosa, with incipient abscess-formation is thus seen to be due to a lateral and not superficial invasion, and the superficial changes occur by the strangulation of the blood-supply.

It is pointed out in this connection that the structural pecularities of Ent.Histolytica alone confer upon them the power of direct invasion, for the terminal points of the pseudopodia of Ent.Histolytica are "horny & resistant", whilst those of E.Coli, are "soft & flaccid".

The feeding experiments of Schaudinn & Strong have put the matter almost upon an unsailable basis the former working with Cysts of Ent.Histolytica in a case of Chronic Amoebic Chinese Dysentery, in which all pathogenic bacteria were excluded, and using ten Coli-free specimens; the latter with sterile Liver-pus containing merely carefully selected material from the walls of the abscess so as to exclude the possibility of an Anaphylactic result due to the introduction of degenerating liver-tissue and massive albuminous content.

But there remains Walker's & Sellard's Human experiments to ~~remove~~ bridge* probably the last gaps in the chain of Experimental evidence at hand. Volunteers from among the Philippino inhabitants of the Bilibid Prison at Manila, were fed on various species of Amoebae, which were carefully studied & defined. The experiments were carried out for 18 months,

* bridge

and when infections occurred, they were promptly treated and cured - the chain of evidence being thus completed. The experiments fall into three groups:-

I. Feeding experiments with cultures of free-living Saprophytic Amoebae, genus Ehrenburg, (not Entamoebae), considered by Musgrave & Clegg to be pathogenic to man. (potential).
The main characterictics are: the greater part of the nuclear Chromatin is arranged in a central Karyosome, the presence of a contractile vacuole, the formation of Mononuclear Cysts and their cultivation on artificial media.

Experiment - 20 feeding experiments with cultures, mainly in the resisting excysted form were made on 10 different men, whose stools had been previously carefully examined, but no trace of Dysentery was produced. The Amoebae were never found microscopically in the faeces, but they were cultivated from the stools between 1 -6 days after feeding - but not later - and all seem to have retained their original characteristics described above.

Result. Cultivable Amoebae are not capable of living as parasites in the human Intestine, and do not cause Dysentery or Disease .

II. Feeding experiments with Ent.Coli.
These are constant parasites of the Human Intestinal Tract, and are very easily found after a Saline purge has been administered. (Craig has investigated the subject in 250 cases for various unselected diseases, and obtained a positive result in 49%.)
E.Coli has no contractile vesicle, the nucleus is excentrically placed, and chromatin is at the periphery of the nucleus and fairly abundant; in the encysted stage, from 4 -8 nuclei are present no growth is possible on artificial media. Very small forma have been described by Wenyon, resembling the Limax saprophytic Type and also the Ent. Histolytica Type. These are however rare.

Experiment.- 20 men, carefully selected after their stools were thoroughly searched, were fed on E.Coli in the Encysted (resistant)stage.

Result. - No dysenteric symptoms were ever induced, the average incubation-period was 4.7 days before they appeared in the stools in 17 cases, and they persisted in the stools for an indefinite time.

III. Feeding experiments with E.Histolytica, (Schaudinn), & its Tetragena Cysts, (Viereck).

This Entamoeba has a distinct refractile ectoplasm and a granular endoplasm non vacuolated. The nucleus is excentric, and the chromatin very fine. The Cysts have at most 4 nuclei( hence Tetragena).

Experiment. -20 men, carefully selected were fed on Ent.Histolytica, in various stages of development. The Ent.Histolytica were given in capsules containing Magnesium Oxide to counteract stomach-acidity. One man was fed three times before he showed signs of the disease.

Result.

i. 17 became parasitised after the first feeding; and one after the 3rd.feeding. In two, the reaction was negative.

ii. Men fed on E.Histolytica developed Tetragena Encysted forms, and vice-versa in the following percentages:-
Encysted E.Histolytica infected in 85.5%
Motile " " " " 75%

iii. Incubation period averaged 5.7 days before Amoebae appeared, and varied from 1- 44 days. One negative case died 165 days later of Tuberculosis, and no amoebic lesions discovered post-mortem.

iv. The incubation period of the attacks varied from 25-95 days - average 64.8 days.

v. Of 18 men parasitised with E.Histolytica, 4 developed Entamoebic Dysentery- 2 mild and 2 severe.

vi. In no case could the Amoebae be recovered by culture from the stools.

vii. No case of Spontaneous Dysentery developed in the Ward during the experiments.
Ergo,
E.Histolytica is a strict and obligatory parasite and it is the essential etiological factor in Endemic Dysentery.

Walkers' conclusions are thoroughly sound, and there appears to be no more complete evidence in the experimental pathology of Induced Amoebiasis than that derived from Walker & Sellard's work. Whitmore* agrees with Walker's views.

*Whitmore,
Phil.Jrnl.Sci.B.Trop.
Med.1913,253.

It is only necessary again to draw attention to the important factors in the Life-history of Amoebae; degenerative phenomena constantly occur; Pleomorphism is characteristically absent in the pathogenic species - and therefore it is well to resist the tendency to create new species and complicate the essential classification laid down by Schaudinn. W.M.James' illustrated & elaborate paper* on The Entamoebae of Man met with in Panama in relationship to the clinical types of disease, is a useful one in solving this vexed question of the artificial creation of new species.

*W.M.James,
Amer.Jrnl.Trop.Dis.
1913, 431.

Viereck's paper, 1907, "Studien der in dem Tropen erworbenem Dysenterie", Beitrag.Z.Arch.Schiffs-u. Tropenhyg.1907,Beiheft I, should also be consulted. Hartmann's "Entamoeba Africana"; & Elmassian's"Ent. Minuta" are all synonymous with the Tetragena Cysts (Viereck),in the Life-history of Ent.Histolytica.

# E T I O L O G Y

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The case for the Pathogenicity of Ent.Histolytica may be summarised thus -

1. There is definite & specific relationship between the occurrence of Amoebic Dysentery and the presence of the organism. In every case Ent.Histolytica is found in either the typical discharges or it may be recovered from the typical lesions post-mortem, even in cases which have remained Latent during life.

2. Man-to-Man Infection occurs directly and through the same agency always.

3. The pathological lesions, whether natural or experimental, are always of a constant & characteristic type, sharply differentiated from what is found in every other known type of Dysentery and all other Intestinal Infections.

4. Subject to certain conditions, notably suitable developmental conditions, the identical disease can be communicated experimentally to Animals or to Man, only when Ent.Histolytica is present or its Cysts.

5. It cannot be cultivated on any of the artificial media, and presents striking differences in shape & structure from all other Intestinal Amoebae, including the Free-living forms. Pleomorphism is exceptionally rare. Its structure and active movements are admirably adapted for deep burrowing; and it also developes a specific Toxin experimentally evident in the paralysis, collapse & death it induces.

Geographical Distribution.

Mainly
Amoebic Dysentery is always Tropical. The Philippine Islands are wholly Tropical, and Amoebic Dysentery is perhaps the commonest of all the serious diseases; in 90 out of every 100 Fatal cases, amoebic lesions can be demonstrated. R.Strong, Amoebic Dysentery, Osler & Mac Rae's System of Medicine, Vol.I, 488, & other articles. On the other hand, only a small area of Japan is Tropical, and although 875,000 cases have been reported by Shiga for 1890-1900, the type of Dysentery responsible for these Epidemics is always Bacillary, and Japanese observers, amongst them Nakagawa, state that Amoebic Disease never occurs in Epidemic form except in Formosa, and the extreme South Provinces. North & Central China have a similar epidemiology - the disease being practically Bacillary, whereas South China, Hong-Kong, and the Treaty-Ports and the South China Coast, the disease is Amoebic (Jürgens).
In the Malay Peninsular & Sumatra, 50% of all cases are Amoebic; while in Java & the Eastern Archipelago, the proportion is still higher.

# E T I O L O G Y

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As in all other diseases, certain ACCESSORY FACTORS are necessary for the propagation of the Disease, and these are in general Epidemiological, Racial & Cultural.

1. Epidemiology & Geographical Distribution.

There is no doubt that in certain seasons of the year the disease increases and at others it is more or less in abeyance (endemic). The prevalence of Dysentery in the Eastern Tropics & India, increases during the Rainy Season, and extends into the Autumn months. The Minimal Dysentery in India occurs in the late cold weather months of Janurary & February, in relationship to the minimum temperature of the year, 46° -70°, and is commonly followed by a slight increase in the early hot weather month of March, 70- 80°, succeeded by a slight fall in the pre-Monsoon period and hot months of May- June 85-100° (what has been called the"Chota Barsath"or the Small Rains). The Monsoon Season may be said to commence at the end of June, and last till end of September, when the temperature falls to 80 -85°., the Dysenteric curve sharply rises, reaching its maximum in Aug- & Septr. With the receding Monsoon in mid-Octobr the curve steadily declines with the cessation of the Rains. In years of excessive Rainfall, the Dysenteric Curve is also unusually high, and vice-versa. (Monsoon Diarrhoea). These statistics relate to all forms of Dysentery - no figures being available for the different varieties. In the parts of India where rainfall is limited to the mid-Summer months of July & August as in Sind, and the N.W.Frontier, the corresponding rise in Dysentery sets in, but Amoebic Dysentery is said to be infrequent. In the very rainy province of Bengal & Assam, the curve is often extremely high.

Geographical Distribution.

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## E T I O L O G Y.

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Anderson * at Port Blair, in the Andamans, in 1905, investigated 2539 cases of Dysentery, and showed that in 920 cases, in which special investigations were carried out, 455 cases or 50%, were Mixed Infections, of Amoebae, Trichomonas, & Lamblia Intestinalis.

* Anderson - Ind.Med. Gaz.Apr.1907; & Ibid-B.M.J.1908,Vol. ii,1243.

In Ceylon where Dysentery of a Malignant Type is common, Amoebic disease is rare. Castellani* could only find two amoebic cases out of 150 dysenteric admissions.

*Castellani, Jrnl of Hygiene, 1904, iv, 495.

In Fiji Islands (cf.B.M.J, Feb.7th,1914, 294- 296) P.H.Bahr publishes an interesting record of an Epidemic of Dysentery during 1910. It is situated between latitude 17- 19° S, & Longitude 177- 179° E. During 1910, some 170 well-marked dysentery cases were studied in detail at the Colonial Hospital, Suva, the Capital of the Group, in only 11 were Amoebae found - 159 being Bacillary.
Throughout Tropical & Sub-Tropical Africa, Amoebic Dysentery is ubiquitous and is exceptionally prevalent in alluvial districts. In Egypt the case incidence is probably higher, in proportion to population, than in any other part of the world, and the disease is almost limited to the low-lying tracts of lands adjacent to the Nile. In S.Africa, the Equatorial provinces & West Coast, Acute Dysentery is apparently less prevalent than in most parts of the Tropics. In Senegal,however, it is endemic. "Amoebic Dysentery appears to be more prevalent in the Temperate Districts of America than in the Isothermal Zones of the old World". (Brown). Osler declared it to be by far the most common type of Dysentery in that country - at Baltimore it was exceptional to find other varieties. Musser of Philadelphia, in B.M.J. 1902, ii, 242, thought that the great prevalence of Amoebic Disease there was a conclusive argument against its being regarded as a Tropical Disease or having any special affinity for the Tropics.
Amoebic Dysentery has been met with in Italy, in the Balkan Peninsula, Germany, Austria-Hungary & Russia. Occasional cases have been reported in England and in France. One typical case in 1907 was reported from France in a man who had never left that country, by Cussade & Joltrain,( & also published in Lancet 1907, i, 694). He had Liver-Abscess and a Lung-Abscess from which Amoebae were recovered.
So much for the Geographical Distribution - it is mainly Tropical.

## 2. CLIMATE.

Tropical climate is indeed a factor which is becoming more & more recognised. A very interesting article and discussion on the "Causes of Invaliding from the Tropics" was published in the B.M.J of Nov.15/1913,pp.1290 -1296. I quote from Law's article (p.1294). "Colonel Gorgas,A.M.S of the U.S.A, in a paper recently read before the Society of Tropical Medicine & Hygiene, is quoted by Dr.David Thompson, as saying -'the work on the Isthmus (Panama Canal Construction) will demonstrate to the World that the White Man can live and work

CLIMATE - cont.

in any part of the world, and that the settling of the Tropics by the Causasian will date from the completion of the Panama Canal.' Law, of British Guiana, maintains that 'there is on the contrary, every reason to believe, even if all Tropical Diseases were wiped out, climate would still remain a powerful enemy to the Settlement of Tropical Countries by the Caucasian".
Not only has climate a subtle influence, but the location of the Individual, whether living in centres of modern commercial life, where there is to be found conditions of life closely approximating to those of Europe as regards cleanliness, &c, or amongst primitive peoples on the outskirts of civilisation with no knowledge of health & sanitation principles;
His Habits - more especially the avoidance of
& Alcohol.
the individual idosyncrasy - liability to catch diseases, reaction to humidity, high average temperatures, thermic influences,
are all important factors.
Long Residence in a Tropical Country lessens the dangers and the new-comer is especially more liable to the Disease.

3. Prophylactic and "Cultural" qualities.

By Cultural Qualities are meant suitable media and conditions for the growth of pathogenic Amoebae, by Prophylaxis, their restraint. Hygiene in the Tropics is all important. The general prophylaxis of amoebic Dysentery can be summed up in one word - cleanliness. Unclean vegetables, domestic arrangements, pollution of drinking water, milk, etc. are responsiblefor outbreaks of the disease. Dysentery is certainly a water-borne disease, and the general use of Ice may be in part responsible; as the Ice-factories may be using contaminated water.
The Fly-Peril is according to some writers exaggerated. Kuenen allowed flies to get contaminated by Cyst-containing faeces. If badly smeared in faeces, they could not fly at first; but as the faeces dried & rolled off, the Cysts died. He therefore concluded that the risk from flies is not a great one. On the other hand Bahr* in his investigations on the Dysentery-Epidemic in Fiji, blamed the house-fly (Musca domestica) as directly responsible for infecting the food. The carriage of pathogenic organisms by flies has been thoroughly worked out by Graham-Smith "Flies & Diseases" Cambridge Univ:Press, 1913. In spite of Kuenen's experiments, it is generally held that Flies are directly responsible, and play an important part in the conveyance of material to foodstufs.

* Bahr - B.M.J. Feb. 7th. 1914. "A study of Epidemic Dysentery in the Fiji Islands, 1910."

## SECTION II. THE MORBID ANATOMY OF AMOEBIC DYSENTERY.

## &

## THE DIFFERENTIAL DIAGNOSIS OF OTHER INTESTINAL LESIONS REGARDED FROM A PATHOLOGICAL ASPECT.

* Pp. 122-127

I. Seat of the Morbid changes.

Before the two types of Dysentery, Amoebic and Bacillary were differentiated from each other, there was hopeless confusion and contradiction in the localisation of the Seat of the Dysenteric processes. Annesley, in 1828, in his coloured illustrated work " Researches into the Diseases of India ", described Amoebic Dysentery very faithfully and by coloured illustrations, esp. Plate 20, Fig. 1 (see Appendix), characteristic of the Disease". ( Rogers ). Thus he noted that the disease often begins in the Caecum, yet rarely involves the Small Bowel.

Reference to the pathology of Amoebic Ulcers in the Bowel when complicated by liver-Abscess will be found in the section of the Thesis on Liver-Abscess. Abscess in the Appendix, Amoebic disease of the lower end of the Ileum, and that the main pathological stress always falls upon the Caecum - and in fact, according to Rogers it is often remarkably limited to the Caecum or Ascending Colon. It hardly ever effects the Sigmoid or Rectum, and is thus sharply differentiated from what occurs in Bacillary Dysentery. Rogers', Strong & Musgraves', & Harris' work will be found reviewed in the section of the Thesis on Liver-Abscess " The Types of Liver Abscess in Relation with the Character & Intensity of the Dysenteric Process ".

II. Malignant or Fulminant Amoebic Dysentery.

The Morbid changes in this rapidly fatal variety are indicative of intense inflammatory reaction throughout the whole Colon. They differ from the lesions of the more common clinical form of Amoebic Dysentery, not only in degree, but also in that the superficial structures are more severely affected. In rapidly fatal instances the Mucous Membrane is invariably hyperaemic, but the changes in the Submucosa are much less conspicuous than they are in the more Chronic form of Amoebic Infection. Rogers emphasises, however, that the characteristic distribution of the changes even in the Gangrenous form is not lost - the lesions are not continuous throughout the large bowel, as they are uniformly in Bacillary Dysentery, but there remains extensive areas of healthy Mucous Membrane between the enormously thickened and raised patches of " tawny yellow

## The Morbid Anatomy of Amoebic Dysentery.

The pathological changes found in Amoebic Dysentry vary with the intensity of the morbid process, and the duration of the disease in both Acute & Chronic Phases. But in the great majority of instances they are characteristic of the infection and are readily distinguished from all other Intestinal disorders, including Bacillary Dysentery. Uniformity of pathological type is especially established in all cases of long duration, in which the characteristic amoebic changes have taken place and been accentuated by repeated infections. Less characteristic will be the Fulminant or Malignant cases, in which the gross lesions are so extensive and so profound that the condition of the Bowel comes to resemble the consistence of wet blotting-paper; and the microscopical changes will be of intense Acute nature to harmonise with the Acute Degenerative process.

### I. Seat of the Morbid changes.

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Reference to the " Tabular Distribution of Amoebic Ulcers in the Bowel when complicated by Liver-Abscess " in the Thesis* will show that amoebic disease never involves the lower end of the Ileum; and that the main pathological stress always falls upon the Caecum - and in fact, according to Rogers it is often remarkably limited to the Caecum or Ascending Colon. It hardly ever effects the Sigmoid or Rectum, and is thus sharply differentiated from what occurs in Bacilliary Dysentery. Rogers', Strong & Musgraves', & Harris' work will be found reviewed in the section of the Thesis on Liver-Abscess " The Types of Liver Abscess in Relation with the Character & Intensity of the Dysenteric Process ".

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II. Malignant or Fulminant Amoebic Dysentery.-continued -

ulceration in advanced lesions of Acute Amoebic Dysentery ". ( Rogers ). According to Brown, even when the disease assumes a malignant type, the gross lesions of all varieties of amoebic infection, present a remarkable similarity, at least to the naked eye. The Colic Mucosa is found to be intense ly swollen & enrorged, of a dark purple colour "with extensive arborisations of congested vessels, and numerous extravasations scattered over the surface". (Brown). There is no deep-seated ulceration as yet, but points of superficial necrosis, red raised dots appear with yellow points - the beginning of ulceration. There is always an excess of Mucous secretion; and here & there patches of exudate become closely incorporated with the disintegrating mucosa and coalesce to form a so-called " Diphtheritic Membrane " - in which will be entangled leucocytes, Amoebae & dead Epithelium. Both the grey or greenish-granular necrosis of the mucous surface of Bacillary Dysentery, and the tawny yellow exposed infiltration of the submucosa of Amoebic Disease have beeh so described by different writers. But these conditions are widely dissimilar. " It is particularly in Acute Epidemic forms of Baccilary Dysentery, that an actual Diptheroid membrane resulting from fibrinous Deposit & necrosis of the Mucous Membrane itself is most frequently seen, so it is well to confine the term to this condition and not to apply it to the very different purulent gelatinous amoebic infiltration of the submucosa." ( Rogers, Dysenteries, p. 261. - "Pathol.Anat. of Bacillary Dysentery ".)

III. When Malignancy is less pronounced, the post-mortem appearances which apparently resemble the Acute Bacillary Type, are essentially differently caused. In the Fulminating type of Bacillary Dysentery which is common - the disease remains centred in the Mucosa and inflammation extends from the surface downwards. In Amoebic Infections, Malignancy is infrequent; and the sub-mucosa is invariably affected and infiltrated, extension taking place from below upwards. In the most acute cases of Bacillary Dysentery, the Mucous Membrane shows a surface-deposit; in Amoebic Disease it is essentially & primarily a sub-mucous infiltration. Vertical sections of the Bacillary infected Bowel show that the Epithelial structures are specially marked out for attack, whilst in the earliest stages the submucosa is quite unaffected. The inflammation of Amoebic Dysentery begins in the Submucosa, and after reaching the Mucous Membrane, is still most accentuated in the deeper parts of the Bowel-wall.

Lastly, in these very acute cases pathognomonic black cob-web-like sloughs of the Mucous Membrane form in Amoebic Disease and are produced by the rapid extension of the exudation deep into the submucous coat, destroying thus the vitality of large areas of the undermined superficial Epithelial layers which die owing to interference with the blood-supply, and are cast off as sloughs "which may be passed in the stools or hang from the anus".(Goodeve, Norman, Chevers & others ).

## The Morbid Anatomy of Amoebic Dysentery.

- continued -

II. In the Ulcerative Stage of an Acute Bacillary Dysentery - the whole extent of the Large Bowel is involved, and there is no extensive area of healthy Mucous Membrane remaining, as in the case of areas of healthy Mucous Membrane in wide-spread and Gangrenous Amoebic Disease. The Ileum is usually also affected in Bacillary Dysentery, the inflammatory process not being limited by the Ileo-Caecal Valve. Throughout the Large Bowel, as well as in the lowest part of the Ileum, there is marked General thickening of the Mucous Membrane with patches of greenish-granulated appearance due to fibrinous deposit in necrosis of the surface Epithelial layers. In addition, there may be Serpiginous ulceration, characteristic by slightly depressed red-inflamed floors, and small areas of raised intact yellowish-white Mucous Membrane which has escaped the necrotic process. Very marked congestion can only be made out by a practically instantaneous post-mortem. The whole Gut will be found to be of a purple-plum colour with the blood-vessels patterned out in a mosaic of red. The Disease however, does not always involve the whole length of the Large Bowel, even in the very Acute fatal cases. But the characterictis point is that wherever inflammation occurs, it is always of the same general type throughout, affecting every portion in the inflamed area in the same degree, and leaving none of the abruptly-defined areas of healthy Mucous Membrane as in Amoebic Disease. The absence of the discrete rounded raised yellow ulcers of early Amoebic Dysentery is conspicuous. The pictures of the two diseases are quite different from each other.

III. Simple Acute Amoebic Dysentery

Opportunities for the investigation of the earliest lesions of ordinary Acute cases of Amoebic Dysentery are infrequent, so that very little can be written definitely upon this stage of the Disease.
A series of autopsies on prisoners in Manila Jail, who died of an Epidemic form of Pneumonia, afforded an amount of material for investigation. Moreover, S. Jürgens * and other Writers have further corroborated these results, and from their observations have shown that the following changes are perhaps invariable:-

* S.Jürgens -"Die Amoben-Enteritis". Zeitsch.f.Exp. Path. Dec.1907.

" i. In the mildest cases, as in all other types of Amoebic Dysentery, the primary lesion is in the Submucosa which is the structure principally affected.
ii. Unless the onset of the Disease is of an exceptionally Malignant character, the lesions of the Mucous Membrane are clearly secondary to those of the Submucosa.
iii. The morbid processes of acquired Amoebic Dysentery in Man, closely correspond to those which result from the Experimental Infection of cats."
(cf.W.C.Brown, Amoebic Dysentery, p.121.).

1st. Stage of Invasion.

In the early stages, when the initial attack is of moderate severity, the gross abdominal lesions are unimportant; but the Great Intestine is always altered in appearance; the colour is brighter than usual, the Peritoneum being exceptionally smooth and glistening, and numerous small patches of

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III. Simple Acute Amoebic Dysentery - continued -

congestion and vascular statis may be seen through the Peritoneum. When the Bowel is laid open, the Mucosa is found but little altered, and though perhaps there is loss of flexibility and a peculiar boggy feeling on pressure, with an excess of mucous on the surface, the changes are principally due to alterations in the submucosa. The earliest lesions are small red raised dots, which may be little larger than a pin's head. They are produced by congestion and even possibly hemmorrhage into the Mucous Membrane, over the early excudation into the submucous coat beneath. When they reach a larger size, a light yellow spot appears in the centre of the purplish congested area - this being explained " as the gelatinous citron-yellow infiltration of the submucous coat seen through the degenerated and thinned superficial Mucous Membrane ", - and this is perhaps the earliest stage of ulceration. At this period the most marked feature is the elevation of the affected patched, " causing them to stand up like small buttons from the healthy Mucous Membrane " Even at this early stage, some of the lesions assume the typical oval form or trans-axial arrangement. Latency of symptoms is often traced to the fact that these early lesions are practically always confined to the upper parts of the Large Bowel, and the Sigmoid & Rectum are thus not affected. The route of invasion of the submucosa can be traced through the Follicles of Lieberkühn, and most Writers are agreed upon this point. The Amoebae assemble in large numbers in these Follicles, push the Epithelium cells upon one side by pseudopodic activity, traverse the basement Membrane, or Muscularis Mucosae, and burrow into the submucosa. The commencing process resembles for a time " Follow the Leader " and chains of Entamoebae may be found lying in the tunnels excavated by the leader. Ultimately they diverge and push into the tissues, coming to rest singly, or in small groups. Ch.Dopter * in his reaearches, is however, strongly opposed to this view. He considers that in Man, primary invasions of the Crypts are impossible, and that the Epithelium of these crypts is never primarily destroyed. On account of the excessive viscid mucous secretion from these glands, the Amoebae are unable to enter the crypts, and they penetrate the mucosa direct from the Intestine. They have thus to traverse the whole thickness of the Interglandular tissue, and the attack upon the Glandular elements takes place from behind with subsequent destruction of the lining Epithelium, before they are able to enter the Crypts. This, therefore, is the reverse process and demands for its acceptance, a direct entrance of the organisms into the deeper Intestinal layers, instead of an invasion via the natural valley caused by the Follicle dipping into the Interglandular tissues - the route of least resistance. There is, however, abundant evidence to show that this route at least is not the common one. In the early stages, the Tube-Glands of the Mucous Membrane are practically healthy right up to the congested margin around the yellow infiltration of the submucosa, clearly showing that the surface layer is not primarily involved in the disease, as we shall see later is the case in Bacillary Dysentery.

* Ch.Dopter ("Anatomie Pathologique de la dysenterie Amibienne" Archives de Medicine Experimentale, July 1907 ).

## The Morbid Anatomy of Amoebic Dysentery.

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### 2nd. The Stage of Pre-Ulceration.

Its earliest appearance has already been described its development is now to be traced in the advancement of the morbid process, which generally takes place (quickest) along the lines of least resistance, viz - the circular extension following the lines of the blood-supply. The lesions therefore take place across the Long Axis of the Bowel, and will, in its earlier stages, be found to be localised in the Caecal-Appendicular region. Once these ulcers have extended round the greater part of the bowel, through extensions of the exudation into the submucous cost, there is not only pressure-necrosis by small-celled infiltration and accumulation of debris, exerted against the more intact and resistant superficial layers, but there is now a commencing strangulation of its blood-supply, which will shortly result in necrosis along these paths. This is why the lesions of an Amoebiasis is always so patchy. This necrosis by an extremely well-marked extensive small-celled infiltration of the submucosa, is caused by a bulging upwards of the Mucous Membrane to form the button-like elevation on the inner-surface of the Bowel-wall, and separates the muscular from the Mucous layer. Degeneration of the Mucous Membrane will therefore show earliest in that portion in which tissue-tension is more raised, and in those parts removed from the already restricted blood-supply. The edges of the " slope" are still supplied with blood; but the plateau on the top will be the 1st. portion to yield. Hence it is that the Tube-Gland in a section, in the early stage are clearly seen nearly up to the central ulcerated area, although the Mucous Membrane shows a considerable amount of small-celled infiltration between the Epithelial columns, which increases in degree as the centre of the patch is approached, to merge into the denuded portions, where the necrosed Mucous Membrane has been thrown off, and this reveals the small-celled submucous accumulation and infiltration constituting the characteristic light yellow centre of the ulcer. Extension toward the Peritoneum occurs exactly in the same way. In the early stages there is but slight infiltration of the adjoining muscular coat. In places, however, there is commencing to show a more intense (patchy) inflammatory effusion, spreading between the muscular fibres and isolating the muscle-bundles. It thus extends deeply to the wall of the Gut, and in the more Acute and advanced lesions it may cause localised Peritonitis, without any actual perforation; but the Peritoneum before adhesions have taken place is perhaps the only structure left to preserve the integrity of the Gut. Thus also it is seen that the Amoebae have approached the radicles of the Portal Vein and reached the area of the lymphatic streams. This inflammatory cellular infiltration also explains the reasons for the marked thickening of the Bowel-wall and its characterictic boggy feeling and opacity.

In the mildest cases however, a temporary or permanent cessation of the morbid process occurs almost immediately after invasion. Fresh immigration of amoebae are arrested, and those who have entered are killed and gradually absorbed. This

*Adami's Monograph on "Inflammation" 1909 should be consulted, "the cells of the Inflammatory Process."

## The Morbid Anatomy of Amoebic Dysentery.

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2nd. The Stage of Pre-Ulceration. - continued -

This corresponds clinically to the period of quiescence and improvement in the condition of the patient. When, however, there are conditions more favorable to the renewed activity of the amoebae and to their development, evidences of further reaction are apparent in the increased Mucous catarrhal process, and patches of false membrane cover the surface. This corresponds clinically to the re-appearance of mucous & blood in the stools and constitutes the relapse. Nothing is more distinctive than the exudation of pus from minute orifices on the apices of these fresh mammillated growths on the bulging mucosa. At a later stage numerous points of suppuration may be seen which unite to form small abscesses These submucosa-collections of pus have seldom any definite limits or abscess-walls; they result from the liquefied remains of debris, Epithelial-cells, the interglandulary substance and inflammatory cells which have been killed in the toxic process; these abscesses therefore communicate freely with each other by tortous sinuses - which perhaps result or correspond to the route of invasion by the amoebae, leaving dead and mutilated cells and substance in their path. The contents of these abscesses exert further superficial pressure causing necrosis of the over-lying structures and finally bursting through the mucosa into the lumen of the Bowel. Hence it is that the additional oval, rounded & separate ulcers may be seen in Intestinal Amoebiasis in addition to the typical trans-axial lesions; and reference should be made to the Thesis section of " The Tabular Distribution of Bowel Lesions Complicated by Amoebic Liver-Abscess ".

The types of cell-necrosis induced in Intestinal Amoebiasis, may be classified as follows:-

i. Cell-death due to purely vascular obstruction and stoppage of the Capillary Circulation by the small round-celled Infiltration induced by the inflammatory process. This may be said to be a Coagulation-necrosis.

ii. Hyaline Degeneration induced principally by the contact of Amoeba Histolytica with the connective tissue-cell. To this may be added the cell-death induced by specific toxins of the amoebae themselves. (Councilman & Lafleur).

iii. Cell-death by suppuration.

A Coagulation-Necrosis is induced by the cell-death of the Wandering Inflammatory cells, derived from the copious effusion of Sero-Fibrinous Fluid; and these cells surround the minute blood-vessels and lymph-channels into which the amoebae have penetrated, as if trying to wall them off from the unaffected fields beyond. * The cells of the infiltration are chiefly lymphocytes. There are a few polymorph cells; and their frequency in all suppurative processes except in this amoebic inflammatory reaction locally induced, is indeed remarkable, seeing that a high degree of General Leucocytosis is rapidly established in the peripheral blood. According to Muir, (B.M.J, vol.ii, 1904, p.585), there is also a large number of Eosinophiles; and this combination of Lymphocytosis & Eosinophilia is indic

*Adami's Monograph on "Inflammation" 1909 should be consulted, "the cells of the Inflammatory Process."

# The Morbid Anatomy of Amoebic Dysentery.

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2nd. The Stage of Pre-Ulceration. - continued -

indicative of recurrent & persistent inflammation. At the point where stasis is completely established, groups of connective tissue-cells undergo hyaline degeneration. Finally, when the effusion is absorbed and the fibrin coagulated, when the inflammatory reaction subsides, numerous interlacing bands of contractile tissue are formed and in the meshes of this the cells of the inflammatory exudate are entangled, further compressed and disorganised. "Except for Entamoebae, and remains of the Solitary and Epthelial Glands, the necrosed tissues and Vascular walls are structureless, homogenous, & impervious to stains" (Brown). This Coagulation necrosis may in part be due to the toxic action of the amoebae, and their direct attack, but as has been indicated, it is chiefly by the strangulation of the tissue elements in the compressed space of the submucosa and in the fibrin meshes that cell-death is induced. It therefore is a purely vascular phenomenon; and the over-lying mucous membrane and Epithelial cells share in the vicious cycle - the cellular elements beneath forming a wedge of compressive cells intervening between the higher intact parts and the blood-stream coming up through the muscular coats.

Cell-death by suppuration. This is most probably due to the association of bacterial toxins with perhaps specific amoebic toxin. This is one of the few instances in the body of "Mononuclear Pus". that is, it is derived solely from the cell-death of lymphocytes in the Inflammatory Exudate. To the compression-phenomena is added the toxic effects of Pyogenic Bacterial activity. It will be most marked in the lymphatic & capillary circulatory areas, in the vascular sheath and vessels around the Solitary Glands, in the smaller muscular venules and the connective tissue lacunae where the Entamoebae are chiefly lodged. Free communication takes place between these death-cell areas and there is a net-work of suppurating sinuses formed by the breaking down of large patches of the submucosa without necessarily involving the mucous layer above. When, however, lateral extension is no longer possible such as, limitation by thrombi or tissue-pressure, the pus escapes along lines of least resistance and bursts through the devitalised mucosa. This is one method of the establishment of the Acute Ulcer, but sometimes on account of the intensive process rapidly undermining the support of the mucosa, this structure rapidly gives way and the amoebic ulcer is thus readily established. Very rarely encystment of these abscesses takes place beneath the intact mucosa. Ofcourse Bacterial infection takes place after the abscess-contents have burst into the lumen of the gut; and it will help to further break down the submucosa. It is said that the Bacteria are only associated with amoebae at a late stage as in earlier stages they themselves are destroyed by the powerful Amoebic toxin or perhaps by amoebae and hence Bacteria as cause of the Inflammatory process is not held to be important , and has little to do with the tissue-reactions as a whole.

## The Morbid Anatomy of Amoebic Dysentery.

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### 3rd. The Stage of Ulceration, Sloughs and the Establishment of the Amoebic Ulcer.

Having traced the morbid-process down to cell-death and pressure necrosis, it is easy to understand that when the Mucosa ruptures, especially by direct pressure, the ulcer resulting will be found principally to effect the Submucosa, and the excessive destruction of deep tissue is therefore the remarkable point of Amoebic ulceration. The classical distinction therefore of such ulceration is its Undermining character. Around the crater the tissues will be found greatly thickened by the repeated infiltration and reaction, and as its edges fall away, a corresponding increase in the size of the cavity is maintained by further loss of deep tissue.

The Types of Ulcers resulting are:-

i. The Infundibuliform, which has been likened to " The Florence Flask" in deep ulcers, with its fundus resting on the Circular inner muscular fibres, and its neck forming the sides of the ulcer, and opening on to the mucosa.

ii. All ulcers are practically alike in method of formation, but the different stages at which they are formed will cause certain changes in their appearances and degree of tissue-destruction. They may vary from the size of a millet-seed, to that of a filbert. Huge patches are always the result of coalescence, These coalescing ulcers, may be derived from the linking-up of the suppurative processes going on beneath the intact mucosa, but instead of causing a large slough of the overlying mucosa, they burst by minute openings through the mucosa - the so-called "ulcères en bouton de chemise " of French Writers. This perhaps results from the early break down of the apex of the bulging mucosa, although the morbid-processes continue to extend laterally in the submucosa.
The smaller ulcers produced at an early stage of the inflammatory lesion taking place in the submucosa, will be found to be few in number and quite separate from the characteristic trans-axial lesion, resulting from the morbid process, cutting off a much larger area of blood supply; and these smaller ulcers will therefore be shallow and their base will be found to rest upon submucosa not undermined to any extent.
Lastly, there is a peculiar type of Ulcer met with in which there is little destruction of tissue - the so-called " punched-out clean cut abrupt ulcer". When they occur, they are met with in the early stages of the disease, and from its Discoverer -Harris, and from its position upon the ridges of the folds of the mucosa, has been named " The Ridge-Ulcers of Harris".
Perhaps they are akin to the smaller ulcers immediately described above, and they have been suggested as being Intermediate Stages between the petechial erosions & the more fully devel - oped undermined cavities, by Woolley & Musgrave* The point not settled is what connection they have with Amoebic Infection as there is some doubt as to its nature.

* Woolley & Musgrave (Jrnl.Amer.Med,Assocn. 1905).

The Morbid Anatomy of Amoebic Dysentery.

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3rd. The Stage of Ulceration, Sloughs and the Establishment of the Amoebic Ulcer. - continued -

ii. When the ulceration is a result of pure coagulation necrosis, the adjacent tissues contain enormous numbers of disorganised lymphocytes and connective-tissue cells encased in a stroma of lymph fibrils. Round the margins of the patch, nests of amoebae may be generally found in abundance.
When the ulceration is a result of Bacterial toxins causing cell-death, the Amoebic Ulcers are covered with ragged shreds of decomposing sloughs which secrete offensive pus; but by degrees, this necrotic tissue is shred, and the cavity of the ulcer assumes a more healthy appearance. The Epithelial cells die, and are replaced by mucous cysts and sometimes they unite with secretions from the damaged membrane to form patches of amorphous "Diptheritic Exudate" - the so-called "Diptheritic form of Heubner". Amoebae Organisms are especially numerous in the tissue immediately surrounding the ulcer, and the so-called Pyogenic membrane often appears to consist almost entirely of Amoeba. With the progress of septic imflammation complete disintegration takes place. The infiltrated oedematous margins break down, and the ulcer widens; but concurrently there is further deep excavation and lateral extension taking place, so that there is no relative change in the shape of the Abscess-cavity.

4th. Perforation complicating Acute Amoebic Dysentery:-

The process of the deepening of the Amoebic ulcer has already been explained, and Local Peritonitis recognised. There however, remains the Acute perforation to be dealt with. In ordinary circumstances, the opposition to the passage of pus which is naturally offered by the External Walls of the Intestine, is much greater than the resistance of the mucosa; but when through deep destruction, the muscular coat is invaded and the Peritoneum itself weakened by the same infiltration and effusion, perforation is likely to occur. This, therefore, may result either from the coagulation-necrosis extending to the Peritonial coat, or by septic burrowing of an infected ulcer. When there is an unusual tension in a submucosa abscess, this abscess may rarely point in both directions, but generally is relieved by the mucosa going first. Hence a direct-pressure necrosis due to abscess-tension, is altogether a rare cause for acute Perforation, but has been known to occur.
In the Gangrenous variety of Amoebic Disease, the Bowel wall is so weakened and sodden as to come to resemble damp blotting-paper. After death, greatest care must be exercised in handling it, to prevent a post-mortem rupture. If rupture occurs, which is uncommon, it is most frequently seen in the Descending Colon or Sigmoid. -
"The comparative rarity of the accident is due to the strength of the serous coat and to the fortunate circumstances that in Amoebic Infections, inflammation is of an unusually plastic and adhesive type.
Where there is deep ulceration; Omentum Colon and other structures are generally closely matted together, and the Peritoneum is thus enabled to maintain

The Morbid Anatomy of Amoebic Dysentery. 26

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4th. Perforation complicating Acute Amoebic Dysentery. - continued -

the integrity of the Intestine".(cf.Brown, p.136). Where the Intestine is not covered by Peritoneum, extra- or Retro-Peritonial Perforation may take place, and its usual sites are the Caecum, Ascending Colon, and even the Appendix giving rise to post-peri-colic Abscess in the Right Iliac or Lumbar regions.
Occasionally in the more Chronic form of Perforation, fibrous bands caused by adhesions may give rise to fatal strangulation of the Small Intestine

5th. Repair.

" In the not infrequent cases in which there was No history of Dysentery during life, the Amoebic Disease will generally be limited to the upper 1/3rd. of the Large Bowel".(Rogers).
In spite of the virulence of the necrotic process, amoebic ulcers display a remarkable tendency to heal, and in some slight cases no traces can be found at post-mortem after minute search. Almost immediately after the slough has been thrown off, red granulations appear to be pushing up from the base of the ulcer, the discharge of blood and serum is replaced by 'Laudable Pus' and complete cicatrisation is ultimately assured, provided the Entamoebae have been destroyed. The formation of permanent structures is incompatable with the continued developement of Entamoebae. The clinical features of the disease is indeed dependant on this one factor. Very often when granules appear the Amoebae enter upon a quiescent stage, and the disorder settles down. Ultimately the Amoebae again begin to quicken and produce the inevitable relapse, with fresh breaking down of the newly found tissue. Relapses indeed form the commonest feature of amoebic Disease, and the condition of the Colon is one of continual new-tissue formation, a certain amount of permanent change to cicatrical formation, alternating with the death of the newly formed granulations. All throughout the Large Intestine, this pathological play of action in its different characters, stages & degrees, may be going on to form what Rogers describes " A Kaleidoscopic picture of all the stages of the protean lesions of this remarkable Disease".
The healed acute ulcer will be shallow, oval or a slit-like depression corresponding entirely to the severity of the pathological change. The edges will be thickened and raised slightly from the mucosa, and the base often still shows the characteristic light yellow bases. If small, there may be no puckering or pigmentation around them, though perhaps only slight scarring may remain. Such fine scars with or without pigmentation are generally seen in the Caecum. In the more Chronic healing ulcers, the floor is smooth and nearly free from the yellow gelatinous infiltration of the earlier stages, separated from each other by fairly healthy mucous membrane, and more or less rounded or oval in shape, being thus quite different from the Serpiginous narrow ulcers running into each other in Bacillary Dysentery. Another characteristic feature is the extensively patchily distributed pigmentation of the mucous membrane, partly

5th. Repair - continued -

surrounding half-healed Chronic ulcers, partly as distinct, more or less circular bluish areas resulting from final complete scarring of the destroyed mucous membrane. Where there has been acute focal sloughing, this bluish-dark pigmentation will also extend some distance away from the site of the actual lesion due to the remains of the acute process which has caused cell-death in the neighbourhood by the intensity of the pathological changes.
In the Gangrenous Variety, and also in the Diptheritic type, the inflammatory changes are very intense, and according to Flexner * the glandular tissue may be almost completely destroyed and replaced by the fibrinous and cellular exudate.

* Flexner, John Hopkins Hosp. Bullett., vol.xi, 1900, p.231.

6th. Chronic Amoebic Dysentery.

After repeated relapses, the Intestine assumes a typical appearance characterictis of lengthened infection. When it is remembered that each relapse is heralded by the death of the newly-formed granulation tissue, it is easily understood the amount of fibrotic changes induced. The same processes of infiltration, cell-death, ulcer and quiescence is renewed over & over again, & the excess of connective tissue therefore completely obliterates and replaces normal structures. There will be changes in the vessel-walls, in the endothelium of the lymph sinuses and vascular spaces, in the follicles of Liberkühn, and in the mucosa. In severe cases on account of the extensive destruction of tissue, the intestinal walls may be almost homogenous. They become pale, thin and parchment-like; the mucous membrane is bare & structureless; the remains of the previous extravasations in cicatrices & slate-coloured patches are scattered over its surface, and the Epithelial Glands have been practically all destroyed. For this reason, the bowel is tough, dry & leathery; at certain places especially where there has been evidence of muscular involvement it is thicker than at others, and this unequal development of connective tissue will produce extreme degrees of contraction & destruction, with secondary dilatations above the narrowed lumen. Such a condition is a frequent result of prolonged Amoebic Dysentery. Together with the concurrently-formed peritoneal adhesions, these structural alterations of the Colon give rise to permanent pain, discomfort and tenderness, and constitute a distinctive sequelae of the disease. The Rectum in Chronic Amoebic Dysentery, often shows more marked ulceration than the rest of the Gut. Occasionally the Sigmoid is the most affected. This variety is often complicated by Liver-Abscess. Seldom however, is the process of fibrotic atrophy typical or complete, and alternating patches of fibrosis, persistent local inflammation and suppurative ulceration due to continued development of Entamoebae are more frequent post-mortem appearances. At some points the Colon, which may be otherwise fairly normal, remains engorged, hypertrophied & disintegrated; ulcers with fringed and undermined edges alternate

The Morbid Anatomy of Amoebic Dysentery.



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6th. Chronic Amoebic Dysentery - continued.

with slate-colored fibrosed patches; & suppurating elevated buttons of Adenoid tissue may be seen in close proximity to Keloid scars & areas of devitalised & homogenous mucosa. Sometimes atrophy of Intestinal mucosa over large areas are met with, & the condition called Chronic Amoebic Enteritis. There is extensive atrophy of glandular material & villi, together with small-celled Infiltration; while patches of Chronic Venous Congestion are seen. Some fibrotic change may also be found in the mucous coat, & minute superficial ulcers may be present. Such cases are not amoebic at all -they are cases of SPRUE. Similar processes in a more advanced degree will be found throughout the Small Intestine The Small Intestine is never, or hardly ever affected in Amoebic Dysentery, and then it is confined to the approximate part of the Ileum. Sigmo-Rectal trouble is not an uncommon sequel to long-standing Sprue. According to the researches of Cantlie, the narrow Sigmoid Flexure is prolapsed into the Rectum for a distance of an inch or two; the invagination leads to Congestion & thickening of the parts. The protruding Sigmoid becomes swollen & ulcerated, & covered by a slimy mucus as it oozes from the lumen of the bowel. Consequent obstruction leads to stricture of this mucus channel; often a clue to this Sigmo-Rectal condition is an alteration in the characters of a Sprue-stools. An affection of the Upper Bowel is said to occur in Cochin-China and the South-Eastern Tropics, consequent on Amoebic Infection; but the endemic diarrhoea of Cochin-China is held to be Sprue, and when Dysentery does occur, it is of the Bacillary Type. In 1904- 1905, 30% of cases occurring in the French Naval Squadron stationed there were amoebic; and it is said that in more than half of all cases in European Officials there, are of amoebic origin. Still, however, these Small bowel lesions are rightly regarded as Sprue.
In Chronic Bacillary Dysentery with a few exceptions the lesions are limited to the lower half or two-thirds of the Large Intestine with general thickening and extensive serpiginous ulceration. In none of the Chronic cases recorded by Rogers, was the lowest part of the Ileum involved, as is so commonly in the Acute & Fulminant varieties." The most essential difference, then, in the characteristic distribution of typical Acute & Chronic Bacillary Dysentery respectively, is, that in the former, the whole or nearly the whole length of the Large Bowel and often also the lowest part of the Ileum are uniformly involved in the Acute Inflammatory process, which may rapidly prove fatal; while in the latter, the process is limited to the less vital and lower portions of the Large Gut, and the patient survives long enough to allow of more extensive destruction of the mucous membrane of the affected areas. (cf. Rogers, Dysenteries, p.267).

## Differential Diagnosis from Other Ulcers.

Amongst the two commonest diseases producing both Acute & Chronic ulceration of the Intestine are - Typhoid Fever and Tuberculosis of the Intestine. Among rarer causes of Intestinal Ulceration must be mentioned " Tertiary Syphilis" (Gummata) and Actinomycosis. Entozoal Dysentery must also be here considered, especially Schistosomiasis; the ova often producing considerable irritation and perhaps Chronic Ulceration and numerous large Papillomatous growths in the lower segments of the Large Gut. Lastly we have to consider Malignant Disease of the Bowel.

i. Tuberculosis of the Intestines - is specially associated with Pulmonary T.B, but it may occur as a Primary affection of the Intestine, esp. in young children. The principal seat of infection is the lower part of the Ileum, but it may occur around the Caecum and in the Appendix. The Pyer's patches and the Solitary glands become swollen, either uniformly or in irregular areas, and T.B.foci may be found in other parts of the Submucous or Mucous coats. The swollen patches undergo central caseous necrosis, and over them the mucous membrane sloughs, forming small ulcers, which by confluence are very irregular. Three types of ulceration are met with, viz - Acute, Subacute and Chronic. In Acute T.B ulceration, there is considerable undermining of the edges which are usually ragged, and the necrotic process is apt to involve the deeper layers of the bowel and cause perforation, which otherwise is not common resembling in general appearances the Acute Amoebic Ulcer, but with this distinction that the floor of the T.B.Ulcer is not infiltrated to any marked degree, but Tubercle follicles undergoing caseation may be made out microscopically. When however, the ulcer is Subacute, these changes are more pronounced but not so Acute. The floor and edges are nodular and thickened; on the peritoneal aspect small T.B granules are seen, and the floor is not formed by one of the coats of the Intestine, but of typical T.B. granular tissue. The ulceration beginning in the Pyer's patch or Solitary Gland spreads peripherally and deep into the bowel-wall and also laterally to Involve the Intestinal mucosa, and may ultimately completely encircle the Gut. The essential condition is the primary formation of typical T.B granulation tissue, and itsbreak down and caseation , and by this method it involves the deeper coats. In the more Chronic Ulcer by the Chronic Inflammatory changes, there is marked thickening of the Serous coat, and adhesions to the surrounding parts. An overgrowth of fibrous tissue within the lumen and its cicatrisation may lead to strictures which are often Multiple and sometimes extremely narrow. The T.B. ulceration of the Caecum and Appendix is generally of an Acute type, tending to spread widely and causing large irregular areas of destruction of the mucous membrane and a feature of Large Intestinal ulceration appears to be excessive pigmentation. In the more Chronic ulcers, pigmentation of the margins and base of the ulcer occur, the edges are raised,

* Prof. Fergusson.
"Bilharzos", Cairo
Scientific Work, 1910
vol. 4.

## Differential Diagnosis from other Ulcers

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Tuberculosis of the Intestines - continued.

and thickened, the floors irregular and nodular When T.B. affects the Mesenteric Glands, the Intestinal mucous membrane very often escapes and when there is T.B. Peritonitis, T.B. ulceration of the Intestine, is said to be rare. Waxy degeneration of the Intestine is generally associated with Chronic T.B. ulceration.

ii. The Typhoid Ulcer.

The early stages of hyperemia occur during the 1st.week of the disease, and the seat of election appears to be in the Adenoid structures of the lower part of the Small Intestine; though the Solitary lymphoid glands in the Large Intestine appear to be swollen. Small areas of necrosis appear in the swollen parts, which coalesce and form irregular sloughs. Towards the end of the 3rd week, these sloughs separate, and irregular ulcers are formed. These ulcers are in the long axis of the bowel generally oval. The floor may be irregular if the sloughs have not been completely separated but it may be smooth and be formed by the muscular wall. The Peritoneal coat is usually unaffected. The edges of the ulcer are undermined. Perforation rarely occurs and is caused by direct thinning and ulceration of the coats. In a healed ulcer, the cicatrix is often pigmented and may remain as a flat depressed area in which the Intestinal wall is thin and transparent and the destroyed lymphoid tissue is not restored.

iii. Gummata of the Large Intestine are generally circular; when they break down they leave irregular, sloughing margins with infiltration of the mucous coat. When healed they are circular, the edges are raised from the surrounding tissue and a good deal of fibrotic change may occur in the ulcer.

iv. Actinomycosis. Secondary abscesses may occur in the Large Bowel, as in the Caecum, Appendix & Hepatic Flexure of the Colon. The pus will contain the characteristic Ray-Fungus. Such cases however, are rare.

v. Entozoal Dysentery - Intestinal Schstomiasis, or Bilharzia Hematobium. A very chronic form of Dysentery or Dysenteric-Diarrhoea, associated with Bilharzial infection of the Large Intestine is a very common disease in Egypt; but it has also been described by Darling in the Panama Canal Zone. Prof.Fergusson's work* in Cairo is perhaps, the best that has been done in the investigation of the disease. It is seldom seen as a primary disease, being nearly always secondary to Bilharzios of the Urinary Organs; but at the Kasr-el-Ainy Hsptl., Cairo, Fergusson has observed exceptional cases of definite Adeno-Papillomatous growths in the Rectum of undoubted Bilharzial origin. These

* Prof.Fergusson. "Bilharzos", Cairo Scientific Work, 1910 vol.4.

Differential Diagnosis from Other Ulcers.

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Intestinal Schistomiasis - continued.

cases have to be distinguished from the "Colitis Polyposa" found in the Bacillary Dysenteries. In these growths, no appearance could be detected of similar vesical or urethral lesions.
The common site is the Sigmoid flexure and Rectum, though the whole of the Large Intestine and Appendix may be involved. The essential pathological condition is the production of Large Adeno-Papillomata, which supervene on the Acute Catarrhal changes undergoing chronicity. The earliest change in the Acute stages is a general congestion of the mucous membrane and it may be with small hemorrhages. This condition in its fresh state is described by Fergusson as " Having a rosy-coloured, velvety appearance". These congested areas are definitely thickened and shows under magnification, " innumerable tumified, glandular orifices filled with mucous; a layer of extremely tenacious transparent mucous, showing here & there flecking and streaking with recently effused blood which covers the congested mucous membrane," (cf.Phillips, Amoebiasis, p.90).
Adeno-Papillomata now arise, at first singly and of very fine vascular structure, and they are especially seen near the Anus; but as they increase in size, they turn more complex in pattern, and remain either as sessile growths or turn pedunculated, hanging down in groups or masses into the lumem of the Gut; but the areas bearing these growths often end quite abruptly. In addition, there are ulcers. These in the great majority result from the sloughing of Papillomata; but other ulcers are seen between the folds of mucous membrane and probably result from the hyper-congestion necrosis of the mucous membrane. They are not deep but when secondary, bacterial infection occurs, sinuses form which burrow deeply and may lead to perforation. The bowel-condition is so characteristic that no error in their being mistaken for Amoebic lesions is possible.
The Disease is essentially Chronic; and the condition arises from the "Spinal" irritation of ova in the submucous coats. In advanced cases, an anchoring of the bowel takes place due to pericolic thickenings and adhesions, and these may occur so firmly as to present a problem in the removal of the bowel in a post-mortem. In such conditions there are very often worms in the Veins supplying these portions of Gut, leading to Pericolic Infiltration with hypertrophy of the muscular coats.

## SECTION III. THE CLINICAL CLASSIFICATION OF INTESTINAL AMOEBIASIS & CLINICAL STUDIES OF ITS VARIOUS TYPES.

## The Clinical Classification of Intestinal Amoebiasis.

A classification to be of clinical interest must fulfill two practical purposes, viz -
as an aid to Prognosis &
as an aid to Treatment.
Certain special types such as Heubner's Diptheritic type is perhaps, of more pathological interest than clinical importance, in as much as there are no special lesions or accentuation of clinical symptoms in its production. This may, however, be included amongst the Acute cases, and it mayn perhaps, be grouped along with the more acute varieties of Amoebic Dysentery.
The cases are therefore divided into the following.

I. Acute Amoebic Dysentery in which there can be distinguished the following types:-
i, Gangrenous or Fulminant type and the Haemorrhagic type of Kelsch and Kiener.
ii. Heubner's Diptheritic type.
iii. The Choleriform type, probably indistinguishable from the Haemorrhagic variety.
iv. The Catarrhal type, or Simple Acute Dysentery of moderate severity.

II. A Special "Ulcerative Typhoid-like Colitis" of Osler.

III. Chronic Intestinal Amoebiasis of the following varieties:-
i. With symptoms, though these may be ill-defined and vague.
ii. The Intermediate Diarrhoeal Group.
iii. The Latent Type, without Diarrhoea -Musgrave's Type.
iv. The Carrier Group.

IV. "Asylum Dysentery".

V. Mixed Cases, both Acute & Chronic.

* q.v. p. 60.

The Clinical Aspects of Intestinal Amoebiasis and Clinical Studies.

I. Simple Acute Dysentery.

The onset of this condition varies. It may be sudden & acute - in 60% it is of this nature - or there may be only Reflex Symptoms of diarrhoea some pains, borborigmi, flatulence, to be followed within a few hours or even days by blood & mucus in the stools. It is impossible to distinguish between these symptoms as indicating the nature of the Dysentery, and only by stool- & blood-examination that we can decide whether a case is of Amoebic nature or not. It is therefore of no importance in detailing Statistics, unless this primary condition has been fulfilled. Even my War-experience of now some 600 cases, cannot be quoted because it was found impossible to examine & report upon the exact nature of the case, beyond including it under the generic name of 'Dysentery'. Laboratory work on Hospital Ships is not always the easy affair it may seem to be; and the constant vibrations alter the field & impart motion to the pathological material under consideration.
Nor can Statistics of the Mesopotamia Cases be quoted, because by the time they have been received heres some 3 weeks or more have elapsed, and we are dependent upon the patients' statements. So far, then, as could be judged, the majority gave a history of only moderate severity, & often the total duration averaged 3 to 10 days.
In some cases which occurred spontaneously in the Hospital & came under direct supervision, I was able to examine the stools straight away, being in charge of the Laboratory, and determine whether the onset was acute, indefinite or otherwise. From a study of 10 such cases, all were of this nature; and in one other case, that of a lady (private case), the disease began with a feeling out of sorts, for a day, followed by 5 or 6 small motions during the next day, and only towards the evening blood & slime were passed. I found Amoebae in the morning stool, and cured the Dysentery in 3 days by the intramuscular injection of 2½ grs. Emetin Hydrochl: (Parke Davis' "Ampoules," sterile solution.)
In the Diarrhoeal cases on the other hand there was either a history of insidious onset, or the symptoms were rather severe, with numerous stools. The majority of these cases belonged to the Coolie class & were very debilitated & of poor physique. Perhaps this plays a more important part in the determination of the onset than might be suspected. Cases which came under my notice in France, are, for the same reasons as already stated, unsatisfactory to quote. Some of them were undoubted relapses; I do not remember any case of Incipient nature; and in some the diagnosis was doubtful because Piles could not be definitely excluded; and when sent to the Clearing Hospl: these cases were lost sight of.
In the cases which were received at No. 5, I.G.H. Alexandria (The Casino Hsptl) most of the cases were reported as being Bacillary in nature, although a sprinkling of Amoebic cases were seen. In these, the disease had been Acute; and as will be found later in the Thesis,* 100 cases were analysed by me which were complicated by Scurvy with Pyorrhoea, to determine if possible whether Amoebae might be the cause; in all these some history was obtainable of recent dysentery.

* cf. P. 60.

## Clinical Studies in Intestinal Amoebiasis.

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### I. Simple Acute Dysentery.

The cause of the delay of Acute symptoms is due to the fact that ulceration has occurred high up and is probably limited to the Caecal Region. General tenderness is often complained of and is most frequently met with over the Caecum and Ascending Colon, or in the Sigmoid, and when well marked in both these situations is very suggestive of Amoebic Disease. Rogers rightly lays stress on the point that this symptom should be very gently illicited, as there may be little but the Peritoneal coat remaining intact to prevent perforation. If tenderness is present over a large proportion of the Great Bowel, the case may be expected to prove a serious one. Fever is usually absent and is a helpful sign to distinguish cases from Bacillary origin. The constitutional symptoms are absolutely no guide to the severity of the case, for occasionally even Gangrenous Amoebic Colitis may present no obvious serious signs. If Fever persists more than a very few days in Amoebic Colitis, complications especially as regards the Liver must be suspected.
Rogers in an analysis of 57 cases, - 34 of which were Acute - and 23 Chronic, differentiates 4 types of fever:-

i. Remittent Fever in 6 Acute cases.
ii. Intermittent to over 100 F. in 2 Acute; & 7 Chronic.
iii. Intermittent to 100 F. or below in 11 Acute cases; & 4 Chronic.
iv. No Fever in 15 Acute cases; & 12 Chronic.

He adds the following clinical notes:-
" In about half of both the Acute & Chronic cases of Amoebic Dysentery, there was no fever during their stay in Hospital, while when present, it was usually of a slight intermittent type only, and seldom lasted more than two or three days under treatment. The few cases in which well-marked fever of the remittent type was present were very severe and frequently fatal, usually from some complication such as Peritonitis or Liver Abscess. In Chronic cases fever is only occasionally met with, and may not rarely be absent even in those proving fatal."(cf.Rogers, Dysenteries,p.90).
Fever then, generally means the presence of some complication, e.g - Malaria, Kala-Azar, Typhoid, Undulant Fever, Lobar Pneumonia, Hepatitis or Acute Abscess, Infectious Jaundice.

As regards subjective abdominal symptoms, fairly severe Amoebic Dysentery is always accompanied by abdominal pain with tenderness, and there is often definite thickening of the Gut to be made out. Tenesmus, which is due to involvement of the Rectum, is fairly well-marked in Bacillary cases, but not so in Amoebic; there are, however, true abdominal pains in the region of the Umbilicus, and the two Ileac foci or, the pain may be localised over one or more Segments and will then correspond to the localised Segment.
Sometimes in the very Acute cases, the Tenesmus, general tenderness, and faintness are alarming. This Tenesmus is then Vesical as well as Rectal; and during Acute attacks of Amoebic Dysentery,

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## I. Simple Acute Dysentery.

spasm of the neck of the Bladder is often one of the most urgent & distressing symptoms.

The Stools. They may be of great frequency upto 30 in the 24 hrs.; but in some cases only 6 to 10 are passed, especially if the patient is about. The Character of the Stools vary according to the severity of the case. Stress has been laid on the information derived from Washed Stools; the practice originating with Norman Chevers*& Goodeve and recently reintroduced by Rogers into practice. As a general rule, numerous separate large pieces of rosy blood-stained mucus are suggestive of the Protozoal Disease; whilst either large white fibrinous masses, or small glairy , raw white-of-egg-like pieces of mucus, intimately mixed with loose fecal matter are more commonly met with in the Bacillary form, esp: the NOT Very Acute Type. Sometimes I have observed that there is a 'splotch' of tomato-looking red in the centre of andd 'encased' by a glairy white-of-egg-like mucus - best described as a recently opened raw egg, but with'tomato-content' instead of the yellow. Numerous Amoebae are readily found in this.

Sometimes no red tinge may be seen at all, though microspically, red corpuscles may be found: & in these cases it may be inferred that the development of the lesions is slow, & that little ulceration has taken place.

If the Caecum is chiefly affected, the blood is dark-brown or black; when the lower segment of the Colon is principally affected, it is fresh, bright red, discrete & clotted; whilst if it comes from above the Sigmoid Flexure, the blood is intimately mixed with mucous & fecal matter, & the evacuations are dark-red or brownish-red. Freee bleeding indicates rapid, rather than extensive, ulceration; but the abscence of haemorrhage does not preclude the possibility of serious mischief, for in the gravest cases, the destruction-process is sometimes so malignant, that perforation takes place before any blood is passed.

Norman Chevers in his "Commentary on the Diseases of India, 1886," quoted Goodeve's Method of Washing Stools; and as that description is to be found universally in all Works on Amoebic Dysentery, I quote from Phillips'"Amoebiasis & Dysenteries"as follows:- (pp.39 & 40).

"The stools passed since the last visit have water poured freely upon them. Any faeculent matter which may be present floats, the water is poured off, & whatever has sunk to the bottom of the vessel is allowed to remain there. The sediment contains the dysenteric products. Water is again poured on and off until the products are left nearly clean. These are then placed in a dish , white & clean & filled with water, which floats them out & apart and displays them clearly. Here it is to be observed, that with the exception of faeces & fluid blood, everything which is worth seeing & which tends to acquaint us with the nature of the case, sinks to the bottom of the vessel, when the stool is washed..... These products consist mainly of sloughs of various character & mucus in various condition. Goodeve's Nomenclature describes 'pus-infiltrated' sloughs; 'tubular sloughs'; & 'cellular or areolar-

* It was introduced originally by Dr. Goodeve, when he was Principal & First Physician of the Calcutta Medical College Hospital, & quoted by Chevers in 1879.

Clinical Studies in Intestinal Amoebiasis.

- continued -

I. Simple Acute Dysentery - continued.

tissue sloughs'; then there were 'rose mucus', 'branny mucus' and 'ropy mucus'. Besides these products, we generally found, with the washed sediments, any article of food which had passed undigested, and which we always knew had greatly irritated the diseased bowel ... and sometimes Ipecacuanha powder and pills which had been given. Thus, a distinct quantity of gelatinous rose mucus with faeculent matter indicated a case of not more than 12 hours' duration. The same mucus without faeculent matter - probably the case has gone on unchecked by treatment for from 6 -36 hours longer than the last. Branny mucus - this is a case from 5 - 8 days old, doing well under treatment. Ropy mucus in great abundance - a very favourable case approaching recovery. Pus-infiltrated sloughs a case of 5 or more days' duration in a tolerably good constitution, which will probably do well under treatment. A Brown or Black cellular slough, scarely distinguishable at first from an old black cobweb, pinched together to the same size and placed in the water beside it - an evidence of gangrene and presage of certain death."
Rogers uses the method in Calcutta and speaks well of it. No mention is, however, made of the occurrence of the sago-like bodies so often seen. The stools are usually alkaline.

A fatal result is however unusual; and even without treatment, the system is generally able to cope with a 1st. attack of Amoebic Dysentery. In the majority of instances, the duration of the Acute stage is only 48 hours; and evidences of improvement begin to manifest themselves within 5 days of the beginning of the illness. For a day or two the patient gets spasms, there may be Diarrhoea, sometimes of a pronouncedly lienteric type, and mucus may ultimately be passed intimately mixed up in the more solid particles. Irregularity of the Intestinal functions, with intermittent persistence of mucous & blood, indicates the continuance of the infection, and about half of all cases pass after the first attack into a Chronic condition, in which, although during the quiescent stages, Dysentery symptoms are but slightly marked, there is constant liability to relapse.
I have met with no cases of Prolapse of the Rectum from straining, though this has been described.

Cases Illustrating The Nature of Pyrexia, when this occurs in Amoebic Dysentery.

From my experience of Acute Dysentery, gathered from the Dardenelles and the Mesopotamia Campaigns, I am able to illustrate this paper with several interesting Cases. Of course, the cases received from Mesopotamia have not often been received here in the Acute condition, for the condition had been established at least two to three weeks on an average, before they were received, except Acute cases at Basra, which were evacuated and brought away, but who had received treatment during the 6-day voyage. On the other hand, the Dardanelles cases were received on boardship H.S."Letitia" in Suvla Bay, in a fresh condition. They were also received at Alexandria, after the disease had been established some time, and in some cases what was labelled " Diarrhoea", blossomed into well-marked Dysentery, from which I was able to recover Amoebae in the stools. In addition, much experience was gained at The Casino Hosptl, No.5, San Stepheno, Alexandria. I am therefore able to detail some interesting cases.

Case 1. The patient was an Australian bushman, aged about 40, who was received at Alexandria with a history of Diarrhoea and Fever about 101°, into my ward. Blood-examination for Malaria was negative, and he was put upon doses of Castor Oil, but in spite of this his Diarrhoea continued, was highly offensive, and he was losing weight. His tongue was dirty and covered with a greyish-fur, and he had on an average, 10 -15 motions a day. He had been ill for some 2 weeks. His stools contained a little mucous at first, but no blood. After he had been on board 2 or 3 days, he began passing blood in the stools, the temperature began to oscillate and turned irregular, and he had sweats. The case was diagnosed as a Typhoid, and his blood was tested against Para A & B, & Typhoid, and found Typhoid plus 80 dilution. I then examined his stools and found Amoebae. He was put upon Emetin 1 gr. daily, and in 3 days there was no more blood in the stools. The patient was landed at Southampton 8 days later.

Commentary. Whether this man had Latent Dysentery or not, is difficult to determine. The blood in the stools with the association of the temperature, suggested Typhoid of the 3rd.week, but the curious part is that all blood vanished after Emetin. There were no griping pains, though he had some tenderness over the Caecum and Sigmoid.

Similar cases have been described by Blair *(Lancet Jan.14/1905), by Strong and others, in which there are Typhoid-like symptoms, but the bleeding depends on a hemorrhagic diathesis, the initial symptoms were those of dysentery; but the hemorrhage from the bowel proved to be a precedent of General purpura & severe bleeding from other mucous membranes.

this occurs in Amoebic Dysentery.

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Case 2. The patient was a man received at Alexandria for transfer to Southampton. He had had irregular f fever, Diarrhoea & colicy pains, and now and again had passed blood in the stools. When seen, he was suffering with fever of the slight remitting type, the temperature not going above 102°, and with Rheumatic-pains in the knees. After a few days, the temperature came to normal, and the pains subsided, but Diarrhoea began with blood in the stools, and tenesmus. After a few days of Apyrexia, his temperature continued swinging and rising ladder-like. On questioning him concerning his place of residence, he gave history of residence in Malta, and stated that he had suffered from "Malta Fever". It was quite clear then that his fever was due to Undulant Fever, and his dysenteric symptoms cleared up under Emetin.

Case 3. Patient was received in a collapsed condition on board-ship at Suvla, with profuse Diarrhoea, blood in stools, and tenesmus. He also had vomiting. His temperature was 104°, and he had signs of Lobar Pneumonia. His Diarrhoea had developed a few days before admission, and he traced it to eating bad food. He was given subcutaneously, 1 gr.Emetin, and the dose repeated for two days in succession. His Diarrhoea decreased, the Pneumonia resolved on the 7th day, and he made a perfect recovery by the time he was discharged at Malta, for our return trip to the Dardanelles.

Commentary. It was feared that perhaps this case was of Gangrenous type, but the rapid improvement under Emetin was remarkable.
These three, are perhaps the most interesting cases from amongst the hundreds which passed through our hands. During June, July & August, we saw practically nothing else but Typhoid, Para-Typhoid, and Dysentery - and much of the Dysentery I should say was Bacillary. We also received a good deal of "Camp Jaundice or Infectious Jaundice" which we now know to be due to the Spirochaeta Icterhaemorrhagica - these cases at that time were thought to be Hepatitis of catarrhal origin, and perhaps of Amoebic origin, and a few of the sases were actually complicated by a present Dysentery. Generally no improvement in the Diarrhoeal condition was manifest after anti-Amoebic measures, though in a few cases, the diarrhoea did clear up, but the Janndice remained. Improvement on the other hand occurred both in the diarrhoeal condition and in the Jaundice, under Liq.Hydrarg.Perchlor: xxx m. t.d.s, in about 60% of cases. Some of these cases were undoubtedly of Flagellate type and due to Trichomonas & Lamblia, but the Trichomonas were found to be more frequent. Whether some of these cases were also due to Spirochete, was unknown, but undoubtedly Spirochital Diarrhoea & Dysentery do occur.

## II. Gangrenous Dysentery.

This is the most formidable type of Acute Dysentery met with, and is generally also associated with Multiple Acute Abscesses of the Liver - ( the Fulminating Type ). Some of these cases have been mistaken for actual Asiatic Cholera, and a few of them have turned out to be of Malignant Malarial origin with Intestinal symptoms So far, the only case suggesting this which I have seen, is Case III recorded. The stools are often black, highly offensive and very liquid. The collapse resembles the Algid Stage met with in True Cholera.* All the symptoms are those of an Acute Dysentery, only greatly aggravated. Finally sloughs may appear in the stools, and the patient die of perforation -peritonitis. The whole thickness of the bowel-wall may become Gangrenous in a number of places, and be so softened as to resemble damp blotting-paper. Clinically, the most frequent symptoms of a Fulminant attack -

i. Very numerous stools with perhaps a preponderance of blood, or sometimes large hemorrhages, as was pointed out by Strong in Manila The blood, however, may be black and tarry as in Duodenal Ulcer, for which the condition may be mistaken, as there is always great thickening and tenderness of the Transverse-Colon in this state.

ii. The appearance of Ominous black-sloughs in the stools.

iii. Severe abdominal pain, tenderness & rigidity-with sausage-like masses of thickening. The Caecum & Ascending Colon are especially liable to be affected, and the case mistaken for Acute Appendicitis. If, however, the Intestine is greatly thickened without tenderness in an Acute case, Gangrene has already occurred.

iv. Less commonly actual perforation occurs, with signs of General peritonitis, and in these cases there is often extreme Gangrene of the Gut. Sometimes the perforation is Post-Caecal or Post-Colic, with Retro-peritoneal Abscess, when the gangrenous area is in the Caecum & Ascending-Colon; whereas in the Sigmoid & Descending Colon, perforation is generally accompanied by General Peritonitis, without localised abscess-formation.

Amongst these Gangrenous Cases, must be put those cases in which there is excessive Intestinal hemorrhage, sometimes of pure blood. Yet again when the Gangrene process is very Acute, perforation may have already occurred before there is evidence of hemorrhage, on account of the rapidity of the involvment of the whole thickness of bowel.

## III. "The Ulcerative Typhoid-like Colitis" Type of Osler.

The clinical features of this condition, which is not uncommon in the Tropics - resemble those of severe Typhoid. The symptoms are, high fever, prostration, pain, frequent hemorrhage, evacuations, and in many cases violent delirium. Entamoebae have been observed but are infrequent.

* A point in connection with the Differential Diagnosis between Gangrenous Bacillary & Amoebic Infections is that in the latter all the symptoms of Toxaemia such as, utter prostration, fever, aphonia, cold extremities, collapse, petechial haemorrhages, vomiting, &c, which one is accustomed to associate with severe Bacillary Infections, and which in fact have often lead to the cases being sent to the Hsptl, with a provisional diagnosis of Cholera. The difficulty is heightened by the fact that the most careful search may fail to reveal Amoebae in the stools, whilst the blood may give a positive agglutination for Bacillary Dysentery. This is just the type of case in which the agglutination reaction fails, as the positive reaction may be due to either past or present benign Bacillary Dysentery. It is only at the autopsy when sections of the Gut-wall are made that the Amoebae are discovered in the Submucosa & none in the Gangrenous mass."
(cf. B.M.J. Nov. 15, 1913, p. 1284, Section of Trop. Med. - Dysentery).

## III. "The Ulcerative Typhoid-like Colitis" Type of Osler. - continued.

As diagnostic points, Osler instances a Normal Spleen, absence of Rose spots and a negative Widal, "but in the Eastern Tropica, these signs are inconstant and unreliable."

## IV. Mixed Types.

In Tropical practice, Dysentery is often seen as a terminal symptom of many widely different Pathological conditions - e.g. Acute T.B, Diabetes, Bright's Disease, and the Severe Anaemias, and it is by far the commonest ultimate cause of death in them. It is also a frequent and fatal complication of the cachectic marasmus condition which originates in Chronic and repeated Malarial Infection, and in advanced cases of Sprue. In these cases however, Entamoebae are rarely met with, and probably in Terminal Dysenteries the infection is largely Bacterial, but may be Flagellate, as I have seen in three instances from cases in Mesopotamia, where, however, it has been more of the nature of a terminal Diarrhoea, followed by blood just before the patient died.
These three cases occurred in Sweepers received from the Expeditionary Force, (Mesopotamia) and may illustrate the above.

* cf. P. 37. Case I.

Case 1. Sweeper admitted in May 1915 with history of Typhoid. He had been ill 1 month; temperature was fluctuating, and he was very weak and emaciated. His Spleen was enlarged, tongue dirty, and he was passing from 10-15 motions a day. There were small mostly watery, greenish or yellowish, foul-smelling and tinged with blood & mucous; his stools showed Trichomas Intestinalis. He improved somewhat under Sour-milk treatment, with Bism. Salicyl. Pulv. Cret. Arom, Cum Opio, Salol & small doses of Calomel. He had numerous relapses, and finally died - No Amoebae were seen by me in his stools.

Case 2. Sweeper admitted in May 1915, with signs of Acute T.B, and history of Diarrhoea and blood in stools. It was first thought that it was T.B. Diarrhoea, but examination showed Trichomonas. He died in a very weak & emaciated condition.

Case 3. Sweeper, with history of Sprue, admitted June 1915. Had typical sore-mouth and his stools were still bulky, white, frothy, but in addition there was recent history of blood & mucous. Amoebae were found by me in the stools. He was put on Emetin, but grew worse in a few days and died.

Case 4. On the other hand, another case Dhobie, admitted in Septr. 1915 in a dying condition with enlarged Spleen and fever & Diarrhoea with mucous of 2 weeks duration, but no blood. His stools averaged 15-20 daily, and he was rapidly getting worse, and there was danger of heart failure. There was no history of Dysentery. He was put on Emetin, 1 gr. daily, and after two injections his stools were reduced to about 10, with but little mucous.

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IV. Mixed Types - continued.

Case 4. A week later, he was out of danger. This case was of the Latent type, and whether it supervened on an old Chronic Malarial condition, or was itself also Chronic, it is impossible to say. He made a perfect recovery, and left the Hosptl. a month afterwards. He had no return of the Diarrhoea or mucous.

Case 5. Another case like the above, only he (Sepoy) was admitted with history of fever and Jaundice. He was rapidly cured under Emetin, and left the Hospital at the same time as the case above.

Typho-Dysentery. A case of this nature has already been detailed. * Other cases have been received of this nature from Mesopotamia, but they were mostly Convalescents, but brought a clinical Transfer Certificate with Typhoid Fever and Dysenteric symptoms or Para-Typhoid & Dysentery In a few, Dysentery relapsed, but after a few injections of Emetin, they were discharged convalescent.

* cf. P. 37. Case I.

It should also be remembered, that Dysentery Carriers have been detected in patients admitted for Typhoid and other conditions, not Dysenteric. In Haemorrhagic Typhoid in the Tropics, the clinical manifestations are generally Atypical, and considerable quantities of Intestinal mucus are passed at intervals throughout the whole course of the disease. " During the early stages the excretion of mucous is sometimes so marked as to suggest a conbimation of Dysentery and Typhoid; and it is especially prominent in those cases which are afterwards complicated by severe bleeding. In these patients, too, the temperature, eruption, and other symptoms are frequently uncharacteristic, and there is, in fact, often great difficulty in arriving at a conclusion as to the actual condition. "(cf. Brown, p. 111).

V. The Choleriform Type.

This perhaps may be in part, the Hemorrhagic Type. This type is attended with severe vomiting, severe hemorrhagic discharges in which there may be found Blackish sloughs or portions of necrosed mucous membrane; and collapse. Such cases have a hopeless prognosis, though it is interesting to note that Rogers had a case which was admitted for suspected Cholera, and was cured by Emetin in a week - a truly marvellous result. So far I have not experienced any such case. Such cases have to be differentiated from the Intestinal "accès pernicieux" in Malignant Malaria, and this can only be done by examining the blood.

VI. The Association of Amoebic & Bacillary Typ

Amoebic cases may be complicated by Bacillary types; and the two diseases may either be acquired together, or one may supervene on the top of the other. It is however interesting to note that H. Fraser, in his reaserches into "The Bacteriology of Dysentery in Malaya, No. 13 of the Studies from the Institute

## Clinical Studies in Intestinal Amoebiasis.

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VI. The Association of Amoebic & Bacillary Types

THE Institute for Medical Reasearch, Federated Malay States", has found that from no case of Amoebic Dysentery in the series was a strain of Bacillary Dysentery (Bacilli) cultivated. Of non-amoebic cases 67 were studied. In 41 no Dysentery bacilli were obtained;failure in some of these cases possibly depended upon defects of technique. In the other 26 cases different types of Dysentery Bacilli were found.
Cf/B.M.J. Nov 4, 1916.
The therapeutic test of Emetin should clear up the diagnosis, with an examination of the faeces for other causes , e.g. Ova.

## CHRONIC INTESTINAL AMOEBIASIS.

I. The Symptomatic Type. The following GROUPS of cases may be indicated for consideration:-

1. Those in which Acute symptoms have subsided, but who suffer from Relapses which grow in frequency until the Disease becomes Chronic with marked thickening of the Bowel & well-prounced lesions of Chronic Amoebiasis. Such cases are the result of neglected dysentery, or perhaps not-sufficiently treated cases, aggravated by chills, exposure & Alcohol, until by the amount of scarring the greater part of the Large Gut becomes converted into an ulcerated scarred tube, and,as it has been pointed out,the kaleidoscopic picture of acute & chronic changes going on side by side are features of Chronic Amoebic Disease.

2. The disease has been chronic to start with. Such cases give a history of Insidious Diarrhoea, which has relapsed frequently, of general ill health & emaciation, with dyspepsia and anaemia. But the patient is not sufficiently ill to take to bed. This condition may go on for years, and be followed by marked changes in the bowel. Such cases are apt to be followed by Liver-abscess.

3. In some the only symptoms may be those of a troublesome recurrent diarrhoea, with passage of blood & mucus, alternating with Constipation. This type is clearly like Type 1, but the changes are often insidious, & either NO history of dysentery can be obtained, or the patient may have had dysentery & forgotten all about it; as it was slight

4. In a certain number of Sprue cases, chronic dysenteric changes may become apparent, as a terminal dysentery complicating Sprue. In these there is a definite history of a transition in the type of stools, the more marked resistance to Dietetic Treatment, and the history of a more troublesome diarrhoea than what had been observed in the past.

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## CHRONIC INTESTINAL AMOEBIASIS.

Rogers in a series of 30 cases was able to ascertain the following data, as regards the DEGREE of FEVER: the period entered is that during which the symptoms had never long been absent, but in addition many of the cases had suffered from previous attacks.
This therefore should be clinically regarded with those cases grouped under Type 1 Chronic. Some like these cases have already been analysed under the Pyrexia seen in ACUTE Amoebiasis.

TABLE of DURATION of the DISEASE in CHRONIC COLITIS.

| | DURATION | | | | |
|---|---|---|---|---|---|
| | 1 mth. | 1-3 mths | 3-6 mths | 6-12 mths | Over 1 yr. |
| No. of cases... | 5 | 12 | 7 | 4 | 2 |

TOTAL of cases 30.

### ANALYSIS.

1. The great Chronicity of these cases.

2. The great majority (nearly½) had a duration of 1 -3 months; and the next most frequent (just over 1/5) of 3 -6 months.

3. In 2 cases the disease was over 1 yr.(no mention is however, made of the number of relapses, or further history of these cases).

The following are some of the more important clinical aspects of such Chronic cases:-

1. FEVER. This is usually absent, especially in those in which the disease has been Chronic from the commencement.
In a minority, low intermittent fever is found, but which yields under treatment. It is especially to be found in cases with a short duration e.g - 1 month; and in those cases where Chronic changes have supervened as relapses of an Acute attack. This fever may be intermittent to over 100° F, or below - 7 chronic cases are published by Rogers in which the fever was intermittent to over 100° F, and of these, 6 recovered and one died; in 4 others, who all recovered it was below 100° F.
This Fever may indicate for the first time, some other Complication, especially Hepatic.

2. NUMBER of STOOLS. No exact figure can be laid down because this will vary according to the process by which the Chronic change has become established, and to the degree of that change. In one of my own cases, the disease had lasted as a more or less continuous Diarrhoea for 3 months after the 1st.attack of Acute Dysentery, and his Stools averaged 10-15 daily. They were mostly composed of water, and but little fecal matter - yet within 2 weeks of Emetin Treatment they had been reduced to about 3 per day, & with return of the more solid elements. " Average cases will vary between 6 & 20,daily".(Rogers).

## Clinical Studies in Intestinal Amoebiasis. 44.

- Continued -

3. Abdominal Pain & tenderness. These are less marked than in the Acute forms, but are similar in distribution, affecting chiefly the Right & Left Iliac regions, and wherever there are adhesions. One symptom is however more marked & that is tenesmus, not only on account of the greater chronic thickening , but also of the more frequent involvment of the Rectum and Sigmoid. On account of adhesions, scarring of the gut, contractions of the lumen take place, and ultimately there may be signs of Chronic Intestinal Obstruction, which may be taken for Malignant disease, especially as there is progressive ill-health, and recurrences of diarrhoea. "The thickening which occurs is generally limited to the Sigmoid & less commonly affects the Caecum, than is the case in the earlier stages of amoebic acute colitis." (Cf/Rogers'Dysenteries, p.109)

## II. The DIARRHOEAL GROUP of Cases.in Chronic Type.

Although many of the above types of cases will be found to be included in this variety, I wish to limit the characteristics of the cases to the one & only symptom - DIARRHOEA. - and which have none of the features of Chronic or mild acute cases. This therefore constitutes an Intermediate Type. It will be difficult to exclude Latent cases of Chronic Amoebiasis, in as much as this may be the only symptom that is complained of.
The clinical types which should be arranged in this class are:-

i. The pseudo-Sprue & Chronic Mucous Colitis
ii. Enteritis(of children); &"Monsoon"Colitis
iii. So-called"Terminal" Dysenteric-Diarrhoea notably in Sprue.

Of these the first is most common in my experience, viz. Chronic Mucous cases.
A.W.Sellards & W.A.Baetjer* report on a careful study of 3 cases of Chronic Diarrhoea, in which they found Entamoebae which differed in some respects from E.Histolytica & E.Coli. The bowel-symptoms were continuous, and not intermittent as is usually the case with Chronic Amoebic dysentery. They concluded that they were atypical E.Histolytica, temporarily modified by environment.
( The Medical Annual, 1916, Amoebiasis,pp78)

* Sellards & Baetjer in Johns Hopk: Hspl: Bull: 1915, 45.

The differentiating point in these Diarrhoeal Cases is that Amoebae are to be found in the stools. The diarrhoea is often intermittent the stools never bulky, and the mucus either intimately adherent to the more solid particles, or forming stringy masses in themselves. Such cases were met with in the Mudros cases. A good deal of diarrhoea did occur in the Gallipoli Peninsula & at Mudros, and they were merely prelude to an attack of True Dysentery; it was a leading symptom in Flaggelate and it was a true condition induced by Chronic sand-irritation, a coarse & monotonous dietary, and unassociated with any form of dysentery or Flaggelate Infection. There

## Clinical Studies in Intestinal Amoebiasis.

- continued -

### II. The Diarrhoeal Group in Chronic Amoebiasis.

still remains the differentiation of the group in which Amoebae were found in the stools. In the Mesopotamia cases there was a similar grouping. In addition the change from Temperate to Tropical climate often induces "Climate Diarrhoea", best illustrated in "Tropical Hill-diarrhoea". Even in these cases Amoebae may be found in the stools. Intimately mixed up with this question is the consideration of the Etiology of "Summer-Diarrhoea in the Tropics". Gordon has called attention to a variety of Acute B.Coli Infection in children in which gastro-intestinal symptoms predominate. IN these the onset is attended by severe colicky pains in the abdomen, vomiting, obstinate constipation, or acute diarrhoea; and sometimes jaundice. Examination of the urine is the key to the diagnosis. At the Boston Floating Hospital, during the summer of 1910, Dysentery Bacilli were found to be the cause; but in 1911 Streptococci were the determining cause - Seasonal Variation had not been recognised hitherto.

Not so in what has been termed MONSOON Diarrhoea. It is chiefly due to Rogers' work in India that the recognition of the condition is now established.

Rogers worked out the Incidence - curves of Dysentery, Diarrhoea & Hepatitis in Calcutta in the Medical College Hospital for 1 yr & the monthly admission to the European General Hospital for 5 years, 1904 -1909, and observed that " they follow very closely, those of the Dysentery, only the maximum incidence is slightly earlier in the case of both classes of patients .... The incidence in European children and adults are practically identical, the maximum of each occurring in July, with the establishment of the Rainy Season, accompanied by a considerable fall in temperature. In the Native out-patients also, the Diarrhoea cases do not materially increase until the heigth of the Monsoon, and reach their maximum in October. Thus, not even in European children is there any marked increase in the incidence of Diarrhoea in the dry hot season, as might at first sight have been expected, in view of the well-known relationship of Infantile Diarrhoea in temperate climates to excess of heat. The important question remains as to what is the nature of the Monsoon Diarrhoea in Calcutta and other parts of India. My recent observations clearly show that the great majority of the dysentery cases at this season are amoebic in nature, and as mild cases of this Infedtion often only produce diarrhoeal symptoms, it appears probable that much of the rainy season diarrhoea is also amoebic in origin." (cf.Rogers pp 41-42; & Diagram 2 -(Appendix)- " The Seasonal Incidence of Dysentery, Diarrhoea & Hepatitis in Calcutta."

## Clinical Studies in Intestinal Amoebiasis.

- continued -

### II. The Diarrhoeal Group in Chronic Amoebiasis.

Much of the "Diarrhoea" in India, at any rate, may be simply due to a Catarrhal Inflammation of the Intestine without neces sarily any blood being passed - the hyperenic condition of the intestine allowing an extra mucous secretion of the bowel to take place. Such diarrhoea will surely be controlled by Emetin, if due to Amoebae. So far as my own experience of Seasonal Incidence is concerned, in the Mesopotamia Group of cases, the period of greatest Diarrhoea & Dysentery were from April to August, 1915, after which cases became extremely infrequent and at present - (Nov - Jan.) are altogether wanting. Perhaps in this analysis the following point should be brought out:-

i. The more perfect feeding & watering arrangements now in force, than during those months and the introduction of the universal practice of Chlorinating all water used for drinking purposes, especially at Basra.

ii. The late arrival of the cooling "Shamal" - wind, with the result that the hot weather was more severe and greatly extended (1916).

iii. The dry weather, as the rainy season is during the winter months.

In the Dardanelles Series of Cases, the incidence was high all through the Summer, especially Mid-Summer, 1915.

i. The Mudros climatic conditions, especially the high winds during Spring & Summer, and the flies & sand-irritation.

ii. Water and fresh food difficulty.

iii. During Novr. & part of Decr. there were still cases, but these had been reduced remarkably. in numbers. (1915).

### III. THE LATENT TYPE

1. The Suppressed Latent Type. The reason why Dysenteric symptoms are so commonly absent in these cases is, that the lesions are generally limited to the Caecum and Ascending Colon. In the Latent type there may have been preceding Acute Dysentery, which is thought to have been cured; but post-mortem supplies evidence of extensive ulceration; or there may be no history of Dysentery & Amoebic Abscess may arise in this class of case, and yet the Gut may be the seat of ulceration.

* Musgrave (Intestinal Amoebiasis without Diarrhoea, 50 Fatal Cases". Phillipine Jrnl. of Science, Sec.B, 1910, Vol.5 p.229).

- continued -

## III. LATENT AMOEBIASIS.

### 2. The Non-Diarrhoeal Type of Musgrave.

Musgrave * has published 50 cases of Intestinal Amoebiasis without Diarrhoea. (cf.Phillips,p.37). The following were the terminations, and the distribution of Bowel-Lesions:-

3 died from perforated Appendix - in 2 of whom Amoebae were the cause.

4 " of Liver-Abscess - 1 perforating the Pleura,& 1 into the Abdomen.

8 " of Pulmonary T.B.

2 " of Chronic Malaria.

5 " from perforation in Large Intestine
4 being in the Caecum &
1 " " " Transverse Colon.

7 " of Acute Beri-Beri.

20 " of Lobar Pneumonia.

" On considering the situation of the lesions in 27 cases, the Caecum and Ascending Colon were affected, including the three Appendicitis cases. In 9, the whole Large Intestine, except the Sigmoid & Rectum was affected. In 2 cases the Sigmoid & Descending Colon were affected. In 2 cases the Transverse Colon and Sigmoid Flexures, and in 5, the Caecum, the Hepatic & Splenic flexures were affected. In 5, the situation was not recorded. Thus the variety of diseases in which dysenteric ulceration was found post-mortem is interesting, the cases of Appendicitis being especially noteworthy". (cf.Phillips, Amoebiasis & the Dysenteries, p. 37).

As regards symptoms - these were indefinite: " some complained of dull aching in the abdomen, worse at night and in early morning flatulence occasionally occurred; there were also occasional constipation, which was not always well relieved by purgatives, sometimes produced excessive action. Neurasthenic symptoms were not uncommon, with perspiration of the hands and feet; in many cases there was no loss of weight. The only positive fact which could make the diagnosis certain, was the presence of the Amoeba in the encysted tetragena stage." (cf.Phillips, p. 38).

* Musgrave ("Intestinal Amoebiasis without Diarrhoea, 50 Fatal Cases". Phillipine Jrnl. of Science, Sec.B, 1910, Vol.5 p.229).

- continued -

## 2. The Non-Diarrhoeal Type of Musgrave(cont.)

### ANALYSIS

1. All the cases were fatal.
2. In all symptoms were very General and even then vague.
3. All cases died of some intercurrent Disease or direct Complication, the largest number of Lobar Pneumonia; and a second group of Pulmonary T.B; and the cases of Appendicitis are especially noteworthy.
4. There was a total of 8 perforative cases, 4 of which occurred in the Caecum.
5. Amongst the Series, there were 4 cases of Liver-Complication.

Experimental evidence in animals also bears out this Latency - infected cats have frequently shewn no signs of the disease, while an extensive ulceration has been found on post-mortem; and the same applies to Experimental Balantidial Infections in monkeys.
The same perhaps is true of Walker & Sellards' * cases.

Under the heading "Latent Dysentery, or Dysentery Carriers in Sarawak, Borneo", W.L.Christie in the B.M.J. July 18th, 1914, p.118, stated that in his experience in Sarawak, that many people, white or Native, may become thin, pale, wasted & weak with what is practically Dysentery, without having loose stools or blood or Mucous. In such cases abundant Amoebae of the histolytica type were found in the stools, and showed rapid improvment under a few injections of Emetin. " It is very probable that much of the debility, invaliding, Anaemia, and 'Fever' put down to Malaria which is rare here, is due to the septic irritated condition of the Colon in patients infested with Amoebae who show no signs of blood or mucous in the stools, till they reach an advanced stage of ulceration."

* Walker & Sellards' (Exptl.Entamoeb.Dys.- Phillipine Jrnl.of Science, Sec.B, Trop. Med, Aug.1913, vol.8, pp.253-332).

## IV. The CARRIER- GROUP.

It is but a step from these Latent cases to the Carrier cases. Walkers' work is especially interesting in this connection, for he has shown that a man may remain as Carrier for years without having suffered from a single symptom of the disease, but he may have Latent lesions. Statistics from all over the World are at hand to quote from.

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The CARRIER-Group.

I. Christie's Statistics from Sarawak, Borneo, published in B.M.J. July 18, 1914 (p.118), states:-

" During 9 months since August, 1913, of 554 cases admitted to Sejijak Hospital, 65 were Dysentery Carriers, and 19 others had usual signs of the Disease. Thus there were 12% of Carriers of Latent Dysentery, and 3.4% of actual cases.
In 100 Unselected cases (Apl & May, 1914), of all kinds, Amoebae were found in 34%; in 100 consecutive Selected cases, during May 1914, Amoebae were found in 34 cases, and in 66, Amoebae were not found, making a percentage of 34 positive results. In none of these cases was Dysentery suspected, nor was blood found.
Of the different Nationalities:-
3 Malays gave 100% positive.
Tamils, (Sth, India), 11 out of 13 cases or 84.6%
Javanese, 16 " " 63 " " 25.4%
Europeans, 2 " " 5 " " 40%

The Conclusion reached is that 30-40% of the entire population are Dysentery Carriers."

II. Dobell's Statistics.

From a valuable article in B.M.J, Nov. 4th, 1916, pp. 612-617, "Incidence & Treatment of Entamoeba Histolytica Infection at Walton Hospital by Clifford Dobell" - the following may be summarised from a Series of," the first 200 men examined at Walton, and 5 others sent there for treatment 205 cases in all. Upon these, more than 800 examinations were made ... The percentage is calculated on 200 cases, leaving the 5 cases as supernumeraries, to be included in considering the Infections with other Protozoa.

1. 22 cases were found infected with Amoebae or 11%.

2. One or two examinations are not sufficient.
It is not only possible but probable, that of the 178 men here included as uninfected with Entamoeba Histolytica, some at least are really infected, for 29 of these were examined only once and 65 only twice; the rest have been examined three or four times.

3. Amongst the 200 Walton men, 130 entered Hospital for Dysentery, Enteric, or other Intestinal ailments, or for debility following these; whereas 70 were in Hospital for wounds or complaints other than Intestinal. Of the 22 men infected with Entamoeba Histolytica - 11 belong to the first group; & 11 to the second category.
Among the Intestinal cases, 90 entered for Dysentery (or debility following); or persistent Diarrhoea - & of these, 9 were found infected with Entamoeba Histolytica; leaving 13 infections among 110 non-Dysenteric patients (including among these, many cases of Intestinal Disorder, expressed as percentagesof Cases infected with Entamoeba Histolytica:-

Clinical Studies of Intestinal Amoebiasis.

- continued -

II. Dobell's Statistics - cont:

| | | |
|---|---|---|
| Intestinal cases | ..... | 8. 2% |
| Dysenteric " | ..... | 10. 0% |
| NON-Dysenteric | ..... | 11. 8% |
| NON-Intestinal | ..... | 15. 7% |

4) Of the 27 TOTAL Cases (i.e -22 plus the 5 supernumeraries) -
4 had no history of Dysentery and should be therefore reckoned as CONTACTS.

22 gave a history of Diarrhoea or Dysentery contracted during their sojourn in the Mediterrænnean Area.

1 had Acute Dysentery.

5) 1 case, in the Series entered Hospital for gunshot wounds, had no official history of Dysentery or previous Emetin treatment and denied that he has ever had any dysenteric symptoms, or even Acute Diarrhoea.

4) 5 cases, had no history of Dysentery, but they had suffered more or less from Diarrhoea - which was not treated - in Gallipoli. One of these cases was an Enteric Convalescent; the other four were not admitted for Intestinal Disorders."

The results of treatment will be found considered in " Treatment of Amoebic Dysentery."

III. Walker Hall, Adam & Savage -Statistics.

In a paper published in B.M.J.- Aug.5, 1916 on "Convalescent Para-Typhoidal & Dysenteric Cases considered from a Preventative Standpoint" - the series of observations made, ranged from Septr.1915 to May 1916. The following is an extract from this report:-

1. In Para-Typhoid Convalescents, of 156 cases from Dec.1915 - Feb.1916 - in 10.06%, Entamoeba Histolyitica were found.

2. The importance of examining stools in conditions other than Dysentery, was not at first recognised, and it was only in middle of November 1915, that such examination was instituted, and the following results noted:-

Dysentery (605 cases) E.Histolytica present in 9. 68%

Paratyphoid (581 cases) E.Histolytica present in 10. 06%

Other conditions, Wounds, Trench Fever, &c, (5 cases) E.Histolytica present in 1 case.

Depot Paratyphoids (23 cases) (marked fit to return) E.Histolytica present in 5 cases.

or

21. 7%

Clinical Studies of Intestinal Amoebiasis.

- continued -

III. Walker Hall, Adam & Savage - Statistics (cont)

3) Table 1.

In a series of 311 TOTAL cases from Jan. 19th to March 31/1916 - it was found that,

| | | | |
|---|---|---|---|
| In 11, | E.Histolytica Cysts alone were present ..... | 3. 6% | |
| In 15, | " plus E.Coli " " ..... | 4. 8% | |
| In 11, | " " " and Lamblia) were present) ..... | 3. 6% | |
| In 1. | " " " and Tetramitus mesnili ..... | 0. 3% | |
| In 2, | " " Lamblia ..... | 0. 6% | |
| In 164 - | Nil were found ..... | 52. 7% | |

That is, in 40 cases, Entamoeba Histolytica was present either alone or with some other Protozoa = 13. 2% of cases, or, leaving out the innocent E.Coli, and reckoning purely on uncomplicated Amoebic Infection, there were 26 cases or 8. 4%. In half of the cases, no Protozoa was found.

4) Table 2.

In another series of 77 TOTAL cases during April 1916 - of which 75 were Para-Typhoids, & 2 Dysentery: the findings were,

| | | | |
|---|---|---|---|
| In 42 cases, | No Protozoa found ..... | 54. 5% | |
| In 1 " | E.Histolytica alone, found ..... | 1. 3% | |
| In 6 " | E.Histolytica plus E.Coli, found ..... | 7. 8% | |
| In 1 " | E.Histolytica plus Lamblia, found ..... | 1. 3% | |

That is, in 7 cases, Entamoeba Histolytica occurred (excluding the innocent E.Coli) = 9. 1% in 1 case Lamblia was found, making a TOTAL of 8 cases in which E.Histolytica occurred = 10.4% of cases.
In slightly over half of the cases, NIL was found.

5) Table 3.

In a series of 630 Dysenteric cases (convalescent)

| | | |
|---|---|---|
| In 56 cases, | E.Histolytica was found alone ..... | 8.8% |
| (mixed cases) | E.Histolytica plus Shiga ..... | 9.68% |
| | No Protozoa or Agglutinins, 310 cases or | 49. 2% |

- continued -

## S U M M A R Y OF TABLES 1, 2 & 3

1. In all Tables, half of the cases gave negative results.

2. In all tables, Pure Entamoeba Histolytica cases were always more numerous than when complicated by any Pathogenic Protozoa.

3. E.Coli alone, occurred in the ratio of 3: 1 when compared with the Total E.Histolytica findings, and yielded a net percentage of about 35% in Tables 1 & 2.

4. Mixed Protozoal cases (excluding E.Coli) yielded for the two Tables - 15 out of 388 cases, or 3. 9%.

5. Mixed Amoebic & Bacillary cases yielded 9. 68%.

6. Amongst Pathogenic Protozoa, Lamblia was the next frequent to E.Histolytica, occurring alone or with innocent E.Coli, which may be excluded, in 37 out of 388 cases or 9.5% of cases; and as a complicating infection with E.Histolytica in 14 out of 388 cases or 3. 5% of cases.

7. Negative findings were recorded in 516 out of 1018 cases or 50%.

8. In all cases Cysts were found.

.....

From this mass of figures, the following deductions may therefore be made:-

1. " It is well known that a small percentage of those who have suffered from Dysentery, act after convalescence, as carriers, and the possibility of those who have NOT suffered from an attack of Dysentery, but have been in a district in which Dysentery is Endemic, serving as carriers must also be borne in mind" - (Ledingham and Arkwright -"The Carrier Problem in Infectious Disease" - London, 1912).

2. Patients other than those who have had Dysentery, viz - Typhoid, Para-Typhoid, may harbour the parasite.

3. All cases showing indefinite symptoms - e.g - Gastric disturbances, progressive anaemia, irregularity of the Bowels, should have their faeces systematically examined for presence of Ankylostoma & Amoebae.

4. It is only on this hypothesis that such spontaneous cases arising in a non-endemic area or Temperate climate by contact-infection are explained. At any rate, before the War, such explanation can be accepted satisfactorily in Spontaneous cases in men who have never been out of England, but now that so many have been invalided there from the Dardanelles & Egypt, it will be difficult to trace contact-infection. Sometimes cases however, arise spontaneously, in whom no contact-infection can be traced.

in the U.K.

The 1st.case in recent times to be diagnosed in the living state,*falls to the credit of Major.D.G.Marshall I.M.S, who published his case in the Edinburgh Medical Jrnl, Mar.1912,(p.229). This was a man who had never left Scotland, and in whose stools Amoebae were repeatedly demonstrated; he made a good recovery. An ex-soldier, living near this patient had spent some time in India, but gave no history of Dysentery. Amoebae were not found in this man's faeces; and feeding experiments on cats were negative.
A similar case that of a soldier, is also published in B.M.J, May 20th,1916, by Worcester- Drought & Rosewarne of Amoebic Dysentery in a man who had never left England. This case appears to be the second reported as occurring in Britain in which Amoebic Dysentery was diagnosed as a Primary condition and during life. All his companions who had had Dysentery were examined and found negative,including the Cook. It is suggested by the Authors,however, that "although we failed to find Pathogenic Amoebae or their cysts in the faeces of those men examined, it is possible that the carrier was among other men of his unit who had been transferrd to duties elsewhere before the patient came under observation."

* Most of the cases recorded prior to this have been conditions of Intestinal ulceration associated with Liver Abscess which have only been diagnosed P.M. In 1862,Dickinson described the occurrence of a Hepatic abscess of considerable size with ulceration of the Large Intestine in a woman who had never been out of England. In 1881 he again recorded a similar case in a man who also had never left England.
Cf.Dickinson,Vol.xiii,1862,p.121. & Vol.xxxii,1881,p.127 London, Trans.Pathol.Soc.

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*Walker & Sellard (Phil.Jrnl Science, B.Trop.Med,1913,253).

Cf. THESIS. Pp 11-12

It is difficult to state exactly what the Incubation period of the disease is. Clinically it is given as a few days, but in Walker's & Sellard's cases * four cases developed Dysentery,20, 57, 87 & 95 days after infection. Of 20 men parasitized by ingesting material containing Entamoebae in different stages, 17 became parasitized after the 1st.feeding, & one more after 3 feedings. The incubation period varied from 1 -44 days, and averaged 5.7 days. Of 18 men parasitized with E.Histolytica -4 developed Entamoebic Dysentery - 2 being mild & 2 severe - lasting 1 -2 weeks. The incubation period of the attacks varied from 25 - 95 days, averaging 64.8 days. No case of Spontaneous Dysentery occurred in the Ward during the experiments.

The classification of Carriers is always a difficult problem. In those diseases (Bacillary) in which agglutinins are found in the blood, the test examination comes to be the agglutination Reaction or the modified macroscopic Castellani Absorption-Test. In Protozoal diseases on the other hand, this method is of no avail, unless perhaps we reckon on the Blood-changes, e.g - finding an absolute or relative Leucocytosis. The test comes to be the finding of specific Amoebae in the stools. This should always be done after free purgation with Salines. The Amoebic Carrier is however, more easily treated than a Typhoid Carrier. The problem is further complicated by the fact that a man may be a carrier of the parasite and then suddenly develop Dysentery, perhaps in Europe in some NON-Endemic area. Repeated examination of the stools are absolutely essential. The following may be found of some service in drawing up some kind of classification after the case has become known as a Dysenteric case.

- continued -

Two types have therefore to be differentiated:-

I. The Non-Diagnosed Latent Type, who may or may not have suffered from the disease. In this type, the classification followsthe lines laid down for Typhoid; and which is controlled by, Emetin.

II. The Known-Dysenteric Type.

Emetin however, is only fatal for Entamoebae Histolytica, and not for its Tetragena cysts.

Nov:4
In the series of cases (Treatment)B.M.J,p.616.1916
" The shortest negative period after the end of treatment which can safely be regarded as indicating a certain cure, can be hardly less than about 3 weeks."

Work done on Typhoid Carriers has been based upon the length of time that Typhoid Bacilli have been found excreted in the urine & faeces. Perhaps a similar classification might be addopted in those who have shown some clinical signs of Intestinal disturbance in known endemic areas. There is however this known difference that Treatment modifies Statistics,and the Carrier-Question is thereby simplified & modified.
Conradi drew up A Carrier-Classification in 1907 dividing up cases into the subheads:-

1. PRIMARY - not suffering from clinical symptoms & hence further differentiated into
   (i). Ambulatory
   (ii). Incubation Period Infected Case
2. SECONDARY - excreting organisms up to the 3rd. month; (Acute Carriers).
3. TERTIARIES- or Chronic carriers. There are many instances throughout the statistics quoted which allow for this important group; and it is probable from these that so-called "Spontaneous" cases arise in non-endemic areas.

In 1910 Sacquepée classified cases into:-

I. Porteurs précoces

II. Porteurs convalescents

III. Porteurs sains.

## Clinical Studies in Intestinal Amoebiasis.



A simple classification can thus be made:-

I. THOSE WHO HAVE HAD THE DISEASE:

Fecal carriers .. (acute - up to 3 mths.
(chronic- any period after.

II. THOSE WHO HAVE NOT HAD THE CLASSICAL SYMPTOMS

i. Contacts.. (acute - up to 3 mths.
(chronic- any time after.

ii. Infectious at the incubation-period

In Group II. we must include obscure cases of diarrhoea, anaemia, and indefinite symptoms perhaps marked at certain definite seasons of the year which is associated with Amoebic infections; e.g. Monsoon diarrhoea; and those cases which develop irregular bowel-symptoms on arrival in a known endemic area, and amongst these must be grouped recent arrivals to the Tropics, though in them such symptoms may be purely the result of change of climate, habits, and food.

The secret of the matter is only unlocked by microscopic examinations, frequently repeated, as in determing any disease, be it Bacillary, or be it Protozoal.

## The Prognosis of Amoebic Dysentery.

The Prognosis varies under the following sets of conditions:-

1. According to the Variety of Acute or Chronic Dysentery, as detailed in the Clinical Classification - that is the severity of the disease.

2. The method of Treatment and the period under which the disease comes under observation.

3. The presence or absence of complications, especially Liver-Abscess.

4. When it occurs as a terminal infection in other diseases, such as, Kala-Azar, Sprue, Tuberculosis; or when other Acute infectious diseases, e.g - Acute Infective Fevers, Typhoid, Pneumonia, &c, or Other Causes of Dysenteries e.g - Acute Bacillary, Other Dysenteric Protozoa, are super-added infections in an Amoebic case.

It is very rare for a Simple Acute attack to be fatal at its first appearance, unless there be added some Acute complication, such as, perforation or a Pneumonia. In the Malignant cases, a fatal result is more likely, but even here the Prognosis is still hopeful if the case has been diagnosed and the patient started on Emetin. Rogers has detailed such a case which was admitted for supposed Cholera, but which recovered in a week under Emetin. In fact, the introduction of Emetin has been hailed as a Therapeutic triumph, and cases which were hopeless in the Pre-Emetin days have now a hopeful Prognosis, provided that no serious complication has arisen, for should the process be so Acute as to rapidly go on to perforation, the Patient may die before his malady is even suspected or he himself show any symptoms of the seriousness of his condition. The whole Prognosis may be summed up in early diagnosis and Emetin Exhibition. In the Chronic cases, complete recovery is still possible if the case be properly treated. Important points which contribute to the judgment of a case are, the appearances seen in washed stools after Goodeve's method, which has already been described. In addition some help may be obtained from the degree of Leucocytosis by blood examination, but even cases showing an extraordinarily high Leucocytosis, e.g - over 30,000, may still recover under Emetin. The condition of the patient, the degree of Pyrexia, the absence of more especially Liver-Abscess, are all points in the Prognosis of the case. The use of Emetin has robbed Amoebic Dysentery of its terrors.

## SECTION IV. COMPLICATIONS & SEQUAELAE OF AMOEBIC DYSENTERY & GENERAL AMOEBIASIS -

The most important complication or sequelae of Amoebic Dysentery is undoubtedly Liver-abscess; and it has been thoroughly studied in every detail. No work could be complete without satisfactory account of what is an absolutely preventable complication. It is the most common complication and though perhaps it follows upon Dysentery as a late feature, yet it is the latent terror of the Disease. It has therefore been treated as a SPECIAL PART of the THESIS; and probably forms its most important feature. The distinction quoted widely between Amoebic & Bacillary disease is the tendency of the former to Liver infection and the latter never. After the Colon the Liver is the organ most frequently attacked by the amoeb

But besides the Liver, A General Amoebiasis, or Amoebaemia, has been described. there being no organ or structure in the body that Amoebae may not attack.
Kartulis has recorded an Amoebic Infection of the Maxillae.

* Williamson & Barris Proceedings of the Royal Society of Medicine, 1910. Apl Vol 3, No.6. Obstetrical & Gynae: Section, p.152.

Ovarian Abscess has been described by Williamson & Barris * from a case of a lady who had suffered from dysentery in India for 3 years.

Amoebic Salpingitis described by Menetier in the Archiv.de.Parasitol 1910. Vol 14, pp. 154-159.

Parotitis, in which amoebae have been demonstrated in the Gland.

Cystitis in the Urine of so-called Granular amoebae, the whole matter will be found discussed under "Amoebic Hepatitis & Jaundice". Cf. Thesis. P.110.

Arthritis. A case was published of this in the B.M.J. April 1st. 1916, p.483 by Capt.Moorehead- Six cases are recorded in which Emetin rapidly cured the arthritis. "In 4 out of 6 cases there was definite proof that amoebic dysentery had been present, either by the finding of the amoebae in the stools, at the time the arthritis was present or owing to the fact that the patient was previously treated in the hospital for amoebic dysentery and that amoebae had been found in the stools at the time of treatment" (Moorehead).
The knee seems to be the special site; in 2 cases the ankles were involved; and in 1 the Right Hip-Joint. In none were the joints of the arm affected. Probably strain & exposure to chill were the determining factors. (Moorehead in B.M.J.).

Abscess of the Skin. Phagedenic Abscess has been described as a complication of Liver abscess opening on the skin-surface; there is another group of Ischio-Rectal Amoebic abscess, where the infection is derived from the gut. These have been dealt with in Complications of Liver-abscess. There is a third group in connection with diseased gut-suppuration, e.g. phagedenic ulceration round an Appendicostomy wound, with amoebae in the pus. Such a case has been recorded in B.M.J. Nov:18, 1913 p.1239 by Major Harrison in the "Discussion on Dysentery (Tropical Sect.) There is still a 4th.group of cases, of Primary cutaneous abscess, not derived from the contamin-

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Amoebic Cutaneous abscess - continued -

ation of a discharging abscess, whether this be of the liver or derived from the affected portion of the intestine. Macgaw & Mukerji*in the Lucknow Medical College Pathological Dept. investigated a case in a Native who came with Multiple Skin Abscesses, a kind of furunculosis. These were wide-spread on the arms, abdomen & lower extremities, & face. Amoebae were found in a scraping of the boils; but unfortunately the man took fright & ran off & they were unable to trace him again; and the case was not published, on that account.

* Lieut.J.G.Mukerji I.M.S. of I. I.G.H. Hospital,Karachi, personally told me of the case, which occurred in the Lucknow Hospl.

Amoebic Appendicitis. Undoubted cases have been published, but by far the most important work in this connection has been published by Musgrave, in his review of 50 fatal cases of Intestinal Amoebiasis, without diarrhoea - and already alluded to earlier in the Thesis, in connection with Chronic Amoebiasis.* In Musgrave's Series 2 patients died from amoebic perforative appendix , and one of apparently ordinary perforative appendix. On considering the situation of the lesions in 27 cases the Caecum & Ascending Colon were affected, including the Appendix cases.

* cf. P. 47.

Rogers maintains that in most cases the ulceration is limited to the Caecum area; hence it is easy enough to understand why an amoebic infection of the Appendix occurs; but the mystery seems to be that the Appendix escapes so frequently, although the diseased process is near its neighbourhood. Harrison states in the B.M.J. Nov:15/16, p.1288, "those patients whose disease is located in the neighbourhood of the caecum, run serious risks of having their appendix removed if they get into the hands of a surgeon who is not familiar with Tropical disease, & even sometimes when he is. "

In one of my more recent cases, recieved in early November from Mesopotamia, the following sequence of events will be found interesting. The patient was a Coolie. aet.35, admitted with "Jaundice & Diarrhoea". His history gave that the diarrhoea was of 4 weeks duration, that he had recently suffered with dysentery, and Jaundice had supervened He was emaciated & had some slight diarrhoea. A day or so after admission he was taken with pains in the abdomen, and said he felt it worse in the two Iliac fossae. I put him on Emetin 1gr. injected(daily). After one injection, the next day he complained of very severe pain more localised to Mc.Burney's Point, extreme hypersensitiveness of the skin in the Right Iliac region. A blood-examination showed 80%Polymorph leucocytosis.
The interesting features of his case are

1. No nausea or vomiting.
2. Pulse good & regular, 76 per min.
3. Temperature 102F. when the pain commenced, coming down to 99.F. when the pain was so bad but pulse steady, rising to 90.
4. No disturbance of respiration, throughout.
5. No appearance of dysentery or diarrhoea, but complaining of constipation.

The case was diagnosed by me of possible Gangrenous nature, and operation was arranged for as soon as possible. The case had to be transferred to the main hosptl. as our operation-theatre was not completed. The operation took place at 3 p.m.

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and a gangrenous appendix was removed. Unfortunately I was unable to be present at the operation and sections of the appendix could not be made to determine definitely if amoebae were the cause of the disease. Three days later the man suddenly collapsed & died, just as there was every hope of a good result. One cannot pronounce definitely on the case which is indeed a pity. But the clinical features, the sequence of events, the fact that Appendicitis is a rare disease to be met with in Natives, the suddeness of onset & the rapidity of the process, which was quite against his unchanged clinical appearance, and pulse, respiration etc - all point to the great possibility of this case being really amoebic in nature, esp as there was distinct history of dysentery, an actual diarrhoea on arrival, which stopped & gave rise to constipation. One cannot help feeling that one is wise after the event; but I deliberately put him on Emetin in case this would modify the pain in case the condition was amoebic. The rapid worsening in his condition unfortunately did not allow the therapeutic action to be studied, and beyond 2 grs. injected there was no further continuance of Emetin.

In Woolley & Musgrave's * Series of 200 cases, the Appendix was found involved in 15.

* Woolley & Musgrave "Reports to the Bureau of Govt: Labs." Manila, June, 1905.

Brown in his "Amoebic Dysentery" p.193. reports upon the Etiology of the condition, and frequent abscence of the Amoebae in the Appendix, and in this connection cites the papers of Leo.Schredel*& Sozo Nishiyama * who were unable to find after careful search Entamoebae in a large number of consequtive cases of appendicitis.

**Leo.Schredel & Sozo Nishiyama - Wiener. klin. Rundschau, March 14,21, 28, 1909.

The appendix may become diseased as part of the general morbid process; that it may be a Metastatic suppuration, strictly so-called, which occasionally originates in amoebic infection; or it may be due to peri-appendicular abscess, secondary to insignificant amoebic lesions in the Colon. "Moreover Ent.Histolytica has frequently been demonstrated in the walls of excised appendices, & in pus in the region of the Caecum, although there has been no history of dysentery & nothing to indicate amoebic infection". (Brown).

Gingivitis & Pyorrhoea Alveolaris.

The discovery of a specific Entamoeba in 1914 by M.F.Barrett & Allen J.Smith * - the E.Buccalis - brings this within the category of amoebic infections, and the successful employment of Emetin ½gr. hypodermically, which causes the disappearance of all amoebas in 99% of the cases in 6 days, brings this condition into the field of practical therapeutics. The further suppurative processes is perhaps the work of other organisms, e.g. Streptococci of the Viridans Group (Hartzell & Henrici; Stewart). An interesting account is given by Robert Hutchison in The Med.Annual,1916,p.488. Against this view, however, should be quoted the paper published in B.M.J. Oct.28/16,p.587. by Dr.Helen Goodrich & Mrs,Moseley on "Certain Parasites of the mouth in cases of pyrrhoea". The authors are of opinion that amoebae have nothing to do with actual suppuration, as they occur not

* Barrett & Smith - Dent.Cosmos., 1914, 948.
&
THESIS. P. 86.

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In the peridontal membrane, but in the tartar of the teeth. "The amoebae bore some resemblance to those of dysentery - E.Histolytica - but showed certain differences, notably that the cell-inclusions were usually remains of Mononuclear cells, & not of red-blood cells. Trichomonas were often found, and were unconnected with the pyorrhoea." The matter seems still to be unsettled.
My own experience in cases of Pyorrhoea is rather clinical than microscopical. Owing to the enormous number of Scurvy cases, both in the Dardanelles, investigated in No.5.I.G.H.; and in the Mesopotamia series of cases received throughout the past year, except in the last 2 mths, a good deal of spongy gums, gingivitis, & pyorrhoea were seen. In the Dardanelles Series of cases, a scheme of work was submitted by the Registrar, Major Mc.Carrison, I.M.S. in order to see what percentage of cases were due to Amoebae, and also to draw up the distribution of the lesions, including the number who gave a history of dysentery & diarrhoea, in order if possible to associate the Saurvy process with definite amoebiasis, esp:as regards the mouth-symptoms. It was noted by me in 100 cases we had in the ward that most, as far as I can remember, about 70% had had dysentery, or diarrhoea. Unfortunately the microscopical part fell through. From the results noted it was thought that thefe was some definite connection between the mouth-symptoms & Dysentery. This was when large numbers of Scurvy cases first appeared. Further extensive experience however has awakened serious doubts as regards this. Because Scurvy has been found to complicate most diseases, at least in Mesopotamia, and the pyorrhoeal condition in most were simply part & parcel of the morbid process. In bad cases of Pyorrhoea I am in the habit of prescribing a lotion of Ipecac & Arsenic* to be swabbed over the gums, together with a Condy Gargle. I have now tested this in some 30 cases and I cannot say that any greater improvment has been manifested than what results from mouth-cleanliness & general Diet treatment. Unless one is prepared to give whole time to the examination of all mouth cases it is quite useless to argue that amoebae are the primary cause. Therapeutic measures, at any rate, lead meto against this view.
There is however one thing which has been observed in Scurvy cases & that is the marked & very characteristic postural tachycardia - the pulse on lying being60 or 70; and as soon as the patients get up within 2 or 3 beats the pulse rises to 110 or 120. This has never been known to occur in Dysentery; and there should be no confusing morbid processes in the two diseases. Dysentery complicated by Scurvy is therefore a well-recognised condition, but it also complicates other diseases, and ought not to be described as a complication of Dysentery, ipso facto.

* My formula is:-
Vin.Ipecac m.xxx
Liq.Arsen. m.x
Glycerine m.xxx.
Aquam oz.½.
Sig:
Local application made twice daily.

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Intestinal Haemorrhage. Dangerous bleeding from the Intestine is rare; but may be encountered in the course of an active dysentery; and according to the researches of Haasler* and Strong* it is especially indicative of formation of an Amoebic Liver abscess - and this has been been further verified by Mugliston & Freer*. In such cases the clinical conditions observed have been altered blood-coagulability (diminution) a tendency to haemorrhages; Jaundice; and persistent & marked fever. The evidence is in favour of predisposition, & failure of resistance to septic infection.

As a rule even when ulceration is both rapid & deep, there is but little blood passed, although as has been shewn in The Morbid Anatomy of Amoebic Dysentery there is so much congestion, & infiltration that it accounts for cell-death; & in Amoebic infection of tissues, as in the Liver, the pathological cycle of events is Infiltration, stasis & thrombosis; and in the more Chronic lesions of Intestinal amoebiasis there is endarteritis & thrombosis which precede tissue-destruction. One explanation offered is that the blood-vessels themselves are remarkably resistant to ulcerative processes, at least of amoebic origin. Serious haemorrhage may occur without the passage of blood per Rectum, as in Fulminant Cases.

Gastro-Intestinal Complications. These are about the most common morbid accompaniments of an acute attack of Amoebic Dysentery. I have repeatedly met with it in most of my cases; and it takes the form of indigestion after food, eructations & flatulence and pain not unlike Gastric Ulcer, esp during convalescence, and in the quiescent stages after an attack. "So frequent are these symptoms, indeed, that it is almost reasonable to assume a definite connection between them & amoebic infection". (Brown). In the poorest classes of patients cancrum oris is a somewhat frequent complication. Stomatitis when occuring in more or less healthy adults should suggest the possibility of Sprue. Irrigation of the lower bowel often reflexly induces gastric derrangements; * " and in young children may be followed by Tetany" Intestinal intoxication is often the cause of this dyspepsia; especially as the preceding "diarrhoea" has been mistaken for the small oft-repeated evacuations from the Rectum; and the large doses of Bismuth Salicylate often produce intestinal stasis.

Sometimes it is the direct result of Splanchnoptosis, or other visceral neurosis, esp: when the condition has become chronic.

The Incidence of Nervous Diseases. This may well result from chronic ill-health, the result of chronic Amoebic changes in the intestine, & chronic relapses. It has been definitely established that the most common cause of invaliding from the Tropics is due to nerve-strain & neurasthenia*; and this may well be due in part to a chronic marasmus resulting from Chronic Amoebiasis In all over the Tropical World this has been the chief cause, averaging about 25%., whereas Dysentery & bowel-disorders have given only some 8%, of which the dysenteric element accounts for 6.4%

* Haasler - 1902 Deutsche.med.Wochen

* Strong - "Publications of the Biological Lab."Manila 1905.

* Mugliston & Freer Jrnl.Trop.Med. 1905

* Brown.Amoebic Dysentery p.196&197.

* Cf."Discussion on The Causes of Invaliding from the Tropics" cf.B.M.J. Nov.15,1913,pp.1290-1296.- by Price, Simpson, Law&others.

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Apart from this which might be reckoned as a sequela of the disease, Amoebic dysentery has been known to be the cause of the incidence of Nervous Disease, e,g. Chorea & Epilepsy. Musgrave* has published two cases which indicate the close association of the two disorders. In one of them an attack & a relapse of Amoebic dysentery were followed in each instance by an attack of Chorea, whereas in the same patient an attack of Typhoid Fever was followed by no nervous complication. The study of Amoebic Toxaemia has hitherto been neglected, although well-recognised by Councilman & Lafleur; and it is just these cases which tend to emphasise the importance of recognising the condition.

* Musgrave - "Amoebiasis: Complications & after-effects" - Phill. Jnl.of Science, June, 1906.

The Seqquaelae of Chronic Amoebiasis apart from chronic ill-health, are more marked in the changes of the Intestinal Tract, than in other Systems of the body - and there is marked thickening of the bowel, adhesions, and it may be ultimate bowel-obstruction, simulating Malignant Disease. According to Cantlie*, the Sigmoid Colon has indeed a special anatomical point hitherto missed by pathologists & anatomists, viz: the existence of a "Sigmo-Rectal Pylorus"* Chronic thickening & ulceration in this the narrowest part of the tube leads to an inversion or invagination of a part of the mucosa into the lower part of this sphincter. Stimulation of this portion of the Great Gut always produces desire for defaecation; and it may be that Chronic irritation & ulceration here may well account for the Chronic diarrhoea; and this condition could be alleviated by distension of a Sigmoidscope-examination. "In a proportion of cases the seat of ulceration becomes malignant". (Cantlie).

* B.M.J. Aug.8,1914, p.303 Sectn.of Trop: Medicine - Discussion on Colitis & Post Dysenteric lesions.
&
* Cf.Plate xxvi-
* "Boundaries of the Sigmoid"- Cantlie - The Medical Annual, 1916,p330.
&
BMJ. Nov.15,1913 p.1297 "Recent Observations on Sprue", No4.para. Cantlie.

Peripheral Neuritis has also been described; but probably there is an element of Beri-Beri, as well,or other cause of Tropical Neuritis. When peripheral Neuritis occurs & is solely due to the Dysentery, there is oedema, which tends to pass off as the ulcerations heal up.

"An acute Suprarenal Syndrome has been described (Cf/Memoranda on Medical Diseases in the War Mediterranean Area). It is however not stated whether this is due to insufficiency or hypersecretion.

<u>There is no doubt that Many Accessory Features are due to Amoebic Toxaemia</u>.

## SECTION V. THE DIAGNOSIS OF AMOEBIC DYSENTERY

## WITH AN ACCOUNT OF

## THE LIFE-HISTORY, & VITAL REACTIONS

## OF THE

## CAUSATIVE ENTAMOEBAE & NON-PATHOGENIC

## TYPES & THEIR ALLIED SPECIES.

The finding of the causative Ent.Histolytica, or its Cysts absolutely clinches the diagnosis.
This is extrenely easy in Acute cases - there is nothing easier in Medicine. Sometimes even in the very acute cases careful search fails to identify the presence of the Amoebae. this is due to the pathological processes being so acute that death has prevented the appearance of the organism in the discharges, but they are abundantly found in the lesions embedded in the bowel.
The diagnosis of Amoebic dysentery may therefore be classified as follows:-

I. DIRECT - by the finding of Amoebae in the discharges, or its Cysts.

II. INDIRECT - by certain changes in the Blood, and when there is Mixed-Infection, by specific agglutination tests, Bacterial cultivation,&c.; or the finding of Other Specific Protozoa.

III. In the abscence of Microscopical facilities, by the THERAPEUTIC TEST of EMETIN- or its Modifications.

## I. The Direct Method.

This I propose to leave till the last, as a detailed account of the Life-History, Morphology ,etc. is called for, for the purpose of a correct diagnosis when seen in the stools.

## II. The Indirect Factors.

### 1. SPECIFIC CHANGES IN THE BLOOD.

The examination of the blood is the second most important clinical test, next to the actual finding of the Amoebae in the stools; for it has been proved by Rogers & other observers that a definite and well-marked leucocytosis is established in the blood, early in the Disease, & persists so long as the patient suffers, even as a Latent case.
Moreover Intestinal Parasites often complicate an Amoebiasis, and notably Ankylostomiasis.
A very careful & full account will be found in the Section of the Thesis devoted to the Diagnosis and Differentiation of Amoebic Liver-Abscess by Blood-Examination. * What is true of this Phase in the Pathological Life-cycle of Human Amoebiasis, holds equally in the more restricted aspects of Entamoebic Infection - that is in Intestinal aspect
The changes induced in the blood by Parasites are often pathognomonic.
Lastly in the blood-serum are developed specific Agglutination-bodies which react with the specific organism - the"Bordet-Gengou Phenomenon".
Recently there has been introduced to the notice of the Profession ready-made dilutions of different Bacteria, The Dysenteric Group, The Typhoidal Group etc. which can be tested by Castellani's Absorption Test, by making suitable dilutions of the patient's blood; and this being macroscopic is easy to read.
An Inverse Method can also be employed where patients'blood suitably diluted can be tested against a ? organism isolated from a stool.
By such methods a ready diagnosis of Bacillary Dysentery, Typhoid & ParaTyphoid, &c. can be made.
I wish to call attention to the very interesting papers, which have been published calling attention to the NEGATIVE-Agglutination met with in cases of

* c/f. Pp.-204-218.

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1. The Haemic Changes. - continued.

Bacillary Dysentery & Typhoid Fever. The first is the article of Drs.Ruffer & GrahamWillmore "The Serum Treatment of Dysentery, with Notes on the Bacteriological Diagnosis", published in the B.M.J. Nov.12,1910,pp.1519-1522.
Another article in the same Journal, by G.H.K. Maclister "Dysenteric Carriers" pp.1505-1508. is worthy of attention.
A more recent study is offered by Graham-Willmore& Savage "The Diagnosis & Treatment of Epidemic Dysentery" in the B.M.J. Nov.15,1913,pp.1283-1286.

Ruffer & Willmore call attention of the failure of the Reaction to the following causes:-

1. In the Early Acute case, when there has not elapsed a period since the onset of infection sufficient to admit of agglutinins being formed.

2. Very severe cases, usually in old men, in which the organism is too exhausted to respond to the infection, by the production of Agglutinins.

3. To these conditions, Maclister calls attention to the fact that in many cases Agglutination no longer occurs a few months after an attack; but, unlike Typhoid, there is no definite time-limit for the dissappearance of specific Agglutinins after termination of an attack.

The whole Question is well reviewed in "IMMUNITY & SPECIFIC THERAPY" by D'ESTE EMERY,1909; and I don't propose to dwell upon these problems further.

The papers on Typhoid referred to above are

1. Scott's article in the Practitioner November, 1913,pp.589-608, a study of over 1500 consecutive examinations of Widal Reactions. Reference is especially invited to "Negative Reactions with B.Typhosis"pp.597-600.

2. "Complement-Fixation & B.Typhosus", by H.R.Dean in the B.M.J.Nov.12,1910,pp.1516-1518.

Therefore there are certain points in the Serum-Diagnosis of Bacterial Diseases which make the question more complex; but yet these tests are of great practical value in the Differential Diagnosis of Mixed Cases.

* Amberg,S. - Bull.Johns Hopkins Hosp: 1901.

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2. The Haemic Changes. - continued -.

The Changes in the cell-contents in the blood.
All Amoebic Infections, whether they be a Primary Amoebiasis of the Intestine, or Infection of the Liver - in all stages; or Secondary Infection of any other viscus; produce the same Type-Reaction in the blood - a well-marked or at any rate a Relative Polymorphonuclear increase. Other changes, e.g. in the Eosinophiles, occur in Abscess-conditions, but the characteristic reaction is the Leucocytosis of the Polymorphonuclear type.
Rogers' Analysis of 60 consecutive cases, in which blood-counts were made, gave the following points:

1. The most characteristic change was a Leucocytosis, commonly of a high degree.
2. Three-fourths of the cases gave an actual increase. In 10 cases a count of 30,000 was obtained, per c.cm.
   In 7, between 20,& 30,000 were found.
   In 21 NON-amoebic cases 15,000 was the highest figure reached - such can be obtained in very severe Bacillary Dysentery, with high fever.
   Any figure over 20,000 is characteristic of Amoebic Dysentery.
3. In 8 cases a relative leucocytosis was present. In one of these cases there was severe anaemia present; & the leucocytosis reached only 10,000 but the proportion of white to red was greater than the normal 1:500
4. In 7 cases or 11.4% there was not even a relative leucocytosis; 3 of these cases had Kala-Azar & enlarged Spleens.
5. TOTAL COUNTS are of Prognostic value - it was found that that counts of over 25,000 were serious, even when treated with Ipecac: as only one out of nine improved.
   Cases with NO Leucocytosis at all, were also very serious - 4 out of 7 cases were fatal.
   It is especially found in Gangrenous Cases.
6. The differential count is of less importance - except that a high proportion of Polymorphs, is a sign of Acute Amoebic Infection.

Probably in every case in which, in the early stage no Leucocytosis is found, the action of alcohol may be suspected - or other inhibitory drugs.

All writers are not agreed upon the question of EOSINOPHILIA. Brown suggests that unless there is a coincident Ankylostomiasis, or a collateral infection by the grosser Entozoa, e.g. Trichinosis, there is no Eosinophilia, at least in early stages. On the other hand Amberg * has found in children suffering from Amoebic Infection, both an absolute and relative increase of these cells.
According to Phillips, changes occur in the Eosin-cells; there may be a local Eosinophilia & some may pass over into the blood. As soon as it, however comes to Abscess-formation, as in the Liver, there is hypo-eosinophilia & finally total disappearance of these cells. (Cf/Haemic Changes in Liver-Abscess Section, THESIS.). P. 204-207 Thesis.
In later stages of the disease, Brown agrees that Eosinophilia is relatively & absolutely increased.

* Amberg, S. - Bull. Johns Hopkins Hosp: 1901.

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together with all Varieties of White Cells.
In a series of blood-counts, in cases of moderate severity in which the average duration of infection was three years, the following results were obtained by Brown.
Twelve blood-counts were made.

| | TOTALS |
|---|---|
| Red Blood cells ..... | 1,850,000 - 3,240.000 |
| Leucocytes ..... | 10,500 - 12,000 |
| Haemoglobin ..... | 65%. |
| DIFFERENTIAL. | |
| Polymorphs ..... | 60 - 65 % |
| Large Mononuclears & Transitionals | 10 - 17 % |
| Lymphocytes ..... | 20 - 25 % |
| Eosinophiles ..... | 5 - 6 % |
| Basophiles (Mast) ..... | 0.4 % |

In Chronic cases therefore the following changes occur, according to Brown's figures;-

1. "During the later stages of untreated or Chronic Amoebic Disease, a typical form of Secondary Anaemia is induced by the absorptions of Intestinal toxins, probably elaborated by the Entamoebae; and the alterations in the blood may come to resemble those seen in Chronic Lead & Arsenic poisoning, Cirrhosis of the Liver, & Ankylostomiasis. There is marked blood-destruction in the Circulation, marked Oligocythaemia Poikilocytosis; Normoblasts, Megalocytes, and Myelocytes are seen, & indicate a somewhat acute phase.* The Colour Index is low, but the Hg. although decreased to 60 or 70 %, is in greater than normal quantity in the individual erythrocytes." (Cf/Brown Amoebic Dysentery, p.97).

* c/f. THESIS P. 209.

2. Eosinophiles are increased, markedly.

3. The Lymphocytes are markedly increased, as they are in any Chronic Disease.

4. There is a Leucocytosis of not more than 12,000 made up of ALL White-cells, the Polymorphs being not more than 65%, which can hardly be called above the Normal count; and the principal elements are the Mononuclear Cells, & the Eosinophiles.

Eosinophilia is found underthe following conditions:
1. In Skin Diseases, especially Pemphigus, - the Eosinophiles do not often reach 10%, and rarely exceed 20% of the Total Count.
2. In Entozoal Dysentery or Helminthic Dysentery, that is when Ankylostomiasis is present, the blood shows an ever-present Eosinophilia. This may reach as high as 52% (Ch.Honore),

or even 72% (Leictenstern); or it may be as low as 5%. Brehaut in Egypt found an average of only 10%. Boycott & Haldane found the highest percentages in recent cases, and the lowest in Chronic cases. To such an extent does its degree indicate the severity of the Infection, that Boycott recommends it as the most important sign, next to the presence of ova in the faeces, in endemic areas.

3. Bothriocephalus Latus is accredited with the production of the most profound forms of anaemia Schauman has found that Dibothriocephalus Latus produces anaemia, in every respect, even to the remissions & exacerbations, equal to True Pernicious Anaemia.

4. Trichinosis. Sporadic cases of Trichina infection are frequently mistaken for Typhoid, Rheumatism, Cholera etc. Eosinophilia is present in <u>every</u> case. In no other condition do the Eosinophiles reach such high percentages & so constantly as in Trichinosis - from 10 to 60 %; though 72% has been recprded in a case by Albert & Norris.
Gaisboek believes that the disease can be diagnosed by blood-examination alone.
Burnham in "Haemocytes & Haemic Infections" p.50, quotes T.R.Brown & summarises his results:-

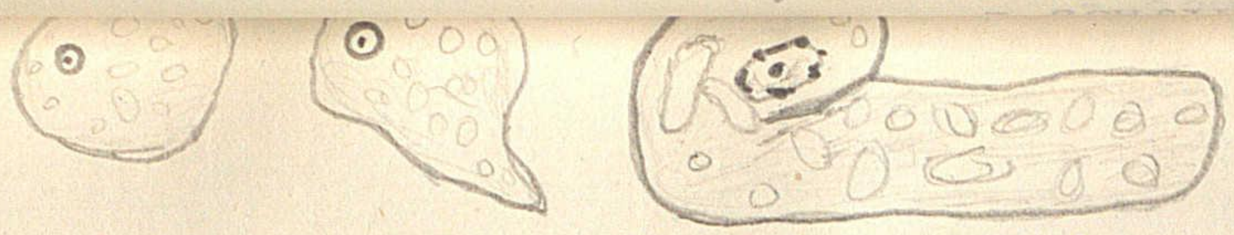
i. In a case of Acute Trichinosis, an extensive leucocytosis with great absolute & relative increase in the number of the Eosin-cells in the blood, associated with a coincident decrease in the quantity of neutrophilic elements.
ii. In degenerated muscles , large number of Polymorph cells (Eosinophile) were especially prevalent in the more degenerated areas.
iii. Increase in the local Eosinophilia takes place in the muscle by the direct transition from the neutrophiles.

Brown concludes as fpllows :-

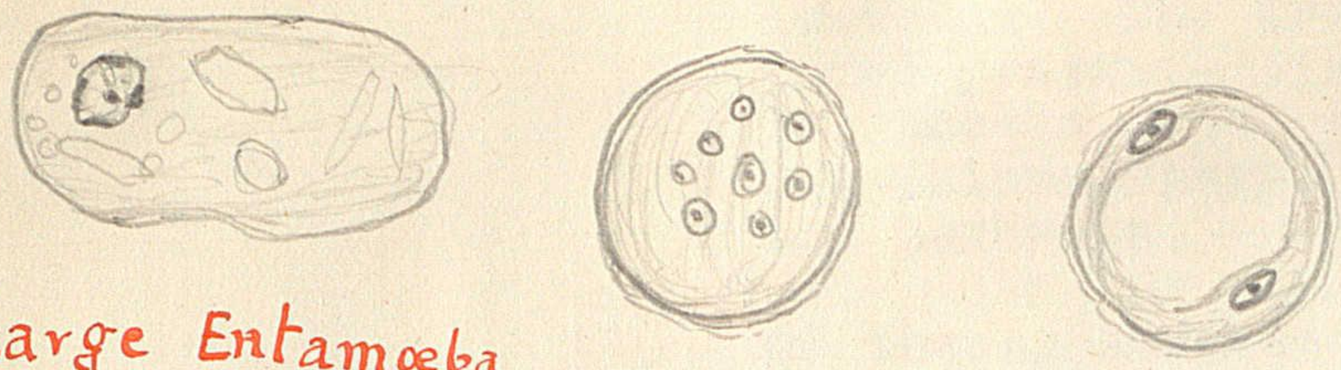
i. That there is a marked increase in the percentage of Eosinophilic cells in the blood of Trichinosis-cases.
ii. That this increase may be used as a diagnostic sign in this disease.
iii. That this disease in its Sporadic form is more common than has hitherto been supposed.
iv. That a systematic examination of the blood should be undertaken, in cases with indefinite Intestinal, Muscular, or articular symptoms, in the hope that of the hitherto doubtful cases in some at least the diagnosis may be reached.

The role of Intestinal Parasites produce definite changes in the blood & by this means & ova-findings they can be accurately differentiated from Amoebiasis

Blood-examination, therefore, is Diagnostic; of Prognostic value, and affords Therapeutical indications. "In fact, I look upon such high leucocyte-counts in amoebic colitis, as well as in Hepatitis of the same origin, as of prognostic value equal to finding numerous Malignant Tertian Parasites in every field of the microscope in Malaria, for as in the latter case, it enables the dangerous nature of the infection to be recognised." (Cf/Rogers'Dysenteries p.101).



Active Forms, and
Large Irregular Amoeba

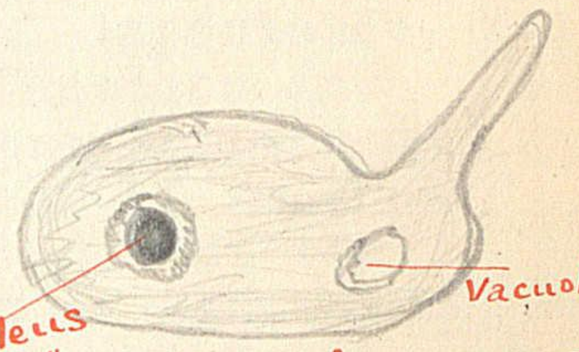


Large Entamoeba with slit-like rectangular vacuoles.

Typical and diagnostic cyst.

Irregular Type with large central vacuole.

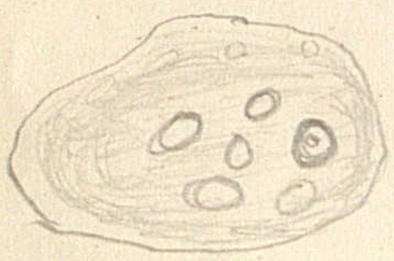
Two Encysted Forms.




Note richness of the Nucleus in chromatin

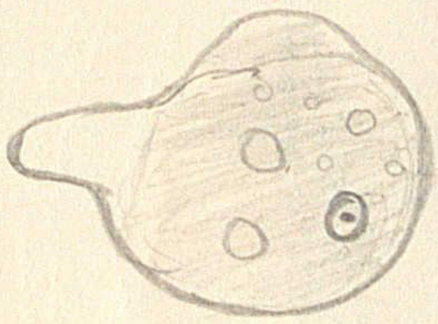
# ENT. COLI. (Schaudinn)

1.



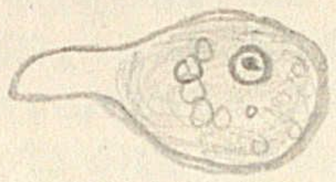
Large tissue-invading form with 5 r.b.c's.
Ent. Histolytica

2.



Ectoplasmic pseudopodium.
Ent. Histolytica

3.



Smaller form of No. 2.
Ent. Histolytica

4

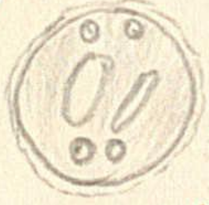


Dead-forms showing "Mulberry Knobs."

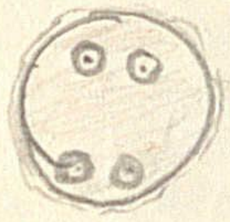
## ENCYSTED FORMS.



Small 'minuta' as in post-dysenteric conditions.



4 nuclei chromidial body and vacuole.



Encysted Typical Form (compare size with E. Coli).



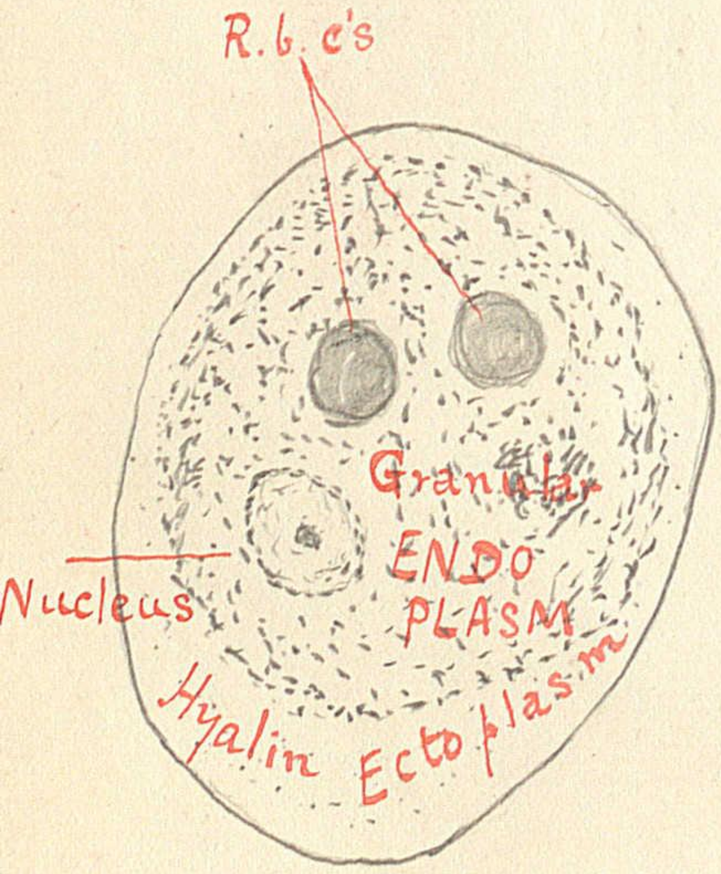
ONE nucleus ONE chromidial body.



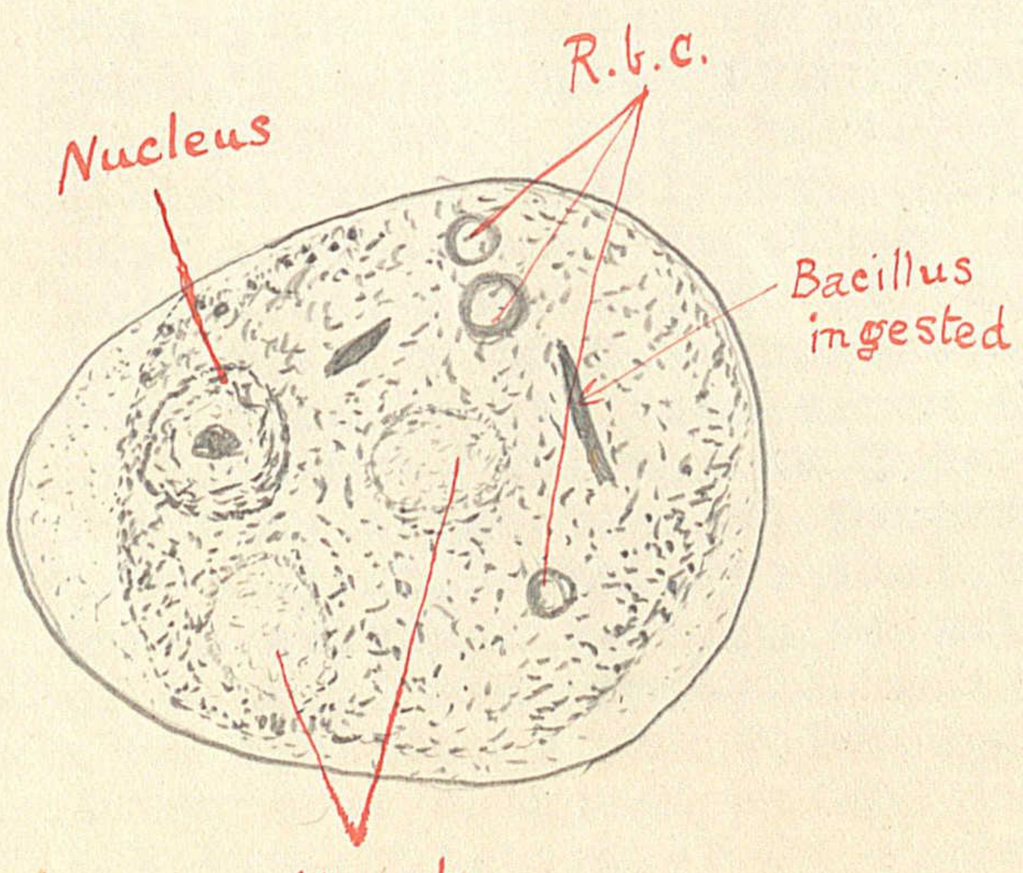
Two nuclei
&
Two chromidial bodies.

Diagrammatic
Not drawn to scale.
Schema I.

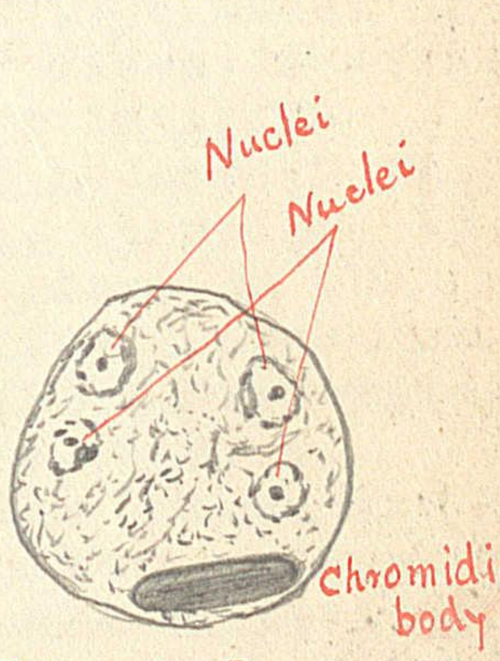
# ENT. HISTOLYTICA (Schaudinn).




Free Vegetative Type
(Ent. Histolytica)
(After Wenyon).




Free Type.
(after Wenyon)




Typical Encysted Form of Ent. HISTOLYTICA.
(after Wenyon).

The Life-History, Morphology & Structure of Ent.Histolytica.

The Classification of Amoebae has already been described & differentiated in the Section on Etiology. The Order Amoebae is divided into its three genera:-

1. Amoeba )
2. Chlamydophrys ) all of them parasitic.
3. Leydenia. )

Of these, Amoebae are of practical importance, for Chlamydophrys has no pathogenic function and Leydenia has been found only in the Peritoneal fluid. In the further subdivision of Amoebae, there is much difference of opinion, but the system now in general use is that of Schaudinn, who in 1903 revised the original work of Cassagrandi & Barbagallo in 1897 and Jürgens in 1902. In this scheme the genus Amoeba is divided into:-

I. Amoeba or Saprophytes - the free-living form (Ehrenberg). Morphologically, the nucleus in the resting organisms is in a more or less central position, and the greater part of its Chromatin is arranged in a central Karyosome; with rare exceptions there is a contractile vacuole, and in the resting stage the Cysts are Monocuclear. There is an absence of Schizogony in the resting stage. They live non-parasitically and can be cultivated on artificial media.

II. Ent.Coli - a harmless Intestinal parasite, subject to variations and the very occasional representation of a free-living type nucleus (AM. Limax) in its smallest forms, especially as regards its Cysts. As a rule it can be sharply differentiated from the Cysts of Ent.Histolytica. (Wenyon).

III. Ent.Histolytica (Schaudinn).- an essential & obligatory parasite. Has a definite Life-Cycle like Ent.Coli, and forms Cysts, which is constant in appearance and does not vary as in the Coli forms. The Cysts are small. In 1907, Viereck described the Life-History of an Amoeba found in cases of Dysentery, which he named Ent. Tetragena, from the fact that well-marked Cysts containing 4 nuclei were formed. This Amoeba he believed to be distinct from E.Histolytica, and to constitute a further pathogenic species. This was again described by Hartmann in 1908 under the name "Ent.Africana" from Dysentery cases in Africa It is now held to be merely a stage in life-history of E.Histolytica. Darling & James, have also investigated "another" Amoeba, described by Elmassian, and believe it to be a stage in the life-history of E.Tetragena. Darling & Ornstein, have come to the conclusion that the E.Nipponica of Koidzumi, belongs to E.Tetregena. Lastly, Fantham, in a critical review of the literature of the subject, considers that E.Tropicalis of Lesage and possibly E.Hominis of Walker, are varieties of E.Coli; & E.Nipponica either belongs to the same species, or to E.Tetregena. Further, the Entamoebae obtained by NOC in Cochin-China in 1909 & E.Phagocytoides of Gauducheau, show close affinities with Schaudinn's E.Histolytica. There are, however, observers -like Craig, Ornstein & James - who believe that there is a pathogenic Amoeba having the life-history described by

Schaudinn, and that there are at least two pathogenic amoebae - the Ent.Histolytica & E.Tetragena. The Ent.Williamsi, Ent.Brasiliensis of Arago, & Ent.Hartmanii of Prowazek, are all variations of Ent.Coli.
"The situation has been admirably summed up by Fantham, who gives his verdict in the following words: 'Recent research strongly suggests that the life-cycle of E.Histolytica described by Schaudinn, is inaccurate as regards the exogenous Cycle - probably degenerative and associated with minute Spores -recorded by him. The correct reproductive cycle of E.Histolytica seems rather to be the formation of four nucleate Cysts, as discovered by Viereck, for E.Tetragena. If I.Histolytica must stand, its life-history would not be that recorded by Schaudinn, but that first described by Viereck and the species named Tetragena must then drop. At present,however, it would be presumptuous to dogmatize on such a difficult subject".(Douglas - B.M.J,Nov 15, 1913, p.1282 -"Discussion on Dysentery").

Lastly,to the above Castellani has described recently at least three "new" species. One - Ent.Castellani Undulans, has been taken to be degenerative forms of Trichomonas (Wenyon); of the other two, not much is known but which have been classified by Castellani as Castellania, Castellani (cf. section "Etiology of Amoebic Dysentery" Thesis)- P.4.
The whole question looked at from a practical point should rule out what really appear to be degenerative or variational forms, and the ordinary Classification of Schaudinn be accepted, that the only pathogenic species is the Ent.Histolytica (Schaudinn).

## Vital Reactions.

The organism may readily be examined in the fresh living state from the stools, by putting it up as an ordinary film-preparation and keeping warm; when its movements may be studied. There is no definite relation between the severity of the symptoms and the number of organisms excreted.
Often in Acute attacks only one or two may be seen, while in mild cases they may be abundant. It is important to search many fields, for sometimes they are only in one particular field where many may be found together, especially if the organism is nearly dead or is dead.
When a study is required - the organism must be fixed and stained. Osmic Acid Vapour, or a saturated watery solution of Alcoholic Mercuric Perchloride may be used (2 parts saturated aqueous soln.Hydrarg.Perchlor, & one part of absolute Alcohol), & the film in the mixture heated to 70° C for 10 mins.(Schaudinn). It is then washed in 70% Alcohol, thoroughly washed & dried; or it may be also washed in a weak Alcoholic solution of Iodine to ensure the complete removal of the Corrosive Sublimate.
It may then be stained in many ways:-

1. In Walker's Alum Hematoxylin, the formula of which is given by Phillips as follows:-

R/

| | |
|---|---|
| Hematoxylin Crystals ..... | 1 |
| Saturated Aqueous Ammonia Alum.. | 100 |
| Distilled Water ..... | 300 |
| Thymol ..... | a crystal. |

Dissolve the hematoxylin in water by the aid of heat, and then add the other substances; allow to ripen (preferably in the Sun) for a week to 10 days in a flask plugged by cotton-wool.
To be kept in the dark in a tightly-stoppered bottle.
A rapid & fairly satisfactory result may be obtained by this method.

2. If fuller Cytological details are required, Heidenhain's Iron- Hematoxylin method is the best. A full description of this can be obtained in Schaffer's Histology; and in the Jrnl of the R.A.M.C, 1908, Hammerton has described "Methods of Study".
Finally, Mallory & Wright in their "Pathological Technique, 1901, p.397, give a modification of this.
I have employed Giemsa's Method, modified, for staining for Spirocheta Pallida, as follows.
It may be used for Amoebae, but 12 hours may be allowed. If understained it can be put back.
Giemsa is made up - 10 drops of the stain in 10 cc. Distilled water. A few drops of Giemsa is then poured on the fixed film (fixed in equal parts of Absolute Alcohol & Ether) and allowed to remain for 1 minute. The excess of stain is then decanted off, and the film immersed in the solution for 24 hours, after which it is washed & air-dried.
Or Grubler's Modification may be used - Giemsa's fluid (Grubler) is slowly added to distilled water until the translucency of the mixture is approximately that of dark port-wine. The specimen is kept immersed for 24 hours. When E.Histolytica is stained in Giemsa, the homogenous ectoplasm remains almost uncoloured and appears as a clearly differentiated slightly tinted area, whilst the granular endoplasm assumes a deeper blue shade. The scanty chromatin of the Nucleus, if at all visible, is seen as minute scarlet points or fibrils and the ingested red blood corpuscles are pink.
E.Coli stains by the same process a dark blue, the outer zones however are fainter in colour. The nucleus, on account of its rich Chromatin, shows numerous deep purple-red fibrils & spots.
A useful method for distinguishing inactive Amoebae recommended by Rogers, without fixation, is by the addition of a drop or two of 1 in 10,000 N/Saline soln. of Neutral Red, which stains both living & dead Amoebae, a rose pink, leaving leucocytes, cells & bacteria unstained.
In the examination of Amoebae found in the dejecta, the following are important points:-

1. Care must be taken not to mistake certain round refractile cells, probably representing disintegrated Intestinal Epithelium & Leucocytes, and in which red blood cells are often enclosed; these in some instances certainly bear a close resemblance in size and form to the pathogenic Amoebae, and they are to be found in considerable numbers in the stools of Acute Bacillary cases, as well as in those of more Chronic Amoebic disease

2. Distinctness or indistinctness of the Nucleus is no guide to the differentiation of Entamoebae. Many Entamoebae have nuclei of different types, but in which one or other of the features of the typical nucleus is shown. The amount of Chromatin varies both on the outer and inner surfaces of the nuclear membrane. In some, no central granule or Karyosome will be seen, and the whole of the interior of the nucleus appears to be madeup of a uniform linin network; in other cases the central clear area will be shown, but no granule within it. (Wenyon - "The Morphology of the Intestinal Entamoebae of Man -B.M.J, Nov. 15/1913, p. 1287).
The Cytoplasm is equally variable, and in the pre-encysting forms, may have the cytoplasm charged with chromidium, which occurs in the form of small round masses, rods often of a spindle shape, or irregular clumps. Chromidium in one form or another is often seen in the Cytoplasm of degenerating entamoebae.

3. Transitions in Ent. Coli Cysts occur, so that they may come to resemble the Pathogenic Cyst, or in some rare cases the Saprophytic Amoeba Limax Type. The Cysts of the Pathogenic Entamoebae, are not subjected to the same extent of variation as are the Cysts of the Non-pathogenic forms. (Wenyon).

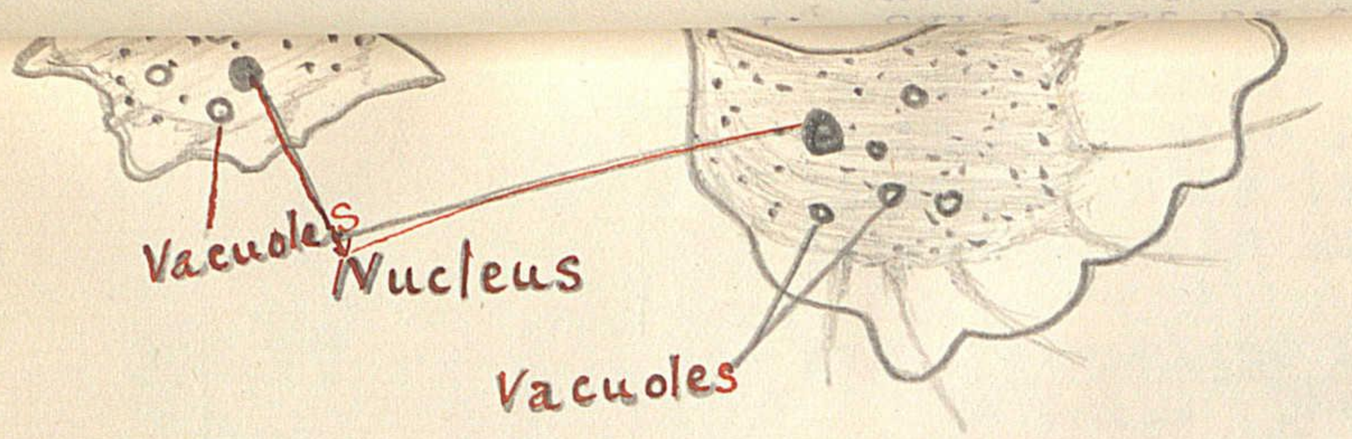
4. Care must be taken not to mistake Oil-Globules for Amoebae - they are highly refringent & irregular in size and may appear as brilliant disks with dark borders and lighter rings. Other bodies are pus-corpuscles and large epitheloid cells in mucous stools. This latter has a ring-shaped nucleus, very large, occupying from a quarter to half the cell.

In the active stage, <u>Flagellates</u> are characteristic, - small size nucleus & a large Karyosome in the nucleus.

i. <u>Prowazekia</u> is ovoid and has two flagellae; in the cystic form they are ovoid or round, and about 5- 7 μ across. It is possibly the same as Tetramitus Mesnili.

ii. <u>Lamblia</u>, a double Flaggellate with 4 pairs of flagellae giving it an owl-like appearance, especially on surface-view, a sucking disc & two large nuclei. They occur as thick form & marrow forms. The encysted form have two to four nuclei. Broad & lightly recurved lines can be seen inside. The existence of the elongated axostyles within the Cyst distinguish it from the Tetragena stage of Ent. Histolytica.

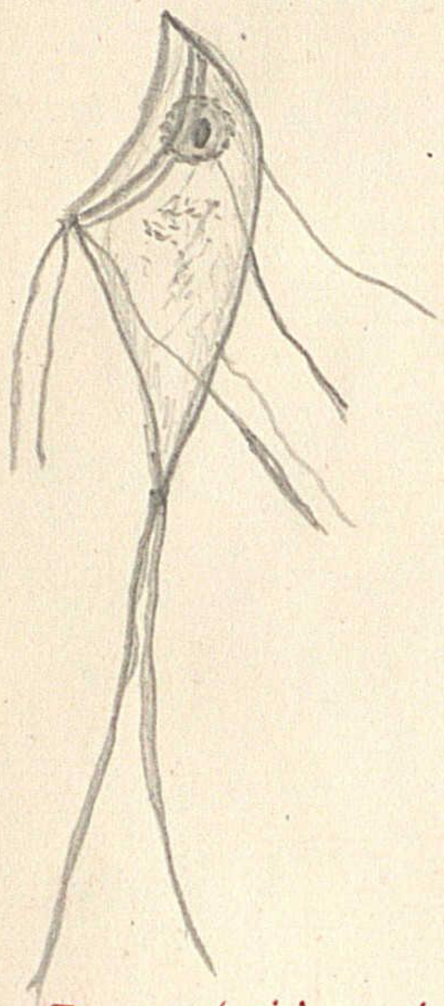
iii. <u>Balantidium</u> is easily distinguished; it is the largest of the parasites; has a funnel-shaped mouth, an anus, two nuclei, two contractile



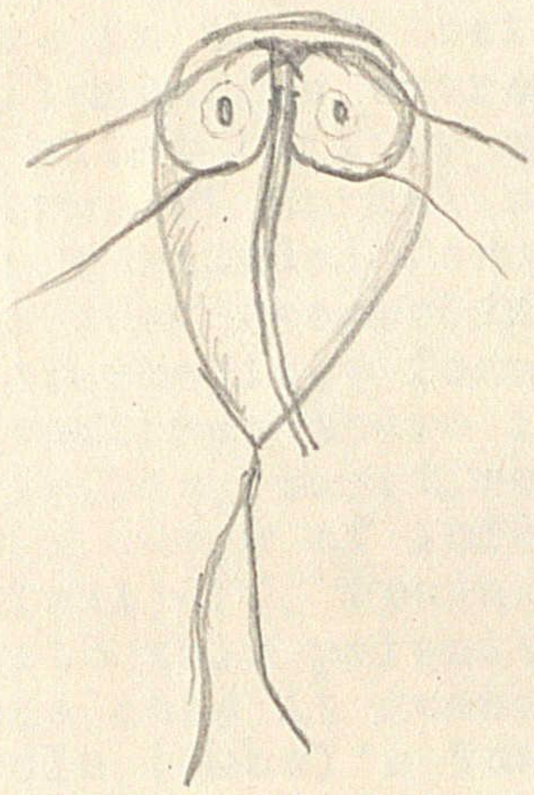

1. Resting Stage

2. Moving.

## Leydenia gemmipara. (Schaudinn).



Free-Form (side view).



Surface-view

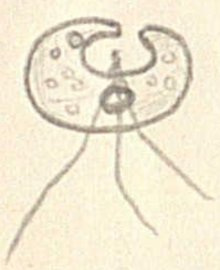


Encysted Forms

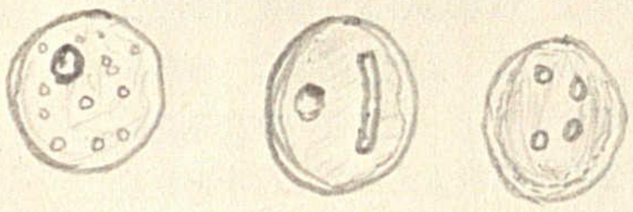
# LAMBLIA.



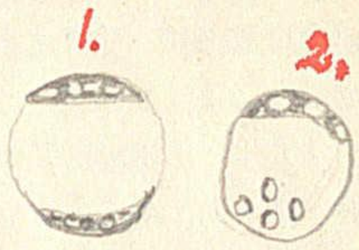
ver lapping cytostome



View on End



Encysted




1. Large spherical form Multinucleat
-ed in semilunar polar protoplasm
2. Somewhat Triangular & Multinuclei

Blastocystis Hominis.

## Tetramitus Mesnili.



orm with ndulating membrane



oval form with undul-ating membr.



Loss of undulating membrane



Amoeboid form Showing a pseudo-podium, and dotted in, the next.



Encysted form of Cercomonas, BODO, Prowazekia.

## TRICHOMONAS.

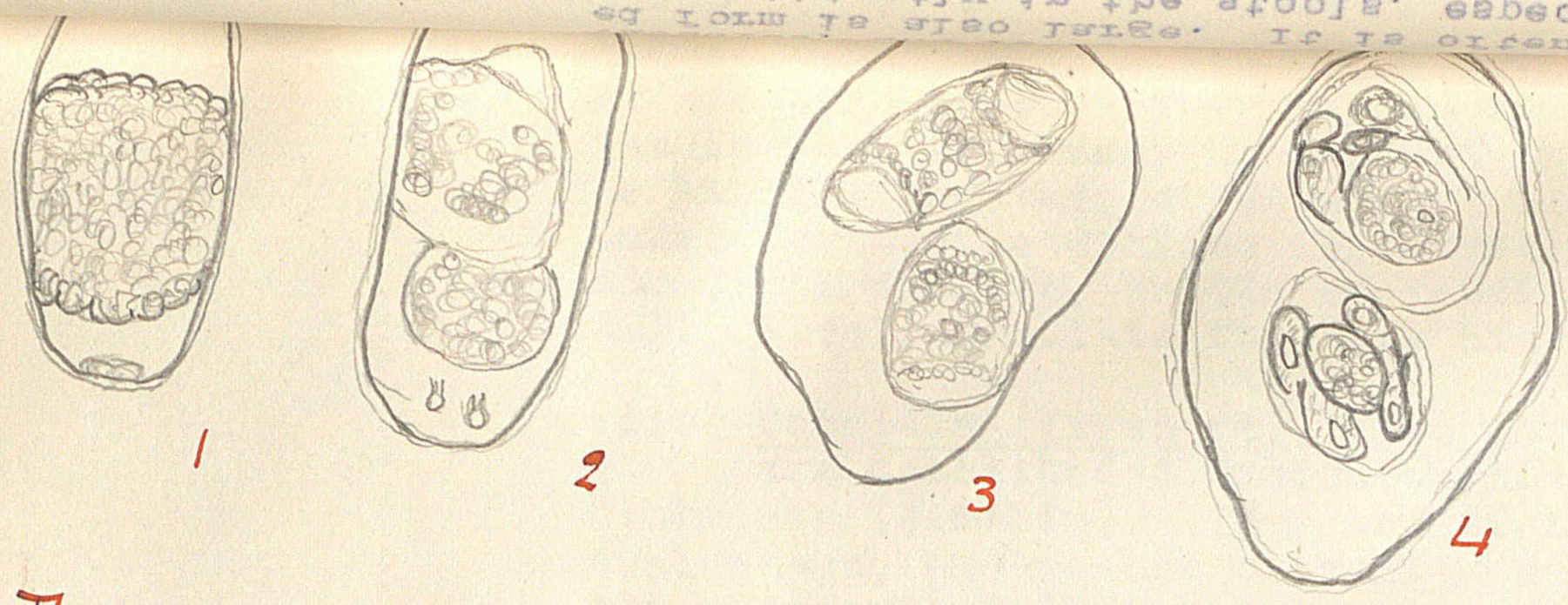
vacuoles, and is covered with cilia. The encysted form is also large. It is often passed intermittently in the stools, especially in Experiments in Monkeys.

iv. Tetramitus Mesnili - has three flagellae & a tail. The undulating membrane with the Cytostome is not always very apparent. The Cytostome with incurved lips is characteristic. Rarer forms, e.g - Hexamastrix Ardin-Delteili, has 5 free flagellae, and one connected with the undulating membrane. Sometimes the flaggellae are in the Sytostome; sometimes the posterior filamentous extremity is either retracted like a blunt tail or altogether retracted. Very small forms of normal shape occur, and sometimes there is a rounded form in which the flagellae are lost so that resemblance to a small Amoeba is marked. Intermediate forms occur. Encysted forms vary - sometimes there is a single nucleus & Cytostome visible, sometimes there are four nuclei. Six cases of infection recorded by Wenyon, Alexijeff, Prowazek, Nattan -Larrier, Brumpt, with this parasite, have been recorded, and in one case it seems to have played a pathogenic role (Gabel's Tunisian case).

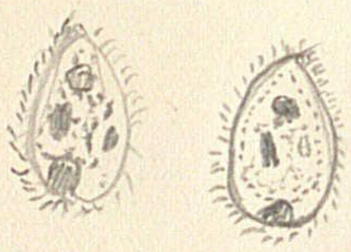
v. Trichomonas - These have three free flagellae and one connected with the undulating membrane sometimes the flaggellae appear to have a common base, due to twisting, sometimes they are free. It may occur as a rounded form with undulating membrane running all round its margin - probably an early stage of its degeneration. The degenerating process is rather important, for according to Wenyon, Castellani's Ent.Undulans*, is merely a degenerated Trichomonas. The large flagellum breaks loose from the undulating membrane, so that the flagellate has the appearance of having one large and three smaller flagellae. If further degeneration occurs, the flagella and axostyle are lost, so that the appearance is of an Amoeba with undulating membrane. Amoeboid activity continues, and finger-like pseudopodia are thrown out - a pseudopodium begins at one extremity, which rapidly passes down in wave-like movements on the same side of the body, and disappears at the opposite end. Another is then produced, and behaves in a like manner. These pseudopodia are produced in rapid succession every few seconds or more slowly. Again, the whole margin of the now-amoeboid organism may move as an undulating membrane. This margin is most probably the remain of the retracted Undulating membrane from which the flagellum has become detached.
Cercomonas - have a backwardly directed flagellum which is adherent to the body. There is only a single nucleus. It ispossibly the same as Tetramitus Mesnili.
Bodo - has two free flagellae with two nucleis.

vi. Blastocystis Hominis. These are very abundant. They usually appear as spherical uncoloured or slightly yellowish corpuscles 10-15 μ containing a homogenous round central mass without any detail, surrounded by a thin, protoplasmic, less refractive envelope in which are a variable number of nuclei. They may occur as large Spherical forms with several nuclei in semilumar protoplasm

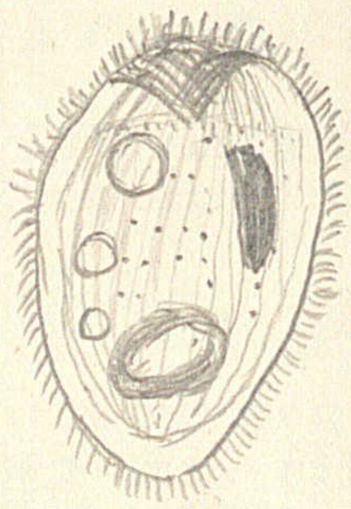
*Castellani, "Researches on Etiology of Dysentery in Ceylon" (Jrnl.of Hygiene, 1904, 495.)



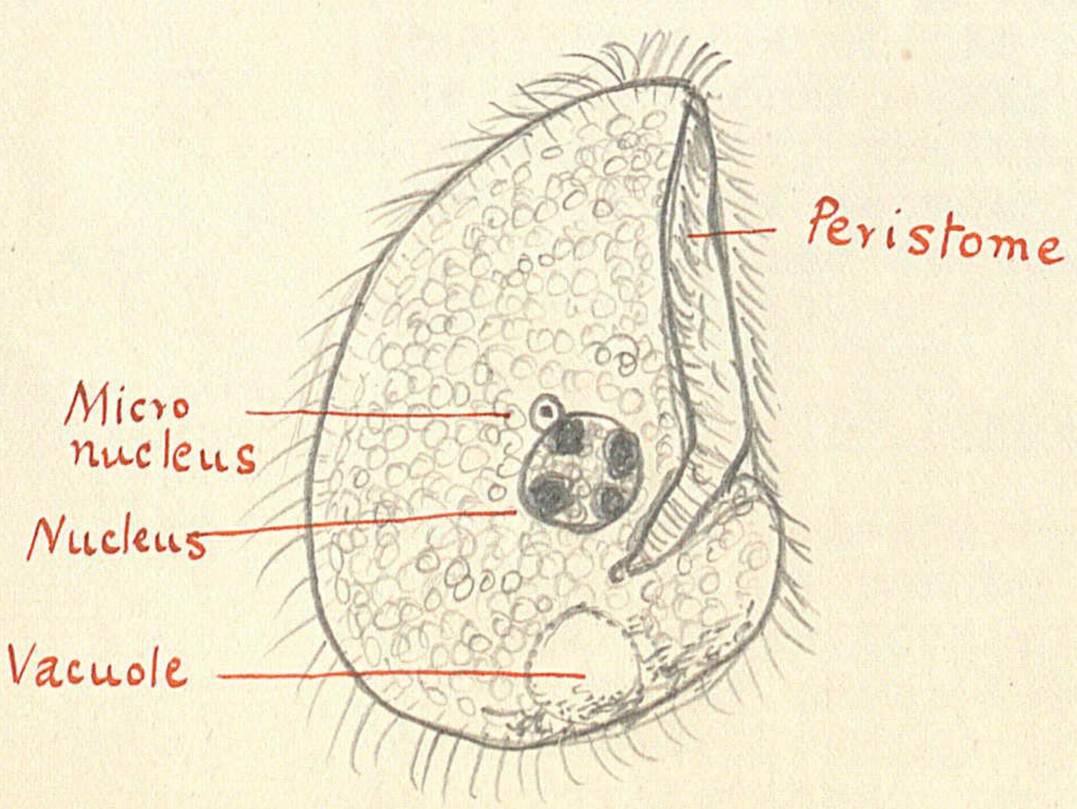

The Extracorporeal development of the Human Coccidium (Isospora) as it occurs after being passed in the faeces. In water the oöcyst becomes infective by development as in Figs 1-4, producing finally within it 2 Sporocysts containing 4 Sporozoites and a residual mass of Cytoplasm. (after Wenyon).



Balantidium Coli in Faeces.



Balantidium Coli (Enlarged).




Schema III

Balantidium Minutum.

at opposite poles. They may be somewhat triangular in form with many nuclei; may be small oval, or small elongated, or elongated dividing form. Under certain conditions degenerating flagellates and small amoebae, or the encysted forms of these will closely simulate the true Blastocystis.

vii. Coccidia (Isospora). Two Intestinal species are described C.Cuniculi (Rivolta), and C.hominis (Eimeria). They are of large size, oval shape, and at one extremity a depression - the micropyle C.Cuniculi is longer & broader than the other. On the ground or in water, the oöcyst becomes infective by development, producing finally within it, two Sporocysts, each containing 4 Sporozoites and a residual mass of cytoplasm. In Eimeria - the oöcyst is Sherical, 20 μ in diameter, and produces 4 Sporocysts each with two sporozoites.

Morphology & Structural Comparison of Ent.Histolytica.

In the living condition, the organism assumes an endless variety of form, on account of incessant movement. Movement is always more marked as the animal begins to die. In E.Histolytica, structural pecularities in the formation of the pseudopodia are distinctive of the species. In the cell itself, the following specific characters may be made out.

1. A clear homogenous field of jelly-like protoplasm the ectoplasm, which when the orgamism is at rest, occupies about one-third of the whole area.

2. A roughly granular endoplasm, constituting the remaining two-thirds of the total contents.

3. A faintly defined nucleus and nucleolus.

4. Cell-inclusions, notably redblood-corpuscles, but also food particles & bacteria.

1. The Ectoplasm.

The arrangement of the Ectoplasm is segmental rather than circumferential owing to movement, and the granular endoplasm is usually in direct contact with the periphery at one or more places. The highly refractive appearance suggests that it is of infinitely greater tenacity and hardness than the rest of the cell, for it is by means of the long & sharp extrusions of hyaline material (pseudopodia), that E.Histolytica is able to thrust itself between the epithelium and glandular structures, and to tear asunder the connective tissue fibres.

2. The Granular Endoplasm.

This varies considerably in appearance and opacity and its limits can be differentiated from those of the homogenous protoplasm only by a deeper shading. The granular protoplasm appears entirely structureless - no fibrillar tissue or areolar network can be distinguished. It is commonly described as

pale or greenish-yellow, while E.Coli is brownish-grey. It is contractile & resillient, and shows marked assimilative functions. In E.Coli, there is no separation of granular from hyaline layer - the granular protoplasm filling the whole of the organism.

i. When locomotion takes place, the absence of a clear field at the anterior pole is especially noticeable, and this marked characteristic is one of the most important indications in the identification of species.

ii. A transparent ectoplasm is then, practically peculiar to E.Histolytica, and the formation of hard and powerful pseudopodia differentiates it from all other Intestinal cells.

iii. A third point and a notable one is that in E.Histolytica, the granular endoplasm invariably contains quantities of ingested redblood-cells - sometimes up to 30. Ingested red cells are never seen in E.Coli, but the vacuoles which abound in this species must be carefully differentiated. The structural granules themselves may be nuclear or fragments of chromatin extruded from the nucleus, resembling shreds of a fibrillary structure; or they may be metaplastic, the residue from digestion of food, when they are angular, & resemble grains of pigment.

iv. The presence of Vacuoles is an important feature in the differentiation of Species,
Briefly stated, the distinction is that:
E.Histolytica, contains blood-cells & no Vacuoles,
E.Coli., " Vacuoles but no blood-cells.
Their presence, however, in E.Coli, is not invariable. Sometimes round transparent faint yellowish tinted bodies occur in the endoplasm of E.Histolytica, and these are suggested as being digested red cells, but if this be so, it is difficult to explain why, although considerably smaller than red cells, they are always uniform in size. They react to pressure and to influence of currents within the Amoeba, and have nothing therefore in common with protoplasmic Vacuolation. As a rule in free-living Amoebae, there is a pulsating or contractile Vacuole - this structure is said never to occur in parasitic species.

v. Size. E.Histolytica is usually described as being considerably larger than E.Coli, and is said to measure 20 -40 μ in diameter, but 10- 12 μ have been described.
In different patients and in different attacks of Amoebic Dysentery, the specific organisms vary considerably in size. Moreover, some of them may have only recently emerged from spores, and not had time to develop. It is also influenced by the density of the surrounding media. Although no relation has been shown to exist between size & pathogenicity, yet it may be probable that different "strains" of E.Histolytica vary in virulence as they do in bulk. More work needs to be done on this subject.

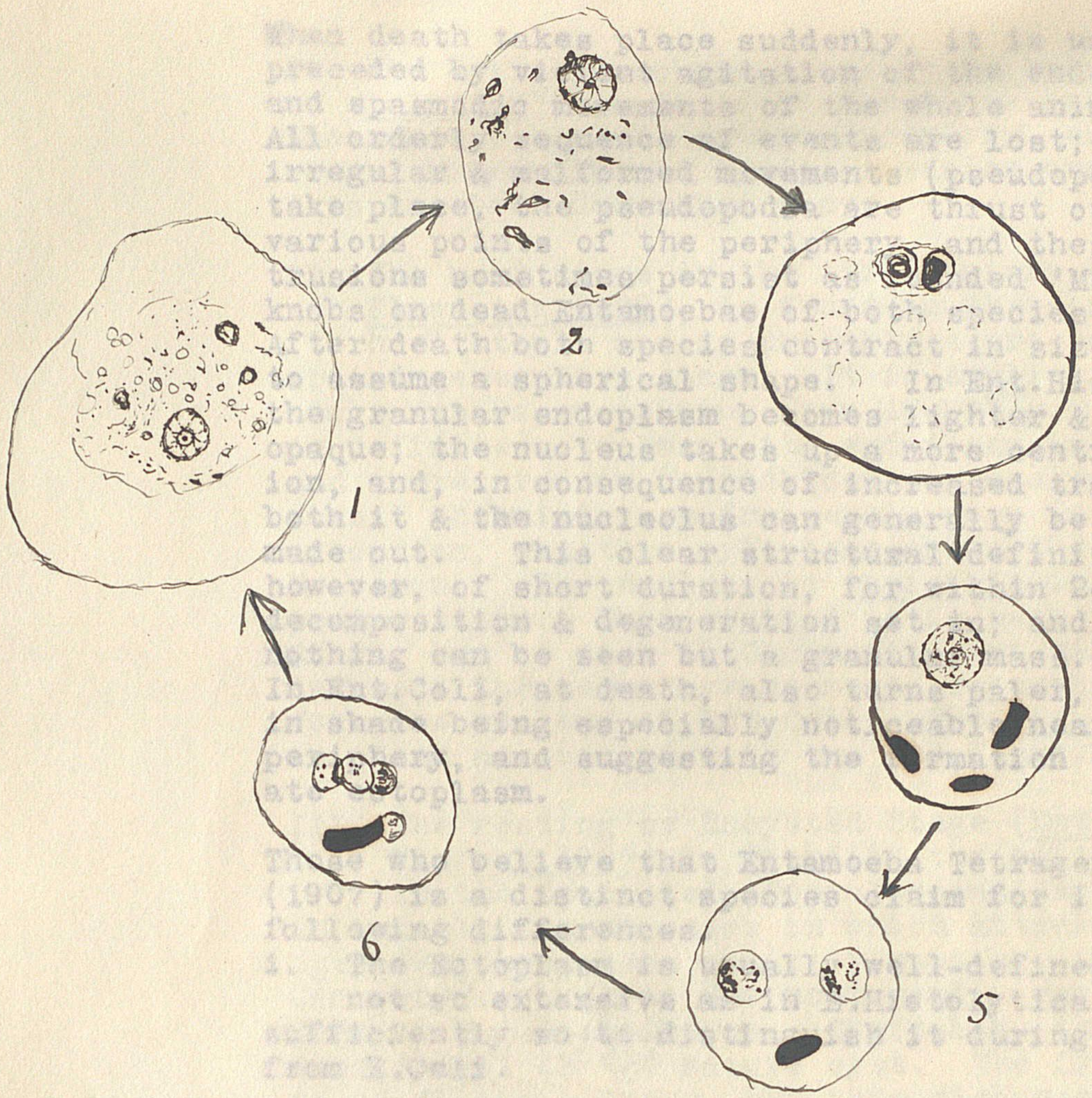
vi. The Nucleus. In both varieties a nucleus is seen, but there are marked differences in position and structural arrangements.
In E.Histolytica - in the living state -is

clearly visible, or it may be seen with difficulty In the latter case, the failure to detect the nucleus may be the result of its having broken up after the Entamoebae have left the body; in other cases it is due to a poverty of refractile chromatin granules. In the stained Amoeba, however, by the Hematoxylin Method, the nucleus is a much less prominent body than in E.Coli; with comparatively little Chromatin, without a well-developed nuclear membrane and with a much smaller central Karyosome. Those who maintain that E.Tetragena is a separate species, point to its resemblance to E.Coli in that it has a well-developed chromatin nuclear-membrane, and a large Karyosome. "There is, however, a definite nuclear membrane upon the inner surface of which Chromatin granules are arranged. These granules are generally small and fairly uniform in size, but occasionally they are massed in more or less irregular clumps. The nuclear membrane is continued within the nucleus as the linin network of fibres upon which some very fine granules are seen. At the centre of the nucleus, a granule can usually be distinguished, and surrounding this a clear area limited by a ring of granules, which represents the inner limit of the linin network. According to Hartmann, the central granule of the nucleus represents a Karyosome with centriole and a kind of Cyclic growth takes place, whereby the granule consisting of little else than the Centriole, increases in size by the deposit of Chromatin material round it till the whole of the clear area is filled up by the ring of granules. A decrease in size then takes place by the passage of the Chromatin into the outer parts of the nucleus, till finally the clear area is formed again, and the Centriole alone occupies the centre On this view, this centriole represents the cestrosome which must necessarily be present for purposes of Nuclear Division." (Wenyon -B.M.J, Nov 15/1913, 1287 "Morphology of the Intestinal Amoebae of Man").
When the endoplasm is opaque and crowded with granules, blood corpuscles, etc, the nucleus may be completely obscured, but the addition of dilute Acetic Acid to the specimen, generally brings it into view. This nucleus is ovoid or elongated in shape, and it is generally placed eccentrically to the granular protoplasm, lying almost on the periphery of that substance.

In E.Coli, the nucleus, which is usually larger in proportion to the size of the Entamoeba than in Ent.Histolytica, has a definite nuclear membrane, not necessarily thicker, according to Wenyon, than of the Pathogenic Entaboema. "The chromatin is arranged as coarse irregular granules upon the inner surface of the membrane, and there is a linin network which usually extends right up to the Karyosome, occupying the centre of the nucleus. This Karyosome, is sometimes comparatively large, having a diameter equal to, or greater than half that of the entire nucleus. At other times, it is smaller, and occasionally a clear area surrounds the Karyosome, as is the case with the nucleus of the pathogenic Entamoebae". (Wenyon -ibid- p, 1288).

- continued -

vii. Movement & Locomotion. The Pseudopodia afe of the greatest diagnostic importance, both as regards the actual movements & the conformation of these pseudopodia.
Briefly stated, in Ent.Coli, they are always granular and scarcely distinguishable from the endoplasm; they are small & blunt,"soft and flaccid;"and the movements are sluggish. In marked contrast to this, the pseudopodia in Ent.Histolytica, are very clear & refractile; sharply differentiated from the endoplasm; they are long & sharp,"horny & resistant"; extremely active movements -"the whole organism, becoming much elongated, flows steadily across the field of the microscope, to pass out of sight at the edge of the field, a degree of motility rarely if ever seen in Ent.Coli." (Rogers).
A distinct sequence of events can be made out leading to the development of pseudopodia. At some particular point of the periphery of Ent.Histolytica, a bulge is seen, under which the hyaline protoplasm (ectoplasm), collects. This swelling subsides almost as soon as it forms, to be succeeded by such an other in some other part of the circumference; without intermission these peripheral changes continue ad.lib.
These apparently ectoplstic processes really are of central origin & spread to the periphery, for they are invariably associated or rather preceded by a change in the granular endoplasm; but the Endoplasm never reaches the periphery, being cut-off sharply as it were, by a thick cushion of hyaline matter between it & the protuberance.
Currents have been demonstrated within this endoplasm by Harris. The first indication of impending change is that all Endoplasmic structures, e.g. Nucleus, granules, and engulfed foreign matter are momentarily swayed to & fro. Ultimately movement towards one sector takes place, probably determined by a positive chemiotaxis & partly perhaps by changes in surface-tension or tissue-tension. In both species locomotion is affected merely by an extension of the pseudopodia in one direction. But there are fundamental differences in the constituted elements composing the content(polar).
In Ent.Coli concentration of endoplasm is marked in the anterior pole, that is, in the direction of the pseudopodial extrusion the body-protoplasm flowing in until nothing is left behind. In Ent.Histolytica, the granular endoplasm is posterior polar, at any rate for an appreciable length of time, the pseudopodia are pale, structureless glassy & homogenous. Ultimately the granular substance pours into it, thus altering what was purely originally a protrusion of hyaline ectoplasm.
Variations occur,in what may be described as the Terminal phase of its life. A Nuclear-storm takes place, to be described overleaf.




Constructed from Hartmann's drawings in the Archiv.fur Schiffs-und Tropen Hygiene. (Castellani & Chalmers).

1. Fully-grown Parasite.

2 -6. Stages in Encystment & Nuclear Division.

Schema IV

- continued -

When death takes place suddenly, it is usually preceded by violent agitation of the endoplasm, and spasmodic movements of the whole animal. All orderly sequence of events are lost; short irregular & malformed movements (pseudopodia) take place, the pseudopodia are thrust out at various points of the periphery, and these extrusions sometimes persist as rounded 'Mulberry' knobs on dead Entamoebae of both species.
After death both species contract in size & tend to assume a spherical shape. In Ent.Histolytica the granular endoplasm becomes lighter & less opaque; the nucleus takes up a more central position, and, in consequence of increased transparency both it & the nucleolus can generally be easily made out. This clear structural definition is however, of short duration, for within 24 hours, decomposition & degeneration set in; and soon after nothing can be seen but a granular mass.
In Ent.Coli, at death, also turns paler, the change in shade being especially noticeable near the periphery, and suggesting the formation of a separate ectoplasm.

Those who believe that Entamoeba Tetragena Viereck (1907) is a distinct species claim for it the following differences.

i. The Ectoplasm is usually well-defined, but is not so extensive as in E.Histolytica, but sufficiently so to distinguish it during movement from E.Coli.

ii. The pseudopodia usually consist of highly refractile hyaline protoplasm, but this differentiation is sometimes difficult to define.

iii. The Endoplasm is greyish in color & contains usually redblood-cells, food particles & debris.

iv. The Nucleus is clearly visible & has a well defined membrane on which chromatic granules are distributed. In the centre, there is a Karyosome surrounded by a clear area & containing a Centrosome. "A cycle of changes is constantly proceeding in the Nucleus: first chromidia break away from the Karyosome & pass outwards into the Nuclear, and this proceeds until little but the Centrosome is left, when it ceases, and chromatin begins to accumulate again, around the Centrosome, until the Karyosome is re-formed, when the cycle begins again."(cf.Castellani & Chalmers,Trop.Med, p.272).

v. Sporogony is rare, and when it occurs tends to cyst-formation, before which the Amoebae becomes small, and their chromidia form 3 - 6 masses. The Cyst sometimes contains a large Vacuole. Nuclear division takes place until four Nuclei are formed.

vi. Wright's Differential Stain gives different results in E.Coli, E.Histolytica, & E.Tetragena

In Ent.Coli - endoplasm is dark-blue
ectoplasm is light-blue.

In Ent.Hist.- endoplasm is light-blue
ectoplasm is dark-blue.

In Ent.Tetr,- not stained well.

## I. ENCYSTATION

I. The active amoeboid stage (original Ent.Histolytica), is found in the mucus passed in the Acute stage of Amoebic Dysentery, and in the body-lesions induced by its invasion and presence. This has been described above.

II. The next stage in the life-history (Ent.Minuta, Elmassian,1909), is found in the soft diarrhoel stools and is probably a pre-encysted, or a degenerative stage. It is smaller than the adult Amoeba, measuring from 12- 17 μ. There is no definite ectoplasm, the endoplasm is vacuolated and there are now no redblood corpuscles to be seen. Chromidia are frequently seen in the cytoplasm, and this cytoplasm shows the Glycogen-Reaction. The nucleus is invisible in fresh preparations. When stained it is seen to be Small, but is rich in Chromatin, but without a definite Karyosome arrangement, resembling therefore the nucleus of Ent.Coli. The Minuta form is often associated with the 3rd.Stage.

III. The resting or Encysted Stage (Ent.Tetragena, Viereck,1907),is found in the solid faeces in the so-called "Convalescent-Carriers", or in totally Latent cases in which attacks of Dysentery have been entirely wanting -the "Contact-Carriers". It is the most easily recognised form of Ent.Histolytica. Typically, there are four nuclei in the mature cyst. The Cyst-wall is of double contour, but this also occurs in the Non-pathogenic Species.
Kuenen* asserts that an Intermediate Form occurs between the Minuta Stage and the Tetragena Stage. This is a one-nucleated Cyst, which Kuenen believes to be very characteristic. E.Coli also forms from 1 -8 nucleated Cysts, so what the special characteristic element is, it would be difficult to state.
The encysted forms of the Entamoebae are more readily differentiated than the free Entamoebae themselves. The pathogenic species become encysted in Cysts which have a diameter of about 10 -12 μ. Within each Cyst is usually a single mass of protoplasm, containing 4 nuclei. Sometimes a medium-sized Vacuole occurs in the protoplasm, and one or two deeply-staining rods or Chromidial Bodies, which have been formed by an aggregation of the Chromidium granules of the encysting Entamoebae. The Cyst-wall is not so thick or so Well-defined as in E.Coli. The Vacuole and Chromidia are evidently of developmental origin, for as the Vacuole diminishes, the Chromidia decrease. In the first stage of development of the Cyst, a large Central Vacuole is formed tinging brown by Lugol's Iodine - the glycogenic Reaction. The nucleus measures 5 -6 μ; it may show division into two with a coincident disappearance of the Vacuole, and later four nuclei appear; sometimes however, the nuclear division is rather rapid before the Cyst-wall has fully formed. Persistence of a large Vacuole retards nuclear division, and such Cysts have rarely more than two nuclei.
In the fully-developed Cyst, all trace of the Vacuole has generally disappeared, and with it

*Kuenen &Swellengrebel, "Die Entamoben des Menschen und ihre praktische Bedentung". Centralbl.f.Bakt (Orig),1913,Vol.71, pp.378 -410 - quoted Bibliography by Phillips -p.132.

ENCYSTATION. cont.

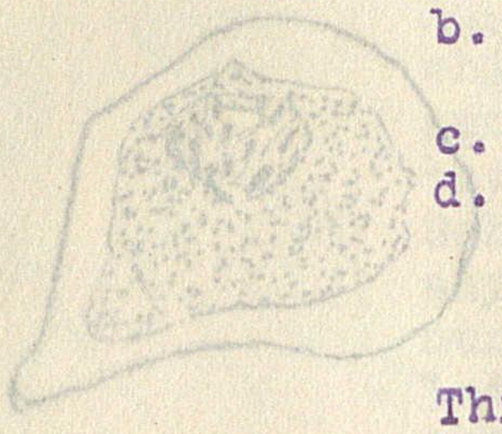
the glycogen-reaction, and the protoplasm turns finely granular. The arrangement of the resultant nuclei is not constant - they may be in pairs, or irregularly distributed; differences in size between the nuclei themselves are not common, & occurs more in the Non-pathogenic species. Wenyon authoritatively states that in his experience, the Cysts of the pathogenic Entamoebae are not subjected to the same extent of variation as are the Cysts of the Non-pathogenic forms. The pathogenic Cyst is more constant in appearance but there is absolutely no known method of differentiating between a smaller Cyst of Ent.Coli, and the pathogenic Cyst.
The nuclei appear to be ring-shaped; as the chromatin is rather abundant and arranged peripherally, there is a definite Karyosome with a clear area around it. Kuenen has on rare occasions observed 8 nuclei.
The Ent.Coli has a Cyst, most usually, though not invariably, Spherical, and has a diameter of about 15 μ. Within the transparent Cyst, there is a single mass of protoplasm containing from 1 - 8 nuclei, according to the stage of development. It is, however, impossible to observe the difference between mature and immature Cyst-formation. The typical Ent.Coli Cyst, as is found in actual examination of faeces, has 8 nuclei, and this is found "in the overwhelming majority of Cysts in the faeces". (Wenyon).
The variations which occur in the Ent.Coli Cysts, and which approximate them to the Pathogenic Species, have been detailed in the Section of the Thesis on "Etiology of Amoebic Dysentery".
There are, however, two main changes of form which may be here alluded to, because they may perhaps be responsible for the Schizogony -cycle which is held to exist in the Pathogenic Species by some Authors, but which Wenyon has thrown some doubt upon. Wenyon writes as follows in the B.M.J. of Nov.15th, 1913, p. 1288, "Morphology of Intestinal Amoebae of Man". -
"The ultimate fate of a Cyst, hampered in its nuclear division by the persistence of a Large Vacuole, is unknown. Again the Cysts, instead of being Spherical, may be distorted, and even elongate structures with the length of one diameter twice that of the other. The surface of the Cyst may be crinkled and creased, so that at first sight in stained specimens, one may have the impression that one is dealing with an irregularly-shaped unencysted Entamoeba, containing 8 nuclei, and conclude that it is an instance of Schizogomy, which is supposed by some to occur in this Entamoeba." (Wenyon).

*Schaudinn, Arbeiten ans dem Kaiserlichen Gesundheitsamte, 1903.

Schaudinn* stated that he was entirely unable to trace the influences that determine maturity in any species of Amoeba; but the condition should be distinguished from the formation of resistant Cysts, which is induced by unfavourable external conditions.

## II. REPRODUCTION

Schema V.



E.Histolytica is supposed to reproduce in four ways:-

a. Binary Fission (Schaudinn).
b. Gemmation or Budding (probably Degenerative) (Schaudinn)
c. Spore-formation.
d. Simple Conjugation.(Craig).

### 1. BINARY FISSION (Schaudinn)

This occurs during the Vegetative stage in both Species. Sexual reproduction or Sporogony is held to occur in E.Coli; Kuenen states he has never observed it in E.Histolytica, or even anything suggestive of a sexual process. Binary Fission occurs in fresh specimens of the Infected Alimentary Canal. The nucleus divides by amitosis into two, and then the cytoplasm splits into two equal daughter cells.

### 2. GEMMATION or BUDDING (Schaudinn).

This, although found more commonly than the above by Schaudinn, is probably a degenerative process. It consists of the division of the nucleus by Amitosis into two or more daughter nuclei, which, together with small portions of the cytoplasm, separate off from the mother-cell; the daughter-cells being smaller than the parent-cell.

### 3. SPORE-FORMATION.

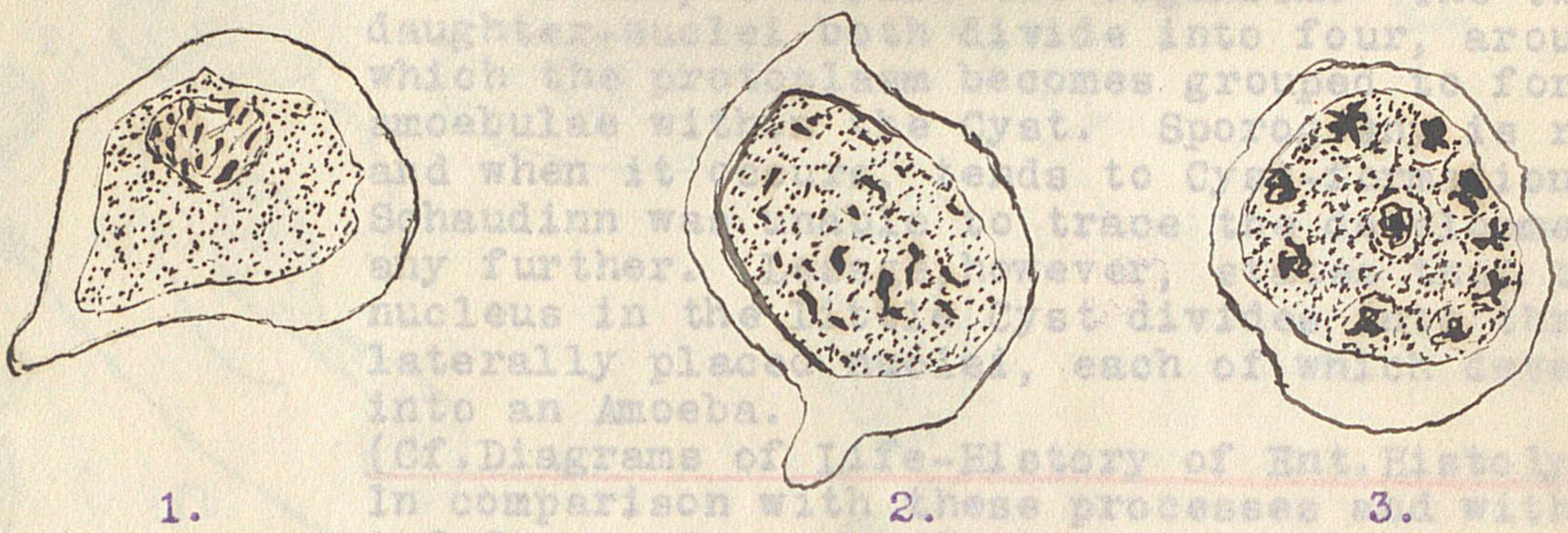
This process only takes place under favourable conditions, such as when recovery is taking place after an attack of Dysentery. After a special form of nuclear division, and subsequent Conjugation, most of the indistinct Chromatin in and around the nucleus is shed off, and becomes diffused into the Cytoplasm (Endoplasm), and comes to Collect near the periphery. The nucleus in consequence rapidly degenerates, and is either absorbed or else extruded. The ectoplasm forms small knobs, containing several chromidia in each - the so-called "Chromidial blocks". These knobs and their chromidia form themselves into an uncertain number of minute refractile spherical Cysts, each 3 -7 μ in diameter; the envelope consisting of a filamentous membrane derived from the hyaline ectoplasm, and being of a yellowish-brown colour. These bodies become separated off as rounded spores which are resistant. These are the spores which are able to produce the disease, as were shewn in Schaudinn's feeding experiments in cats, which developed typical Dysentery with the Amoebae in the discharges, and in the lumen of the Gut, and in the Intestinal walls themselves These spores may require to pass through another phase, as has been suggested by Brown, before they are capable of developing into new individuals. The remaining portion of the parent Entamoeba after spore-formation has matured, rapidly degenerates and dies. At a certain period in the life of the organism, it becomes mature, and it then enters on a resting or quiescent stage of existence. By those who claim that E.Tetragena is a new Species, the following life-history is attached to it.

Schema V.

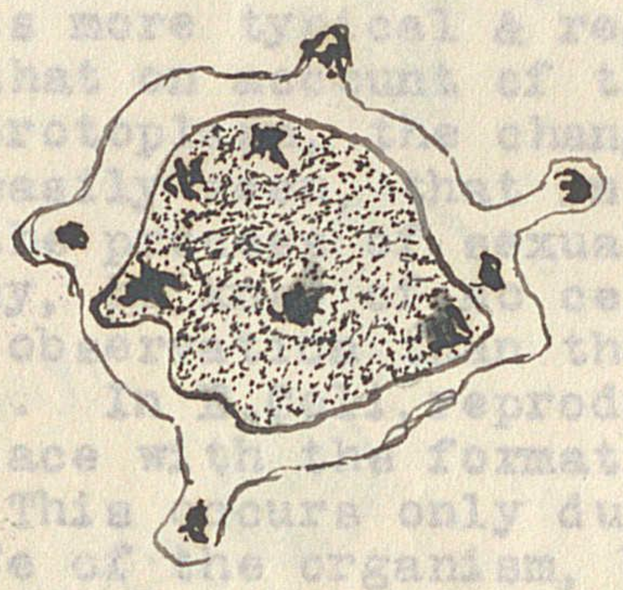
## Ent.Histolytica - Asexual Multiplication by Budding.

(Schaudinn).

After Brown.



1. 2. 3.



4.

Figs.1 & 2. Dispersion of Nuclear Contents in the Granular Endoplasm.

Fig.3. Collection of Chromatin for the Nuclei of the Amoebulae.

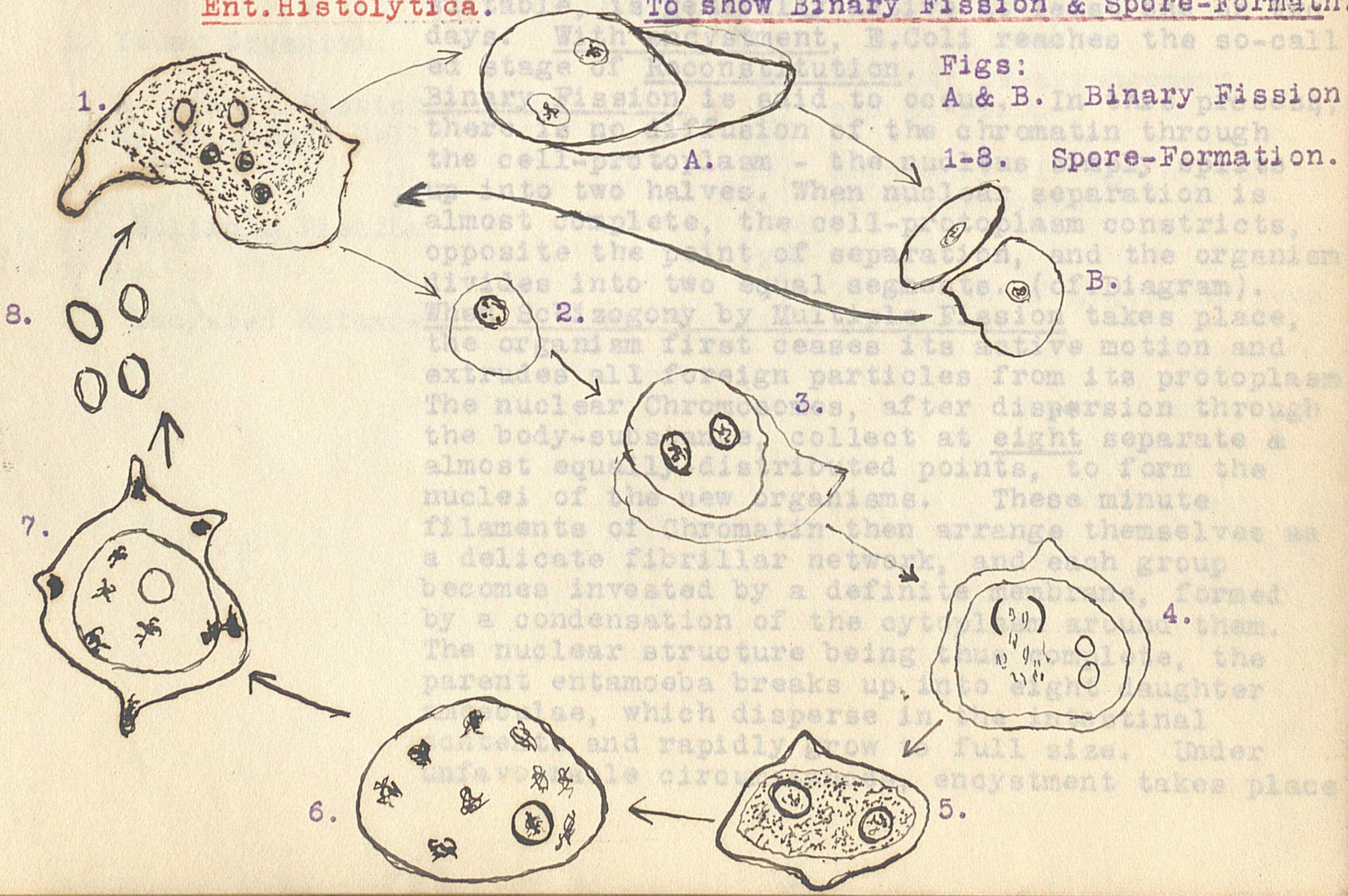
Fig.4. Formation of Buds.

* * * * * * * * * * * * * * * * * * *

(After Castellani & Chalmers).

Constructed from Craig's drawing in "Jrnl.Infectious Dis."

Ent.Histolytica. To show Binary Fission & Spore-Formatn.



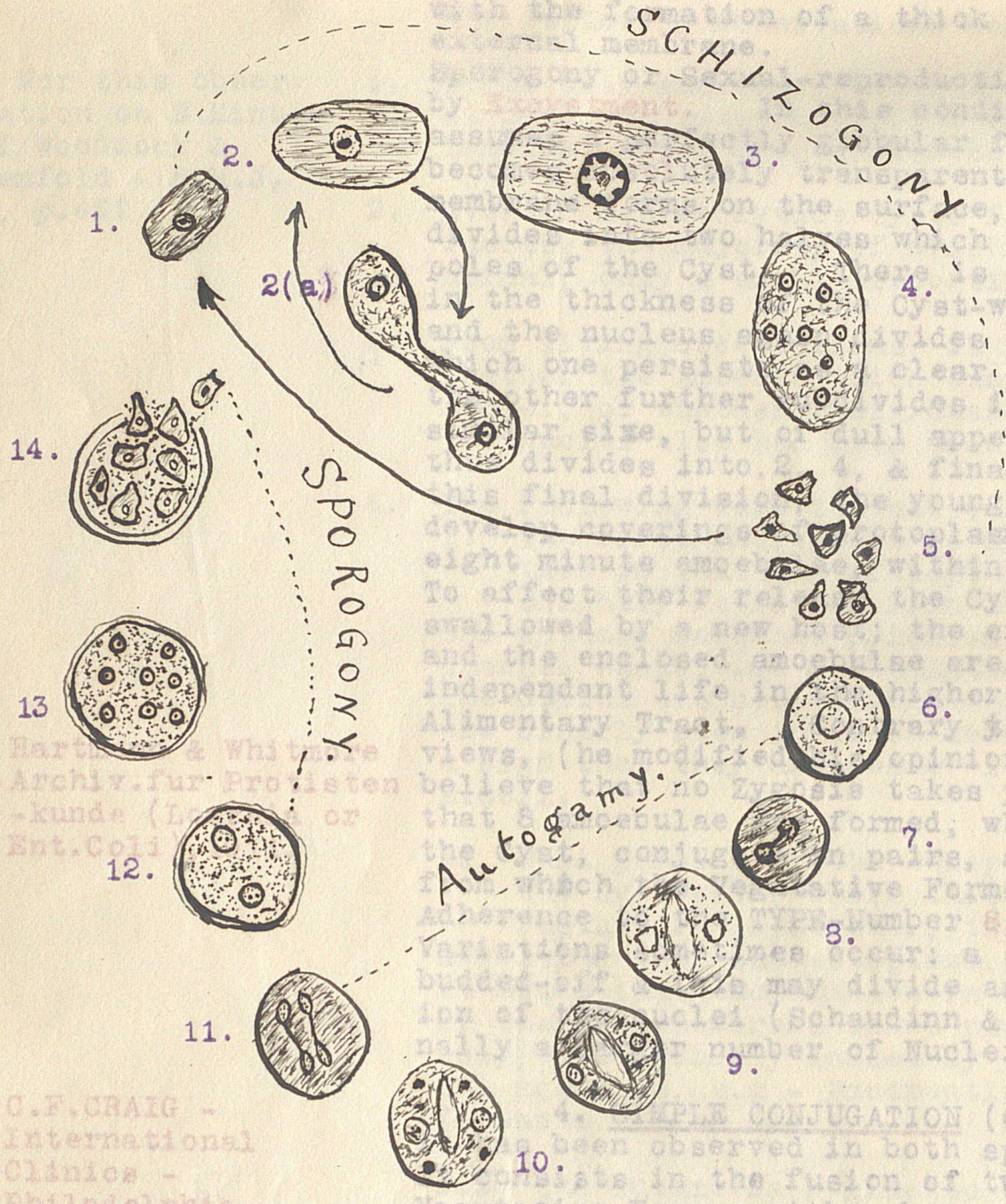

Figs:
A & B. Binary Fission
1-8. Spore-Formation.

SPORE-FORMATION. Cont.




The process is simpler. After the extrusion of the foreign matter, the nucleus enlarges and divides into two, and at the same time a Cyst-wall developes around the organism. The two daughter-nuclei both divide into four, around which the protoplasm becomes grouped to form four amoebulae within the Cyst. Sporogony is rare, and when it occurs, tends to Cyst-formation. Schaudinn was unable to trace the development any further. Lesage, however, states that the nucleus in the little Cyst divides into three laterally placed nuclei, each of which develops into an Amoeba.
(Cf. Diagrams of Life-History of Ent. Histolytica).
In comparison with these processes and with the indefinite formation and number of buds & Spore-Cysts in Ent. Histolytica, the reproduction of E. Coli is more typical & regular. Schaudinn has stated that on account of the extreme clearness of the protoplasm, the changes in the nucleus are so easily seen, that in spite of the Complexity of the process of sexual-reproduction or Sporogony, he knew of no cell more suitable for nuclear observation than the encysted stage of Ent. Coli. In E. Coli, reproduction by Schizogony takes place with the formation of eight daughter-cells. This occurs only during the intra-intestinal life of the organism, but when active life ceases and the organism arrives at maturity.
At this stage, encystment always occurs, but the process differs from the reproductive encystment of E. Histolytica, in that it is certainly hastened, if not invariably produced, by unfavourable conditions. The gradual solidification and concentration of Intestinal contents in their downward passage, is adverse to the continuation of active life; hence when it is found in the solid dejecta, E. Coli is never in the active state but always encysted. In this respect, it offers a marked contrast to E. Histolytica, which under similar conditions, and if the temperature be suitable, is generally active at least one or two days. With encystment, E. Coli reaches the so-called stage of Reconstitution.
Binary Fission is said to occur. In this process, there is no diffusion of the chromatin through the cell-protoplasm - the nucleus simply splits up into two halves. When nuclear separation is almost complete, the cell-protoplasm constricts, opposite the point of separation, and the organism divides into two equal segments. (cf. Diagram).
When Schizogony by Multiple Fission takes place, the organism first ceases its active motion and extrudes all foreign particles from its protoplasm. The nuclear Chromosomes, after dispersion through the body-substance, collect at eight separate & almost equally-distributed points, to form the nuclei of the new organisms. These minute filaments of Chromatin then arrange themselves as a delicate fibrillar network, and each group becomes invested by a definite membrane, formed by a condensation of the cytoplasm around them. The nuclear structure being thus complete, the parent entamoeba breaks up into eight daughter amoebulae, which disperse in the intestinal contents and rapidly grow to full size. Under unfavourable circumstances, encystment takes place

Schema VI




Figs. 1-5. Schizogony. Figs. 6-11 Autogamy.

Figs. 12-14. Sporogony.

1. Young Organism.

2. & Binary Fission
2.(a). of Mature Cell.

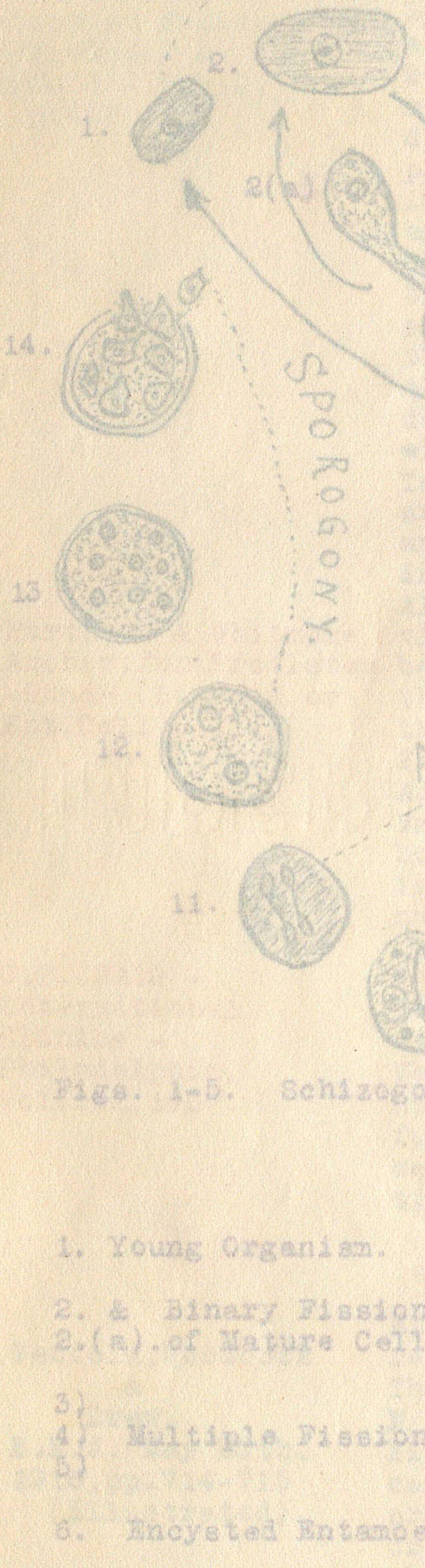
3)
4) Multiple Fission.
5)

6. Encysted Entamoeba.

7)
8) Nuclear re-arrangement
9) and Division.
9)
10) Secondary clevage & reunion
11) of Chromosomes.

12)
13) Formation of Zygote-nucleus
14) and spores.

SPORE-FORMATION. Contt.




The process is simpler. After the extrusion of the foreign matter, the nucleus enlarges and divides into two, and at the same time a Cyst-wall developes around the organism. The two daughter-nuclei both divide into four, around which the protoplasm becomes grouped to form four amoebulae within the Cyst. Sporogony is rare, and when it occurs, tends to Cyst-formation. Schaudinn was unable to trace the development any further. Lesage, however, states that the nucleus in the little Cyst divides into three laterally placed nuclei, each of which develops into an Amoeba.
(Cf. Diagrams of Life-History of Ent. Histolytica).
In comparison with these processes and with the indefinite formation and number of buds & Spore-Cysts in Ent. Histolytica, the reproduction of E. Coli is more typical & regular. Schaudinn has stated that on account of the extreme clearness of the protoplasm, the changes in the nucleus are so easily seen, that in spite of the Complexity of the process of sexual-reproduction or Sporogony, he knew of no cell more suitable for nuclear observation than the encysted stage of Ent. Coli. In E. Coli, reproduction by Schizogony takes place with the formation of eight daughter-cells. This occurs only during the intra-intestinal life of the organism, but when active life ceases and the organism arrives at maturity.
At this stage, encystment always occurs, but the process differs from the reproductive encystment of E. Histolytica, in that it is certainly hastened, if not invariably produced, by unfavourable conditions. The gradual solidification and concentration of Intestinal contents in their downward passage, is adverse to the continuation of active life; hence when it is found in the solid dejecta, E. Coli is never in the active state but always encysted. In this respect, it offers a marked contrast to E. Histolytica, which under similar conditions, and if the temperature be suitable, is generally active at least one or two days. With encystment, E. Coli reaches the so-called stage of Reconstitution.
Binary Fission is said to occur. In this process, there is no diffusion of the chromatin through the cell-protoplasm - the nucleus simply splits up into two halves. When nuclear separation is almost complete, the cell-protoplasm constricts, opposite the point of separation, and the organism divides into two equal segments. (cf. Diagram).
When Schizogony by Multiple Fission takes place, the organism first ceases its active motion and extrudes all foreign particles from its protoplasm. The nuclear Chromosomes, after dispersion through the body-substance, collect at eight separate & almost equally-distributed points, to form the nuclei of the new organisms. These minute filaments of Chromatin then arrange themselves as a delicate fibrillar network, and each group becomes invested by a definite membrane, formed by a condensation of the cytoplasm around them. The nuclear structure being thus complete, the parent entamoeba breaks up into eight daughter amoebulae, which disperse in the intestinal contents and rapidly grow to full size. Under unfavourable circumstances, encystment takes place

III. EXCYSTATION. Cont.

The following observations were made:-

* For this observation on E.Minuta cf/Woodcock & Penfold - B.M.J, i, p.407.

1. It is only successful in E.Histolytica & E.Minuta.* It does not occur in E.Coli & Lamblia. In the Lamblial Cyst, Conjugation and not division occurs.

2. Even of E.Histolytica Cysts freshly passed in the faeces, the majority of which appeared quite normal, only a small proportion excysted.

3. From living observations, it was impossible to say whether the Amoebae which excysted had always 4 nuclei, or whether individuals with only one or two nuclei also had been able to excyst.

4. The following were the steps in the process:-

i. The first indication of approaching excystation is that the protoplasm becomes very slightly retracted from the Cyst-membrane, and appears somewhat crinkled. The body very slowly changes shape, i.e - The Entamoeba turns amoeboid. The nuclei are not visible - whenthe nuclear rings are clearly seen in fresh Tetragena Cysts, it is a sign that they are dead. It thus differs from E.Coli.

ii. That portion of the endoplasm is applied to the Cyst-wall, where this is going to be ruptured. If,however, there occur a slight development of the ectoplasm, which is unusual, it means that excystation is delayed. Dis-solution of the Cyst-membrane takes place over a small area only, and probably caused by the results of external agencies, e.g - Pancreatic Juice or Bacterial ferments.

iii. The Entamoeba begins to emerge. A kind of ectoplastic pseudopodia is thrust out. The whole of the protoplasm gradually flows out of the Cyst - average time about ten mins. In every instance, the entire protoplasm leaves the Cyst as a single Entamoeba. After the Entamoeba has come out completely, the Cyst-membrane left behind appears as a single-contoured, very delicate, usually spherical ring - by careful focussing can the break be detected in the wall.

iv. There is absolutely no indication of division while still inside the Cyst. No division into four amoebulae therefore takes place as a rule, within the Cyst.

v. Excystation has been observed equally to apply to Amoebae with no Chromidial-blocks, and to Amoebae having these. Hence, this is no determination of maturity or ripeness of the organism.

vi. By subculture of active excystation forms on blood-agar tubes and incubation at 37° C, for 18 -20 hours, small & moderate-sized Amoebae Histolytica have been seen, and some with redblood-cells within them. Multiplication is exceedingly doubtful, but probably division of some of the originally-encysted forms into four,may have

occurred - but this is exceedingly doubtful. In spite of all efforts, the growth of bacteria were excessive. After a further 24 hrs, only one or two Entamoebae were still alive, but in a moribund state.

vii. Cysts were kept alive in very slowly running water for 15 days.

viii. Conclusions.

1. "We are strongly of opinion that this is the normal method of excystation".

2. Successful cultivation of Entamoebae from excystation - stocks are exceedingly doubtful.

3. Water contaminated with Cyst-containing faeces, may remain a source of infection for a considerable period.

## S U M M A R Y

1. Reproduction in Ent.Histolytica occurs either Asexually by binary fission, or by budding. The Nuclear chromogen is dispersed in protoplasm, and young forms containing parts of it, bud off. This is perhaps a degenerative form described by Schaudinn. There is a Sexual Type too, but denied by some Authors (Rogers & Wenyon), and upheld by Brown & Castellani, who describe Sporogony occurring under favourable circumstances in contrast to what obtains in E.Coli, which develops spores in unfavourable conditions.

2. In E.Coli, although 8-nucleated forms without definite evidence of Encystment are produced by divisions (Asexual); yet there is a definite Sexual stage, after reconstitution & nuclear changes by formation of a Zygote-nucleus, which divides into 8 smaller nuclei and Amoebulae. Hartmann & Whitmore have modified Schaudinn's original view that no Zygosis takes place in the Cyst; they believe that eight amoebulae result, which, on escaping from the Cyst, conjugate in pairs and form the Zygote from which the vegetative forms arise. Schaudinn & Hartmann found that a small nucleus may be budded off, and this may divide as well. This budding-off they consider a kind of sexual process, copulation of the two nuclei occurring.

3. The process of Excystation has been studied by Penfold, Woodcock & Drew. The results were only successful for Ent.Histolytica & Ent.Minuta - a further point in the identification of the two into one - the E.Histolytica. The resulting organism appeared to leave the cell as a Single Amoeba.

## SUMMARY Continued.

4. Vegetative Conjugation has been announced by Craig and recognised by Rogers. It has not been thoroughly investigated.

5. Lastly, some appear to work out the life-history of E.Tetragena as a separate organism.
Rogers & Castellani both describe life-histories; Phillips, Fantham, Wenyon and other, maintain that it is a stage in life-history of E.Histolytica

### The Life-History of Doubtful Species.

1. E.Tropicalis- Lesage (1908) *

* Lesage - "Bulletin de la Societe de Pathol. Exotique, Vol i, No.2, Paris. (E.Tropicalis).

It is probably identical with E.Coli. It is non-Pathogenic. It resembles E.Coli in having a nucleus which contains much chromatin, and by becoming encysted and being non-Pathogenic.
It differs in having a clearly visible ectoplasm, by the small size of its Cysts,(the variation-forms described by Wenyon), and the nucleus breaks up into a number of nuclei varying from 3 -13.
It shows Binary Fission and spore-formation.
This organism was again described by Walker in 1908 as **E.Hominis.**
Lesage considers that this organism contaminated Musgrave's & Clegg's experimental work with Non-Pathogenic Amoeba.

2. E.Phagocytoides - Gauducheau* 1908.

* Gauducheau, Bulletin de la Soc. de Pathol.Exotique, 1909.

It shows close affinities to E.Histolytica.
It was discovered in a case of Dysentery in Indo-China. It is very small - 2-15 μ in diameter- very mobile, and has a well-developed Ectoplasm.
It can however, be readily cultivated in Symbiosis with E.Typhosus.

3. E.Nipponica, Koidzumi*, 1909.

*Koidzumi, Centralbl.fur Bakt. (E.Nipponica), 1909.

It was disvovered in Japan. Said to belong either to E.Coli or E.Histolytica (Rogers). When it occurs in cases of Dysentery, it is associated with E.Histolytica, which it resembles in size, and in the marked difference between ecto & endoplasm. It differs in that the pseudopodia are never spinose; the endoplasm is vacuolated and more granular than E.Histolytica; the nucleus is well-defined and rich in Chromatin; and reproduction is by fission, schizogony and sporogony.
It is therefore reported on by Darling and Ornstein as a form of E.Tetragena.

4. Ent.Hartmanni, Prowazek* 1912.

*Prowazek, Arch.f.Protist, 1912.

Found in Man in Savaii. It is 4- 13 μ in diameter; nucleus vesicular, 2- 3 μ; Cysts small, quadrinucleate, characterised by a thin, bacteria-like arrangement of Chromidia.

5. Ent Minuta, Elmassian* 1909

* Elmassian, Centralbl.f.Bakt. ( E.Minuta, 1909.)

Discovered in a case of Chromic Dysentery in

Ent.Minuta, Elmassian (Continued.)

South America. Resembles E.Tetragena; but it is much smaller, rarely exceeding 14 μ in diameter. No differentiation between ecto- & endoplasm and the nucleus in fresh preparations is invisible; but when stained, shows rich Chromatin. Encysted forms have 4 nuclei.

6. E.Undulans, Castellani* (1905)

Obtained in faeces from Chronic diarrhoeal cases in Ceylon, together with Cercomonas & Trichomonas. Wenyon for this very reason considers it a degenerated form of Trichomonas It had no flagellae, but possessed undulating membrane, and straight pseudopodia, which were rapidly emitted and retracted; only one pseudopodium being extruded at one time.(cf.Section of Etiology of Amoebic Dysentery, Thesis).
Castellani himself states that he regarded this at one time as a developmental stage of Cercomonas hominis. The cytoplasm was not differentiated into ecto- and endoplasm; and there was a non-contractile vacuole usually present. The cytoplasm was finely granular, and often contained bacteria.

* Castellani, Centralbl.f.Bakt, 1905.

7. Castellania, Castellani.

Cf.Section on Etiology of Amoebic Dysentery - a full description has been given.

8. Granular Amoebae in Urine. - cf. P. 110.

These have been described by Jürgens & others notably Posner, Kartulis, & Wijnhoff.
The matter has been dealt with under ~~xx~~ Amoebic Hepatitis of the Jaundice- Diarrhoeal & Pseudo-Sprue Type ( Type XI), & in Cystitis as a Complication & Sequaela of Amoebic Dysentery, Thesis.
These bodies were found in the sanguineous Urine of patients -Amoeburia.

9. E.Buccalis, Prowazek, 1904.

This has been described in connection with dental Caries & Endamoebic Tonsillitis. It possesses a distinct ectoplasm & pseudopodia. The nucleus is large, subcentral in position, poor in Chromatin. Development is by binary fission, & a spore-formation somewhat like E.Histolytica. (Castellani). A full description of the Etiology of Pyorrhoea Alveolaris, will be found in the Section of the Thesis* on "Gingivitis & Pyorrhoea as Complications of Amoebic Dysentery.

* cf. P. 59.

For a fuller description of "Doubtful Species", cf.Castellani & Chalmers, Trop.Med., 1913, pp, 274- 276 & Bibliography, p.279.

## SECTION VI. THE TREATMENT OF AMOEBIC DYSENTERY

### & A CONSIDERATION OF

### THE CARRIER-PROBLEM.

The History of Ipecacuanha and Emetin.

"Maclean, Diseases of Tropical Climates, 1886.

* The first mention of Emetin as a substitute for Ipecacuanha was in 1813, when Magendie & Pelitier recommended its use.

* Vedder, " An experimental Study of the Action of Ipecac. on Amoebae", Far Eastern Assoc. Trop. Med. Trans, 2nd Bienn. Congress held at Hong-Kong, 1912, pp. 97-91 &.

The treatment of Amoebic Dysentery falls under three main heads:-

I. The treatment of Acute Dysentery.

II. Of Chronic Dysentery.

III. The Carrier Problem.

The Treatment of Acute Dysentery.

1. Treatment by Drugs.

Ipecacuanha is the drug par excellence, which is historically associated with the treatment of the Disease, though for many years it was under a cloud. That this very effectual remedy passed from the ken of medicine, was most probably due to the difficulty of Diagnosing the difference between Amoebic & Bacillary Dysentery. Ipecacuanha or Brazillian Root was first brought to Europe in 1658 by Pisc and given in the form of an infusion or decoction. It appears to have been used in India as early as 1680, but to here again largely fallen out of use there. The same fate seems to have overtaken the drug in Europe, for " After having been sold to Louis XIV as a secret remedy, and looked on as a specific for Dysentery (Rogers in Dysenteries " History of our knowledge" pp. 27- ) it was revived by Annesley in India, and in 1835 Twining in India advocated its use, though in small doses; but it was only in 1848 that Parkes advocated it in doses of 30-60 grs. at a time, and this practice was further emphasised by Docker in 1858. In 1886, W.C.Maclean & Norman Chevers, recognised its influence in full doses in preventing serious hepatic complications ending in Liver-Abscess. Maclean writes as follows:- " How this remedy, almost deserving the name of a specific, came to be superseded by Calomel & Opium in the treatment of Dysentery in the East, is one of the most curious questions of Tropical Medicine". (Rogers) After this it again fell largely out of use and was supplanted by Saline Treatment. Attention was then paid to the Alkaloids. These have been isolated by Pelletier in 1817 under the name Emetin; this was really a mixture of 3 Alkaloids: Emetin, Cephaelin & Psychotrine.* In 1829 Bardsley of Manchester pointed out the value of Emetin in Dysentery and Chronic Diarrhoea; itwas forgotten, however, until Tull-Walsh in 1891, used a compound of Emetin with Mercuric-Iodide " under its use in 22 cases, only one patient died and only one did not improve. The average duration of the dysenteric stools in his cases was 4.9 days, while controlled cases lasted 5.7days".(cf. Phillips, Amoebiasis, p. 61).

Emetin again was forgotten until Vedder's investigations in 1910. A full account of Vedder's work has been given by Capt. S.R.Douglas, I.M.S., in B.M.J, Nov. 16, 1913, p. 1082 " Treatment". In June 1912 and in the following months of that year, Rogers published several papers on Amoebic Dysentery & its complications treated with sub-

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* Vedder," An experimental Study of the Action of Ipecac. on Amoebae", Far Eastern Assoc.Trop.Med.Trans, 2nd.Bienn.Congress held at Hong-Kong, 1912, pp. 87-91. &,
"Origin & Present Status of the Emetin Treatment of Amoebic Dysentery", Jl.Amer.Med.Assoc. 1914, Vol.62, pp. 501-506.

subcutaneous injections of the soluble salts of Emetin. Rogers in the first paper mentions that Vedder found that cultures of Amoebae were rapidly killed by solutions of Emetin Salts, even in dilutions of 1 in 100,000. To quote from Douglas' paper (B.M.J. Nov.15/ 1913) "Vedder having shown that solutions of fluid extract of Ipecacuanha had no specific bactericidal power on Dysentery Bacilli then proceeded to investigate if Amoebae were affected by this drug. As cultures of pathogenic amoebae are unobtainable, he used cultures isolated from tap-water, or the stools of a healthy man, and found that fluid extract of Ipecac. had a very high amoebaecidal action which varied markedly with the different extracts used .... he found that Emetin even in the strengths of 1 in 100,000 sterilised his cultures and Cephaline was equally amoebaecidal; and the Ipecac. sine Emetina of commerce had no deleterious effect on the cultures. The physiological effects on dogs showed that Emetin even in doses of 0.5 grs, had no emetic or depressant effect; Cephalein in doses of 0.1 gr, produced violent vomiting and marked depression. He concluded by saying ' If further experiments show that Emetin has no emetic or depressant action and a constantly high amoebaecidal action, we have a drug which may prove as active an agent against Amoebic Dysentery as Quinine is against Malaria' .... Rogers by his application of these principles has found a simple method of administering the drug, and that the differential diagnosis between Amoebic & Bacillary Dysentery, can be readily and is most easily made .... Whether this treatment is a radical one, as is claimed by Rogers, can only be solved by time and further careful experiments on animals."

Such then is the detail of this drug, and its history throughout coincides with the Non-differentiation between the two main types of Dysentery. It has however, finally come to stay, and the glamour of its worth may perhaps be most nearly akin to Ehrlich's happy phrase - "Therapia Magna Sterilisans" Amoebae. But as in all Protozoal infections in which a specific drug is known, prolonged use is necessary to effect a complete sterilisation of the body from the parasite, a result seldom achieved. During however, the past year, the curative action of Emetin Hydrochloride has indeed been put to severe test. Emetin itself kills only Amoebae in the vegetative stage - never their cysts or Tetragena stage, and it is from the Cysts that not only does relapse take place, but the parasitisation of the healthy occurs.

In Walker & Sellard's experiments on Convicts, Amoebae when administered were given in capsules containing Magnesium Oxide, to neutralise the gastric HCl. Cysts on the other hand do not require precautionary measures. One cannot but feel that Emetin itself acts rather as a charm than a specific drug, for in this one crucial test it fails. Moreover, it has been claimed that prolonged doses of Emetin render Amoebae Emetin-proof, and that the succeeding generations are more resistant to it. This is Mc.Donaugh's view of Salvarsan-sterilisation, and by his discovery of a definite Spore-stage and Gametocytic cycle of the Spirocheta Pallida or as he prefers it -

the "Lymphocytozoon", he has precisely brought this question into the field of Practical Therapeutics in which the question is raised to what extent Salvarsan kills the Spores and renders Arsenic-proof, the generations that follow, as evidenced by the increase of Cerebro-Spinal Syphilis as distinct from Systemic Syphilis.
I have been able, as member of the"West London Medico-Chirugical Society", to follow a lecture given by Mc.Donaugh there in middle of 1913. when I was able to see his lantern-slides and hear the results of his own investigations. What I than heard and saw, has impressed me considerably in accepting any dogmatic assertion about any drug, however "specific" that may be. The further relative proof lies in Malaria and its Quinine specific, especially in the treatment of the Malignant Infection. And what has all along appeared probable has now been greatly emphasised by Dobell in his recent work in connection with the Treatment of the Carriers. Emetin therefore, judged by the supreme standard of Complete Sterilisation, is found wanting; as a prophylactic drug, it stands the test of years, more especially in warding off Liver-Abscess and Hepatitis.
This can well be understood, because it is the active Entamoebae which are carried to the Liver, and such forms are readily enough destroyed, both in the Bowel and elsewhere.
Happily even this bar to complete sterilisation appears to have been passed, but it is too recent yet to be fully accepted, although the work in this direction is full of promise - that is the treatment by a double-Salt. In two of Dobell's cases in which two full courses of Emetin Hydrochloride completely failed to cure, had been completely cured by a single course of the Double Iodide of Bismuth & Emetin. Fuller Reference will be made again to Dobell's work in the Treatment of the Carrier-Problem. It was Tull-Walsh who first, in 1891 treated cases with Emetin plus Mercuric Iodide, with good results.
The results of Emetin alone has been tested now throughout the World, and there is testimony of all Writers on the efficacy of the salt to cut short an incipient Amoebic attack, to hasten convalescence and abolish the possibility of Liver-Abscess and Hepatitis. It has been used in Fulminant cases with remarkable results. In my hands the same has been the case. But whether this will always be held to afford a permanent cure, only time and labour will solve. Rogers' published papers and his work "on Dysentery", afford most optimistic reading (cf."60 cases of Amoebic Dysentery illustrating the Treatment by Ipecac. & Emetin respectively" - Ind.Med.Gaz.1912, Vol.47,pp.421-427; and "The Emetin & other Treatment of Amoebic Dysentery & Liver-Abscess" - Ind.Med.Gaz.1914,Vol.49, pp.85-88).

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Treatment of Acute Dysentery - continued -

E.B.Vedder, in Jrnl.Amer.Med.Assocn.1914, i, 501, publishes an interesting review of the present position of the Emetin treatment. He analyses 110 cases of Amoebic Dysentery so treated by different workers, concluding that any patient who is not moribund can be cured. As it is irritating, he prefers to give one-third gr. hypodermically, three times daily.

Jerome Wagner, in Ind.Med.Gaz.1914, 85., records some very interesting cases in which E.Histolytica were found, and the ulcers in the Rectum watched with the Protoscope. ½ gr.doses were given daily for one week. In no case were Amoebae found after 24 hrs, by which time the daily stools had been reduced from 15-20 to 1-2, which became formed in 3 days. At the end of the week, the protoscope showed little signs of ulcers remaining, however numerous they had been at first. There was no vomiting or nausea. "The immediate action of the drug must be described as nothing short of marvellous or gratifying".

L.J.Rosenthal, in Medl.Rec.1914; i; 190, obtained similar results in 9 cases, and after 2 or 3 injections, the Rectal ulcers showed signs of healing, and disappeared in a week or ten days.

M.L.Legane, in "Presse Med." 1914; 465, emphasises the value of a repitition of the dose after 10-15 days, so as to prevent relapse due to the Encysted Stage.

Roger Brooke, in the Philippines Jnl.Amer,Med, Assocn.1914; i; 1009, states that Quinine is a useful alternate remedy in place of Emetin in refractory cases of Dysentery. Its action is general rather than local. He advises Quin.Sulph. in doses of 20-30 grs.daily by the mouth, for a period of 6 days. Ten Chronic cases treated by this method, gave satisfactory results.

It is very interesting to note in such a work as W.C.Brown, 1910, the total absence of mention of Emetin in the Treatment of Dysentery, although he devotes 40 pages to Treatment. He however emphasises the value of Ipecacuanha.

THE DOSAGE

On account of its irritating effects, some recommend small doses repeatedly - one-third gr. t.d.s, subcutaneously. The dose should be kept up for 10 days.
In Adults Rogers recommends 1 gr.for 3 or 4 days, preferably in ½ gr.doses morning & evening." IN severe cases I frequently give a gr. at a time - (this being equivalent to 90 grs.Ipecac) & repeat it two or even three times daily, although this is not often necessary. Intravenously from ½ to 1 gr may also be given at a time with perfect safety in adults." (cf.Rogers'Dysenteries, p.129).

- continued -

THE DOSAGE and METHOD I employ is as follows:-

As soon as the case is diagnosed, the patient receives 1 gr.Emetin Hydrochloride (either B.W &Co or Parke Davis' preparation Tabloid or"Sterilised" Ampoules in solution). This is entered on his temperature Chart; I give it always deep into the muscle, and perhaps the best locality is deep into the outer side of the arm. I have also injected it into the Deltoid, but I find that often there is considerable bruising of that muscle. Subcutaneous injections I have now given up, as they always cause considerable pain and swelling. Even Intramuscular injections are not altogether free from pain, though this is much less than in the Subcutaneous Method. The pain is much relieved by hot-water compress.
I have not seen a sterile abscess form, however.
This injection is followed by an ounce of Castor-Oil, or a big dose of Saline made up as follows:-

R/

| | | |
|---|---|---|
| Mag.Sulph. ) | aa | 60 grs. |
| Soda Sulph ) | | |
| Soda Bicarb..... | xv | grs. |
| Aquam ad ....1 oz. | | |

This mixture is given every 3 hrs, till full purgation starts, when it is given thrice daily. The patient next morning receives 1 gr.more (Emetin) and the salts are continued thrice daily for that day. The 2nd. night, Calomel grs.2 are given followed by the salts next morning, after which the 3rd.grain of Emetin is injected. The Salts are only given once more that evening, and on the 4th.day another grain Emetin & Salts twice daily ordered. This is kept up till that evening, when the Salts are given once daily from the 5th.morning, with another grain Emetin.
After 5 grs.Emetin, I stop, but continue with Salines once daily for a week longer.
In the Acute cases I keep on the Emetin until 7 grs. are given, and then after a week, 2 more injections of a grain each. In all cases I give 2 more grs. on the 10th & 11th.days,followed by Salines. The Saline Treatment I fully recommend for two chief reasons -

i. To keep the bowels thoroughly flushed and to wash out the dead Amoebae, &
ii. To avoid any trouble with "Intestinal absorption".

I do not give any Ipecac.treatment besides this, and unless the patient is markedly constipated, I do not give Enemas.

It is interesting to note that Quinine Irrigations are recommended by Veddar. With so powerful a drug as Emetin, I have not come upon a case in which I had to institute any other treatment.

After the 5th.day, I give the patient large doses of Bismuth, in the following prescription:-

- continued -

THE DOSAGE and METHOD I employ - continued.

R/
Bism.Salicyl) aa grs.xv
Soda Bicarm.)
Ol Menth Pip. m.ii
Gum Acac )
or ) q.s.
Mucilage )
Aq.Chloroformi ad 1 oz.
t. d. s.

- OR -

R/
Bismuth Carb) aa grs.x
Soda Bicarb )
Salol ..... grs x
Ol.Menth Pip ..... m.ii
Mucilage ..... q.s
Aq.Aurantic,ad.... 1 oz.
t. d. s.

This prescription is continued from the 5th to 10th day, after which the Salines are again instituted, and the Bismuth mixture held over. This mixture I have found very useful in combating the Dyspepsia which so often follows.

Finally, after the 11th.day, the patient is put upon an Iron & Arsenic tonic as follows:-

R/
Ferri et Quin.Citras grs v
Liq.Arsenii Hydrochlor. m ii
Acid Hydrochlor.dil m v
Aquam ad 1 oz.
t. d. s

- OR -

R/
Ferri et Ammon.Citr. grs v
Liq.Arsenicalis m ii
Sod.Bicarb. grs x
Aquam ad 1 oz.
t. d. s.

I do not recommend Iron during the treatment of the Acute stage while the patient has Diarrhoea ( & the same applies to Bismuth) because the character of the stools are altered and are so profoundly black that little information can be obtained about the progress of the case. Moreover, the Iron particles are rather irritating to the sore bowel-lesions which have not as yet healed, and I therefore recommend this in the Convalescent stage. While the Iron Tonic is being kept up, the patient should take Salts from time to time, or perhaps " Laximel" may be given - a disguised preparation of Castor Oil. In lieu of this, the old-fashioned remedy of Sweet Oil should be tried. I have had a good deal of experience now in the treatment of Constipation by Sweet Oil given thrice daily in ½ - 1 oz. doses, and it is exceedingly useful. Being bland, it occassions

- continued -

ADJUVANTS to EMETIN TREATMENT - cont.

are prepared from 2 drachms of bruised root-bark
i. by soaking it in 6 ozs. of cold water for 24 hrs
ii. by infusing the root-bark after exhaustion in this way in 6 ozs. of boiling water for 2 hrs, &
iii. by afterwards boiling it for ½ an hour in a similar quantity of water. The 3 solutions are given in their proper order in ½ oz. doses on 3 following days, the whole of one solution being taken each day. During the administration of the remedy, no food except soup, arrowroot, etc, is allowed." (cf. Brown, Amoebic Dysentery, p.234). Ipecacuanha sine Emetina is useless; a fit name for it should be Emasculated Ipecac. Ipecac. can only act by virtue of its chief alkaloid -Emetin.

ENEMATA.

The chief Enemata that have been used are

1. Quinine, 1 in 1000 Quinine Sulph or Bi-hydroch: and this has been recommended by Haines in China; Vedder & others. Phillips however states that it is useless against Cysts, though Quinine has undoubted anti-amoebic properties.
2. Silver Nitrate,* 10 - 20 grs. to the ounce. Recently there is a marked tendency to use Colloidal preparations of Silver - Collosal Argentum (Crookes), - which is non-toxic. Other preparations are Argyrol (25%); Collargol 1 per cent; Protargol (15-20%); Albargin (½-1%). But as Emetin has a distinct healing action on Rectal Dysenteric Ulcers, there is no indication for the use of any such preparations.
3. Kerosene Oil. American writers have advised this in its pure state 1 pint to be given at a time. G.M.Niles in Amer. Jnl.Med.Sci.1914, Oct., 526 advises 1 pint for 3 or 4 days & to be retained for 30-40 minutes.
4. "Enema Kartulis". It consists essentially of an emulsion of Iodoform & Tannic Acid. An appreciation will be found in the B.M.J. Nov.12, 1910, p.1522 & footnote. It appears to be of use in early cases but of no use in old chronic & gangrenous cases. (Ruffer & Willmore). The same authors in the same paper find that 0.5% Pararosaniline Acetate is absolutely useless," & in no case was it absorbed sufficiently to tinge the urine". The idea of the use of this drug was that it might benefit during its absorption.
5. Tannin. This was very highly praised by Kartulis in acute cases. A solution of 0.5% kills Amoebae in 2 minutes, and this strength is easily borne in acute cases. It should be given very slowly, and be retained at least 10 minutes. Up to 2 litres may be given. It is sometimes painful. 4 or 5 injections are sufficient.
Andels recommends the following formula, modified by the addition of Iodoform, as follows:-

* " We particularly dislike the much-vaunted injections of Silver Nitrate. In any case we use lavage, as a rule only in cases of post-dysenteric constipation." Willmore & Savage. B.M.J.Nov.15, 1913 p.1286.

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ADJUVANTS to EMETIN TREATMENT.- cont.

Andels' Formula.

℞

| | | |
|---|---|---|
| Tannic Acid | .... | 4.00 grams. |
| Iodoform | .... | 3.00 " |
| Sod.Chlor. | .... | 6.00 " |
| Starch | .... | 25.00 " |
| Tinct.Opii | .... | 3.00 " |
| Aq.Dest. | ... | 1000.00 cc. |

Sig. This is sufficient for two Enemata.

Kartulis by further trials found that rapid cure is brought about also by the hypodermic use of Tannin; he uses a 10% soln, Merck's Tannic Acid in distilled water, which is sterilised and kept in a dark place; the dose is, 2.00 cc, which is given either subcutaneously or into the Gluteal muscles. One to two injections in most cases cures the patient; he has treated more than 40 cases in this way. Phillips summarises these cases as follows:-
"In only one was there a relapse after 14 days; one died, a Chronic case with Liver-Abscess, partly healed.
It seems to have been as efficient in Kartulis' hands as the Emetin treatment usually is."
(cf.Phillips, Amoebiasis, p.65).
Tannalbin & Tannigen, are preparations which may be used. (cf.The Extra Pharmacopoeia,Martindale & Westcott,14th.edn.p.82).

## THE TREATMENT by OTHER DRUGS

Bismuth Salts. Deeks in The Jrnl.Amer.Med.Assoc. 1913, vol 60,No.1,pp.38-42, has drawn attention to the value of Bismuth treatment in Dysentery due to Ent.Histolytica. He gives 3 drachms of Bismuth Subnitrate in a glass of water every 3 hrs in conjunction with Saline Enemata. The treatment must be prolonged, about 10 days. In cases so treated there were only 4 cases of Bismuth poisoning; in those that recovered the only region in which Amoebae could be demonstrated was the Appendix. Most Authors however, believe that relapses occur. E.F.Haines, in the Boston Med.& Surg.Jrnl.1914,ii,816, has found that this gives poor results in Acute cases, while Chronic cases go from bad to worse, and in one instance he thinks fatal perforation was caused by a coating of Bismuth bottling up the Amoebae in the depths of an ulcer; he has never seen any form of Bismuth cure a case of Amoebic Dysentery. Sandwith, however, recommends its continued use with a view to getting rid of the Cysts. I have found Bismuth Salts especially the Salicylate useful in the convalescent period after an Acute Dysenteric attack, which has recovered under Emetin.

Calomel. This has been recommended in small divided doses of 1/3rd.gr.every 2 hrs until free purgation is established. Annesley and the older Writers used to use this drug in the enormous doses of 20 or 30 grs, and that is how it fell into disrepute. It may have a direct action on Cysts as experiment shows that it kills them

- continued -

## THE TREATMENT by OTHER DRUGS . cont.

outside the body. I use the drug in order to thoroughly clear out the bowels, stimulate the Liver, & get rid of dead Amoebae from the Intestines, in other words - as a Cholagogue.

Salvarsan. Winn in a report of 12 cases published in Proc.Canal Zone Med.Assoc., 1912, Vol.5, Pt.I. pp. 7-10.; found that in all cases except 1 the amoebae disappeared in 24-72 hrs.after; the number of stool diminished & altered in character & there was marked improvement. He however does not mention if the result was permanent or that it was fatal to Cysts. Undoubtedly in so-called Spirochaetal Dysentery it may have good **resukts**. Emetin is surely the simpler & most potent agent known & should be used in preference.

Tatar Emetic. Tartar Emetic has been recently recommended for Amoebiasis, and been used in Brazil I have had no experience of its use in Amoebiasis, but I have used it with success in Oriental Sore. There is however **Castellani's** Formula which I quote from his paper published in B.M.J. Oct.21, 1916, p552

1. Oral Administration:-

℞

| | |
|---|---|
| Tartar Emetic | grj. |
| Sod.Bicarb | grs xv. |
| Sod.Salicyl. | grs x |
| Pot.Iodid | grs 60 |
| Glycerin | drs ij. |
| Aq. ad | ozs j. |

Sig.

"This dose is given diluted in 3 or 4 ozs.water thrice daily to adults and young persons above 16 yrs. ½ doses are given to children from 8-14 yrs.; & 1/3rd. or less to younger children . To European patients I generally give half the doses mentioned." (Castellani)

2. Intramuscular Injections.

℞

| | |
|---|---|
| Tartar Emetic | grs viij. |
| Acid Carbol | m. x |
| Glycerin | 3. iij. |
| Aq.dest ad | ozs j. |

Sig.

½ - 1 c.cm. every other day in the gluteal muscles.

This preparation made alkaline by adding to the above gr1/3rd.Sod. Bicarb. does not produce different results than the acid preparation, & is equally painful.

3. Both Methods may be combined.

## OTHER INDIGENOUS DRUGS.

Uzara. **Waldow** gives a good account of this in the Cameroons. 30-60 drops t.d.s. of its solution. (Phillips Amoebiasis, p.66.

Kho-sam. The dried seeds of Brucea Sumatrana & called by the Japanese "Kho-sam

- continued -

## OTHER INDIGENOUS DRUGS.

called by the Japanese "Kho-sam". Brown gives a good account of it in his Amoebic Dysentery, p.236. and quotes MOUGEOT, of Saigon, who treated more than 870 cases (879), and found that it was successful in more than 90%- i.e. in 871. The alkaloid is contained in the kernel - Chosamine. Compressed tablets are in the market under the name Elkossam, each of which represents one kernel, & 5 or 6 tablets are taken daily. Phillips quotes GAILLARD & BRUMPT 's work * and states that the drug had good effects.

* Gaillard & Brumpt - "Un Cas de Dysenterie Amibienne Autochotone" Bull.et Mem. Soc.Med des Hopit.de Paris, 1912, 3e.Ser.,Vol.28 No.36, pp.736-741.

Simaruba. This is the root-bark of the Mountain Damson, and is a popular remedy in Java & The East Indies. The usual method of administration is to soak ½ oz. of root-bark in a pint of boiling water for 15 mins, the whole of the infusion being taken in doses of 2 or 3 ozs at short intervals within 24 hours. It has a bitter & slightly astringent taste, and its anti-Dysenteric action is said to be sometimes very remarkable. It may be combined with Pomegranite and the following prescription is given by Phillips:-

℞

| | | |
|---|---|---|
| Simaruba Bark<br>Pomegranite Fruit rind<br>Gum Arabic | aa | 15.00 grams |
| Water | | 1 litre. |

Sig.Boil down to ½ litre, and the dose 30.00 cc 3 or 4 times daily

Bael Fruit. This flourishes abundantly in Bengal, and it has been prized throughout the Tropics as an anti-Dysenteric, anti-Scorbutic remedy, and is often used iced for its great thirst-quenching properties. The unripe fruit is generally used. Its stringy contents are mashed with water and strained through linen, and then cold water is added to fill a large jug. This is iced and sugar added, and this infusion or sherbet is drunk ad lib from 30 -60 ozs in the 24 hours.

Chaparro Amargosa.* A good account is published in the Medical Annual 1916, p.10. Nixon*has employed it in 12 cases of Amoebic Dysentery. Clinically it resulted in prompt improvement in the stools which became normal in a couple of days. He used it as follows:- " After preliminary administration of Mag.Sulph. 6-8 ozs of the infusion are given 30 mins. before each meal,and rectal enemata of 500 to 2,000 cc twice daily in the knee-chest position. The treatment is continued for a couple of weeks after symptoms subside. Experiments show that the drug even in weak solutions has a special affinity for the protoplasm of Ent.Histolytica. The action seems a specific one as the drug is not curative of other parasitic infections. Such a dilution as 1- 1,000,000 acts on the Amoebae in vitro in 2 mins.

*It belongs to the Simarubaceoe, and its botanical name is, Castela Nicholsoni (Hook).

* Nixon, Amer.Jrnl.Trop. Dis. vol.ii,No.9.

## SYNTHETIC INTERNAL GERMICIDES.

Brown gives a series of these in his Amoebic Dysentery pp.238-245. Amongst these may be mentioned Benzosol, Benzoyl-Acetyl-Peroxide; Salol; & Acetozone. A detailed description is given by Brown.

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2. Treatment by Diet.

In the earliest stages of an Acute attack food must be reduced to a minimum, and the diet should be fluid, at any rate for the 1st. 48 hours. Probably the best is Albumin Water. Milk should not be given - it often aggravates the symptoms and produces a good deal of flatulence. If milk is given, it should be Citrated & diluted. Light Chicken soup is often useful. There is, however, one preparation of milk Yaghurt, advocated by most Writers and which has been further Commended by Willmore & Savage in their paper on the Treatment of Epidemic Bacillary Dysentery -Nov.15, 1913, p.1285 -note. They state "Yaghurt, was always taken with the greatest avidity, being in one form or another, the staple diet of many Oriental peoples; while examination of the stools showed it not to be completely digested, yet it had an undoubted effect in arresting the putrefaction of the Intestinal contents, and never gave rise to the Meteorism and colics which were so often seen in the days of the plain milk diet,.... Yaghurt must be prepared with the greatest care. It has been our practice to buy in Suez at the commencement of the pilgrimage season several samples of Leben Zibad, and to innoculate them into sterilised milk. That which gave the softest and most homogenous curd was then plated out on Mac Conkey or Lactose Cochineal Agar, and pure cultures obtained of a large Lactic Acid-producing Baccillus and a Long Streptococcus (? S.Lebensis). These were then innoculated into Sterilised Milk ("Natura"brand) - the Australian condensed milk is unsuitable - and each batch of Yaghurt, prepared in covered sterilised jars in an incubator at 37° C. was innoculated with a flamed spoon from the preceding one. The curdled milk prepared from the various so-called "Lactic Acid Tablets" on the market, should, in our opinion, never be used." (Willmore & Savage).

The great point in all foods is that they be taken very slowly and warm - not hot, otherwise they are very apt to cause lienteric diarrhoea and griping. As the stools clear up, a gradual return to solid food should be instituted - or, as the late Professor Wylie used to teach in Edinburgh " The patient be made to gradually ascend the 'ladder of diet' - roast beef & Potatoes being on the topmost rung."
Solid food can be commenced about the 4th.day of treatment.

II. The Treatment of Chronic Amoebic Dysentery.

There is perhaps, no more difficult subject to write upon than the Treatment of a Chronic relapsing Dysentery. In the pre-Emetin days, there was practically only one type of thing to do, and that was irrigation through an appendicostomy-opening, and if that failed - the short-circuting of Ileum to Rectum or Sigmoid. But this in itself was pretty useless, as there are numerous ulcers often situated in the "Sigmo-Rectal Pylorus" & Rectum, and unless these were cured, the constant pain & tendency to defecation were always present.

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## Treatment of Chronic Dysentery. (cont.)

Now that Emetin has been introduced and widely * accepted, there is held to be almost no class of case who will not benefit from its use. To these measures may be added the use of Enemas. "Previously Ipecacuanha had given uncertain results and Lynch had performed Appendicostomies in 100 cases with ultimate success from irrigations of the bowel, the appendicostomy wound not being closed on the average in less than 2 years. The results now obtained with Emetin appears to show that the day of this operation in Amoebic Dysentery is over." (cf. The Medl. Annl. 1915, p.106 - "Amoebiasis" by Sir Leonard Rogers). Rogers in his own book on Dysentery says - " I have long been on the look out for suitable cases of Dysentery in which to try appendicostomy, but have found that Chronic Amoebic cases generally do so well on continued full doses of Ipecac. and Calcium permanganate bowel wash, and are so rapidly cured by Emetin injections, that I have not yet met with an instance in which I felt justified in recommending surgical procedures. Moreover, cases have been recently recorded in which after the complete failure of prolonged irrigation through an appendicostomy wound, persistence with Ipecac. has cured the patients, while with the Emetin treatment I feel sure that operative interference will rarely if ever, be necessary or admissible."

* The conclusion reached by W.L.Christie in the Treatment of Carriers in Sarawak, and published in B.M.J. July 18, 1914, p.118, are "that Emetin is most valuable in obstinate Latent cases, & essential in dangerous, acute, amoebic dysenteries, robbing them of their terrors".

In Keen's Surgery, 1908* Vol.IV.pp.1105-1108 a very good account of the Surgical indications are given; and the following is summarised from the Treatment.

* The date of the Work should be noted.

### Appendicostomy.

Appendicostomy is urged as an efficacious form of treatment for Chronic Dysentery.

i. for Local applications or irrigations. High irrigation of Quin. Soln. in warm Sterile Saline 1-1000, or hot soln. Copper Sulphate, 1-10,000 ( as hot as can be borne) - (Storck - New Orleans Medl & Surgl. Jrnl. Lxiv, 39). Massive injections are necessary.

ii. Relief of Chronic constipation (post-Dysenteric WITH auto-intoxication; and of the extension of diet so as to include any ordinary food.

iii. Great relief to distressing Neurasthenic symptoms.

iv. In a few cases of Acute Dysentery with threatening symptoms to save life.

v. In Chronic Dysentery <u>apparent</u> cures are often obtained, and at least, there is always very great improvement in the condition of the patient. A <u>FINAL</u> cure is much more likely to occur than under any other treatment. ( This was written in 1908 before the introduction of Emetin).

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vi. Daily irrigation becomes the only daily evacuation, and there is rest to the Bowel.

vii. The class of case which reaches fairly satisfactory state of improvement are those who show by **respense** to treatment by Rest, Diet, or Medication that their Large Intestines are not entirely crippled; and it is in these, that the irrigation from the Caecum to the outlet is most suitable.

Thomas, in "Amer.Jnl. Med. Sciences, Janry.1906, investigated the bionomic relation of Intestinal bacteria to Entamoebae from the view of definite Therapeutic results, and the germicidal effects of various solutions on organisms have been studied by numerous observers. Life-destruction of the Bacteriae is held to produce cessation of Amoebic activity on this theory. Thomas' investigations were on Symbiotic cultures of Amoebae, and reputed Spirillae of Asiatic Cholera:-

" 1. Boric Acid, Eucalyptus, Ichthyol & Oleum Cassia had little or no effect on either organisms.

2. Tannic Acid 1 in 100, Copper Sulphate 1 in 2000 Pot.Permanganate 1 in 4000; Quinine Bisulphate 1 in 1000, partially destroyed both Amoebic organisms & Spirillae.

3. Pot.Permang. 1 in 2000; Quin.Bisulph. 1 in 500 Nitrate of Silver 1 in 2000; Argyrol 1 in 500; Protargol 1 in 500; promptly killed the Spirillae, but failed to affect some of the Amoebae. All life was, nowever, destroyed by doubling the strength of these solutions.

4. Thymol 1 in 2,500, destroyed the Amoebae withou affecting the Spirilla." (cf.W.C.Brown - Amoebic Dysentery - p. 252).

*Chantemesse & Rodriguez. Bulletin, Soc.de Pathol.Exotique, ii, 1909.

Chantemesse & Rodriguez* in a case of Hemorrhagic Amoebic Dysentery, records complete recovery by use of douches of ½% Creosote. " In a similar case who had passed blood & mucus for 3 months and which had resisted treatment by Ipecac. & Argyrol injections, the symptoms yielded almost at once to injections of Creosote of a similar strength. Although the breath smelt of Creosote for some time the evidences of absorption were inconsiderable, and the urine remained unaffected." ( Brown, ibid, p. 253).

Intestinal Lavage with Enemata of medicinal substances may be employed, and perhaps Pot. Permang. or Quinine are amongst the two most useful. Emetin however, is our main stand-by. All Authors state that even after a single injection of 1 gr.Emetin in Chronic cases, perceptible improvement was noted and many hopeless cases are " cured " or at any rate their condition so vastly improved, that it is indeed reasonable to suppose that ultimate recovery may result, though perhaps a thickened and scarred gut remain.

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## III. The Treatment of the Carrier-Problem.

The successful treatment lies firstly in the recognition of cases, and secondly the erradication of the Cysts. Up till now even Emetin has given disappointing results concerning the treatment of "Cysts"; and therefore various drugs have been resorted to e.g. Bismuth, Quinine irrigations & the like, which might erradicate Tetragena Cysts. More recently the problem has at any rate been partly solved, which offers great hope for the future in solving allproblems as regards the treatment of Intestinal Amoebiasis, if not for other aspects of amoebic infection, by using a DOUBLE SALT of Emetin and Bismuth - EMETIN BISMUTHOUS IODIDE.

The first instance of the use of a double salt was by Tull-Walsh in 1891, when he combined Emetin with Mercuric Chloride, and obtained good results. The new salt was introduced by Du Mez 2 years ago and his paper was published in the Philippine Jrnl. of Science, Janry.1915, Vol.x, Sec.B. No.1,p.73. It is a brick-red powder, insoluble in water, or water acidulated with dilute Hydrochloric Acid, & stable in air. It contains, according to Du Mez 58% Iodine, 12% Bismuth, & 29% Emetin. Three grs. of the double-salt, containing about 1 gr. Emetin, is a good average daily dose, and should be given in cachets of 1 gr.each, until 36 grs.are taken. (Dobell). It is recommended that the dose should be given after a full meal, when the stomach-contents are acid, and on the whole the drug is well tolerated. If vomiting occurs, the best method is to continue with full doses when it is found that tolerance is established more quickly than if the drug is reduced. Tolerance is usually effected in 1 to 2 days. Clifford Dobell has published his results on a series of 205 cases in whom more than 800 examinations were made, in the B.M.J, Nov.4th,1916, 612-616. Dobells' results have been confirmed by reports*on isolated cases and some interim accounts* of further systematic trials. "There is no evidence to weaken the conviction from any source, that the chance of curing a Carrier with the double Iodide is very much greater than with Emetin given as any other Salt, or as Ipecac. The curative results have indeed, been far beyond the original expectation." B.M.J. Nov.4, 1916,626.

Acute Diarrhoea is often excited during the treatment but stops as soon as this is discontinued. Dobells' results may here be summarised. According to him the standard laid down of judging cases is, " That the shortest negative period after the end of treatment which can safely be regarded as indicating certain cure (that is, absence of Amoebae or Cysts), is hardly less than 3 weeks."

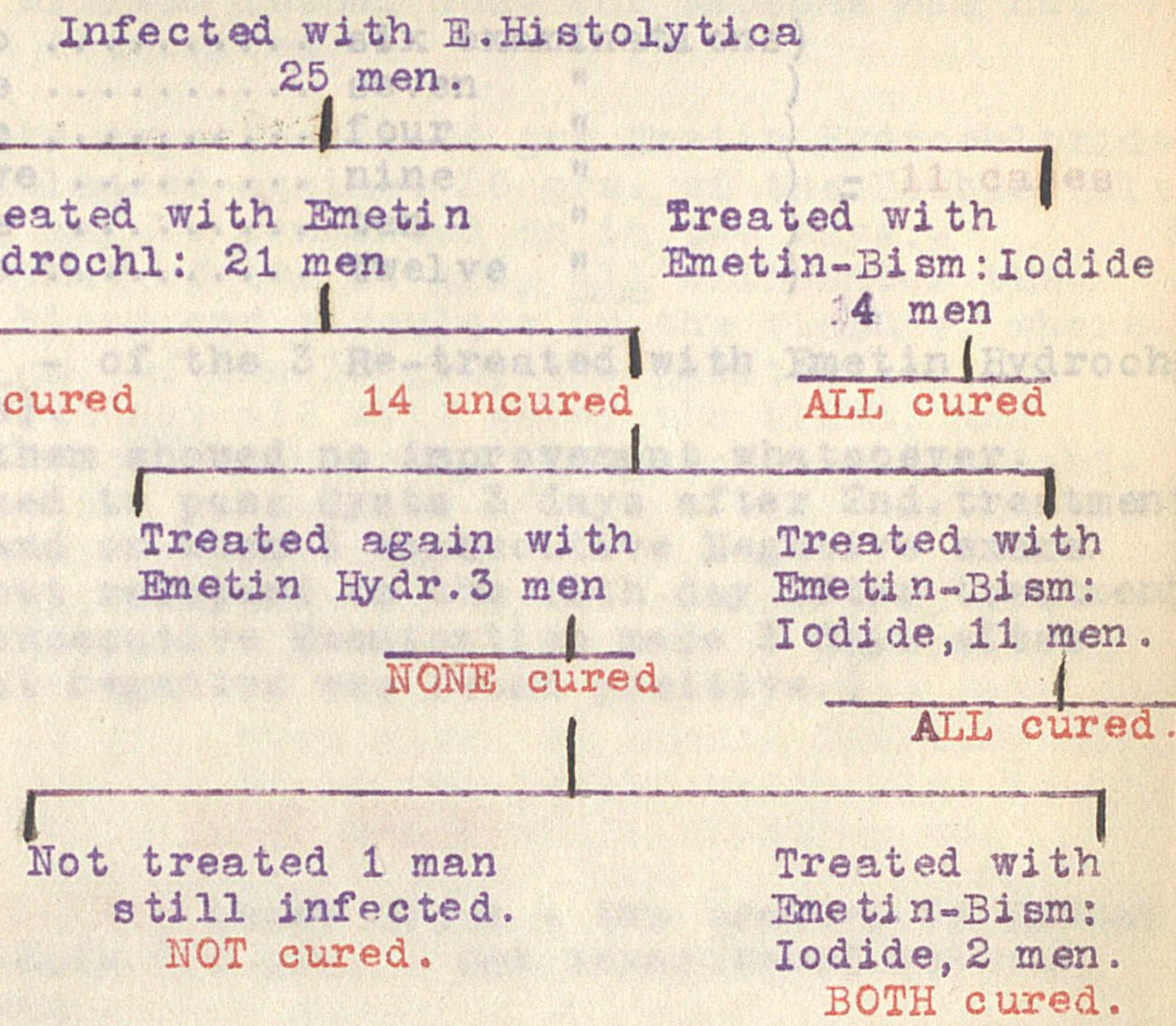
* Dale- Treatment of Carriers of Amoebic Dysentery,etc, Lancet July 29,1916.
Low & Dobell, 3 cases of Ent.Histolytica Infection treated with Emetin Bismuth Iodide,Lancet,Aug.19, 1916.

1. Results obtained:-

| | with Emetin Hyd: Hypoderm: | with Emetin Bismuthous Iodide. |
|---|---|---|
| TOTAL number of Treatments ... | 24 | 17 |
| Number of CERTAIN cures ... | 5 | 9 |
| Number of UNCERTAIN cures ... | 2 | 8 |
| Number of RELAPSES ... | 17 | 0 |

- continued -

2. Summary of Treatments.




3. ANALYSIS of the Tabular Results.

FIRST SERIES.

21 cases - Emetin Hydrochlor: Hypodermically of 11 -14 grs.

Result. Out of 21 cases, no fewer than 14 had not been cured 66.6% as Amoebae were still found in the faeces.
The remaining 7 had between 4 -10 Consecutive negative examinations before being discharged cured. Whether they are so or not is doubtful, based on what has been found below.
OF THE 14 UNCURED:-

5, showed no improvement whatsoever under Emetin, and Cysts were found on every occassion both during and after treatment.

9, passed no Cysts or Amoebae during or immediately after treatment, during 1- 6 consecutive examinations, but relapsed at varying intervals of time, averaging 1- 16 days after treatment - one on the 1st.day, two on the 3rd; three on the 4th; one on the 13th; two on the 16th.

SECOND SERIES.

Made up of the 14 UNCURED CASES of 1st.Series -
11, treated by Emetin Bismuth Iodide, and
3, treated by Emetin Hypodermically.

Result. of the 11 treated by 36 grs. Emetin Bism. Iodide, every one became negative ( No Amoebae or Cysts), within a few days after beginning treatment, and all remained negative throughout. From 4- 12 Consecutive Negative examinations were obtained done 2- 5 days after each other, as follows:-

- continued -

SECOND SERIES - cont.

In Two ..... six examinations)
" One ..... seven " )
" One ..... four " )
" Five ..... nine " ) = 11 cases
" One ..... ten " )
" One ..... twelve " )

Result - of the 3 Re-treated with Emetin Hydroch: (12 grs).
2, of them showed no improvement whatsoever.
1, ceased to pass Cysts 3 days after 2nd. treatment began and on whom 6 consecutive Negative exams. made, but relapsed on the 12th day after treatment (7th. Consecutive Examination made 3 days after the last negative was found positive.)

THIRD SERIES.

The 3 UNCURED cases above - two treated by Emetin Bism. Iodide (36 grs) - one transferred without treatment -

The two treated were the refractory cases of the 2nd. Emetin Hydrochloride period. Both were CURED, and 16 & 15 consecutive Negative examinations were made respectively - "They had been cured by a single course of the Double Iodide."

FOURTH SERIES.

Four fresh cases treated with 36 grs Emetin Bism. Iodide only - two had never been treated with Emetin in any form; two had the usual Emetin injections a year previously and were said to be cured.
In One ..... four Consecutive Negative Exams.
" One ..... nine " " "
" Two ..... six " " "

4. CONCLUSIONS & DISCUSSION.

i. Emetin Hydrochlor. undoubtedly modifies the Acute nature of the disease, removing the blood & mucus and bringing about an apparent cure. It seems, however, to induce the 2nd. or more Latent stage of the Dysenteric process - this coming about more quickly by Emetin than by natural resolution. From this Latent Stage, the cases pass into the Chronic or Carrier State, and Emetin then though it may again clear up any visible signs of the 'relapse' does not influence the Amoebae in their Cystic state, though all active Amoebae may be killed as before.

ii. Emetin in as much as 24 grs. does not cure Carriers.

iii. A single course of 36 grs of the DOUBLE SALT cures refractory cases to Emetin.

iv. It is important to notice that a single course is held to contain 36 grs. TOTAL.

- continued -

iv.(cont.) Dobell does not mention whether less dosage yields as satisfactory results, i.e - the minimum lethal dose for Amoebae has not been determined.

v. In the experiments 24 grs.Emetin Hydrochloride is balanced against 36 grs. of the Double Salt. This may be commented on in two ways:-
(a) That of the 24 grs, all will enter the blood and circulate in the tissues, whereas, of the 36 grs, the greater portion but not all will enter the blood, and hence undoubtedly the greater antiamoebicidal properties of the latter are undoubtedly manifested.
(b) Against this it may be quoted (but not necessarily truly judging by the results of the 3rd.series of cases), that only 24 grs. were given of Emetin Hydrochloride against 36 of the Double Salt; that in the latter the Emetin administration was continuously longer than in the former; and to judge between the two, the same dosage and same period of administration should be strictly observed.

vi. It is difficult to state exactly what number of consecutive negative examinations can be permitted before a case can be judged finally cured, and how long a period should elapse after the last treatment. According to Dobell it is three weeks.

vii. Amoebic Carriers do not exhibit the intermittency one finds in Typhoid Carriers. An Amoebic Carrier does not become positive and negative without treatment, nor are the Amoebae passed intermittently as is well-known to be the case in the Typhoid State, when Bacilli are present and absent from the faeces

viii. "It seems therefore that in Emetin Bismuth Iodide, we have a specific drug, which,whilst unpleasant to the patient, is very deadly to the specific E.Histolytica, but harmless to all other Protozoa of the human bowel" - be they Pathogenic or innocent.

ix. There is a similarity displayed by all drugs pathogenic to Ent.Histolytica in that they are harmless to all other Protozoa - viz - Emetin, Emetin Bism, Iodide, Chaparro, Amargosa, Kho-sam.

x. Cases often refractory to Ipecac. have yielded to other Anti-Protozoal Remedies, excluding Emetin Bism.Iodide.

## IV. TREATMENT of MIXED CASES.

There still remains the Group of Mixed Infections producing Dysentery to be considered, and amongst these may be classed ASYLUM DYSENTERY.
Asylum Dysentery is usually held to be produced by the Bacillus of the Flexner Type; but Morgan No.I, Shiga-Kruse; Y-infection, Streptococci are

- continued -

also causes. Occasionally it may be produced by Entamoeba Histolytica.

The 1st. Group to be considered is Amoebae & Bacilli of the different types now definitely grouped into Mannite and Non-Mannite fermenters. The Diagnosis is generally made by the non-reaction to Emetin; by the plating out cultivation, and Sugar fermentation tests (principally Mannite), and a specific Widal. When such a complication is present, the Polyvalent Serum 20 cc may be injected and the Salines instituted.

The next Group is with the Ciliate Type. (C/f. P. 8.)
(Balantidiasis) - Emetin is no use against this parasite, but a combination of Emetin for Amoebae and a large Rectal Enemata of Collargol or Protargol with Thymol administration is effective.

The 3rd. Group, is with the Flagellate Type (Lamblia Trichomonas, Tetramitus Mesnili).
Saline treatment has been used with effect.
I have found Hydrargy Perchlor. xxx ,. doses t.d.s, useful; also Salol & Bismuth - though Hydrargy cum Creta; Liq. Ferri Perchlor. (10 m.t.d.s), are practically useless. Escomel recommends Turpentine 2 grams by the mouth, and three enemata daily prepared as follows:-

℞

| | |
|---|---|
| Essence of Turpentine | 20 m. |
| Tinctr. Opii | 10 m. |
| Yolk of Egg | one |
| Distilled water | 250 c.c. |

The 4th. Group is with Bilharzios. This perhaps, is the most difficult to treat, especially the Chronic form. Astringent enemata, e.g - Tannin, Zinc Chloride, Silver preparations, may be tried. When Adeno-Papillomata have formed, they must be removed surgically. Salines are useful in keeping the bowels clear. Thymol may be tried.
The treatment is very unsatisfactory, for even were all the living worms to be killed, the destruction of tissue and new growth present an almost insuperable obstacle to recovery.
Phillips warns against the use of Filix Mas, for to be of any use, absorption is necessary, and this may be followed by Optic Atrophy.

## SECTION VII. AMOEBIC INFECTION OF THE LIVER AND OTHER ORGANS.

### PART I. AMOEBIC HEPATITIS.

This term is here used to indicate only the pre-suppurative stage of Amoebic Infection of the Liver. Its connection with Antecedent Dysentery is firmly established, but cases occur in which this is not at all evident; and in fact the classification which is to follow is based largely on this point. In the Etiology of Liver Abscess the connection with Dysentery will be found argued out, so that there is no further use of following up this point.

The classification of Amoebic Hepatitis results in the recognition of 3 types, viz - Acute, Chronic & Insidious or Latent. In addition a sub-variety may be added when the Hepatitis accompanies some other condition, for which it may be mistaken.

Amoebic Hepatitis is held to be a Remote Complication of Amoebic Dysentery, for it tends to occur after months or even years following the Primary Dysenteric attack, which by no means may have been Acute; and it is especially in long continued Chronic Dysentery untreated in which Liver infection ultimately occurs. The importance of the recognition of Hepatitis in this stage lies in the fact that by energetic anti-Amoebic measures its development into its suppurative stage is absolutely prevented.

From a study of recorded cases the following Types may be made out:-

Type I. <u>Acute Hepatitis complicating or shortly following on an Acute attack of Amoebic Dysentery</u>.

The salient points of this are:-

(a). An Acute attack of Dysentery with blood & slime in the stools. Such attack may be cut short by the advent of the Hepatic condition, and the Dysentery ceases to be a feature for the remainder of the life-history of the Acute pathological process; or, there may be a recrudescence of the Dysentery once the hepatic condition has been established.

(b). Severe pain in the hepatic region but relieved by Emetin.

(c). The temperature rises and often turns remittent.

(d). There is a rapid enlargement of the Liver, without Jaundice, but in some cases Jaundice is a well-marked feature.

(e). There is Leucocytosis but the Eosinophiles are still present in the blood.

In those cases where the dysenteric symptoms continue after the onset of Acute Hepatitis, there is danger of a severe and rapid onset of so-called " Miliary Abscesses ", that is, small amoebic abscesses of the Fulminant type breaking down and leading to a fatal termination by exhaustion or Peritonitis.

This condition is the early clinical picture of a pre-suppurative hepatitis. In this class of case Liver-puncture may yield negative results at first, but even a day later pus may be discovered. It is the ideal case for immediate treatment by Emetin.

As a typical example, Rogers cites the case of a European male, developing Acute Hepatitis not treated with Ipecac: and developing into Liver-Abscess while in Hospital after 38 days, with a fatal result.

Type II. Antecedent Dysentery and very Acute Hepatitis, simulating Liver Abscess; the Dysentery being very recent.

In this class of case, the clinical features are rather of actual abscess than of Hepatitis. Rogers case of a European male ( aet. 25 ), may be here mentioned as illustrating this. The patient was admitted for Dysentery of 6 weeks total duration, with 6 stools daily. Seven days after admission, severe pain developed in the hepatic region, with rise of temperature and profuse sweats daily; and X-Rays revealed a shadow in the Right Lobe. An abscess was diagnosed, but the patient was put upon xxx grs Ipecac: and immediate improvement set in, and within the next 3 days, the patient was better, and no operation was required. The Ipecac: had averted impending Acute suppuration in the Liver.

Type III. Acute Hepatitis with non-antecedent history of Dysentery: the case being very Acute.

Two such cases are detailed in Rogers' Series, the one with supposed suppurative involvment of the base of the Right Lung which cleared up under Ipecacuanha; the other, admitted with Acute Hepatitis, profuse sweats, & rapid oscillations in the temperature and rigors simulating abscess but clearing up under xx grs Ipecac: administration.

Type IV. Insidious Hepatitis with antecedent history of Dysentery.

This type is exceedingly difficult to diagnose from clinical symptoms alone, for these are either suppressed altogether, or are obscure. It is principally by blood examination and the exhibition of Ipecac: or Emetin that the disease clears up. The antecedent history in such cases has to be carefully enquired into.

Type V. Chronic Hepatitis with non-antecedent history of Dysentery.

This class of case, like the above, and which perhaps has resulted from long continued insidious Hepatitis, can also only be discovered by blood examination and the use of Ipecac: after the failure of other drugs. It is further complicated by the fact that there is no antecedent history of Dysentry.

Type VI. Latent Hepatitis with non-antecedent history of Dysentery, but with fever.

Such cases are extremely difficult. There are very few signs of Liver enlargement, which is painless, and there is Chronic Pyrexia as in Chronic Malaria. The blood, however, shows Leucocytosis, and the fever yields to Ipecacuanha. Rogers writes of this type as follows:-
" I only discovered this important condition during a prolonged investigation of Fevers in the Calcutta European General Hospital, during which I made blood examinations and obtained full clinical notes and 4-hourly temperature charts of 1,350 consecutive

- continued -

Type VI. 1,350 consecutive Fever admissions, in the course of which I met with several cases of Chronic Pyrexia showing Leucocytosis .... suspecting them to be Latent forms of Amoebic Hepatitis, I advised full doses of Ipecacuanha, with the happy result of rapidly curing the fever." (Rogers'Dysenteries p146) Two such cases of the same puzzling nature are related by Rogers illustrating the above.

Type VII. Latent Hepatitis with antecedent history of Dysentery and Fever, but the Fever resembling Para-Typhoid & "South-African Camp Jaundice Fever".

This class of case has suggested itself to me in a case of an Indian Officer admitted from Mesopotamia in Sept. 1916, with a diagnosis of Para-Typhoid. The Widal reaction against Para-Typhoids A & B, and Typhoid were found negative. He gave history of Dysentery, about 10 weeks old, though he had quite recovered from that and his stools were normal. The interest of the case lies in the fact as will be seen from his temperature that no drug (except Ipecac: which unfortunately was not tried until about the time of his departure in the form of Emetin ), influenced his temperature, which showed a remarkable similarity to Infectious Jaundice temperature, an illustration of which appears in a "Memoranda on some Medical Diseases in the Mediterranean War Area, printed by H.M. Stationery Office, London, W.C, 1916. pp 62 -66." The patient had well-marked Jaundice and slight Enlargement of the Liver, and the condition was thought to be of the Infectious Jaundice Type; and therefore no Emetin was given. Another similar case of Pyrexia occurred shortly afterwards in a Gurkha patient who developed Acute Hepatitis, with marked Enlargement of the Liver, and some enlargement of the Spleen, and intense Jaundice; the Liver and Spleen conditions clearing up under Emetin, but the condition was succeeded by a characteristic type of temperature in which Emetin had no effect whatsoever. Whether these kinds of cases are in reallity of the Infectious Jaundice Type complicated by Dysentery, & Hepatitis, or whether they result from Amoebic Hepatitis, cannot be determined but it is very probable that at least in the Gurkha patient the following Fever may have resulted from the Acute condition of the Liver, which although subsiding, may have left behind some toxic changes in the Liver, from which the temperature curve was raised.

Type VIII. The Cirrhotic Dysenteric Type.

Phillips met with several cases in Egypt, and Rogers in Calcutta, in which the Liver was Cirrhosed but for which no cause could be definitely attributed; and in these cases there is history of antecedent Dysentery. It therefore follows upon Chronic unsuspected Amoebic Hepatitis.

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Type IX, Hepatitis with complicated blood-pictures.

In those cases in which the diagnosis depends chiefly upon the blood and the finding of the characterictic Leucocytosis, the blood-picture may be complicated by one of the blood diseases fully dealt with in "Special Points in the Diagnosis of Tropical Abscess from Blood Diseases". Moreover, there may be a complicating type of Anaemia present which, together with the Liver enlargement may be mistaken for cases of Pernicious Anaemia, in which owing to remissions the C.I is normal. In all such cases the therapeutic test may alone form the sole method of diagnosis.

Type X. Hepatitis with other complications, notably enlargement of the Spleen, inflammation of the Appendix, Abscess of the Lung, & Infection of the Brain.

Amoebic Appendicitis has been definitely established as a complication of Amoebic Dysentery, and rare cases may exist when there is both Appendicular Abscess & Amoebic Hepatitis.
In the other cases the inflammation in the Spleen, Lung, & Brain, may co-exist with Hepatitis in the pre-suppurative stage, although such a condition must be uncommon; for they generally result from a co-existent Abscess of the Liver.

Type XI. The Jaundice- Diarrhoeal-and Pseudo-Sprue Type.

This perhaps is a sympton-complex rather than strictly a Hepatitis Type, but I have met with a few such cases, that it is necessary to call attention to the features of this condition, as it is apt to be taken for a Latent Type of Hepatitis, as a history of previous dysentery can be obtained, which perhaps may be regarded as being of the nature of an accident than of direct Etiological value. Some of these are old Sprues, or give a history of Sprue-diarrhoea, and present other evidences of that condition; the majority give a history of chronic diarrhoea, have often symptoms of dyspeptic disorder, including small ulcers in the mouth, and suffer from Jaundice & "chronic or torpid liver", and state that they have noticed the condition to start after an attack of Dysentery. All sorts of queer symptoms are complained of & different diseases, e.g. Malaria, Typhoid, Hill-diarrhoea, and other Tropical affections can be generally stringed-tied together.
The Jaundice as far as one can observe is Catarrhal in nature; but one must not forget the possibility of Malignant Disease in these cases- the painful enlargement of the liver being of the nature of Secondary Metastases to that organ, & the Jaundice and diarrhoea being also explained in the same way.
I have seen the Sprue & pseudo-Sprue cases, and the only explanation of Liver-enlargement may be attributed to that condition, but the blood test & the reaction to Emetin have been deciding factors against True Amoebic Hepatitis ; and some of these cases were also of the nature of Hepatic Congestion summed up in that peculiar Tropical condition "Tropical Liver". These cases are difficult.

- continued -

## Hepatitis with complicated blood-pictures.

Type XI. - continued -

There still remains the group of the Infectious Jaundice cases to be considered under this heading Amoebae have been from time to time seen in Urine in cases of Infectious Jaundice, and such cases have been reported betwen 1892 & 1895 by Jürgens, Kartulis, Posner & Wijnhoff and as early as 1883 "Amoeba Urogenital " was described by Baelz. These amoebae might be considered nowadays to belong to the genus Endamoeba. A case was described in the B.M.J, Apl.8th. 1916, p.526 in a Memorandum by Ward, Coles & Friel, from the South African Genrl. Hospital, Bournemouth, in which peculiar granular bodies with Pseudopodia were seen in a case of Jaundice with Albuminuria, from Mudros, and these bodies were totally unlike Entamoeba Coli & Histolytica; and it was named provisionally "Amoeba Urinae Granulata". In the B.M.J of Apl 15. 1916, H.B.Fantham, of the Liverpool School of Tropical Medicine, called attention to the above series of cases, and took exception to the provisional name of Granular Amoebae. In all the cases mentioned, the organisms were found in sanguineous Urine, and were generally complicated by Albuminuria. A very good Review of the Cases of Epidemic Jaundice & the causative parasites - The Spirochaetae Icterohaemorrhagica - is given. Reference should also be made to the War-Office Manual or "Memorandum on some Medical Diseases in the Mediterranean War Area", on JAUNDICE pp.59-66. There is associated Hepatic & Splenic enlargements, fever and intense Jaundice. The fever at first is high 103-104°F., and remains so for several days while there is considerable pain in the Epigastrium, and Right Hypochondrium, with Hepatic & Splenic enlargements, and the urine is often albuminous, & may contain casts and red blood-cells. The jaundice appears from the 3rd. to the 6th.day, and lasts usually from the 7th.to the 9th.day. The fever drops abruptly on the 5th.or 6th.day, and with it the albuminuria, and Visceral enlargements also dissapear. Secondary fever sets in on the 7th.or 9th.day and continues often for three weeks or more. In two of my recent cases a history of Dysentery was obtained, and as will be seen in one of them Emetin absolutely controlled the Hepatic & Splenic enlargement, but had very little effect on the secondary fever. I certainly regard this case as of undoubted Amoebic origin; the other was I think of Infectious Jaundice, although the jaundice persisted for the 47 days he was in my ward.
In the set of cases we received on boardship from Mudros Camps, the disease was often of recent origin, and I was able to observe the clinical features of this then-imperfectly understood disease.
Some of the cases were of longer duration, and in many there was persistent jaundice, hepatic enlargement, and pain & often a characteristic Bradycardia Comparing with what obtains in Hepatitis, the clinical features are not at all dissimilar; but I have no experience of the Blood-condition of cases of Infectious Jaundice. In the B.M.J. Sep.23, 1916 pp.413-417 "Weil's Disease in the Army in Flanders"

## The Infectious Jaundice Group of Cases.

several cases are given with Charts, and a consise account of the Experimental evidence in favour of Spirochaetae. According to the Japanese workers Inada, Ido, Hoki, Kaneko, Ito in the "Jrnl.of Experimental Medicine", p.383, the most characteristic changes are to be found in the Lungs of Guinea-Pigs innoculated, "the Lungs present small and large haemorrhagic spots, like the wing of a mottled butterfly. This change is one of the most important in the diagnosis of the disease. The intestines show haemorrhages in the walls."
Reference to the literature of Spirochaetae in this disease - Jnl: Expermtl:Med: Vol XXIII, No.3,4,5:-
March 1,1916,pp377-402 & Plates 56-62;
April 1,1916,pp557-562 & Plates 88-89;
Novr: 1,1916,pp471-496.

The Etiology of this condition is therefore most interesting, and in the light of the more recent research,the Amoebic Question seems to be replaced by a Spirochaetae Infection.
The following are some of the features culled from the Flanders' set of cases:
Vomiting in the early stages occurred in every case
Diarrhoea was not noted in any case. (This is unlike what was observed in Gallipoli & Mudros).
Hiccough occurred in two most severe cases. This is a common feature in Amoebic Hepatitis.
One fatal case had uncontrollable diarrhoea, and in one other case traces of blood were passed in the stools. On the other hand, in the Mudros cases there was often history of blood & diarrhoea, which was often severe, probably due to sand-irritation of the Intestine, for I was told that mules & horses suffered from Sand-Colic.
All cases showed an irregular pyrexia descending by lysis.
All cases showed enlarged glands, esp: the Pectoral Group & Cervical.
Even in acute cases, attended with unconsciousness, profound jaundice, and weakness & Conjunctival Congestion, the Spleen & Liver were not enlarged; and in7 out of 9 cases no enlargement of Spleen & Liver were noticed; in one the Liver was slightly enlarged, butnot the Spleen; in the other there was slight tenderness over the Liver, but the Spleen was not enlarged. This was in direct opposition to what has been observed & recorded in "Memorandum of Mediterranean Area War Diseases", and to what occurred in my own series of Mudros & Gallipoli Cases.
The diagnosis from Hepatitis of Amoebic origin,lies in the observation of a series of cases in any one area, occurring with practically the same symptoms, with intense Jaundice & albuminuria in the urine.
It is only when an issolated case occurs that the diagnosis is more difficult. The principal points and clinical features have been indicated, and I therefore now leave this interesting condition, and refer to the two Jaundice cases, alluded to above, with Charts & figures of the Hepatic condition.

Infectious Jaundice Types of Temperature.
Chart I.

1.

# CLINICAL CHART.

(To be attached to the case sheet.)

A. F. B181.
*Gratis.*
15-2-10.

*Corps* _____ *Hospital Station* _____

*No.* _____ *Rank and Name* _____ *Age* _____ *Service* _____

*Disease* Infectious Jaundice *Date of admission* _____ *Date of Discharge* _____ *Result* _____

Type of Temperature seen in "South African Camp Jaundice" — cf. Chart II - P. 63. "Memorandum of Medical DISEASES IN MEDITERRANEAN WAR AREA."

| Dates of Observation. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of Disease. | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | | | | | | | | | | | |
| Temperature, Fahrenheit. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. |
| 107° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 106° | | 1st Week. | | | | | | | | 2nd Week. | | | | | | 3rd Week. | | | | | | | | | | | | | | |
| 105° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 104° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 103° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 102° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 101° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 100° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 99° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 98° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 97° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PULSE PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| RESPIRATIONS PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Motions. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Infectious Jaundice Types of Temperature.
Chart-II.

# CLINICAL CHART.

(To be attached to the case sheet.)

A. F. B181.
*Gratis.*
15-2-10.

*Corps*_____ *Hospital Station*_____

*No.*_____ *Rank and Name*_____ *Age*_____ *Service*_____

*Disease*_____ *Date of admission*_____ *Date of Discharge*_____ *Result*_____

Type of Temperature Chart seen in "South African Camp Jaundice". Chart III of "Memorandum Diseases of War Mediterranean Area - p. 64.

| Dates of Observation. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of Disease. | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | | | | | | | | | | | | |
| Temperature, Fahrenheit. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. |
| 107° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 106° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 105° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 104° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 103° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 102° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 101° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 100° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 99° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 98° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 97° | ·8 ·6 ·4 ·2 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| | ·8 ·6 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PULSE PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| RESPIRATIONS PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Motions | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

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Diagram.

Case. I. Rifleman Gurkha, aet:22, admitted into "Annexe" Hospl: Karachi, on Oct: 28th./16, from Mesopotamia with history of diarrhoea & dysentery, contracted one month ago. Had no dysentery or diarrhoea on admission, but was debilitated.
Heart-sounds weak; Tricuspid & Pulmonary 2nd. sds: reduplicated. (No jaundice)

6/11/16. Markedly jaundiced, temperature 100°.F. and complains of tenderness in the Right Hypochondrium. Abdomen distended, & Liver and Spleen enlarged, esp:Liver.

8/11/16. Liver dulness increasing, and can be felt in the Left hypochondrium; patient has a rigor, like Malaria. Emetin 1.gr injected. Blood-exam: shows Benign Tertian Rings;(this was examined by me) Quinine X grs. t.i.d.

9/11/16. No parasites in the blood, after the Quinine; leucocytosis of Polymorphs 75%; temperature still raised to 100.4 Emetin 1 gr. injected.
Liver-dulness extends to Left Hypochondrium, and a distinct liver-notch can be determined, quite easily. (see Fig). Dulness made out at level of Umbilicus, and can be traced to the Left Iliac & M.V.L.lines. The Spleen is felt distinctly & is seperate from the Liver mass, and extends for 3 fingers'breadth below costal margin. No pain now; & no resistance of the Antr:Abdl:Wall. Jaundice still well-marked. Case thought by some to be Specific & doses of Iodide of Potash advised; & some think that it may be some acute condition in a Malarial Liver cirrhosed. I however took the view that this is an Amoebic Hepatitis, and to persevere with Emetin, before trying any other line of treatment .

10/11/16. Emetin 1 gr. to be injected daily.

14/11/16. Liver remarkably reduced in size; jaundicemuch improved, and the patient better. Fever normal since the 11th. Quinine still continued xxx grs.daily
(See Temperature-Chart & Figs.)

23/11/16. No Splenic enlargement made out; Liver remarkably further reduced in size, and extends 3 fingers' breadth below c.m. and immediately below Rt.Nipple Transv: plane. Emetin stopped on the 18th. & Quinine discontinued on the 21st.

30/11/16. Spleen normal; Liver still slightly enlarged; no jaundice; running a slight temperature; was on Chlorine-mixture from 23rd to 28th, without benefit; & Emetin ½ gr. daily from 25th-28th.
Was normal during 28th & 29th.

8/12/16. No Spleen; no jaundice; Liver 2 fingers' breadth below c.m; still has same type of temperature, but feels well.
Evening rise & morning fall throughout from 16th-to date. Is discharged to Ambulance-train today.

Diagram.

## Diagrammatic Representation of the Liver & Spleen Enlargements in a Case of Acute Hepatitis after Dysentery.

Case of Gurkha Rifleman treated in the Annexe-Indian General Hospital, Karachi.

Case Treated throughout with Emetin Injections.

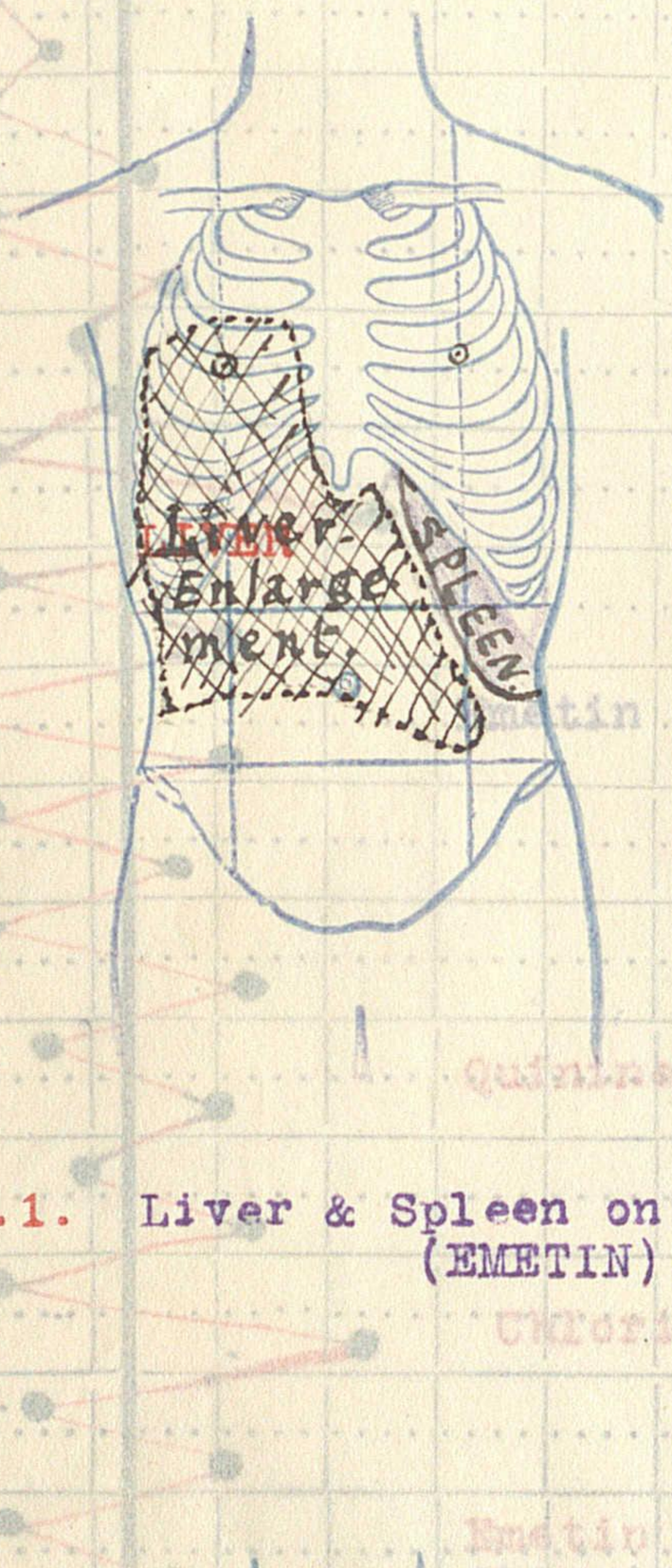


Fig.1. Liver & Spleen on Nov.9/16. (EMETIN).

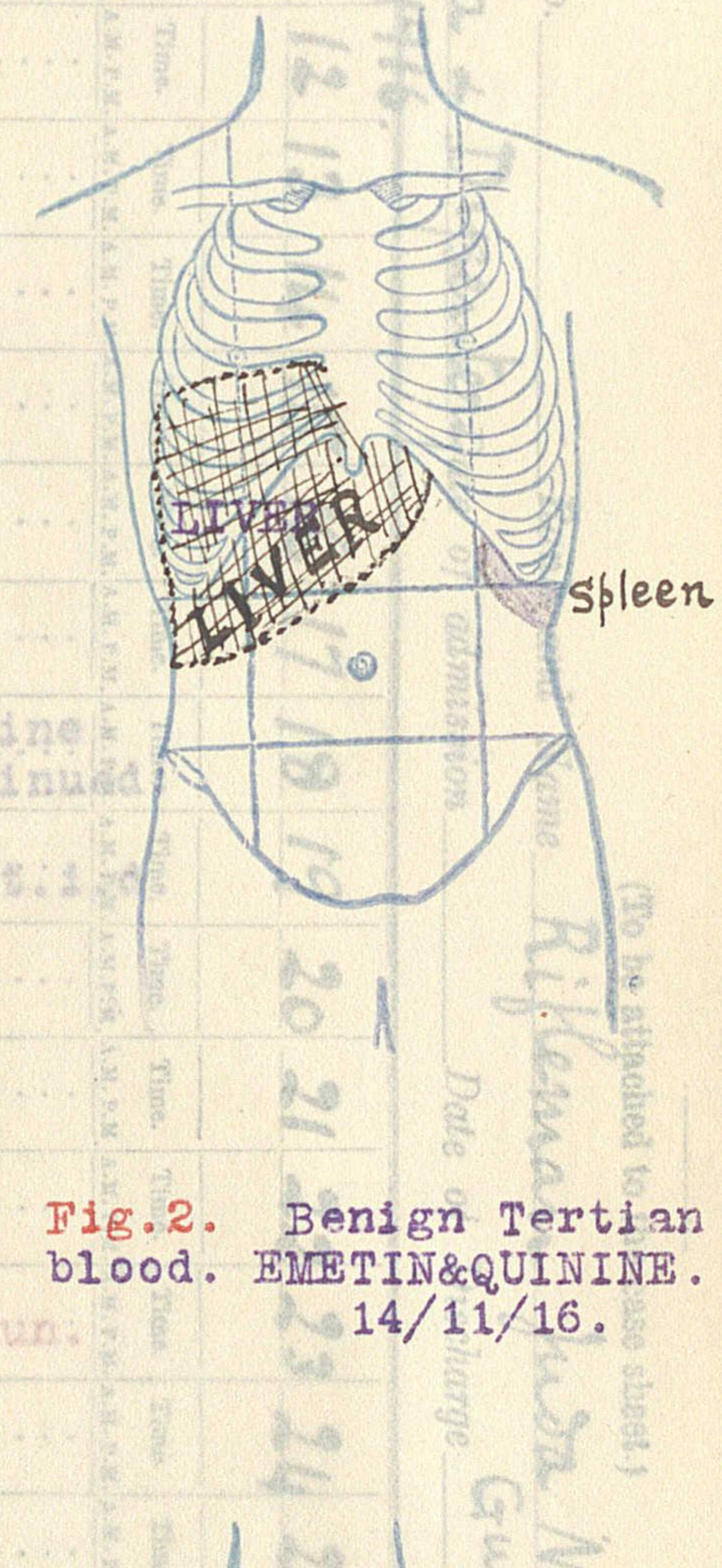


Fig.2. Benign Tertian in the blood. EMETIN&QUININE. 14/11/16.

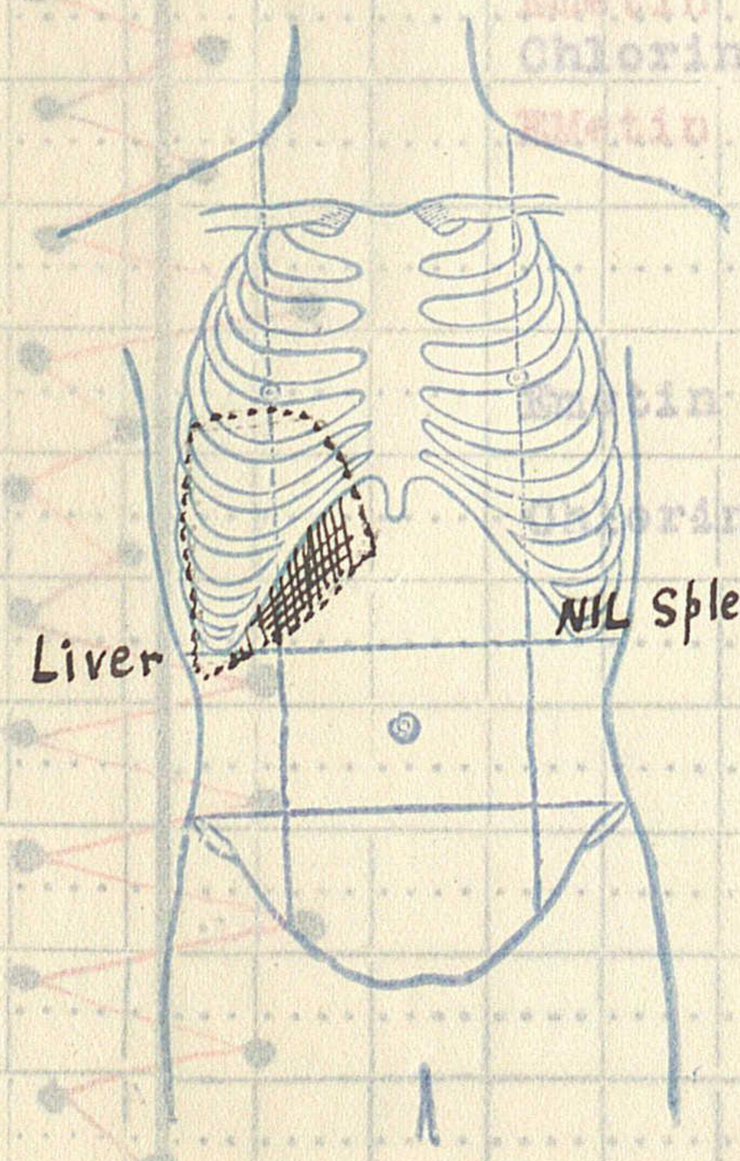


Fig.3. EMETIN ONLY - No Parasites. State of Liver & Spleen on 23/11/16.

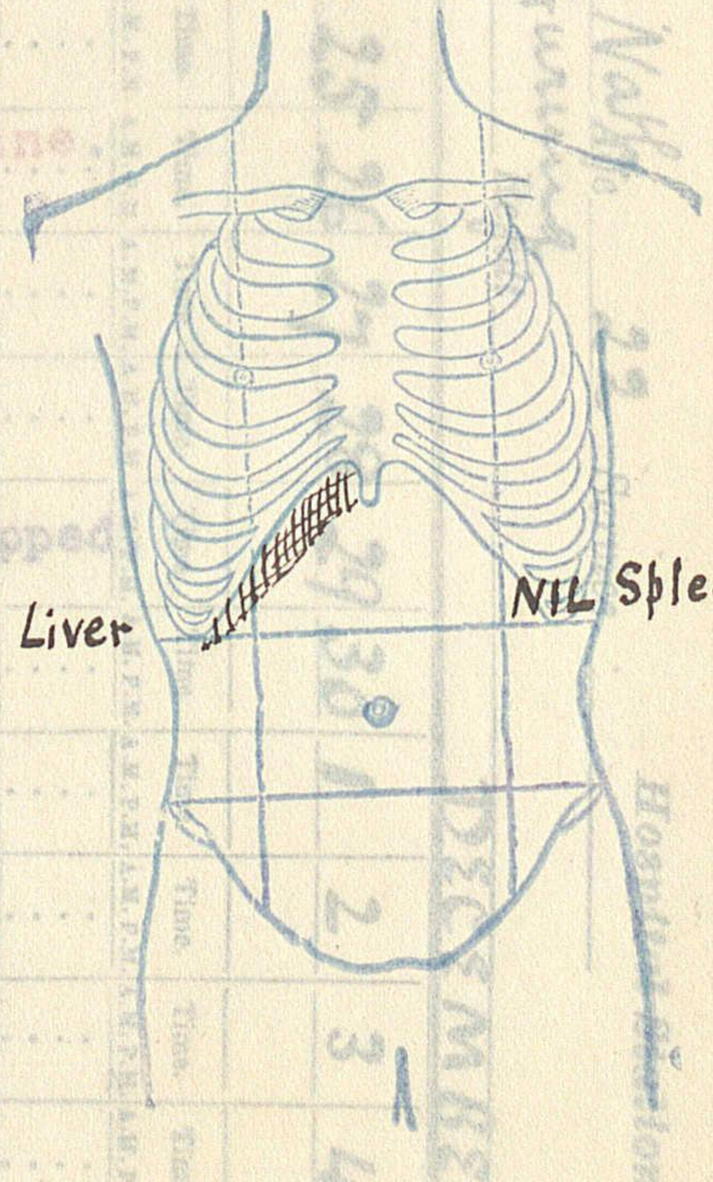


Fig.4. State of Liver & the Spleen on 30/11/16. EMETIN.

Hepatitis.

2.

# CLINICAL CHART.

(To be attached to the case sheet.)

A. F. B18
*Gratis.*
15-2-10.

*Corps* Gurkha *No.* *Rank and Name* Rifleman Juda Nath Gurung *Age* 22 *Service* *Hospital Station* "Annexe" Karachi.

*Original Disease* Diarrhoea & Dysentery *Date of admission* *Date of Discharge* *Result*

NOVEMBER/1916. DECEMBER-1916

| Dates of Observation. | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of Disease. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Temperature, Fahrenheit. Time. A.M. P.M. | Benign Ter. MALARIAL PARASITES Rigor; Emetin 1.gr.injected | Emetin 1.gr. No Parasites Leucocytosis | Emetin 1.gr. & Quinine x.grs | Emetin 1.gr & Quinine x grs. t.i.d. | DO. | DO. | DO. | DO. | DO. | DO. | Emetin stopped - Quinine continued. | Quinine x.grs.t.i.d. | DO | Quinine Discontinued. | DO. | Chlorine Mixture begun. | DO | Emetin ½.gr.injected. Chlorine Mix.contd. | Emetin ½.gr. & Chlorine. | DO. | Emetin stopped. | Chlorine Mixture stopped | DO. | DO. | DO. | DO. | DO. | DO. | Discharged from Hospl. & sent by Ambulance Train. |
| 107° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 106° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 105° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 104° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 103° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 102° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 101° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 100° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 99° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 98° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 97° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PULSE PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| RESPIRATIONS PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Motions. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

- continued -

Comments on Case I.-

The out-standing features of this case are:-

1. Sudden development, with pain and enlargement of the Liver & Spleen.

2. Intense Jaundice.

3. Rigor which was explained by the Benign Tertian found in the blood.

4. A Leucocytosis of 75% Polymorphs.

5. The remarkable diminution of the huge Liver mass and the absence of pain under Emetin within a period of five days after the onset.

6, In 14 days after the onset, the liver was only enlarged 3 fingers' breadth; and the Jaundice totally disappeared.

7. Fall of the temperature to normal three days after the onset, and its continuation thus for some 4 days, after which it rose in the evening with the morning remission throughout the rest of his stay in Hospital, & uninfluenced by Emetin, Quinine or Chlorine mixture. The pulse also varied with the fever, 74 - 90. What the cause of the secondary fever was, is impossible to say, but it resembled what has been observed in " The South African Camp Jaundice type ".

Case II. Indian Officer, aet: 39, received on 29/8/16, with diagnosis of Para-Typhoid. He had Dysentery on 1st.July/16 - it lasted till 7th.July, when he developed Fever; the fever lasted until the 30th, July, when it came down for the first time.
The fever came on again on the 4th Aug: & lasted till the 13th Aug: it was intermittent. From the 18th till the 28th Aug: he was again attacked with fever on the voyage out to India.
On admission the Spleen & Liver were normal, the Circulatory system normal, and Respiratory system normal. No fever from the 29th Aug: to Sep.3rd, when the fever again rose to 99.2. No Malarial parasites found in the blood. Fever again on the 5th.Sep. Widal reaction negative to Typhoid and Para-Typhoid A & B in all dilutions. Fever of the continuous type from the 7th Sep. to 15th Oct: 99.2 in the evenings, & 98.6 in the mornings. Salol & Bismuth tried without effect; Quinine also useless; Calomel ½ gr. t.d.s without effect, from 21st to 28th Sept; Triple Sulphate mixture of Mag; Sulph, Ferri Sulph. & Quinine Sulph: & Acid Sulph: dil: āā 5 grs, without effect, from 29th Sep. to 5th.Oct; Emetin ½ gr. daily from 11th.to 15th Oct. useless; fresh air drives no benefit. Pulse throughout 96 morning & 108 evening. Lung normal. States that his condition started after he had the Dysentery. No other history obtainable Discharged to Ambulance Train on Oct.15th.
He had slight Jaundice throughout his stay in Hospital, and was passing bile in the Urine.

I.

# The original Chart of Jamadar Nikah Gul.

## CLINICAL CHART.

(To be attached to the case sheet.)

No 1 Ld H Amb 3

A. F. B181
Gratis.
15-2-10.

Corps 2/4th Punjabis  No.  Rank and Name Jamadar Nikah Gul  Age 39  Service 21  Hospital Station Kanaela.

Disease Para-Typhoid (?)  Date of admission 29/8/16  Date of Discharge  Result

| Dates of Observation | Aug. 29/8/16 | 30 | 31 | Sept. 1/9/16 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of Disease. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 |
| Temperature, Fahrenheit. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time, A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. |
| 107° | | | | | | | | | | | | | | | | | | * | | | * | | | | | * | | | | | |
| 106° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 105° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 104° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 103° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 102° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 101° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 100° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 99° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 98° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| 97° | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| PULSE PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| RESPIRATIONS PER MINUTE | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Motions. | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |

Tonic of Iron & Arsenic

Salol & Bismuth mixture

Salol. & Quinine mixture

Fresh air. Diet

Fresh air Diet

Quinine Fresh air

Calomel & Kt. 7th

Fresh air Diet

Fresh air Diet

Calomel & Kt. 7th

Temperature: 98/96 | 102/100 | 98/96 | 98/97 | 99/98 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96 | 98/96

Pulse: 120 | 90/76 | 96/96 | 102/100 | 98/96 | 78/72 | 88/82 | 96/84 | 96/82 | 94/96 | 92/92 | 96/96 | 96/92 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96 | 96/96

Respirations: 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20 | 20

Motions: 1 | 2 | 2 | 3 | 4 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 2

Vomited 4 times i/c. Case.

II continued

# CLINICAL CHART.

(To be attached to the case sheet.)

No 1 IS H Amb

A. F. B181.
Gratis.
15-2-10.

Corps 28th Panjabee No. — Rank and Name Jamadar Nikah Gul Age 39 Service 21 Hospital Station Karachi amb

Disease Para Typhoid Date of admission 29.8.16 Date of Discharge Result

| Date of Observation. | 29 | 30 | 1st Oct/16 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of Disease. | 32 | 33 | 34 | 35 | 36 | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 |
| Temperature, Fahrenheit. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. | Time. A.M. P.M. |
| Pulse per minute | 96/104 | 96/96 | 90/96 | 96/96 | 90/104 | 102/107 | 96/108 | 108/100 | 96/120 | 96/96 | 96/108 | 94/96 | 92/98 | 98/102 | 92/102 | 100/96 | 93/102 |
| Respirations per minute | | | | | | | | | | | | | | | | | |
| Motions | 2 | 2 | 1 | 2 | 2 | 2 | 1/1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 |

Temperature, Fahrenheit: 107° 106° 105° 104° 103° 102° 101° 100° 99° 98° 97°

Time: 8 6 4 2

Triple sulphate mixture (Mag. Sulph. Ferri Sulph. Quin Sulph.)

Triple sulphate mix. stopped * Fresh air drives Chlorine mix. 4s

Emetin 1 gr. injected * Fresh air drive. Do EMETIN

Do - EMETIN.

Do - EMETIN.

Transf. to Hululose train

J. G. Moses. Lt. Ins. i/c. Case.

- continued -

## Comments on Case II.

The interesting features in this case are:-

1. History of Dysentery.

2. Continued Pyrexia, after which he had intermittent bouts of fever, until 8th Sept.

3. Widal reaction to Para-Typhoid A & B and Typhoid negative in all dilutions; and no Malarial parasites in the blood.

4. Persistent Jaundice, but Liver not enlarged.

5. No second attack of Dysentery or Diarrhoea.

6. The continued fever uninfluenced by any drug, even Emetin, though this latter was only given for 4 days prior to his departure.

7. The pulse-rate remaining high throughout, though it showed remarkable stability in type, being 96 in the morning, and with the evening rise of temperature, rising to 108.

8. Temperature not unlike that seen in Infectious Jaundice, though Infectious Jaundice cases from Mesopotamia distinctly rare.

9. This case should be contrasted with Case I, above; and the temperature compared with the type temperature of Infectious Jaundice.

## The Treatment of Amoebic Hepatitis.

From a study of the types met with in Amoebic Hepatitis, and the frequency of which it simulates actual suppuration, no case of Liver Abscess should be operated on without a course of Emetin Treatment. The diagnosis of Latent cases are extremely difficult; but blood examination clinches the diagnosis by the finding of the characteristic Leucocytosis. The treatment of Hepatitis is early successful diagnosis; and no case however severe, will fail to re-act to Emetin if the cause be Amoebic. It is in the question of diagnosis alone that greatest difficulty will be experienced. The treatment can be carried out by Intra-Muscular Injections of Emetin Hydrochlor: 1 gr. daily, until all evidence of Liver Enlargement and abnormal percentage of Polymorphs disappears. This may be reinforced by Ipecac: 20 grs. orally, t.d.s but Emetin alone will be found curative. There is practically no other method of treatment so quickly and so thoroughly efficacious as Emetin.

## SECTION VII. AMOEBIC INFECTION OF THE LIVER AND OTHER ORGANS.

### PART 2. THE ETIOLOGY OF TROPICAL ABSCESS.

ITS HISTORICAL & PATHOLOGICAL ASPECTS.

ITS DIRECT & ACCESSORY FACTORS.

## Historical.

The Primary early condition is what has been termed " Pre-Suppurative Hepatitis ". After the Colon the liver is the organ most frequently attacked by the Amoeba. The etiology of Tropical abscess is linked up with the etiology of Amoebic Hepatitis, of which it is the final stage, for the symptoms are at first those of acute Hepatitis, and the course of this Hepatitis is variable. For many years the relationship between Dysentery & Liver abscess has been well known, but the relationship of Acute Hepatitis to Amoebic Infection has been largely overlooked. The differentiation of Amoebic Dysentery from the Bacillary Type has principally a historical interest. In 1887 the pioneer work of Kartulis in Egypt placed the ultimate establishment of Amoebic Dysentery as a distinctive disease. In 1887 he pointed out the definite association of what was then known as Amoeba Coli with hepatic suppuration, and his results were promptly confirmed by Hlava of Prague. In 1891 Lutz observed the same phenomena. Councilman & Lafleur working under Prof. Osler at Baltimore, were able to work out the Pathology of Amoebic Dysentery, and publish their results in the Johns Hopkins Hospital reports 1891 ii. Prof. Osler himself was the first to record the presence of Amoebae in Liver abscess in 1890; the first case to be recorded in America. In 1901 Rogers recorded the occurrence of Amoebic Dysentery in India, and showed that the Amoebae is the sole organism constantly found in Liver abscesses secondary to Amoebic Dysentery. In the early part of the 19th. Century, Annesley in his "Researches into the Diseases of India", 1841, recognised the connection between Amoebae & Hepatitis, and called it Hepatic Dysentery. But it is through the work of Rogers in Calcutta that this pre-suppurative inflammation of the liver secondary to Amoebic Dysentery has been thoroughly recognised, and the whole Pathology put upon a sure foundation.

## Relationship of Liver abscess to Antecedent Amoebic Dysentery.

There can be no question as to the existence of an intimate relationship between Dysentery & Liver abscess. ( Manson ). " It is more than doubtful whether abscess ever occurs as a Primary Lesion of Amoebiasis; in all cases, dysentery is present or has previously existed. Patients often have dysentery in such mild chronic form, that it does not attract the attention it deserves; the occasional looseness of the bowels being considered merely diarrhoea, which is too common an occurrence in the Tropics, to provoke a second thought unless profuse or painful. " (cf. Keen's Surgery, vol iv, 1909, p. 1109 ).

## Geographical Distribution & Statistical Returns.

Statistics are available from all over the world to corroborate this intimate relationship. All over the world where Amoebic Dysentery is endemic, hepatic suppuration is known.- there being no immunity from liver abscess in endemic areas of Amoebic Dysentery. The Dysentery which occurred in the Fiji Islands as an epidemic in 1910, was of the Bacillary Type, and no Hepatic Complications were found either during life or post-mortem in the 159 cases of Bacillary Dysentery. In only 11, were Dysenteric Amoebae found, and 5 of them showed Hepatitis or liver abscess. R.H.Bahr published his papers in the B.M.J of 1914, i, 294.

- continued -

## Geographical Distribution & Statistical Returns.

Evidently judging by the returns from Fiji, Amoebic Dysentery is uncommon. Liver abscess is common in Indian immigrants in Fiji, in whom also Amoebic Dysentery is common; whereas in the native Fijian Dysentery due to amoebae & liver abscess is rare. (Bahr). Tropical Africa, Cochin-China, Malaya, Sth Eastern - Asia, yield sufficient statistics to put the sure relationship on an exact foundation.
In 3680 Dysenteric autopsies made in various Tropical countries, and collated by Woodward, 779 or 21 % revealed abscess of the Liver.
Kartulis* in Egypt , in an experience of over 500 cases of Liver abscess, elicited a history of dysentery in from 55 - 60 %,
Zancarol, also in Egypt, in 444cases elicited a similar history in 59 %.
Edwards & Waterman in 699 collated cases obtained a similar history in 72.1 %.
Johnston Smith in 45 cases treated at the Seaman's Hospital Greenwich, for Liver abscess, during 1870 - 1895, recorded that 38 , or 844 (84.4 ) %, gave a distinct history of dysentery or post-mortem evidence. A
According to the Annual Report of the Sanitary Commisioner with the Government of India for 1894 out of 465 European Soldiers who dies from Dysentery in India during the period 1888- 1894, 161 or 35% had, in addition to dysenteric lesions abscess of the liver. ( Manson , Trop.Med, p. 563 )
As has been pointed out by Macleod and others, the occurrence of antecedent dysentery in cases of liver abscess is very often overlooked; for without a post-mortem it may be impossible to pronounce definitely on this point in every instance.
Extensive dysenteric ulceration may be present, and yet give rise to no active symptoms whatsoever. Further patients either forget previous records of their disease or call it " diarrhoea "; lastly even at post-mortems, fine superficial ulceration may have so healed or disappeared, that they have been overlooked.
Macleod's statistics in Shanghai work out at 99 % for in 40 cases of liver abscess he had evidence of dysentery in all save one, which even could not be positively negatived. However, Geographical relationships which certainly occur in the determining of the segmental distribution of dysenteric lesions in the Colon, may play some important part, in explaining some paradoxical and ill-understood reasons why there should be differences in the statistics and the liver abscess readings varying in the very same statistics of the country from which the y are drawn. Thus in the Commissioner's Report reffered to above, it is stated that out of 74 cases of Liver abscess occurring in the Bombay Presidency, only in 2 were there dysenteric associations (3%). "It is difficult to believe that the liver abscess in the Bombay Presidency is associated so rarely (3%) with dysentery, whilst according to the same Authority, in the whole of India, it is certainly so associated in at least 30% of the Total cases; and it is also difficult to believe that so important and evident a circumstance

*Kartulis- "Zur Aetiologie der Dysenterie in Aegypten" Virchows Arch. BD. 105 1886, pp. 521-531. (quoted by Phillips).

- continued -

Geographical Distribution & Statistical Returns.

circumstance as dysentery had been overlooked in 72 out of 74 cases..... so that it is just possible that what holds good for one place may not hold good for all places." (Manson- ibid, p.564).
"In 75% of all cases of Tropical Abscess of the Liver, there is a distinct history of dysenteric symptoms ..... including definite post-mortem evidence of Amoebic Infection of the Colon ....In Calcutta 95% of all cases had, previously, suffered with dysentery." (Rogers*).
Musgrave* in the Phillipine Islands, also found even more than this proportion of all liver abscesses being Amoebic.
Rogers, gives the following table of 63 cases abscesses showing their relationship to Dysentery:-

*Rogers- B.M.J. 1903, i, p.1315.

*Musgrave. W.E. - Phillipine Jrnl.of Science, June 1906.

| | | | |
|---|---|---|---|
| Clinical & P.M. evidence of Dys: | 35 cases | | ...55.5% |
| No history but P.M | " | " " | 13 " ...20.6% |
| No History or P.M | " | " " | 6 " ,.. 9.5% |
| History but no P.M | " | " " | 9 " ...14.3% |

thus, in 90.4% of cases, a positive history of Dysentery was obtained. (cf. Rogers, Dysenteries, p. 169 ).
The cases in the above Table include old records dating back to 1872, when the relationship of the two diseases to each other was less understood than later.

Rogers European Hospital Notes for 1904 - 1913 yield the following:-

| | | | | Tot:% |
|---|---|---|---|---|
| 86%.... | Dysentery.. | In hospital..... | 18... 18 | 86-72 |
| | | Within 3 mths. of admission... | 10 | |
| | | Over 3 " before " .... | 8 | |
| | Diarrhoea only ..... | | 7.. 14.. | 14 |
| 14%.... | Nil ..... | | 7.... | 14 |

Rogers, loc;cit:p.170.

"There existed thus a definite history or symptoms of Dysentery in 72%, while in 14% more there was one of Diarrhoea only, which is the only symptom produced by some mild cases of Amoebic disease of the large bowel. This leaves only 14% with no evidence of Intestinal flux: this symptom may, not rarely, be absent when typical Amoebic ulcers are found after death from liver abscess.... Dysenteric symptoms frequently abate when those of acute Hepatitis supervene, and the previous bowel trouble may not be mentioned by the patient unless carefully looked for. Moreover, the dysentery is nearly always clearly antecedent in date to the Hepatitis.. In the Native series, the Dysentery certainly preceded the liver abscess in 80% of the cases, in which full histories were recorded, while when the bowel trouble supervened after signs of Hepatitis it was frequently only a recrudescence of old

- continued -

The Statistical Returns.

old Intestinal Disease. The whole of the evidence, then, points to Amoebic Dysentery, often of a latent character, as constantly preceding the formation of Tropical Liver abscess. " (cf, Rogers, ibid, pp. 170 - 171 ).
Some clinicians have held that the two diseases from the very commencement are concurrent; whilst in others, Hepatitis alternates with active dysenteric symptoms. If the abscess antedate the Dysentery, then the dysentery cannot be the cause of the abscess. On these grounds some have regarded liver abscess & Dysentery as but different expressions of one morbid condition; reacting to some extent on each other, but not directly related the one to the other as cause and effect. Here again the Latency as regards symptoms of some Dysenteries, has to be discounted in attempting to settle the question on clinical grounds alone.
" All these discrepancies and differences of opinio have to be re-studied in the light of the acknowledged relationship of the Amoeba to Dysentery & Liver abscess ". ( Manson ). Some difficulties and anomalies can only be explained by Racial or Geographical considerations - factors which are to be considered in the Pre-disposing causes of Liver abscess.

The Relationship between Abscess of the Liver & Dysentery from a clinical point of view.

i. Abscess in the liver associated with concurrent well marked Dysentery.

ii. Abscess in the liver developing first, followed later by the appearance of blood & slime in the stools; as for instance occurs after an abscess has been opened, i.e, a recrudescence of old Dysentery. This must not be mistaken for a rupture of the abscess into the bowels.

iii.* Well marked signs of abscess, with either no history of Dysentery or no appearance of it. This may be graphically described as Clinical abscess, non-clinical dysentery.

iv. Latent or insidious abscess and Latent Dysentery.

v. Clinical abscess, non-clinical dysentery, but pathological evidence ( P.M ) of active ulceration and scars in the bowel-wall of former dysentery.

vi. Pathological abscess, & Clinical Dysentery. i.e, abscess only found at post-mortem and Dysentery during life.

vii. Pathological abscess & Pathological Dysentery. The term Pathalogical here refers to the conditions being found only at the post-mortem.

* Anderson;"Abcess of Liver with Amoebae, but without antecedent Bowel Disease ". Indian Med. Gaz.1912 vol 47.No.10,pp.398-399.

- continued -

## The Pathological Relationship between Abscess of the Liver & Amoebic Dysentery.

" The ratio between the Admission Rates for Liver abscess & dysentery, may be taken as an index of the prevalence of amoebic disease..... The returns of dysentery & liver abscess in the British Army in India for the period 1901 - 1910, gave the following results:

i. The whole of India returns gave one admission for liver abscess for each 7 of dysentery.

ii. A remarkable uniformity in the results were obtained over different areas, for in the whole of the Central & Northern parts of India which includes the great bulk of the entire Country, the ratio was still 1 in 7 - although the climatic conditions vary intensely from the steamy heat of Bengal to the very dry hot N.W.Frontier. "

## The Types of Liver Abscess in Relation with The Character & Intensity of the Dysentery.

1. Acute Ulcerative Amoebic Dysentery is occasionally complicated by Multiple Small Liver Abscesses.

2. Multiple Large Liver Abscess is associated with a comparative paucity of ulcers and their marked tendency to limitation in the upper third of the large Intestine, especially situated in the Caecum alone. In this conditio the bowel lesions are never so acute or sloughing in character as in the acute ulcerative or gangrenous type. This is the characteristic condition in Chronic Amoebic Dysentery in which there is often total abscence of dysenteric symptoms.

3. In active dysentery complicating liver-abscess the hepatic suppuration is usually Multiple.

This is Rogers' experience as detailed by his clinical & pathological observations in Calcutta. They do not coincide with what has been observed in other parts of the world. There is considerable Geographical variation in the extent to which particular sections in the Alimentary canal are liable to attack. Thus in the East Indies, the lesions are confined to the Descending Colon, and Sigmoid Flexures in about 25% of all cases, but in Strong & Musgraves * 1st.series of 100 autopsies in the Phillipine Islands, limitation to these areas "were never once observed; whilst in their 2nd.series it was found only 9 times.

*Strong & Musgrave - " The Pathology of Intestinal Amoebiasis" Reports of the Bureau of Govt. Labs.Manila 1905.

## The Types of Liver Abscess in relation with The character & intensity of the Dysentery.

*Harris -American Jrnl. of Medical Science, 1898, p.384.

*Rogers- B.M.J. 1903 No.1. 1315.

Harris*states that in America the lesions rarely extend above the Hepatic Flexure of the Colon; while Rogers*finds that they are almost invariably marked in the Caecum and Ascending Colon, and that they are frequently limited to these areas. The Transverse Colon is alone affected in only 1 out of 100 cases of Amoebic Dysentery. Ulcers are occasionally seen in the lower part of the Ileum; but lesions of the upper segments of the Small Intestine, are very rare. (Brown). No statistics are available to show the type-abscess arising from ulcers in the Transverse & Descending Colons. It is however very curious to find that dysentery has this tendency to localise itself in the Caecum; and also that Large Multiple Abscess is more associated with Chronic Amoebic Dysentery, than with the Acute Ulcerative Type, probably because there is repeated doses of Amoebae from the diseased gut, plus a certain amount of toxic absorption & perhaps bacterial flora passing to the liver.
In relation to the above, attention is called to "Amoebic Appendicitis", for an analysis of the distributional lesions in Musgrave's "50 Fatal Cases of Intestinal Amoebiasis, without Diarrhoea"

## Statistics of the Bowel-Condition in Recent Fatal Liver Abscess.

"In patients dying of Liver Abscess, Chronic dysenteric lesions are often met with.
Evidence of Active or previous dysenteric disease were found in 98% of 50 post-mortems- whilst the single exceptional case may easily have been due to slight earlier ulceration which had healed and been overlooked, especially as Ipecac: having been given during life." (Rogers).

## Relation of Dysentery to Hepatitis.

In European patients the maximum of the Hepatitis cases occurs 2 months after that of the Dysentery and three months later than the milder Diarrhoeal cases; just as might be expected if the liver Disease is secondary to the bowel. (Rogers' Dysenterie p.43.).

The Distribution of Dysenteric Ulcers in the Bowel when complicating Liver Abscess.

1. 5cases of very Acute Gangrenous Dysentery were complicated by Small Multiple Abscesses unsuspected during life, and were clinically severe dysentery. In all these cases, the abscesses were only found post- mortem, and had not been clinically in evidence, the bowel-disease having been too rapidly fatal to allow of the symptoms of hepatic suppuration becoming clear during life.

2. Post-Colic Abscess - cf/Table IV.below - one ulcer in Caecum extending to Ascending Colon - the case ended fatally by perforation. Multiple Liver abscesses were found.

3. The complicated Dysentery cases by abscess of the Liver, are more numerous and fatal, than when no such complications accompany Acute or Chronic Dysentery. Ulcers occurred in Caecum, Ascending, Transverse & Descending Colons. Cf/Table II.

4. "More than One Large Liver abscess" (Rogers). In these cases we find a very different distribution of the bowel-lesions to that in the Acute dysenteries, with or without Multiple abscesses. The most noteworthy feature is the comparative paucity of ulcers &, the marked tendency to their limitation in the upper 1/3rd.of the Large Intestine, and esp: in the Caecum alone. In only 3 of 13 cases were fairly numerous ulcers present through the greater part of the Large Bowel, and in none of these were they anything like so extensive or of such a sloughing character as in the cases showing Multiple Small Liver abscesses In5 of the cases scars of old ulcers were recorded, proving the Chronic nature of the Bowel - Disease. (cf. Rogers' Dysenteries p.83.). The differences between the ulcers associated with 2 abscesses and those with 3 abscesses are shewn in Table II. 4 cases had smaller round ulcers in the Caecum in the Liver with 2abscesses; whereasthe 3-abscess cases had 3 ulcers. The differences are most marked in the Transverse Colon, Descending Colon, Sigmoid & Rectum The larger & widespread lesions in the Descending Colon, were thus more marked in cases of 3-abscesses. None of these ulcers hpwever were so extensive or of such gangrenous or sloughy character as in cases showing Multiple Small Liver abscesses.

5. "A Single Large Liver Abscess" - Cf/Rogers, ibid p.83.- Series of 23 cases, in Table I. The bowel-lesions are similar to those described as being associated with 2 or more Multiple Large Abscesses, only the limitation of the disease to the first part of the Large Intestine is even more marked in a considerable majority.

- continued -

5. A Single Large Liver Abscess. -continued -

Out of 23 cases:-
in 9 ulceration was absolutely limited to Caecum
in 4 it extended to Ascending Colon
in 1 it extended to Ascending " & Transv:Colon
in 6 scarring of old ulcers alone were found after death from a Large Single Liver Abscess, being also generally limited to the upper 1/3rd. of the Great Bowel

6. In the same series of 23 cases, one case who died of Cirrhosis of the Liver, had amoebic ulcers & scars limited to the upper 1/3rd. of the Large Bowel-the association of which to antecedent Amoebic Dysentery has already been established* by Rogers' Cases of Hepatic Cirrhosis in Calcutta which were directly the result of a "chronic amoebic infection of the liver derived from a long-existing ulceration of the bowel.

* Rogers- Indian Med. Gaz. 1911 Feb.

Four Tables will be found appended explaining Rogers' diagramatic Distribution of dysentery of his cases - distribution of dysentery in the Intestine, associated with Liver abscess.

Table I. Amoebic Dysentery & Small Liver Abscess.-- 24 cases.

Table II. Multiple Large Liver Abscess --12

Table III. Amoebic Dysentery & Multiple Small Liver Abscess. ---5 cases.

Table IV. Post-Colic Abscess --- 3 cases;
two uncomplicated and
one complicated by Liver abscess:
Perforative cases.

Tabular Distribution of Dysenteric lesions in the Bowel when complicated by Liver abscess.

## Table I.

### Amoebic Dysentery & Single Liver Abscess. 24 cases

| Segment of Gut involved | Ulcers across Axis of Gut with healthy muc:membrane between them | Smaller round or oval ulcers (seperate) on an otherwise nor-mal muc:membrane of less advanced Amoebic Disease. | Large thick ened patch of ulcerated gut in Acute amoebic dyse nteric cases. | scars of healed ulcers |
|---|---|---|---|---|
| Ileum | nil | nil | nil | nil |
| Caecum | 1 case - 3) ulcers ) | 12--in 6...2) in 2...1)=12 in 4...3) | 6 cases:- (4...2patches 6(1...1 " (1...3 " | cases cases 5 each 2 scars |
| Ascending Colon | 1(1 case with (1 ulcer | cases ulcers (4 2 7(2 1 (1 3 | nil | nil |
| Transverse Colon | nil | cases ulcers (7 2 9-(1 1 (1 3 | nil | nil |
| Descending Colon | nil | cases ulcers 7-(6 2 (1 1 | nil | (1 case (2 scars |
| Sigmoid | nil | cases ulcers 5-(4 2 (1 1 | nil | 2 cases (1 cases (2 scars (1 case (1 scar |
| Rectum | nil | cases ulcers 2-(1 1 (1 1 | nil | 2 cases each with two scars |

NOTES.

1. In none of these cases were there any perforation of the bowel.

2. In all, the mucous membrane affected showed the characteristic patchy manner in which Amoebic Dysentery causes lesions in the bowel-wall. This is always in marked contrast to what results in Bacillary Dysentery.

Tabular Distribution of Dysenteric Lesions in the Bowel when complicated by Liver Abscess.

## Table II.

### Amoebic Dysentery & Multiple Large Liver Abscess. 12 cases.

| Segment of Gut Involved & No. of Abscesses. | Ulcers across Axis of Gut with healthy muc:membrane between them. | Smaller round or oval separate ulcers on an otherwise normal muc:membrane of less advanced Amoebic Disease. | Large thickened patch of ulcerated Gut in acute Amoebic Dysenteric cases. | Scars of healed Ulcers. |
|---|---|---|---|---|
| Ileum | nil | nil | nil | nil |
| Caecum. | cases- ulcers | cases -ulcers | | |
| 6 cases with 2 abscesses | 1 case - 2 | 4 - (2 - 2; 1 - 1; 1 - 3) | nil | 3 cases & 1 scar in each. |
| 5 cases with 3 abscesses | 1 - 3 | 3 - (1 - 1; 1 - 1; 1 - 1) | nil | nil |
| 1 case with 4 abscesses | nil | nil | nil | 1 case with 2 scars. |
| Ascending Colon. | cases - ulcers | | | |
| 6 cases with 2 abscesses | * 1 case with one ulcer between Ascdg: & Trans: Colon. (cf. Transv: Colon) | 1 - 2 | nil | 1 case with 1 scar. |
| 5 cases with 3 abscesses | 1 case with 2 ulcers | 2 - (1 - 2; 1 - 3) | nil | 1 case with 1 sca |
| 1 case with 4 abscesses | nil | nil | nil | nil |
| Transverse Colon. | cases - ulcers | cases -ulcers | | |
| 6 cases with 2 abscesses | 1 - 1 | 1 - 1 | nil | nil |
| | (* 1 with 1 ulcer( cf* above ). | | | |
| | (* 1 with 1 ulcer between Trans: & Descdg: Colon.(Cf.* next page ). | | | |

Tabular Distribution of Dysenteric Lesions in the Bowel when complicated by Liver Abscess.

Table II. - continued -

| Segment of Gut involv-ed & No. of Abscesses. | Ulcers across Axis of Gut with healthy Muc:Membrane between them. | Smaller round or oval sep-arate ulcers on an other-wise normal muc:membrane of less adv-anced Amoebic Disease. | Large thick-ened patch of ulcerated Gut in Acute Amoebic Dys-enteric Cases. | Scars Of Healed Ulcers. |
|---|---|---|---|---|
| Transverse Colon (continued):- | | cases - ulcers | | |
| 5 cases with 3 abscesses) - | 1 case with 2 ulcers | 2 - (1 - 2; (1 - 1 | nil | nil. |
| 1 case with 4 abscesses) - | nil | nil | nil | nil. |
| Descending Colon. :- | | cases - ulcers | | |
| 6 cases with 2 abscesses) - | nil | 3 - (2 - 2; (1 - 1 | nil | nil. |
| 5 cases with 3 abscesses) - | 1 case with 1 ulcer & *1 case with 1 ulcer between Transverse & Descending Colon. | 3 - (1 - 2; (1 - 1; (1 - 1 | nil | nil. |
| 1 cases with 4 abscesses) - | nil | nil | nil | nil. |
| Sigmoid Flexure:- | | cases - ulcers | | |
| 6 cases with 2 abscesses) - | nil | 1 - 1 | nil | nil. |
| 5 cases with 3 abscesses) - | 1case with 2 ulcers. | 1 - 3 | nil | nil. |
| 1 cases with 4 abscesses) - | nil | nil | nil | 1 case with one scars. |
| Rectum :- | | | | |
| 6 cases with 2 abscesses) - | nil | nil | nil | nil. |
| 5 cases with 3 abscesses) - | 1case with2 ulcers; 1 " " 1 " | nil | nil | nil. |
| 1 case with 4abscesses ) - | nil | nil | nil | 1 case with one scar. |

Tabular Distribution of Dysenteric Lesions in the Bowel when complicated by Liver Abscess.

## Table III.

## Amoebic Dysentery & Multiple Small Liver Abscess.

### 5 Cases.

| Segment of Gut involved. | Ulcers across Axis of Gut With healthy Muc:Membrane between them. | Smaller round or oval separate ulcers on an otherwise normal muc:membrane of less advanced Amoebic Disease. | Large thickened patch of Ulcerated Gut in Acute Amoebic Dysentery. | Scars of Healed Ulcers. |
|---|---|---|---|---|
| Ileum | nil | nil | nil | nil. |
| Caecum | nil | nil | 4 - (3 cases with 2 transverse patches (1 case with one vertical patch. | nil. |
| Ascending Colon :- | nil | 1 case with 3 ulcers | 2 - (1 case with 2 transverse patches & (1 patch between Ascdg: & Transverse Colon. (1 case with 2 transverse patches. | nil. |
| Transverse Colon. | nil | 1 case with 3 ulcers. | 2 - (1 case with 3 transverse patches (1 case with 2 transverse patches | nil. |
| Sigmoid | nil | 1 case with 2 ulcers | 3 - (2 cases with 2 transverse patches (1 case with 1 transverse patch. | 1 case with 2 scars. |
| Rectum | nil | nil | 2 - (1 case with 1 vertical patch (1 case with 1 transverse patch. | nil. |

Tabular Distribution of Dysenteric Lesions in the Bowel when complicated by Liver Abscess.

## Table IV.

Post Colic Abscess - 3 cases - (2 uncomplicated & 1 with Multiple Liver Abscess ).
Acute Amoebic Dysentery.

| Segment of Gut involved. | Ulcers across Axis of Gut with healthy Muc:Membrane between them. | Smaller round or oval separate ulcers on an otherwise normal Mucous Membrane of less advanced Amoebic Disease. | Scars of healed ulcers. | Perforation at Points. |
|---|---|---|---|---|
| Ileum. | nil | nil | nil | nil |
| Caecum. | | | | |
| 2 Uncmpltd: | 2 cases(each with 2 ulcers) | nil | nil | nil |
| 1 Compltd: | 1 case with 1 ulcer. | nil | 1 case with 1 scar. | 1 perforation. |
| Ascending Colon. | | | | |
| 2 Uncmpltd: | 2 cases(each with 1 ulcer) | nil | nil | 2 cases with 1 perforation. |
| 1 Compltd: | 1 case with 1 ulcer. | nil | nil | 1 case with 1 perforation. |
| Transverse Colon. | | | | |
| 2 uncompltd: | 1 case with 2 ulcers. | nil | nil | nil |
| 1 Compltd: | nil | nil | nil | nil |
| Descending Colon. | | | | |
| 2 Uncmpltd: | 1 case with 2 ulcers. | 1 case with 1 ulcer. | nil | nil |
| 1 Cmpltd: | nil | nil | nil | nil |

Tabular Distribution of Dysenteric Lesions in the Bowel when complicated by Liver Abscess.

## Table IV. - continued -

Post Colic Abscess - 3 cases - (2 uncomplicated & 1 with Multiple Liver Abscess ).
Acute Amoebic Dysentery.

| Segment of Gut involved | Ulcers across Axis of Gut with healthy Muc:Membrane between them. | Smaller round or oval separate ulcers on an otherwise normal Mucous Membrane of less advanced Amoebic Disease. | Scars of healed ulcers. | Perforation at Points. |
|---|---|---|---|---|
| Sigmoid | | | | |
| 2 uncmpltd: | 1 case with 2 ulcers. | nil. | nil | nil |
| 1 Cmpltd: | nil | nil | nil | nil |
| Rectum | | | | |
| 2 Uncmpltd: | 1 case with 1 ulcer. | nil | nil | nil |
| 1 Cmpltd: | nil | nil | nil | nil |

NOTES.

In Table IV, there were no thickened patches of ulcerated bowel, as in Tables I, II, & III, - but complicated by Perforations of the Bowel.

- continued -

## Analysis of the Tabular Distribution of Dysenteric Lesions in the Bowel with Liver Abscess secondary to it.

### Analysis of Table I.

1. The Ileum was unaffected in all the 24 cases.

2. The Caecum shows the greatest number of pathological findings. Moreover, the large thickened patches of ulceration were alone recorded in the Caecum.

3. The Ascending Colon, showed only one case with the typical Dysenteric Ulcer, and 7 cases with the smaller round or oval ulcers.

4. The Transverse Colon, had no case of typical trans-axial arrangement of ulcer, but yielded the second largest number of cases of smaller round or oval separate ulcers; 2 ulcers being found in 7 cases out of 9.

5. In the Descending Colon, 7 separate ulcers were found, the great majority of cases showed 2 ulcers.

6. In the Sigmoid, 5 cases of separate ulcers were found, 4 out of 5 cases showed 2 ulcers.

7. In the Rectum, 2 such cases were found, but each had only 1 ulcer.

8. The typical Trans-axial arrangement of the ulcer were limited to Caecum & Ascending Colon. The smaller round or oval separate ulcers were found in all segments of the Gut, being most numerous in the Caecum of equal proportions in the Ascending & Descending Colons, least in the Rectum & next highest to the Caecum in the Transverse Colon. The great majority had 2 separate ulcers. Up to 3 ulcer were found in Caecum, Ascending Colon & Transverse Colon, the most numerous of these 3 -ulcer cases occurring in the Caecum.

9. Scars of healed ulcers were found in 5 cases in the Caecum; the Sigmoid being the next frequent with 2 Cases; the Rectum also showed 2 cases; the least common being the Descending Colon. No scars were found in the Ascending & Transverse Colons.

10. The main incidence of the disease therefore fell upon the Caecum.

Liver Abscess secondary to Dysenteric Ulcer. of the Bowel - A Tabular Distribution & Analysis of the Dysenteric Lesions.

## Analysis of Table II

1. The 12 cases in this series are divided up into
6 cases with 2 abscesses
5 " " 3 "
1 " " 4 "

2. First as regards the Trans-axial arrangement of the typical Lesion. The greatest number of cases showing this, were Caecal. The next highest was in the Ascending Colon. Already in the Transverse Colon this is beginning to be lost, for only 1 case can be found; 1 case is mixed up with the Ascending Colon Lesion, & 1 case with the Descending Colon. In the Descending Colon, there is similarly 1 pure case; 1 ulcer occurring as a mixed distributional one (cf. above). In the Sigmoid & Rectum, there were 1 & 2 cases respectively, but these were limited to the 5 cases with the three abscesses, in both instances.
The 6 cases with 2 abscesses, & the 5 cases with 3 abscesses were about equal in this respect, except in the Descending Colon, Sigmoid & Rectum, when they were limited to the 5 cases with 3 abscesses.
The 1 case with 4 abscesses was absolutely negative throughout, and in all Segments of the Gut.

3. Next, as regards the smaller round or oval separate ulcers.
The greatest number of cases occurred in the Caecum the next commonest being the Descending Colon.
The Ascending Colon & Sigmoid are about equal.
The Rectum was nil throughout.
The 6 cases with 2 abscesses gave a larger percentage of cases with these ulcers, in the Caecum than anywhere else; the Descending Colon being the next most frequent.
The 5 cases with 3 abscesses were about equal in the Descending Colon & Caecum.
The Sigmoid showed an equal number of cases of ulcer in the 2 abscess group cases as in the 3 abscess group.
The 2 abscess group cases in the Caecum were the most, as compared with the 3 abscess group throughout the whole of the Large Bowel.
The Rectum seemed to be the least affected.
The 1 abscess group cases yielded the fewest pathological lesions.

4. Large thickened patches were found in not a single case of all abscess groups & in all Segments, contrasting with the 6 cases in Table I, which showed Single Large Liver abscess.

5. Scars of healed ulcers were found in 75% of cases in the Caecum being most numerous (%) in the 2 abscess group.
Both in the Sigmoid & Rectum, 1 case with 1 scar was found in the 4 abscess case. Scars of healed ulcers were more numerous in the 24 cases of Table I.
The Caecum again showed the maximum stress of the total pathological lesions.

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Liver abscess secondary to Dysenteric Ulcer of the Bowel - A Tabular Distribution & Analysis of the Dysenteric Lesions.

## Analysis of Table III.

1. The Ileum was negative throughout.

2. The Caecum showed the largest number of Large thickened patches of ulcerated Gut. The Transverse patches were found in 3 out of the 4 cases. That is, 4 out of 5 cases (total) showed this thickening. No ulcers of any description were recorded.

3. The Sigmoid showed 3 cases all with Transverse thickened patches. In addition, 1 case with 2 ulcers were found.

4. The Ascending Colon showed 1 pure case with 2 Transverse patches & 1 mixed case of patch between Ascending & Transverse Colons. In addition 1 case with 3 ulcers were found.

5. In the Rectum, 2 cases of thickened patches were found, and no ulcers.

6. In the Sigmoid alone, 1 case with 2 healed scars were found.

7. The typical Trans-axial ulcer was absent throughout the 5 cases, & from every segment of the Gut. The smaller round or oval separate ulcers were found in the Ascending&Transverse Colons & in the Sigmoid - in the former two, 3 ulcers, in the latter one, 2 ulcers.

8. The maximum intensity of the pathological lesions, were manifested in the Sigmoid. If we are to judge of Single Liver abscess & Multiple Large Liver abscess, as having origin from maximum intensive processes, then the seat of origin would be in both cases the Caecum. In, however, Multiple Small Liver abscess, if we apply the same test, the seat would be the Sigmoid.

Liver abscess secondary to Dysenteric Ulcer of the Bowel - A Tabular Distribution & Analysis of the Dysenteric Lesions.

## Analysis of Table IV.

1. The Ileum was negative throughout.

2. This Table is a valuable one, although having only 3 cases, for comparing the lesions found in the liver & Intestine with the lesions found in the Intestine alone. The Post Colic abscess can be looked upon for convenience as a more exaggerated stage of the acute dysenteric process in the Gut.

3. The maximum stress of the uncomplicated cases falls in the Caecum, as both cases showed 2 ulcers. In the Ascending Colon the two uncomplicated cases had each 1 ulcer, and in the Transverse Descending Sigmoid & Rectum segments, only 1 case occurred having two ulcers except in the Rectum, where there was only 1 ulcer. In the complicated cases 1 ulcer was found in the Caecum & in the Ascending Colon; all the other segments of the Gut were normal. These ulcers refer to the typical Trans-axial arrangement.

4. Only 1 case of the uncomplicated group had 1 smaller round or oval separate ulcer and that in the Descending Colon.

5. The complicated case alone showed 1 healed scar in the Caecum.

6. The only perforation which occurred in the Caecum was that of the uncomplicated case; who also had a perforation in the Ascending Colon.
Both the uncomplicated cases had 1 perforation only in the Ascending Colon.

7. The maximum intensity of both the complicated & the uncomplicated cases were found to be the Caecum & Ascending Colon; the uncomplicated case showed its maximum intensity of lesions in the Caecum by reason of its typical 1 ulcer Trans-axially arranged, and 1 healed scar.

8. Comparing all Tables, the maximum group of lesions were found most frequently in the Caecum or Caecum & Ascending Colon. Only in one set of cases ( Table III ) was the Sigmoid found chiefly involved.

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## The Pathological Role of Amoeba Histolytica in the production of Liver Abscess.

### Amoeba Histolytica as the Exciting Cause.

"To what extent the Amoeba is concerned in the production of Tropical Liver abscess, it is as yet impossible to state. If the frequency of its presence is any indication, it must be the usual if not, the only cause. If we watch the movements of this animal on the warm stage .... and reflect that it wanders about in the same very active way among the structures forming the walls of the Liver abscess .... and consider that it lives at the expense of these tissues, it is hard to resist the conclusion that the Amoeba must operate as a disintergrating and irritating agency.... As yet experimental pathology has not given a decisive answer to this, one of the most important questions in Tropical Pathology, though later experiments are very suggestive; Amoebic Dysentery & Liver abscesses have been produced in cats by rectal injection both of amoebic dysenteric stools, and sterile liver pus containing Amoebae; and these organisms have been demonstrated in the liver-pus & intestinal walls after death. Further Harris & Gauducheau have been able to produce dysentery & Liver abscess in dogs by similar injections of amoebic pus, the latter by the intravenous route. Calmette, in view of the frequency with which he and others have found liver abscesses sterile, suggests that the exciting agency is of a chemical nature, some irritating liquefying body derived from the decomposition processes going on upon the surface of the dysenteric ulcer. " (cf.Manson, Trop: Med: pp 573 - 574 ).

* Councilman & Lafleur Johns Hopkins. Hsptl: Reports, ii, 1891, p. 395.

Councilman & Lafleur * found only amoebae in small abscesses in the earliest stage and think that they alone are the initial active agents.

The experimental production of liver abscess were carried out originally in 1893 by W.Kruse & Alessandro Pasquale; and a contemporary observer Zancarol of Alexandria.

* Kruse & Pasquale, " Eine Expedition nach Egypten zum studium der Dysentery und Leber Abzess ". Deutsch Med.Wochenschr, 1893, 354.

W.Kruse*(of the Hygienic Institute of Berlin ) & his confrere Staff Surgeon Alessandro Pasquale of the Royal Italian Navy in the course of their experiments in 1893, conducted principally in the Greek Hospital at Alexandria, were the first to prove that Amoeba-containing pus from a hepatic abscess, which was otherwise sterile, if injected into the Rectum of cats, induced true amoebic dysentery.

* Zancarol -" Pathogenie des Abces du Foie ". Revue de Chirurgie, 1893, 677.

A contemporary observer Zancarol*of Alexandria, showed that amoebic dysentery & liver abscess could be successfully transferred to domestic animals.

* Kartulis"Zur Aetiologie der Dysenterie in Aegypten ". Virchow's Archiv. 1886. Bd. cv, p.521 & " Centralbl.für Bakt." 1891, ix, p.365. & Bd.ii, 1887, p.745.

Kartulis * in 1887, discovered for the first time amoebae in liver abscess. His numerous papers appeared in Virchow's Archives & Centralblatt F. Bakt.

"Strong reports a case in which an Orang-utan in Manila developed a hepatic abscess after amoebic disease of the appendix; and, in a report presented to the first Egyptian Medical Congress in 1904, mention is made of a badger which died at the Zoological Gardens in Cairo, from dysentery with subsequent suppuration of the liver. In this case Ent: Histolytica was demonstrated in all the lesions."( cf.Brown, Amoebic Dysentery, p.173 ).

For complete list of works, cf.Brown, Amoebic Dysentery, pp 11 - 12.

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The Pathological Role of Amoeba Histolytica in the production of Liver abscess.

The most recent and by far the most important experimental work is that of Walker & Sellards* They fed convicts with the organism in the amoebic stage, and some of these became parasitised, and tetragena cysts appeared in their faeces; none developed dysentery. However, of those who ingested the cysts, 4 developed typical dysentery up to the time of writing, the amoebic form appearing in the stools, thus proving the identity of the various forms. 18 out of 20 became parasitised, therefore the percentage developing dysentery was 22.2%. Although the percentage is small, it must be remembered that dysenteric lesions may remain latent; thus in animals that have been infected and which have shown no symptoms, dysenteric ulceration had been found after death. The same applies to man.

If liver abscess be the result of specific absorption from a dysenteric ulcer in the bowel, the reason why it is not a common sequel of Typhoidal or Tubercular ulceration in the Tropics has been explained by Macleod. In Tubercular & Typhoidal ulcerations, the lesion is a surface -lesion, unattended with abscess formation in the wall of the Gut. Hence there is free escape of the products and germs of ulceration, whereas in the dysenteric lesions, in addition to the superficial ulceration, there is often real abscess formation with burrowing and retention of pus below the mucous membrane; therefore, there is increased liability for the causative organism to penetrate into the radicles of the Portal Vein.

The constancy of the presence of Amoebae in the walls of active Tropical Liver abscess.

Early observers pointed out that the habitat of the Amoeba is not in the liver pus but in the walls of the liver abscess, and is more readily found therein than in the contents. Rogers showed that living amoebae were present in the walls of liver abscesses in 35 out of 37 consecutive cases examined either at the time of operation, or within 9 days afterwards. In the 2 cases which were negative, a lapse of 12 & 14 days respectively after operation was allowed togo by before examination. In two-thirds of these cases, the contents of the abscess were sterile, and amoebae were the only organisms to be constantly associated with the condition. According to Manson, amoebae can be detected in considerably over ½ the cases.

Primary Sterility as regards Bacteria of the great majority of Amoebic Abscesses of the Liver.

Many views have been held on the subject - the above is what is now almost universally accepted.

i. It has been held, especially by French Writers, that Pyogenic organisms may be present in the earlier stages of abscess formation but die out later. This view is in part the " Symbiotic Theory " founded on cultural experiments of the older writers. This view receives a measure of support from the fact that in a certain proportion of cases the ordinary Pyogenic Bacteria, B.Proteus & sometimes B.Coli or Typhoid-like Bacilli have been found. Kruse & Pasquale believed that Bacteri were necessarily associated with the Amoebae in suppuration. Kartulis believed that Bacteria were always brought in with the parasites, but

* Walker & Sellards; " Experimental Ent- amoebic dysentery " Phillipine Jl. of Science, Sec.B. Trop Med. Aug: 1913, Vol.8, pp 253 -332.

i. Primary Sterility as regards Bacteria of the great majority of Amoebic Abscesses of the Liver.

sometimes die out in long-standing cases, having less resistance than the animal organism. Rogers is completely opposed to this view. " Why", he asks, " should this occur in liver-abscess than elsewhere ? Moreover, amoebic pus & coccal pus are so dissimilar, as to absolutely contradict any such view. Liver abscess occuring secondary to infection has quite a distinctive pathology of its own - for this type of septic abscess is invariably Multiple; the abscess wall has none of the limiting characters known to occur in the majority of liver abscesses; and the clinical phases are profoundly altered and indicative of Toxemia, with probably secondary abscesses elsewhere. " For these reasons, he condemns this view.

ii. The Symbiotic Theory.

* Celli & Fiocca. " Ueber die Aetiologie der Dysenterie" & other papers in Centralbl.f. Bakt Bd.xv - xvii. & " Annali d'igene speriment, " 1896,vi, 204. & " Intorno alla Biologia delle Amoebae ". Bull R. Accad.Med. Rome,1894-95.

*Tsujitani - "Ueber die Reincultur der Amoben Centralbl.f.Bakt.1898 xxiv, 666.

Prof.Celli & R.Fiocca * maintained that as B.Coli & A.Coli were so frequently found in Symbiosis, they suggested that these organisms exercised a definite influence on each other.
In 1898, Tsujitani * claimed he had successfully grown Intestinal amoebae with the Spirillum of Cholera, and he suggested an inter-dependent relationship between specific protozoa & virulent bacteria.
The recent work of Musgrave in Manila, demonstrated the necessity of Symbiosis in artificial cultivation of amoebae, and this would rather indicate bacterial co-operation in all the lesions of Amoebiasis.
"Reference has also been made to this in the Cytology of the fluid in amoebic Brain Abscess; in some of the cases "symbiotic" Anaerobic micro-organisms have been described.

iii. Primary Sterility.

Rogers found during an investigation of 87 consecutive cases, 75 cases were sterile ( 86%), as regards Bacteria, both microscopically & on culture Cantlie states that in 1895 he had observed the same thing in China.

iv. Anti-Dysenteric Measures.

Quinine which in a solution of 1 in 500 will readily kill amoebae, has no action on Pyogenic organisms. Emetin which is specific for Amoeba Histolytica & Dysenteric processes caused by this organism, will not influence any other Protozoal organism. A.Coli certainly disappears while Emetin is being used but it re-appears when the Emetin is stopped. Emetin has no action at all on Flagellate & Ciliate Dysenteric organisms.

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## Routes of Amoebae to the Liver.

There are four routes by which Amoebae may reach the organ:-

1. Direct - from the lumen of the Alimentary Canal.
2. Transperitoneally - due to perforation of the Colon by an amoebic ulcer, with adhesions to the Liver & direct infiltration of the organ with pus.
3. By the Portal Vessels - the great majority of cases, Amoebae having been demonstrated by Marshall in a thrombus in a branch of the Portal Vein.
4. Through the Systemic Circulation.

## THE DIRECT ROUTE.

This is quite uncommon&can only be explained by invasion through the Bile-Duct. Living Entamoebae have been found in the Gall-Bladder, where the bile is generally more concentrated than in the ducts. This direct method has been held to explain the rare instances of Hepatic Suppuration in which there has been no antecedent dysentery, & the most minute post-mortem search has failed to reveal any lesion of the bowel. It is almost inconceivable in these cases that Intestinal Amoebiasis should have been so slight as to leave absolutely no trace of its presence & yet have allowed a submucosal penetration into the radicles of the Portal Vein & transmission of the amoebae to the Liver. And unless Primary infection of the Liver is admitted a possibility, it is most difficult to explain the origin of such suppuration. Encysted Amoebae become excysted when they reach the alkaline Duodenum, & apart from the fact that bile is not secreted continuously, there are many conditions in which it is not fatal to Protozoal life, especially as Tetragena cysts are mainly the cause of an ingested dysentery.

## DIRECT MIGRATION OR TRANSPERITONEAL INFECTION.

Rogers has seen it occur in a case of Post-Colic abscess due to perforation of the Ascending Colon by an amoebic ulcer, with adhesions to the Liver and direct infiltration of the organ with amoebic pus.

Direct migration, according to Brown is a frequent method of infection. Superficial Amoebic Abscesses are often seen on the lower surface of the Right Lobe, & a direct extension may here take place in the simple extension of the morbid proces from the bowel-wall. In most of these cases the Hepatic Flexure is ulcerated, markedly thickened and adherent to the under surface of the Liver. Even in those cases where there are no adhesions, amoebae may pass across the Peritoneum, from one Serous surface to another; & they have been found in the Peritoneal Cavity, & on the Capsule of the Liver, in the bare area, uncovered.

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## AMOEBAE REACH THE LIVER BY THE PORTAL VESSELS.

This is the most common highway & occurs in the great majority of cases. Marshall found the amoebae in a thrombus in a branch of the Portal Vein. When the submucosa is deeply infiltrated amoebae in large numbers can be found in the tortuous & dilated venous radicles, & at times may be traced in the thrombi throught the whole length of the Portal System, to their distribution in the Interlobular Veins. As ulceration takes place & extends more deeply "enormous swarms of entamoebae are swept into the portal circulation and come to rest in the Perilobular Veins". Brown. Infection by the Portal Route might be expected to produce Multiple Abscesses in the Liver of the Pylephlebitic Type, such as occasionally arise from septic Bacterial infections in sloughing of some part of the Gastro-Intestinal Tract. *

* Jurgens has described amoebae inside the crypts of Liberkühn, into which they have crept; they spread into the submucosa They may also be found in the Mesenteric Glands, having got there by the lymphatics. Lymphatic spread to the Liver may form a hitherto unrecognised & important route to the Liver. THE LYMPHATIC ROUTE MAY BE INCLUDED AS A FIFTH WAY OF CONVECTION.

## INFECTION THROUGH THE SYSTEMIC CIRCULATION.

Infection through the general circulation is infrequent. The amoebae have been found in the Vena Cava & right heart; and they may, according to Brown reach the tissues by squeezing through the capillaries of the lungs.

### I. Age-Sex & Race Incidence.

In a Table shewing Liver Abscess in 300 cases among Natives of India & 92 Europeans, treated in Calcutta Hospitals, the following figures are instructive, and when analysed reveal facts, which show that all the factors must be grouped together, to understand the Etiology of Tropical Abscess.

| | NATIVES. | | | | | EUROPEANS. | | | |
|---|---|---|---|---|---|---|---|---|---|
| Age-Periods | Hindus | Muhmedans. | Males | Females | TOTAL % | Males | Females. | TOTAL | % |
| YEARS: | | | | | | | | | |
| 0 - 10 | 0 | 2 | 2 | 0 | 2 0.7 | 0 | 0 | 0 | 0 |
| 11- 20 | 15 | 1 | 16 | 0 | 16 5.3 | 4 | 0 | 4 | 4.4 |
| 21- 30 | 86 | 19 | 102 | 3 | 105 35.0 | 24 | 1 | 25 | 27. |
| 31- 40 | 94 | 17 | 107 | 4 | 111 37.0 | 34 | 1 | 35 | 38. |
| 41- 50 | 46 | 7 | 58 | 1 | 59 17.6 | 19 | 1 | 20 | 21. |
| Over50 | 11 | 2 | 13 | 0 | 13 4.3 | 7 | 1 | 8 | 8. |
| TOTALS | 252 | 48 | 353 | 8 | 300 - | 88 | 4 | 92 | - |
| | % | % | % | | | % | | % | |
| Percentages | 84 | 16 | 97.3 | 2.7 | - - | 95.6 | - | 4.4 | - |

## Accessory Factors or the Predisposing Causes.

These must be looked upon as rather important factors in the pathological cycle of amoebic infection of the Liver, for although many may get dysentery, yet only a certain percentage go on to its more serious complication of Tropical Abscess; and as it is rare in Females & Children unless we accept these points in the explanation of the incidence of abscess, we are quite unable to explain what would be conundrums in Medicine. What exact percentage of amoebic dysenteries develop Hepatitis & abscess-formation, is variable, because the whole question turns upon adequate & early treatment, which in turn depends upon early diagnosis. There is, however, no doubt as has been shown by G.Padoa * and others, the protective influence of the healthy liver is sufficient to resist and counteract the entrance of Intestinal organisms & their toxins into the systemic circulation, and in ordinary circumstances, these Entamoebae are all destroyed & absorbed. " When, however, the Gland is impaired by Chronic Congestion infiltration, & Fibrosis, it loses its protective function, and the tissues break down around the infecting organism. If in such cases, the Entamoebae are unattended by septic Bacteria, the Abscess is Solitary and sterile; but should there be large numbers of putrefactive germs, normal resistance is overcome, and suppuration is them Multiple & Septic!" (cf.Brown, Amoebic Dysentery p.177 ).

The following may be considered as Predisposing:-

1. Age, Sex Race, & Climate.
2. Duration of residence in the Tropics.
3. Causes of Liver-Congestion & " Tropical Liver ".

* G.PADOA - Revue Crit. de Med.Clin. Sep.& Oct. 1904.

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| | NATIVES. | | | | | | EUROPEANS. | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Age-Periods | Hindus | Muhmdans. | Males | Females. | TOTAL | % | Males | Females. | TOT: | % |
| YEARS: | | | | | | | | | | |
| 0 - 10 | 0 | 2 | 2 | 0 | 2 | 0.7 | 0 | 0 | 0 | 0.0 |
| 11- 20 | 15 | 1 | 16 | 0 | 16 | 5.3 | 4 | 0 | 4 | 4.4 |
| 21- 30 | 86 | 19 | 102 | 3 | 105 | 35.0 | 24 | 1 | 25 | 27.2 |
| 31- 40 | 94 | 17 | 107 | 4 | 111 | 37.0 | 34 | 1 | 35 | 38. |
| 41- 50 | 46 | 7 | 58 | 1 | 53 | 17.6 | 19 | 1 | 20 | 21.7 |
| Over50 | 11 | 2 | 13 | 0 | 13 | 4.3 | 7 | 1 | 8 | 8.7 |
| TOTALS | 252 | 48 | 353 | 8 | 298 | - | 88 | 4 | 92 | - |
| Percent-ages | % 84 | % 16 | % 97.3 | % 2.7 | - | - | % 95.6 | - | % 4.4 | - |

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Analysis of Age-Sex-&-Race Table.

1. The lowest incidence is in age-group 0 - 10. & there were no females. The European cases gave a nil-return.

2. The numbers gradually rise to a crescendo of 37 & 38 % in the Native & European Series respectively, between 31 - 40 (age-group). The males give a total of 107 to 4 females in the Native & 34 to 1 in the European Series.i.eor 27:1 & 34:1, in the two series.

3. The Native Percentages for Age-Groups 21-30 & 31-40 are approximately equal; but in the European Series the difference is as much as 11%. The female Total figures do not vary, so that these differences are wholly due in the Male-Incidence Rate.

4. From over 40 the case-incidence falls steadily,& is least in age-period over50, in both series. This is again due to the Male-Rate.

5. As regards differences in the Native Series, theMale Hindu Total admission , for all ages, are 252 against a similar Muhmdn:case- incidence of 48. And the Percentages are respectively 84% & 16% the Ratio therefore being as 5.25 : 1. The higher case-rate for Hindus appear to be in the age-group 31-40; & in the other denomination 21-30; but the difference in the case-rate between these two age-groups in the case of the Muhmdms: appears trifling whereas in the Hindus there is a greater difference. The case-rate difference between these two denominations is most strikingly marked throughout all age-periods, but moreeespecially between 11-20 & over50. By a curious"accident" age-group 0-10 gave 2 cases in Muhmdms-boys & nil in Hindus.

6. The female rate seems practically unaffected by age remaining so low throughout that it appears a matter of accident than otherwise; though the European female rate is always smaller than the corresponding Native rate.

7. Between 41-50 the figures (Total) are ½ of the age-groups 31-40 in Native Series & slightly less than ½ in the Europeans, for the same periods.
Over 50 the figures are further lowered to 1/9th. of what obtains in ages 31-40, in the Natives & to 1/5th. in the Europeans,in the same age-groups.

Notes. The figures for the Native age-groups must be read with an eye to the fact that in most cases the Native can only give his approximate age, for ages are amongst them often a matter of heresay or anHoroscopic affair, & a difference may well exist in what they state to what they are by a matter of 10 years. We may therefore take it that the European age-groups figures, although slightly higher are approximately equal in the corresponding age-groups.

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## The Influence of Sex.

One must not strictly look upon this as a factor ipse se. For there is no doubt that habits, less exposure etc. are most important factors in the consideration of this side of the question.
"It is noteworthy that Pre-suppurative Hepatitis is equally rare among females of both races, only one-outof 50 cases in my European series being females." (Rogers' Dysenteries p.158).
The lesser consumption of alcohol by females may in part account for these low figures, & perhaps also to the fact that in the Tropics they are not exposed to the same extent as the men, but this however is only a portion of the truth & until we have more exact knowledge of the Etiology of the disease, these more or less generalised statements can alone be put forward.

## The Influence of Race.

Authors disagree on this point. The common view held is that fresh & unacclimatised arrivals to the Tropics are more susceptible to Dysentery than the habituated Indigenous sojurners. There is undoubtedly a great amount of truth in this. The newly-arrived European not only does not take the necessary amount of care of himself but often undermines his health with late hours, drinking etc. and being unaccustomed to boiling milk etc. before use he gets Dysentery, which is often unproperly treated & turns into Chronic Neglected Case. The Native, it is equally true, also takes no extra precaution, but he is acclimatised in his very infancy to hardships that fashion his life and he gets a certain amount of protection; and his cruder habits of life allow him more ample scope than can be reasonably run by the new-arrival.
Turning to the Indian Army Statistics, according to Manson, in the Native army the proportion of DEATHS from Liverabscess, to TOTAL mortality in 1894 was only 0.6 %; whereas in European army inIndia it was 7.4 %. Man for man, the relative liability of the European & the Native soldier was as 95.2:4.8. This disproportion is in spite of the fact that the Native is more liable to Dysentery than the European Thus in 1894, in the Indian Army the Admission-Rate for Native Troops for dysentery was 43.8 per 1000; whereas in European Troops it was only 28.60 ; & in every 100 deaths in the Native Army, 4.7 were from dysentery, against only 3.8 in the European Army.
Cf/Manson - Trop. Med. p.565.
Rogers is entirely opposed to this view & to the quotation of mere figures, without attempting at the same time to recognise the differences between the conditions under which these statistics were drawn up. Jail figures are least important as the type of Dysentery-is almost wholly Bacillary, & Amoebic cases are only 0.1%.
"During the 14 years 1894 - 1908, the admission rate per1000 for Liver abscess averaged 2.35 amongst the British Troops, but only 0.1 in the Native Army....
Nor are the conditions under which Europeans & Native Troops serve strictly comparable, for the two races are unequally distributed over Indian Stations, & British Troops are alone sent to the Hills, in large numbers in the hot & rainy seasons, while sudden

The Etiology of Tropical Abscess of the Liver.

- continued -

The Influence of Race - continued.

sudden change to high altitudes & climate notoriously predispose to both dysentery & hepatitis. Alcohol is also more largely consumed by British than by Native Troops. For these reasons the figures for a number of years' admissions to the large Calcutta Hospitals may be expected to furnish more reliable data for comparrison of incidence of Tropical abscess in the different races." Cf/Rogers' Dysenteries p.159.

These cases are admissions for 1899-1908, & in addition the post-mortems for the last 35 years. "They show a case-incidence of 300 Natives & only "31 Europeans, so 1/11th. of the patients belonged to the latter race, while 1/3rd. of the beds available there are for Europeans; so that in proportion to the beds available there were three times as many cases among the Natives . On the other hand, if the Incidence is calculated on the relative proportions of Natives & Europeans in the population from which the Admissions are derived, then the disease is more common among Europeans." (cf/Rogers - ibid p.160).

These Statistics therefore may be made to read in any direction one wills. The Race-Question is always a most complicated affair to draw any trustworthy data from. In my mind not sufficient attention has been devoted upon the characteristic differences that exist in ithe way an Indian looks upon Disease & how difficult it is to remove their prejudices with regard to Western Medicine . Their outlook upon disease & its treatment depends mostly upon their time-honoured remidies & their Hakims or Native-doctors. They therefore cannot be regarded as forming suitable classes in comparing the Incidence-Rate with others. Moreover their population is so enormously larger than the White population, that many more cases will surely result amongst them, than amongst the lesser. Further, even amongst Europeans, there exist such enormous differences both as regards the fact that a certain large % have lived so long in India that that comparrison cannot be made with the new-comer, and this further fact that the climate of India differs so much, even often at a distance of 50 miles, that there is weighty objection in the comparrison of sets of figures taken in any given place & weighed with what obtains in others. The only safe solution is to compare class with class, but with this reservation, that the members live pratically in one community, as regards habits and as regards Climate. The compared rates amongst Hindus & Mumhdns. are only useful in as much as it accentuates the differences of Custom which perhaps has a greater bearing upon the Etiology of Disease, than a gross comparision of Race. Abscess is twice as high amongst Hindus probably because of their greater indulgence in Alcohol. Manson makes this interesting remark that when the Natives take to European habits in the matter of eating and especially drinking, their liability to Liver abscess is greatly & prpportionately increased.

The Etiology of Tropical Abscessof the Liver.

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Climate & the Duration of Residence in the Tropics as Factors .

Liver Abscesses, due to Amoebae, are very rare in Temperate climates.
Rogers Tables of a comparrison of Liver Abscess in 45 cases amongst Europeans , regarding the TIME they had been there, 1/3rd, had been born & bred there, and 2/3rds. were Immigramts. The duration of these latter were as follows:-

| Time in India | Under 1 Years. | 1 - 3 Years | 3-10 Years | Over 10 | Tot |
|---|---|---|---|---|---|
| CASES ..... | 8 | 6 | 8 | 8 | 30 |
| PERCENTAGES ... | 26.7 | 20.0 | 26.7 | 26.7 | 100 |

"Thus just over 1/4th, were attacked in the 1st. year, and another 1/5th. in from 1-3 years of coming to India, so that long residence does not appear to increase the predisposition to the disease as much as might have been expected."
Rogers'Dysenteries p. 161.

Commentary. Although at first glance one might agree with Rogers'Figures, yet he seems to have lost sight of his own statement that out of 45 cases one-third ~~were~~ were born & bred in India, i.e. 15 cases, whereas two-thirds were Immigrantsi.e. 30 Surely these facts speak for themselves. The Immigrant cases evidently were not, inter se, affected by length of residence, but when compared with the Indigenous cases, they were in the ratio of 2;1.
My experience has been that all Gastro- Intestinal disorders are much more common & more severe among Europeans than among Natives. One was able to test this practically among the Indian Troops & the British & Australasian Troops in the Gallipoli Expedition in 1915. The largest numbers we took back in the Hospital Ship "Letitia" were for Dysentery & Typhoid. While attached to No.5.Ind. Gen. Hospl: in Alexandria although we received a good number of such cases in October 1915, they did not come up to the sick-rate for these diseases in the case of British troops, & in Nov.1915 while I was in Suvula Bay, the high rate of such cases while they did not equal the Summer sick rate were high enough to judge of the case-incidence among Indians & among British & Australasian troops.
It is also the common experience of many that Dysentery is more common among among newly-arrived persons in the Tropics than those who have been in those parts a long time. W.C.Brown definitely asserts"That Length of Residence appears to be a predisposing cause than otherwise". (cf/Brown - Amoebic Dysentery p.172).
Manson too agrees with this dictum. (cf/Manson - Trop.Med. p.565; 567-568.).

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## Disturbances of the Liver as a Factor in Etiology.

Opium-Eaters or Habitues, seem like Alcoholics to be more prone to Hepatitis & Abscess than abstemious indivudals. This perhaps works out as a lowering agent to the successful resistance of the body in infections, and a narcotised body cannot resist baneful influences to the same degree as a healthy person.

Alcoholics. The influence of over-indulgence in Alcoholics, in the production of Abscess, is universally held by all writers, who have experience in Tropical conditions & practice.
Waring states that 65% of liver-abscesses observed by him were in Alcoholics.
Megaw, of the I.M.S., collected in the Medical College Calcutta, a series of Notes of 229 cases, & found that in 170 there was a record of the use of Alcohol, in the cases of Liver Abscess, as follows:-

In 119 it was habitually used - 70%.
In 51 habit was denied - 30%.

Rogers'European Hospital cases of 55 , showed :-

All took Alcohol, generally as Whisky.
In 62 % the quantity was unrecorded.
38%- (In 22 % 2 - 3"Whisky-Pegs" daily (moderate)
(In 16 % excess was noted.

i.e. Out of 38 % where a definite quantity was known, nearly ½ were in excess - "a very high proportion, clearly indicating a marked effect of alcoholism in predisposing to liver abscess. "
Cf/Rogers'Dysenteries p. 162.

It has also been pointed out that the low incidence of liver abscess in the Native Army, among Muhmdms: and in the female sex, are all in accordance with the view that alcohol markedly predisposes to the disease, so that there is no doubt that its habitual use is an important factor, though ofcourse not an absolutely essential one.
The reason of this condemnation of the habitual use of the drink is that it certainly leads to what is a now-recognised condition of TROPICAL LIVER.
This condition is an artifically-induced condition, physiological however in the earlier stage & due to the excitation & congestion of the liver by the overwork required in a temperature continuously high, and caused by alcohol & incidentally aided by the want of excercise and over-eating: but as time goes on this chronic stimulation passes on to a pathological result, attended by enlargement of the organ to a greater size than that induced by the initial reaction, and by diarrhoea. One step further, and such a condition passes into actual, but Simple Hepatitis, with accentuation of the symptoms. Given the causative Amoebae, the soil is quite fertile for their lodgement and pernicious activity; & a rapid deterioration of the remains of what may be called its Protective Influence, follows upon the necrotic processes induced by Amoebic activity.

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## Disturbances of the Liver as a Factor in Etiology.

Malaria. Rogers denies all possibilities of Malarial Fever as predisposing to abscess. The very fact that there is an almost constant Leucocytosis present, is alone sufficient to exclude this Fever as a determing cause. However, there is no reason to doubt that a Chronic Malarial condition, with its cachexia & degenerative phenomena in the blood, evidenced by an increase of the Large Lymphocytes, Megalobytes, & polychromatophilic degeneration in the staining reactions of the Red cells; & also a Liver weakened by a Chronic Malarial Cirrhosis, will act as causes by weakening the Liver-tonus to resist Amoebic activity.

Chills. Tropical chills are commonly looked upon as predisposing causes. Temperature conditions are so variable in these hot climates, that chills are of common occurrences, due solely to the body being unable to adapt itself to sudden drops in the temperature. Even a drop of a few degrees, although the temperature is still high, will immediately cause shivering. Moreover, as has been remarked before, sudden changes of climate undoubtedly cause severe Hepatic Symptoms. A change from the hot plains to the "Hills" - an average of altitude is 5000 feet - often induces acute Hepatitis in persons who have suffered from previous Dysentery or Hepatic Congestion; and Chills therefore are certainly of importance & do explain cases of Liver abscess, when the exciting Cause, Amoebae, are present or there are indications of an associated Dysentery. Often however one has to infer the presence of Latent Dysentery, when a change to the Hills has been followed by incipient Liver abscess; the change having been undertaken for Chronic ill-health, without obvious cause.
"Chills"however must be always be carefully differentiated from the actual Rigor of an Amoebic Hepatitis or of actual Amoebic Suppuration.

## S U M M A R Y.

The causes of Liver abscess are two in number & both these two conditions are essential to Hepatic Suppuration after Dysentery.

1. Predisposition - owing to Alcoholism, exposure. Race & Sex Influence are too ill ill-understood to say definitel what exact influence they have & it probably turns upon the above. Length of Residence is undoubtedly important.
2. Implantation of Amoeba Histolytica in the Liver. Abscess is always secondary to Dysentery- esp: chronic untreated cases. They reach the organ by the Portal Stream, in the great majority of cases. Lymphatic spread is important, though not properly recognised. The great majority of such abscesses are **Primarily sterile.** Abscess is undoubtedly due to the action of the Amoebae themselves; some however think there is an active cellular toxin secreted by the Amoebae. How far Bacteria are responsible in the initial process of abscess formation is not quite settled; but the Amoebae are in themselves quite active enough to explain all lesions.

SECTION VII. AMOEBIC INFECTION OF THE LIVER.

PART 3. ITS CLASSIFICATION-TYPES AND METHODS OF FORMATION.

1. Its Method of Formation.

1. The essential factor is the presence of Ent.Histolytica, derived in all instances from the Intestine - a Secondary Phenomenon therefore to Amoebiasis of the Intestine. Such passage occurs generally by the PORTAL blood-stream. (Cf/Etiology of Liver-Abscess, supra, THESIS).

2. CLASSIFICATION OF ABSCESS. This has been usually divided into:-

I. The Single Large Abscess - the commonest

II.Multiple Abscess.

III.The Single Small Abscess.

Method of Production of the Single Large Abscess.

This, as will be seen from the TABLES of Frequency is the commonest Type of Abscess.

* Cf/Rogers'Dysenteries, p.172.

1. Its Method of Formation.

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III.The Single Small Abscess.

Method of Production of the Single Large Abscess.

This, as will be seen from the TABLES of Frequency is the commonest Type of Abscess. Necrosis of the Liver & its disorganisation produces in time a dense fibrous wall, shutting off the abscess from surrounding tissue a Limiting Membrane. Expansion occurs by the pushing on one side the liver-substance rather than active destruction. In extreme cases of Amoebic abscess most of the liver-substance escapes destruction. Rogers in his "Fevers in the Tropics" & his "Dysenteries"* records a case of an enlarged Right Lobe Abscess, reaching down to the Anterior Superior Iliac Spine & containing more than four pints of pus; the fluid resulting from secretion of the lining-membrane,

The greater part of the Right Lobe as well

* Cf/Rogers'Dysenteries, p.172.

as the whole of the Left remained quite healthy in appearance.

3. Method of production of Multiple Abscesses.

The most acute and rapidly advancing Amoebic Hepatitis usually produces multiple abscesses, some being of considerable size, and some also at a very early stage.

The condition is essentially a vascular obstruction and thrombosis of the veins. Zones of Liver substance break down and the process extends. The minute distributional arears of the Portal Vein ( the Intralobular veins ) are filled with Amoebae which get entangled in and break down the blood-clots. The Amoebae have been introduced by the blood-stream into the Liver. Councilman and Lafleur think that some of the destruction is due to a soluble toxin.

Councilman and Lafleur ( Johns Hopkins Hospl: Reports ii 1891, P. 395 ) have carefully described the microscopical appearances. The loss of tissue may be replaced by a cellular proliferation as well as by connective tissue overgrowth; but in other parts entirely by new connective tissue and a degree of Cirrhosis of the Multi-lobular Type results. This necrosis is sometimes confined to the Central portion of the lobule, the portal areas escaping, at other times the whole lobule is involved. In more chronic cases where a capsule forms, granulation tissue is formed followed by reticular fibrous tissue with spindle- cells; outside this is a zone with new bile-ducts and numerous blood-vessels; further out there is regeneration of new Liver cells in groups passing on to masses; and outside this

a zone of Liver cells which have been compressed by the abscess. Kartulis sums up these zones into

(i.) Detritus Zone, or zone of actual destruction of the cell.

(ii.) The active cell zone of regenerating Liver tissue etc.,

(iii) The Boundary zone or peripheral zone of pressure and compression.

The changes are always produced by the following sequence of events ( Phillips Amoebiasis and the Dysenteries, 1915, P. 26. ), " At first thrombosis of the small vessels occurs, and amoebae may be seen within them; then liquefaction of the thrombosed area occurs and the amoebae escape. The amoebae are most easily found in the wall of the cavity where they cause necrosis of the Liver cells; the cellular protoplasm is destroyed with degeneration of the nuclei. "

"This breaking up of the nuclei and formation of granular detritus seen in bacterial infections do not occur" - Ibid, P. 26.

4. <u>Mode of Production of the Single or very few, Chronic circumscribed Large abscess with dense fibrous walls.</u>

The original hepatitis set up is due entirely to the presence of amoebae in large numbers carried through the Portal circulation to the Liver, producing Acute Congestion and probably some clotting in some of the smaller vessels. Here they undergo degenerative changes ( sometimes with calcification ) without being able to escape through the vessel walls to break down and liquefy the Liver-substance into

into an abscess. As long as these Protozoan Parasites are widely distributed in small numbers through the organ no suppuration may take place, but if at any one or more parts of the Liver they should chance to be sufficiently numerous to produce clotting in numbers of contiguous vessels and interfere with the circulation, foci of necrosis must form which will enable the organism to revert to the process outlined in Mode of Production,(3). Thus the cavity produced by disintegration by concentric layers enlarges till it becomes limited by the chromic fibrous capsule, when all the conditions attached to Mode 1, will be called into play and a huge Single localised Tropical Abscess will result.

The following account of Intra-Hepatic Circulation is taken from Beattie and Dickson Special Pathology P. 274, and illustrates spread by the Portal Vein.

" The branches of the Portal Vein ( interlobular veins ) by which most of the blood comes to the Liver, sends capillaries into the Lobule, and these at the centre open into the Central or Intralobular Veins. These Central Veins unite to form larger branches ( the Sublobular ) which open into the Hepatic Veins. Between these capillaries lie the columns of hepatic cells and separating these blood-channels from the Liver cells there are at places the stellate cells of Kupffer. "

Cirrhotic condition of the Liver has already been referred to above. This cirrhosis is resultant upon the destruction of the hepatic cells plus the blocking of the intra-hepatic circulation by amoebae which will at first produce Acute and then this be followed by Chronic Venous Congestion.

In purely uncomplicated cases " there is no overgrowth of fibrous tissue extending from the Portal tracts or from the rest of the fibrous tissue framework, and therefore such Cirrhosis following on Chronic Venous Congestion is not a sequel of mere Chronic Venous Congestion of the Liver ( Beattie and Dickson Ibid P. 280") .

In the Embolism and Thrombosis of the Portal Capillaries the blocking of the veins supplying the lobule may cause complete necrosis of the Central two-thirds of the lobules, though comparatively little damage to the Liver tissue results as nutrition is still carried on especially at the periphery of the lobule by the Hepatic Artery. When the Interlobular and other branches of the vein get blocked and infected large irregular suppurative areas result with considerable destruction of the Liver tissue. Cirrhosis may also be purely of the Biliary Type, when persistent Jaundice usually occurs. The so called proliferation of the bile-capillaries are due according to Lindsay-Milne " to the swelling of the flattened endothelial-like cells lining the minute biliary channels running between the columns of Liver cells ( Monolobular Type ) ", The nature and distribution of the resulting histological lesions will therefore depend on the rapidity or chronicity of the destructive changes in the Liver cells, the fibrous tissue overgrowth being induced by the irritant action of the irritant not upon the pre-existing fibrous tissue, but upon the cell-death of the Liver cells; and it is according to the capacity of the cells to undergo reconstructive and reparative processes that

that a wide- spread or diffuse or localised and restricted cirrhosis will result. (cf. beattie& Dickson, ibid, p. 290. ).

Sir Leonard Rogers has described a peculiar type of Leucocytisis in Cirrhosis of the Liver, esp: if the case is going to end in cholemia - about 93% of cells being POLY-MORPHONUCLEAR.

A secondary cirrhosis of theLiver has been describ-ed by Rogers associated with Chronic amoebic disease of the bowel- wall. ''Much of the excess-ive prevalence of hepatic cirrhosis in Calcutta is directly the result of a chronic amoebic infection of the Liver, derived from a long existing ulceration of the bowel." CF.Rogers' Dysenteries p. 73.) *

Rogers' cases
* IND: MED: GAZ.
Feb: 1911.

Infantile Biliary Cirrhosis. (Tropical. ). *

This special type of Tropical Biliary Cirrhosis in infants up to one year of age is of unknown origin. IT has an insidious course, ending in cholemia. It is apparently not the Aeute Congenital Acholuric Jaundice, either of the Minkowski type or other known form of Hereditary Familial Icterus (cf, Osler, The Principles & Practice of Medicine 7th edn, pp 537- 538.).

*Ref: Infantile Biliary Cirrhosis
Mackenzie& Ghose
Lancet 1895, i, p 321.

The pathology of this condition has been worked out by Gibbons who concludes " that it is a peculiar form of Biliary Cirrhosis, the consequences of the action on the Liver cells of some irritant of gastric origin which leads to degeneration of the

cells in the first instance, with subsequent increase of intercellular connective tissue, and, later, of the portal sheets. The formation of new bile-ducts between the hepatic cells, which is a well marked feature is evidence of a natural curative effort having for its object a regeneration of the Liver cells ".( cf.Manson Tropical Diseases, 5th.edition, 1914, pp 597 - 598).

In these cases enormous Livers have been noted - probably the result of Chronic toxemia from the intestine. Such cases may date from time of birth attacks children generally under one year of age and tends to run in families. It usually runs a fatal course in about three months. Whether such a condition may be due to a latent amoebic infection or to some other Protozoal organism e.g.in Leishmaniasis ( Kala-Azar) is undetermined. It is not due to Syphilis or Malaria. If this be due to an amoebic infection, the possibility of the mother being a chronic carrier should not be lost sight of. Possibly infection may take place through the mother's milk. It seems to be very prevalent in Calcutta but may occur in other large towns of India.

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continued

2. The distribution in the Liver; the varieties of and courses of amoebic abscess.

The convection of the amoebae to the Liver is fully described in the Routes and Pathways of amoebae to the Liver.

1. The relative frequencies of the Multiple and Single abscess.

On an analysis of cases from 1886 - 1908, Rogers has collected data and drawn up Tables of relative frequencies. A summary of his findings is given below and classified by me as follows ;-

Multiple Abscess.

(i). Those in which two or more Large or moderate sized well-circumscribed abscesses were found which are similar in nature to the typical Single Large Abscess.

(ii). One or more Large or fair sized cavities together with numerous small acute suppurative foci of more recent and acute formation. These run clinically an acute course, are accompanied by well marked Dysentery; non-ammenable to surgical measures but may be influenced by Emetin in their earlier pre-suppurative stage.

continued

(iii). Small Multiple abscesses in addition to a Single Large cavaty of much earlier date which has been operated on some time ago. This Type which results <u>after operation</u> in one of the ways as follows:-

(a) by the non-exhibition of Ipecac. treatment; permitting of infection of the Liver from a pre-existing persisting Amoebic Dysentery, perhaps of a Latent Type - the whole case being often regarded as a Chronic Malaria.previously.

(b) Advent of pyogenic bacteria after operation for its evacuation. This is really a Pyemia and is specially influenced by a hot moist climate, as of Bengal. Pyemic Abscesses may also occur secondary to a septic phlebitis of the portal vein - the source of the infection being usually in the Large Intestine and freguently causing a septic thrombosis of one of the mesenteric veins. The septic focus therefore may primarily be in the large bowel and sepsis therefore is not caused by the advent at the time of operation but derived from the unhealthy gut.

(c)

Beattie and Dickson

Special Pathology P.288.

(iii) (d) Other abscesses of the Liver occur but present no important features which dintinguish them. The most important are those which arise as result of infection by the Streptothriceae ( Actinomycosis); and from suppuration in Hydatid Cysts. (cf.Beattie & Dickson, Ibid, P.289 ). Pneumococcal Abscess of the Liver has been also described. ( cf.Lancet June 18. 1910 ).

## The Single Abscess

These form the greatest number of cases statistics of which will be given below. They may be Acute or Chronic. They are more commonly situated in the Right Lobe. " The seat of election " is the upper part of the Right Lobe ( Manson ). The posterior part of the upper portion of the Right Lobe is the commonest locus of such an abscess. ( Castellani ). Roux gives the proportions in 639 cases as 70.85% Right Lobe; 3% Left Lobe; and 0.3% Lobus Spigelii. ( Manson Tropical Diseases 5th edn. p. 569 ).

Musgrave's statistics yield an average of 40 -65% as Solitary .

Zancarol gives his Egyptian figures as562 total cases of which 60.2-%were solitary.

* Zancarol
Progrès Médicale
No.24 p. 393.

These abscesses , like the Multiple, are secondary to dysentery.

ITS earliest stage is an acute hyperemia, akin to

the condition known as, Tropical Liver or Hepatic Hyperaemia ( Manson Tropical Diseases, 5th. edn, pp. 556 - 560.).

Budd's theory expresses in modern terms becomes a "Theory of Chance". " If the weakened Liver is efficiently innoculated at one point only there is only one Liver abscess; if at many then there are several. " ( cf. Manson ibid, p. 573 ).

Rogers, however, compiles important Tables of Frequency from periods 1873 - 1908. He divides up his cases under the following heads:-

THE FREQUENCY of SINGLE and MULTIPLE LIVER - ABSCESSES.

| No. of Abscesses | 1873-1886 cases ....% | | 1886-1908 cases....% | | TOTAL cases....% | |
|---|---|---|---|---|---|---|
| 1. SINGLE abscess ..... | 33 | 55.9 | 52 | 49.5 | 85 | 51.8 |
| 2. TWO or more LARGE..... | 16 | 27.1 | 23 | 21.9 | 39 | 23.8 |
| 3. LARGE plus Several Small... | 10 | 17.0 | 30 | 28.6 | 40 | 24.4 |

"The recovery rate during the last two decades is just 40% which will almost invariably be composed of Single abscess cases. To get the proportion of SINGLE abscesses among the total admissions we must add this 40% of recovery to HALF the 60% death-total. Thus 70% of the total admissions are SINGLE abscess ". (cf.Rogers Dysenteries, their Differentiation and Treatment, 1913, p. 179.)

SUMMARY

of THE MULTIPLE and SINGLE ABSCESS TYPES.

1. The Multiple abscess type.

These average about 23.8% of all cases - 2 abscesses being the commonest about 44.7% of cases. (cf. Table of Frequencies given below.)

This type may occur as,

(a) a localised abscess with limiting membrane spreading by pressure necrosis causing focal degeneration, similar in type to the typical Single Tropical abscess.

(b) those associated with more numerous small suppurating foci caused by hepatitis going on to pus-formation and running an acute course often accompanied by a well-marked dysentery.

(c) small Multiple abscesses( evidently a further stage of the preceding one)and associated with a chronic fibrotic abscess undergone secondary changes due to reaction of the Liver to chronic inflammatory processes. This abscess clinically is a Pyemic abscess associated with the presence of Pyococci capable of producing septic metasteses in other organs e.g Brain, Lung & Spleen.

2. The Single abscess type

This is the commoner of the two varieties forming about 51.8% of cases resulting from a hepatitis going on the lines of an acute inflammatory process resulting in abscess; spreading by pressure necrosis and pus secretion from its lining membrane. Such abscess may, however, result from insidious formation with chronic fever corresponding to type 5 chronic insidious hepatitis clinically marked with a Malarial-like cachexia and low fever; resolving readily enough in their pre-suppurative stage to

## S U M M A R Y

- continued -

Emetin, or perforce surgical measures; and being often of a considerable size, but leaving an astonishing amount of healthy Liver-tissue, in its immediate vicinity.

Note

It is always important to bear in mind that an enlarged Lobe does not necessarily mean hepatitis or abscess. There is also the condition known as Riedel's Lobe enlargement, which may cause errors in diagnosis. There are a few symptoms, the mass moves on respiration, is continuous with the Liver dullness without any intervening area of resonance between it and the Liver.
(cf. Index of Differential Diagnosis of Main Symptoms, ed. by French, 1912, p. 737.).

* Rogers - B.M.J, 1903 vol ii, p. 706.

1. Portal Pyemia ( Pylephlebitis ).

This is due to septic infection arising in some part of the Gastro-Intestinal Tract, and producing Multiple acute abscesses throughout the liver, originating in the distribution of the Portal Veins. This form of Portal Pyemia, may arise from sloughing dysentery in the Tropics. It is exceedingly uncommon. Rogers has not met with a single case among over 1,000 post-mortems in Calcutta during the last few years. (cf.Rogers, Dysenteries, p. 154.).

2. Multiple abscesses in the liver in the Biliary Canals.

These abscesses are always secondary to some infection of the bile-passages; the great majority secondary to gall-stones. Among 20 cases of this rare disease which Rogers collected, 18 were found secondary to gall-stones, the infection probably spreading up the Common Bile-Duct from the Duodenum; one was due to an Hydatid Cyst, and the remaining one to a Primary Cancer of the Bile-Duct. Most of these cases are very rare to diagnose during life; only one such case occurring in Calcutta which was diagnosed during life, and in which Rogers removed a large mass of gall-stones from the Hepatic Ducts; but the suppuration tracked along the Inferior Vena Cava to open into the lungs with fatal results.
(cf.Rogers' *Dysenteries, p. 155 ).
The clinical history of such cases are very widely different from the so-called Tropical liver abscess, for they are of a very acute nature, and dependant upon the Primary diseases which they complicate.
In typical Tropical liver abscess, a Primary more or less acute hepatitis is the usual antecedent, the collections of pus are always large and localised with or without smaller Multiple abscesses quite unconnected with each other, and entirely free of secondary pyogenic bacteria throughout the course of their existence. The Biliary variety, in contra distinction to Tropical abscess, occurs quite as commonly in the Temperate, as Tropical zones - the Tropical abscess being limited as its name suggests, to Tropical or Sub-Tropical Climates.

* Rogers - B.M.J, 1903 vol ii, p. 706.

PART 4. RIGHT & LEFT LOBE SINGLE & MULTIPLE LIVER ABSCESSES:

THEIR FREQUENCIES & A RESUMÉ OF THEIR CLINICAL COMPLICATIONS & TERMINATIONS

TABLES of FREQUENCIES of SINGLE and MULTIPLE LIVER-ABSCESSES

1. Rogers Tables

Two abscesses 44.7% ..... 17 cases

three " 26.3% ..... 10 "

four " 18.4% ..... 7 "

over four " 10.6% ..... 4 "

Total 48 "

In roughly half of the cases 44.7% were dual Liver abscesses.(cf.Rogers' Dysenteries p.179 ) et.seq:-

2. Rogers Table of Multiple Liver abscesses - their distribution.

1. All occurring in Right Lobe, 15%

3. Distributed in both Lobes .. 13%

3. Rogers Table of Single Liver abscess distribution

1. Abscess of the Right Lobe - the great majority.

2. Abscess of the Left Lobe - 16.4%

3. Subdiaphragmatic or Juxtaphrenic ) .....v 3.8% (Sambuc) (rather than in the Liver itself)...

4. The Pathological course of Single Large abscess

1. Spontaneous Rupture: statistics of the terminations of abscess.

Sambuc*gives the following:-

Into the Lung.....9
Into the Pleura.....4
Into Intestine .....4
Into Peritoneal cavity.....2
Into Pericardium
Into Kidney
Into Skin .....1

* Sambuc Notes cliniques sur les abcès du Foie au Tonkin -- Annls d'Hyg. et Méd.Colon: 1913 Vol.16 No.1 pp. 42 - 103.

TABLES of FREQUENCIES of SINGLE and MULTIPLE

LIVER-ABSCESSES

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1. Rogers Tables

Two abscesses 44.7% ..... 17 cases

three " 26.3% ..... 10 "

four " 18.4% ..... 7 "

over four " 10.6% ..... 4 "

Total 48 "

In roughly half of the cases 44.7% were dual Liver abscesses.(cf.Rogers' Dysenteries p.179 ) et.seq:-

2. Rogers Table of Multiple Liver abscesses - their distribution.

1. All occurring in Right Lobe, 15%

2. " " " Left Lobe, nil

3. Distributed in both Lobes .. 13%

3. Rogers Table of Single Liver abscess distribution

1. Abscess of the Right Lobe - the great majority.

2. Abscess of the Left Lobe -16.4%

3. Subdiaphragmatic or Juxtaphrenic ) ..... 3.8% (Sambuc) (rather than in the Liver itself)...

4. The Pathological course of Single Large abscess

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Into Skin ) .....1

* Sambuc Notes cliniques sur les abcès du Foie au Tonkin -- Annls d'Hyg. et Méd.Colon; 1913 Vol.16 No.1 pp. 48 - 103.

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1. Spontaneous Rupture ; statistics of terminations

Rendu gives the following:-

In a series of 563 cases of Liver abscess the Table shows the direction of Rupture in 159 cases which open spontaneously. They are arranged in their order of frequency by me. (cf.Manson,Tropical Diseases,p.582 )

| | | | |
|---|---|---|---|
| Into the Lung | 59 | cases... | 10.5% |
| " " Peritoneum | 39 | " ... | 6.9% |
| " " Pleura | 31 | " ... | 5.5% |
| " " Stomach & Duodenum | 8 | " ... | 1.4% |
| " " Colon | 6 | " ... | 1% |
| " " Lumbo-Iliac region | 6 | " ... | 1% |
| " " Bile-Ducts | 4 | " ... | 0.7% |
| " " Vena Cava | 3 | " ... | 0.5% |
| " " Kidney | 2 | " ... | 0.3% |
| " " Pericardium | 1 | " ... | 0.1% |

i.e. 28% of Liver abscesses rupture spontaneously and most generally into the Lungs.

Rogers gives the following:-(cf.Dysenteries pp.181-183).
( re-arranged in their order of frequency)

2 These cases are sub-divided into those associated with Single Right Lobe Liver abscess and Single Left Lobe Liver abscess.

Complications and terminations of Right Lobe Liver abscess.

1. Secondary abscess in base of Right Lung. — 26 cases
   *(Cantlie sub-divides into
   i. those invading through the Diaphragm and the Ligament Latum Pulmonis.
   ii. Adhesions of the Pleura at the base & extension direct to the Lung.)

* Cantlie "Liver abscess opening through the Lung" Jl.Trop.Med.& Hyg. 1913, vol.16 pp.345-347.

2. Empyema - after operation through the Right Pleura — 16 cases

Summary.

Complications and terminations of Right Lobe abscess

- continued -

3. Acute genrl: peritonitus following operation..... 10 cases

4. Hemorrhage after operation..... 5 cases

5. (Empyema preceding operation..... 3 cases
(Empyema doubtful if after operation or not )..... 3 cases

6. Opening into Right Flexure of the Colon ..... 3 cases

(Brown's statistics give 10%)

7. Opening into Caecum )
" " Duodenum )
" " Pericardium )
" " Infr.Vena Cava) ..... 1 case

Complications and terminations of Left Lobe abscess.

Occurred in 11.9% of European cases and 18.3%

Natives.

1. Abscess in base of Left Lung ..... 3 cases

2. Opening into Pericardium ..... 2 cases

3. " " Stomach ..... 2 cases

4. Supra-hepatic abscess
Abscess in base of Right Lung
Suppurative Pericarditis without perforation)
Sub-hepatic abscess ..... 1 case
Opening into Stomach and Pericardium )
Opening into Omental Bursa

5. Uncomplicated ..... 1 case

These Tables have been compiled from records in Calcutta for 35 years by Rogers.

The out-standing features of all these Tables of Frequencies are ,

Summary.

i. Abscess of the Lung is the commonest complication
ii. Surgical operation more often induces complication than either natural case-incidence or spontaneous evacuation through other hollow viscera.
iii. Spontaneous evacuation into the Colon is ten times more common than into the Duodenum or small Intestine (cf.W.Carnegie Brown, Amoebic Dysentery 1910, p.186 ).

- continued -

Analysis of the data-supply from all the Tables of Frequency.

- continued -

iv. Empyema is much more commonly produced when draining a Liver abscess by the trans-pleural route before adhesions have taken place.

v. The onset of a Peritonitis is more commonly induced after operation. Not less than one out of every five cases tend to terminate by spontaneous rupture into the Peritoneal cavity (cf.W.C.Brown, ibid p.186 ).

vi. Discharging into the Stomach is infrequent.

vii. None of the statistics give a reference to the number of cases where Encystment of the abscess takes place. They are generally discovered at a Sectiocadaveris.

viii. The frequency of Metastatic abscesses of the Brain as a complication of Liver abscess will be described later on.

3. The Clinical complications and terminations of Hepatic abscesses with an account of the Pathological course.

(a) Single Large abscess of the Right Lobe

i. In relation with the Anterior abdominal wall---- a fairly large group of cases.

ii. In relation with the Thoracic wall --- this is the commonest situation; 45.5% of cases. Others give 40.7%.

iii. In relation with the Right Lung ( Hepato-Pulmonary ) Indirect abscess.

iv. Hepato-Pulmonary-direct abscess, involving the Lung through the Pleura.

v. Intra-thoracic abscess taking an extra-pleural route and tracking between the Pleura and the Ribs, often with necrosis of the ribs. This may be considered a sub-variety of ii above,

vi. Opening into the Bowel - generally the Colon, (Hepatic Flexure).

vii. In relation with Appendicular abscess, and post-colic perforation involving the Liver.

viii. Opening into the Peritoneal cavity.

ix. Retro-Peritoneal relationships (morbid).

x. Sub-Diaphragmatic or Juxtaphrenic (Vault abscess).

xi. Metastatic abscess of the Brain.

- continued -

(b). Single Large Abscess of the Left Lobe.

i. In relation with the Anterior Abdominal Wall (Epigastrium).

ii. In relation with the under surface of the Liver. (Sub-Hepatic).

iii. In relation with the upper surface of the Liver. (Supra-Hepatic).

iv. In relation with the Pericardium.

v. In relation with the upper edge of the Left Lobe, & involving the Left Lung. It is less common than on the Right side.

vi. In relation with the Stomach.

vii. In relation with the Peritoneum & its Lesser Sac (the Foramen of Winslow).

viii. In relation with the Spleen (Splenic Abscess).

ix. Metastatic Abscess of the Brain.

x. Uncomplicated by any Visceral Involvement.

(c). Peri-Hepatic Abscess & Hepatitis.

(d). The Insidious Type of Chronic Abscess.

(e). General Amoebaemia - Secondary to Liver-Abscess.

The Detailed Account of the Clinical Pathology of Right Lobe Liver Abscess.

1. In relation with the Anterior Abdominal Wall.

The organ enlarges downwards into the right Hypochondrium. The swelling differs from the common variety of Left Lobe Liver abscess, in being much larger and placed more to the right. Tender adhesions form tender swellings, but they are mostly localised. There is marked extension of the Liver dullness below the Costal margin. In some very advanced cases, a fluctuating swelling continuous with the Liver dullness may extend far down into the Right Lumbar Region and even reach the Iliac area. Abscess has to be differentiated from other Acute diseases of the Liver, e.g. Acute Congestion, Hydatid disease, Neoplasms of Malignant Type, the associated enlargement of the Liver which accompanies diseases of the Blood, e.g -Pernicious Anaemia; the Leucocythemias & Banti's Disease, the Tropical febrile Splenomegaly & Indian Kala-Azar, and from other Chronic diseases of the Liver associated with enlargement of the organ due to Hypertrophic cirrhosis (Hanot) & others - Fatty Liver, Lardaceous or Waxy Disease, & Chronic Congestion, & backward pressure from Heart disease. Diagnosis is also required from certain more or less physiological conditions such as Reidel's Lobe; Hepatoptosis or wandering Liver; & very [illegible] which may push the liver up.

There are three moderately common Tumours in the [illegible] of increase in the size of the Liver. They are:-

i. A Stomach affected with Malignant disease, especially [illegible] of the Greater Curvature.

ii. Malignant disease of, or impaction of faeces in the Transverse Colon.

iii. Chronic Peritonitis causing a thickened and puckered up Omentum towards the transverse Colon.

Enlargement or Disease of associated structures, such as Kidney, Hydro or Pyo-Nephrosis, may simulate enlargement due to disease of the Liver itself. Probably the largest Livers that occur are due to Secondary Carcinoma or Sarcoma.

(cf. Index of Differential Diagnosis of Main Symptoms, French, pp. 404 -415, & pp.54, 59 -64).

SECTION VII. AMOEBIC INFECTION OF THE LIVER.

PART 5. A DETAILED ACCOUNT OF RIGHT LOBE LIVER ABSCESS IN RELATION WITH THE ANTERIOR ABDOMINAL & THORACIC WALLS.

The Detailed Account of the Clinical Pathology of Right Lobe Liver Abscess.

1. In relation with the Anterior Abdominal Wall.

The organ enlarges downwards into the right Hypochondrium. The swelling differs from the common variety of Left Lobe Liver abscess, in being much larger and placed more to the right. Tender adhesions form tender swellings, but they are mostly localised. There is marked extension of the Liver dullness below the Costal margin. In some very advanced cases, a fluctuating swelling continuous with the Liver dullness may extend far down into the Right Lumbar Region and even reach the Iliac area. Abscess has to be differentiated from other Acute diseases of the Liver, e.g. Acute Congestion Hydatid disease, Neoplasms of Malignant Type, the associated enlargement of the Liver which accompanies diseases of the Blood, e.g -Pernicious Anaemia; the Leucocythemias & Banti's Disease, the Tropical febrile Splenomegaly & Indian Kala-Azar, and from other Chronic diseases of the Liver associated with enlargement of the organ due to Hypertrophic cirrhosis (Hanot) & others - Fatty Liver, Lardaceous or Waxy Disease, & Chronic Congestion, & backward pressure from Heart disease. Diagnosis is also required from certain more or less physiological conditions such as Reidel's Lobe; Hepatoptosis or wandering Liver; & very large collections of Ascitic fluid which may push the liver up.
There are three moderately common Tumours in the Abdomen which may give rise to a false impression of increase in the size of the Liver. They are:-

i. A Stomach affected with Malignant disease, especially when the growth infiltrates much ofthe Greater Curvature.

ii. Malignant disease of, or impaction of faeces in the Transverse Colon.

iii. Chronic Peritonitis causing a thickened and puckered up Omentum towards the transverse Colon.

Enlargement or Disease of associated structures, such as Kidney, Hydro or Pyo-Nephrosis, may simulate enlargement due to disease of the Liver itself. Probably the largest Livers that occur are due to Secondary Carcinoma or Sarcoma.

(cf. Index of Differential Diagnosis of Main Symptoms, French, pp. 404 -415, & pp.54, 59 -64).

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In relation with the Anterior abdominal wall.

Differential Diagnoses.

(cf. System of Clinical Medicine, Savill 3rd. edn., pp. 347- 370. for what follows )

i. The patient complains of pain and discomfort in the Hepatic Region. The Liver area may be increased, slight jaundice and numerous vague dyspeptic symptoms are present, but there is little or no fever. The disease is probably Acute Congestion of the Liver.

ii The patient usually an elderly female is suddenly seized with Paroxysims of severe pain in the Hepatic Region, and in the course of 12 - 24 hours becomes jaundiced, the stools becoming clay-coloured, the attack is one of Biliary Colic

iii The patient complains of pain and tenderness in the Hepatic Region, agravated by movement; there is NO JAUNDICE, and other hepatic symptoms are absent. The disease is probably Perihepatitis. Often the think rounded distorted edge of the puckered Liver can be made out. It may be associated with an abscess, tumour, or cirrhosis, or be part of an inflammation of the Liver itself or result from Syphilis, its commonest cause.

iv. There is enlargement of the Liver accompanied by pain and tenderness and the boundaries of dulness is Irregular there are Shiverings Sweatings and Intermittent Pyrexia. The disease is ABSCESS OF THE LIVER.

v. The Liver is enlarged and painless; its surface is hard, jaundice is present, but little or no Ascites, and there is a long history of failing health. The organ is enlarged throughout the whole course of the disease. The disease is probably Hypertrophic Cirrhosis.

vi. The enlargement of the Liver is painless and uniform, the surface is smooth and soft; there is no jaundice or ascites, and the Spleen is not enlarged. There is a history of alcoholism or Phthisis, the disease is probably FATTY LIVER.

vii The enlargement of the Liver is uniform and painless, the surface is smooth and hard, there is no jaundice or ascites, the Spleen is enlarged, there is a history of prolonged suppuration or Syphilis. The disease is WAXY LIVER.

The detailed account of the Right Lobe abscesses.

- continued -

1. In relation with the Anterior abdominal wall.

Differential Diagnoses.

viii. There are three diseases in which enlargement of the Liver is attended with pain and tenderness, viz - Chronic Congestion, Cancer of the Liver, & Abscess of the Liver. The enlargement is moderate, smooth and uniform; painful; some jaundice and ascites may be present, the Spleen is enlarged, and there are signs of Congestion of the Abdominal Viscera and signs of general venous obstruction. The disease is probably CHRONIC CONGESTION OF THE LIVER(Nutmeg Liver)

ix. The enlargement of the Liver is irregular, with perhaps nodules; the pain and tenderness may be great; jaundice and ascites are present; the Spleen is not enlarged; the patient is advanced in years, feeble and emaciated; fever may occur at intervals; the disease is CANCER OF THE LIVER. Probably the largest Livers that occur are due to secondary Carcinoma or Sarcoma. They may reach a weight of 22 lbs. or more. The nodules on its surface are said to be ' Umblicated '.

x. Enlargement due to Chronic Blood diseases will be found discussed under Condition of the Blood in Dysentery; that due to Kala-Azar will be described under ABSCESS OF THE SPLEEN.

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xi. The commonest error in diagnosis is to confound a case of Liver abscess with Malaria. Osler states that he has hardly ever met with a case of Liver abscess which has not been drenched with Quinine. Manson's experience is the same. The Diagnostic points in abscess of the Liver are, " A history of Dysentery; fever generally of a Serotine type with sweatings, not yielding to Quinine; painful enlargement of the Liver; the characteristic referred pain to the tip of the shoulder on the right side ( especially when the upper surface of the Lobe just beneath the diaphragm is the seat of the abscess; this symptom is seldom noticed in abscess of the Left Lobe); the rigidity of the Right Rectus; the loss of movement in the Right side of the diaphragm, and the frequent cupola-shape of the Liver on radioscopy and above all the discovery of the pus by puncture. "
(cf. Castellani & Chalmers, Tropical Medicine 2nd. edn, page 1410.)

Differential Diagnosis. - continued -

xii. General symptoms.

1. Pain. The referred pain to the tip of the Right shoulder has already been outlined above. It is most frequent and indeed rarely absent in those Right Lobe abscesses which perforate the diaphragm to involve the base of the Right Lung. When the abscess involves the anterior portion of the Liver, the organ is enlarged below the costal margin, and the pain is felt chiefly in the right Hypochondriac region and Epigastrium. In Left Lobe abscesses it may extend into the left Hypochondrium where it may be mistaken for a Splenic Tumour.

2. Oedema of the abdominal wall. This generally appears when the abscess is near the surface or pointing. It may be mistaken for an abscess of the abdominal wall or a softening guma of the Liver in which there is often fever of a hectic type. I have seen sterile abscess of the abdominal wall caused by Quinine-solution injection into the parieties for the treatment of resistant Malarial cases produce such soft fluctuation over rather a wide area as to suggest dealing with a hernia through the abdominal wall or cyst in the abdominal wall. These cases give a history of Quinine injection for Malaria.

3. Fever, Rigors ( recurrent) and Sweatings. There is nothing distinctive about the fever which is of the ordinary suppurative hectic type. Recurrent Rigors are common in various septic conditions which will be given later under Classification of Causes of Multiple Rigors. * Cold sweats generally of a very diffuse character are common accompaniments of abscess.

* c/f. P.196-197.

4. Blood examination This is the key stone of a successful diagnosis, the point will be emphasised in the differential diagnosis of Blood diseases, but it may be mentioned here that a Hypo-Eosinophilia which may pass into a total disappearance of the Eosinophiles when abscess formation has taken place. In Hepatitis the Eosinophile percentage may be normal, in abscess formation it is diminished or abolished. This is in striking contrast to suppurative changes in an abscess due to Hydatid Disease. A polymorpholeucocytosis always results commonly of a high degree in Hepatitis as well as in Liver Abscess.

Right Lobe Liver abscess in relation with the Anterior abdominal wall.

Differential Diagnosis - continued -

xii. General symptoms - continued.

5. Boinet* gives the following as valueable localising symptoms:-

i. Superficial abscess - peritonitis; the pain is acute and spreading; the diaphragm is elevated, if in the Right Lobe; there is possible displacement of the heart or dyspnoea ( Left Lobe ); there is fixation of the abdominal wall and friction sounds.

ii. Deep Central abscess.
The pains are vague; deep and increased by shaking the Liver;
There is change in the shape,(dulness) of the Liver but this is slight.
Patient is able to move about with difficulty.
There is seldom any serious gastric disturbances.

iii. Abscess of the Concave Surface of the Liver
There is pain in the Lumbar Region, gastric disturbances, such as vomiting, Icterus.

* Boinet - Gaz. des Hopitaux, Paris, 1901, lxxiv P.257.

6. Jaundice.
This does not necessarily accompany abscess formation. The jaundice may be a sequel of the Acute Hepatitis which has passed into the suppurative stage. An analysis of such cases will be found discussed under the section of Hepatitis of the Liver.

All the foregoing symptoms including even a slight degree of tumour formation in the Epigastrium are common to both the pre-suppurative stage & to the actual abscess formation in the Liver. In fact, there is no symptom other than some of the physical signs to be still mentioned with the further complications of the Liver abscess which is absolutely diagnostic of pus. Blood examination and even a positive Iodiphylia is common to both Hepatitis and abscess. Exploratory puncture may be the final means of diagnosis, or the actual appearance of pus, either vomited by the mouth, or passed per Rectum may herald the presence of an abscess cavity of the Liver.

2. Right Lobe Liver abscess in relation with the Thoracic wall. - The Clinical Pathology -

This is the commonest situation in which it appears; the European Tables giving 40.7%, and the Native Series, 45.5%. It is often of large size yeilding more than three pints of pus. The chief clinical points of note are -

i. Insidious symptoms and signs are often met with in the earlier stages, the earliest being increase of Liver dulness in an upward direction.

ii. Later, when the abscess has more fully formed, there is marked bulging of the ribs, with an extension of dulness below; and an increase in the circumference of the chest.

iii. Auscultation. On account of rigidity of the right half of the diaphragm, there will be a diminution of breath sounds at the base of the Right Lung. The physical signs may correspond with those obtained in a Purulent Pleurisy or in a Pleurisy with Effusion or Metastatic abscess of the Lung, or Neoplastic process ( Intra-thoracic ).

iv. Actual fluctuation may appear in the lower intercostal spaces and previous even to this, Oedema of the superficial parieties is often a valueable sign of suppuration already having occurred. X-Rays may be of use. The difficulties of interpreting X-Ray readings, will be found discussed under the diagnosis of Hepato-Pulmonary Abscess.

v. The Extra-Pleural route of an Intra-Thoracic abscess, will also be considered under the Hepato-Pulmonary Lesion.

vi. Basal Pheumonias of Chronic type will give rise to some errors in diagnosis. Blood examination must always be done.

vii Hepatic abscess will have to be differentiated from Neoplastic processes; Tuberculosis of the Lung; Fungus diseases such as Spirochaetosis; (Castellani ) of the acute or chronic broncial condition; Tropical Broncho Mycoses; Aspergillosis of the Lung; Sporotrichosis of the Lung; ( for detailed description of Tropical Fungus diseases, cf. Castellani & Chamlmers, 1913 1284 - 1289). Much of this course of Intra-Thoracic relationship of Liver abscess, belongs to a secondary Pulmonary lesion which will be described below.

By far the commonest complication is the spread of the disease through the diaphragm to involve the base of the Right Lung; and it is especially noteworthy how rarely an Empyema is produced owing to failure of the formation of adhesions between the base of the Lung and the perforated diaphragm. Empyema is much more commonly produced when draining a Liver abscess by the trans-pleural route before adhesions have taken place. The same remarks apply exactly to the onset of a peritonitis which is much more commonly induced after operation. (cf. Rogers Tables of Frequencies).

## SECTION VII. AMOEBIC INFECTION OF THE LIVER.

### PART 6. THE CLINICAL PATHOLOGY OF RIGHT LOBE LIVER ABSCESS IN RELATION WITH THE LUNG.

Cantlie * has divided up his cases as follows:-

i. Liver abscess opening through the Lungs. (i.e. from the surface of the Liver through the diaphragm itself, and then into the Lung. Pulmonary involvement of the Pleura.

ii. Non-Adherent Pleura at the base causes abscess extension to the lung without involvment of the Pleural Cavity.

iii. Involvment of the Cavity (Empyema) with secondary extension to the lung.

iv. Occasionally an Intra-Thoracic abscess may take an extra-Pleural route and track up between the Pleura and the ribs. Necrosis of the Ribs with extension to the Sternum has been noticed by Legrand after such cases, and will be considered with Amoebemia of the Bones.in general.

v. Phillips observes that some cases are not truly Hepato-Pulmonary at all, especially those cases in which after a time the discharge of pus from the lung becomes continuous instead of being intermittent, with bouts of coughing and periods of expectoration of the characteristic pus. Such cases may be Secondary abscesses in which the original hepatic abscess has healed and the track into the lung cicatrised, leaving merely the active secondary lesion in the lung; or,

vi. It may be a Primary lung condition ( a rarer group) produced in the same way as the metastatic abscess of the Brain, Spleen, Salivary Glands, the Alveolar, & Dental tissues, and the Skin, i.e a blood borne infection.

* Cantlie, Liver abscess opening through the Lungs. Jl.Trpl.Med. & Hyg. 1913, Vol.16, pp.345- 347.

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Cantlie * has divided up his cases as follows:-

i. Invasion from the upper surface of the Liver through the diaphragm itself, and the Ligamentum Pulmonis without involvment of the Pleura.

ii. Non-Adherent Pleura at the base causes abscess extension to the lung without involvment of the Pleural Cavity.

iii. Involvment of the Cavity (Empyema) with secondary extension to the lung.

iv. Occasionally an Intra-Thoracic abscess may take an extra-Pleural route and track up between the Pleura and the ribs. Necrosis of the Ribs with extension to the Sternum has been noticed by Legrand after such cases, and will be considered with Amoebemia of the Bones.in general.

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The Hepato-Pulmonary abscess may be therefore produced by,

i. A direct spread into the lung

ii. A secondary spread from an Empyema.

iii. A Metastatic or Primary Blood-borne lesion.

The diagnosis between these types are few; X-Ray examination is the principal with absence of signs of Liver disease.

The Hepato-Pulmonary abscess give a larger percentage of returns than the native series of cases; there being a difference of some 13% in Rogers collected series, although this percentage Rogers thinks is erroneous owing to the missing of such cases in the natives.

The clinical histories of such cases are so important, that greater stress is laid upon the hepatic condition rather than the pulmonary resulting abscess; for such abscess can be stopped early enough with Emetin exhibited in an early stage of the disease.

The lung cases often reveal themselves only after the appearance of the typical anchovy sauce pus evacuated through the respiratory passages.

The condition is often immediately preceded by a sharp critical rise of temperature, ~~slight~~ some irregular fever, a hacking cough coming on in paroxysms and muco-purulent expectoration, with disturbances of the respiration, cold sweats, and pain in the chest referrable to the tip of the right shoulder or going down the inner side of the arm. The opening of a Liver abscess through the lung may bring the Patient under observation for

Right Lobe Liver abscess in relation with the Right Lung.

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the first time. This will be the case where an Insidious Chronic abscess of the Liver has burst into the Lung.

The clinical classification of hepato-pulmonary cases may be divided into:-

i. The Acute cases - in which the diaphragm is rapidly perforated, and there are acute signs of lung involvment, and the speedy spitting-up of typical Amoebic pus. There will be no signs of a Pleural Empyema, owing to the absence of adhesions of the Pleura. There will be an acute rise of temperature respiratory embarrasment, a boring deep pain referrable to the shoulder, a rigor followed by cold sweat, and then a severe paroxysmal cough with vomiting and the coughing up of the pus. Spontaneous evacuation may be followed by spontaneous cure.

ii. The Acute cases, with marked symptoms of an early Empyema in the first instance, followed later by evidence of the involvment of the lung itself. Such cases will be clinically indistinguishable from Purulent Pleurisy which infact it is. When the lung has become involved, the case may run the same acute course as when the lung has been directly involved, but the coughing up of the abscess-pus will naturally depend upon whether there is direct continuation between the cavity of the Liver abscess and the lung. Pus of course may go from the lung into the Pleural Cavity and then find its way into the lung and be expectorated.

iii. The Chronic insidious cases. These form the larger group of cases and are characterised by obscure fever, obscure physical signs in the chest, Chronic ill-health - the clinical features are suggestive of a T.B of the lung. Some of these cases ultimately turn out to be of Acute type when they give rise to an Empyema which the Liver abscess may produce by rupture into the Pleura, owing to the Chronic adhesions at the base. They may only be revealed by an unexpected coughing up of copious thick reddish purulent expectoration with a mawkish fish-like odour, or semen-like smell so characteristic of amoebic pus.

Clinical classification - continued.

iv. The purely Pulmonary type. These may be Acute or Chronic, and when Chronic they are often insidious. They are, however, generally Acute and may result from, as has been shown, by Metastases when they are Primary, or may result from secondary Liver abscess in which the connecting tract has cicatrised. When Primary there is naturally a negative clinical history of hepatic trouble. They are further differentiated from the secondary group by the absence of paroxysms of cough, the periodical disturbances of the respiration and by Acute Exaccerbations of temperature which take place with the emptying of a liver abscess into the lung for expulsion by the Respiratory Passages. In these cases the expectoration of the pus is quite a sudden affair; it may however, be preceded by sweats, some haemoptosis, diffused pain in the chest, feeling of nausea and faintness, and then the violent expulsion of the pus. There is, thus, nothing to distinguish them at times from the discharging abscess secondary to Liver disease In the insidious group, there is often the diagnosis of T.B. made in error, and this class of case may be entirely missed until the pus is expectorated.
Sometimes the Acute Pulmonary group may be mistaken for commencing Gangrene of the Lung, or a Bronchiectasis. The condition due to the Amoebae generally improves after such expectoration, and may go on to spontaneous cure - valuable clinical points in their differentiation from Gangrene. Moreover, amoebae will be found in such pus, which also has not the characteristic putrid odour of Gangrene cases. One further error in diagnosis must be warned against, and that is the condition due to Malignant Pernicious Fever ( Malaria ) with Pulmonary symptoms.( cf. Castellani & Chalmers, Tropical Medicine, 2nd. end; p. 886 ). These Malignant Malarial cases may occur in either of two forms - the Pneumonic and the Pleuritic; In the Pneumonic variety the symptoms are that of a Broncho-Pneumonia, and is accompanied with blood expectoration; the red corpuscles in which parasites may be seen, and therefore characteristic of the condition. There is dyspnoea and cough. The symptoms are better during remission of the fever, and worse during the attack; the blood is full of parasites. This Broncho-Pneumonia in malarial patients in many cases is not due directly to the parasites, but is a complication due to the Pneumococcus. The Pleuritic cases are characterised by intermittent pleuritic pernicious fever with sharp pricking pain, dry cough, and friction sounds, also characterised by the fact that they improve in the remission and become worse again in the attack. The parasites will also be found in the blood. A differential diagnosis of the causes of the Haemoptysis is most necessary. Haemoptysis due to the changes in the lungs may be tabulated thus :-

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Haemoptysis due to changes in the Lungs, continued.

i. Phthisis - early and late

ii. Cirrhosis of the Lung; Pneumonoconiosis or Fibroid Phthisis.

iii Chronic Valvular Heart disease, esp. Mitral Stenosis.

iv. Violent coughing efforts.

v. Injuries to the chest.

vi. Acute Lobar Pneumonia.

vii. Broncho Pneumonia.

vii Septic Pneumonia with or without abscess,

ix. Gangrene of the Lungs.

x. Infarction or Pulmonary Appoplexy & Brown Induration.
(a) Embolic Infarction
(b) Thrombotic Infarction

xi. Neoplasm of the Lung - Primary and Secondary.

xii. Sporotrichosis of the Lung.
(a) Aspergillosis
(b) Actinomycosis
(c) Other Fungi

xiii Aortic Aneurysm, with erosion of small vessels in the wall of a bronchos.

xiv. Hydatid Cyst.

xv. An Empyema bursting through the Lung.

xvi. An Hepatic abscess draining through the Lung.

(cf. Index of Differential Diagnosis of Main Symptoms by French, 1912, pp. 317 - 323 ).

Phthisis is by far the most common cause of Haemoptysis, the sputum should always be examined. Mitral Stenosis is the second commonest cause of Haemoptysis. In failing cases of Mitral Stenosis, it is due to Infarction or to Pulmonary Apoplexy. An Embolic Infarct occurs suddenly causes acute pain in the corresponding part of the Thorax, Orthopnoea, increased Cyanosis, Dyspnoea and Haemoptysis; a Thrombotic Infarct which is formed gradually owing to Atheroma and failing circulation, arises gradually & causes Haemoptysis without the other symptoms.
Primary Pulmonary abscess is therefore a most difficult condition to diagnose and most cases will only be clear after the voiding of Amoebic pus.

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Other Protozoan organisms may also cause Hepatic abscess with a secondary lung complication. In this connection reference must be made to Balantidium Coli. It may reach the Liver and other organs through the lymph vessels and must be considered as an intra-vascular parasite. In Balantidium infections, necrotic areas and abscesses produced by embolisms of the parasite are frequently found in the liver; only occasionally as a primary infection in the lung. "Balantidium"has moreover been observed in pus from a hepatic abscess which was expectorated through a pulmonary sinus." (cf.W.Carnegie Brown,Amoebic Dysentery, 1910,p.89 )

Terminations. A Hepato-Pulmonary abscess or a Pulmonary abscess, may go on discharging for weeks or months and end fatally from exhaustion, Waxy Disease - the results of chronic suppuration, or the patient be carried off from some intercurrent malady such as Tubercle or Pneumonia. Or the pus gradually diminishes, the abscess sicatrises and beyond the permanent signs of a chronic healed pulmonary lesion, with perhaps some sinking in of the chest wall. Spontaneous cure may result from spontaneous evacuation or the patient may be gradually restored to health even up to a duration of 18 months of trouble.

Pathology. Amoebic abscess of the Lung is irregular in form and compares in every detail to Liver abscess, as regards the method of extension and naked eye appearance. In Chronic cases there may be some attempt at the formation of a lining membrane, but the cavity generally is in relation to a Bronchus. The histological changes are partly those of degeneration and destruction. Amoebae may be found in the Alveoli which may contain in addition Charcot-Leyden crystals, fibrin lymphoid cells, catarrhal cells & red blood corpuscles. Changes indicative of Interstitial Pneumonia. Pneumonic consolidation occurs at distant parts, where however, no amoebae may be found. This is explained by the general reaction of the Pulmonary tissue to the morbid changes occurring elsewhere.

## SECTION VII. AMOEBIC INFECTION OF THE LIVER. AND OTHER ORGANS.

### PART 7. METASTATIC BRAIN ABSCESS SECONDARY TO RIGHT OR LEFT LOBE LIVER ABSCESS.

Next to the Lung abscess, of all the viscera far removed from the areas of original infection, the Brain is perhaps the most frequently affected. In Countries where Amoebiasis is endemic, Brain abscess is unusually prevalent. This condition is always like the hepatic abscess, secondary to dysentery. Kartulis* in Egypt, found secondary cerebral suppuration in 3% of a series of cases of amoebic abscess of the Liver. It is equally prevalent in Java and the East Indies. " Out of 184 cases of hepatic abscesses treated in the Hospital ( Egypt), seven were complicated with four brain abscesses developed, or about 3% of all cases ". (cf.Keen's Surgery, Vol.vi,1913, p.796.). Legrand* in Alexandria has collected and published 45 such cases.

Legrand & Phillips have published two more such cases together "making 47 in all on record ". (cf.Phillips Amoebiasis & the Dysenteries;1915,p.

Clinical history. From published cases, the following points are summarised:-

i. All have been secondary to hepatic or hepato-pulmonary lesion. Habershon in Guy's Hospl. London, published a case in 1855 in which this relationship was noted.(W.C.Brown details the case on p.191 Amoebic Dysentery,1910.) In two cases published by Legrand, no such previous lesion existed.

ii. The Cerebrum is generally the seat of the abscess - only in one case has Cerebellar abscess occurred.

iii. In the recorded cases all were fatal; in 27 of Legrand's cases, the patients were resident in the endemic area ( Egypt ); in five others who had contracted Dysentery in France and in England, the patients had never left those Countries.

*Kartulis - Central f.Bakt.Bd.37, 1904. xxxvii, 527.

*Legrand "Les abcès Dysentériques du Cerveau ( Amibe Encephalique )" - Archives Provin: de Chirurgie, 1912, No.1.

4. Metastatic Brain abscess secondary to Right or Left Lobe Liver abscess.

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Metastatic brain abscess secondary to Right or Left Lobe Liver abscess.
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iv. Absence of Meningitis and absence of adhesions of the Dura with underlying structures is a feature. Purulent Meningitis is very rare. Wildt of Cairo, has reported such a case. A patchy Meningitis may however occur on the surface of the brain or in the convolutions, from which amoebae have been obtained, and recorded by Legrand.

v. The abscesses are usually very small - in many cases they are microscopic - and they are generally situated near the surface of the Cerebrum, in close proximity to a large Venous sinus or lymph-channel. It may turn very large and finally burst into the Ventricles; this is its usual line of progress according to Phillips.

vi. Intracranial tension is greater than usual, and headache most intense; not even lumbar-puncture relieving it. In spite of this there is no Optic Neuritis (Phillips).

vii. The symptoms are often very insidious, or there may be no symptoms at all; and an abscess unsuspected during life may be found at the post-mortem encysted and complete. Generally the abscess after partial encystment bursts and spreads. Such a case is recorded by Dubujadoux who found at an Autopsy a Cerebral abscess with a partial capsule showing a recent rupture through the Fornix into the Ventricle; an old encysted six months old Liver abscess was present; and there was also a second abscess of more recent origin.

viii In several cases slight swelling of the face has been observed by Legrand, as in cases of Myxoedema.

ix. There is no vomiting, the temperature is not usually raised as in other types of fully developed Cerebral abscess. Mental acuteness is diminished. A comatose condition supervenes at the point of death. Localising <u>focal</u> symptoms depend upon position of the lesion in the Brain. A burst into the Ventricles causes Hyperpyrexia, Nystagmus, vomiting, convulsions, coma and death. The onset of symptoms of Brain abscess may be sudden, with signs of Jacksonian Epilepsy. There may be no associated Dysentery. Abscess may occur months, or even years after the Dysentery, or abscess of the Liver cured Vomiting may be the first symptom of an actual abscess forming.

x. Unless located and opened at an early stage, they are almost invariably fatal

Legrand classifies his cases into:

i. Acute Necrotic abscess - a pure amoebic infection with a hemorrhagic tendency.

ii. Residual abscess, with blood stained content containing but few living or dead amoebae.

iii Phlegmonous abscess - in which virulent bacterial infection is super-added.

iv. Encysted abscess, in which at one time there may have been bacterial infection but which might since have become sterile.

Pathology. The fluid obtained from a Brain abscess, is usually sterile, bacteriologically. Bac.Pyocyaneus has however, been found in one case by Kartulis; and cocci have been described by others. Legrand states that amoebic abscess of the Brain are seldom sterile; and that besides Entamoebae, various bacteria both anaerobic and aerobic have been found - he looks upon them as possibly growing symbiotically. Jacob & Legrand with the addition of Hydrocele fluid to cultures have been able to cultivate Anaerobes. The question of anaerobic occurrence in the abscess fluid has not been settled, nor the functions of the Anaerobes.
The resemblance between a Cerebral abscess and Hepatic abscess is remarkable in point of view of Pathology and Pathological conditions.
Amoebae reached the Brain from the gut, by multiplying in the submucosa and penetrating throu to the peritoneal coat, and then through the lymphatics and blood-vessels to the Liver which is the first great barrier. This however, may be passed and an abscess occur in the Brain by metastasis. From the Lung amoebae pass into the circulation and reach the Brain.
The appearance of the cavities is characteristic In contradistinction to the greenish- tinted and extremely offensive pus which result from intra-cranial suppuration, such as the extension of Otic suppuration, the contents of the amoebic cavity are generally odourless and vary from a deep yellow to a brownish - red. There is generally no true pyogenic membrane; though W.C.Brown states the very reverse. Amoebae may be found in the pus, but they occur specially as in the liver in the edges of a cavity. If secondary bacterial infection has occurred, then the abscess may resemble the regular type of septic Cerebral abscess. The implication and degree of inflammation of the meninges varies. The condition of the Pia Mater depends on the situation of the abscess. Morehead in 1838 also describes a suffusion of the meninges in cases of Dysentery apart from abscess. Meningitis of a widespread purulent nature is very uncommon; but a localised patchy Meningitis as has already been described may occur in patches. In old cases there is often an attempt made for encapsulation to take place - such encapsulation however, is often more partial than complete.

Metastatic Brain abscess secondary to Right or Left Lobe Liver abscess.
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Pathology - continued.

This encapsulation becomes rusty coloured owing to hematin being formed. The microscopic appearances again resemble those in the Liver. In the earliest stages, the Pia Blood vessels are distended and thrombosed, especially when the Pia Mater itself is involved. In the Acute Necrotic abscess described by Legrand, there is oedema and commencing softening of the Brain - tissue with hemorrhages. The presence or absence of leucocytes in the disintergrating Brain matter, depends upon secondary bacterial infection. In the perivascular spaces leucocytes and Eosinophile cells occur with the grouping of the parasites in large numbers round the edges of the cavity. A certain amount of this disintergration and softening of Brain tissue is due to the arterial obstruction and thrombosis.
Within the Brain the regions most affected by Arterial obstruction and Thrombosis correspond with the distribution of embolic changes due to the transmission of clots from the Auricular Appendix to the Brain in Ulcerative Endocarditis. (cf.Beattie & Dickson,Special Pathology,p.440 et seq.).
The regions most affected by arterial obstruction by Embolism -

i. Left Middle Cerebral Artery and branches.

ii. Right " " "

iii. Posterior Cerebral

iv, Vertebral.

v. Cerebellar.

For this reason also, the Cerebral abscess is commoner than the Cerebellar.
The effects of such obstruction will depend on its situation in the Brain, its extent, the amount of collateral circulation. Obstruction in "The end arteries of Cohnheim " will produce the most elaborate results. The nutrient arteries supplying the Brain tissue do not anastomose freely with one another.
Occlusion of the middle Cerebral Artery and its branches.
In the Cortex , there is a considerable amount of collateral circulation, and therefore the softened area will be much smaller than the area supplied by the Artery, and will correspond with the parts furthest removed from the collateral circulation. Thus the damage will correspond with the posterior extremity of the Third Frontal and lower part of the Ascending Parietal Convolutions and the Temporo-Sphenoidal Lobe.
It is on this account that Cerebral abscesses are small, and the area of degeneration not large unless by the direct extension of the abscess.

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Pathology - continued.

In the Basal Ganglia there may be no change if the obstruction occurs beyond the origin of the branches of the Middle Cerebral which supply them. If these branches become involved, softening will occur in practically the whole of the Corpus Striatum; in the greater part of the Caudate Nucleus except the tip; and in the anterior and middle third but not the posterior third of the Optic Thalamus. The arterial branches to the Basal Ganglia are terminal; there being no anastomosis amongst themselves or with neighbouring vessels.
It is not necessary to dwell upon the nature of symptoms produced by a burst of the amoebic abscess into the Ventricles, or into one of the large Brain sinuses. They will correspond to symptoms produced by a burst of any pus into these parts.

Differential Diagnosis.

The condition is not apt to be mistaken for a Tubercular Meningitis. It may, however, bear some resemblance to the Cerebral type of Epidemic Cerebro-Spinal Meningitis. In this disease, however, the exudate specially accumulates in the posterior Arachnoid cistern, and is most marked at the base posterially. Lumbar puncture will reveal the causative Diplococcus of Weichselbaum. It may also have some resemblance to Posterior Basal Meningitis, when the exudate extends to the vertex of the Brain, but it is usually confined to and always most marked at the base. Lumbar puncture and cultural experiments in the fermentation of Saccharose will reveal the Diplococcus of Still.
Infective Sinus Thrombosis. In this condition there is always a chronic or intermittent otorrhoea. Its symptoms are general - those of Septicemia or Pyema; often with an initial rigor and vomiting followed by high temperature characteristically hectic, going from the abcissa to 105º and down again to normal, followed by repeated rigors and sweating. The local symptoms are very severe pain about the ear excruciating headache and venous congestion of the optic disc, with others that vary with the site of thrombosis. In Pyogenic Sinus Thrombosis the Lateral Sinus is the favourite position ( secondary to Middle Ear disease ). The localising signs are Oedema and tenderness over the Mastoid and by extension a hard brawny swelling down the course of the Jugular Vein is felt.
In Cavernous Sinus Thrombosis, the localising signs are, oedema of the eye-lids and root of the nose, exophthalmos, and paralysis of the second, third, fourth, ophthalmic division of the fifth and the sixth nerves, with the consequent muscular paralysis of the eye.
In Non-Pyogenic Sinus Thrombosis. The Superior Longitudinal Sinus is most often affected. Headache passing on to drowsiness and coma are the leading symptons. Epistaxis and convulsions

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Differential Diagnosis - continued.

in children are suggestive of the disease even in absence of localising signs. The localising signs consist of Oedema of the scalp, distension of the veins over the forehead, and sometimes strabismus, associated with convulsions at the onset.
In Cerebral abscess, the temperature is normal or sub-normal after the initial rise, is unaccompanied by so much stupor, and widespread paralysis of the cranial nerves. ( cf.System of Clinical Medicine - Savill, 3rd.edn.p.776.).
Lastly one condition has always to be borne in mind, viz - the Cerebral type of Malignant Malarial fever; and what is also known as " Masked Malaria ". No diagnosis of Hemiplegia Cerebral abscess and other acute Intracranial conditions should be made without examination of the blood in Tropical Countries, and in known Malarious localities. "Thus after an accident the symptoms may point to Cerebral abscess, but on examination of the blood and the discovery of the parasites followed by treatment with Quinine, the urgent symptoms disappear. Malaria is capable of being masked or concealed by some concurrent disease, e.g. Dysentery or Phthisis. The more important forms of masked malaria are, neuralgias, particularly of the Trigeminal, especially of its Frontal branch, paralyses and chronic diarrhoea, and also according to Craig, pneumonia." ( cf.Castellani & Chalmers, Tropical Medicine, 2nd.edn,p.888 ).
Masked Malaria is generally due to the Subtertian parasite.

Pernicious Fevers are classified into:-

I. Pernicious Fevers without local symptoms
  i. Algide Pernicious Fever.
  ii. Diaphoretic " "
  iii. The Hemorrhagic type
  iv. Scarlatiniform "

II. Pernicious Fever with local symptoms.
  i. With Cerebro-Spinal symptoms.
  ii. With Gastro-Intestinal "
  iii With Cardiac symptoms.
  iv. With Pulmonary " ( already considered)

It is with this second type with local symptoms that we are to deal.
To these series of phenomena the French Writers have given the name " accès pernicieux ".

Differential Diagnosis - continued.

The Cerebral type may be further classifie into many forms which this protean malady may assume.

i. Comatose Pernicious Fever.
In this, the symptoms are mostly of weakness, stupor or delirium ending in coma. There are usually no paralyses or alteration in the reflexes. Cases which are going to be fatal, develop syncope and the temperature tends to drop below sub-normal. This condition has further to be differentiated from, sun-stroke or heat-stroke, which is a common error in diagnosis.

ii. Delirious Fever
Delirium is the most marked feature, and apt to come on suddenly.

iii Tetanic Pernicious Fever.
In this there is trismus, opisthotonos, retraction of the abdomen, and conjugate deviation of the eyes.

iv. Meningitic Pernicious Fever.
The symptoms are, vomiting, headache slow pulse, retraction of the head, rigidity of the neck, a well-marked tache-cerebral and convulsions.

v. Bulbar Pernicious Fever.
This may be mistaken for a case of Glosso-Labio-Laryngo-Facial Paralysis. Acute Bulbar symptoms may be well-marked, and there may be disturbance of the equilibrium. Such cases can only be re-diagnosed by a blood examination. Along with this, Ataxic Pernicious Fever may be included.

vi. The Cerebral form may be associated with Pernicious Fever with Gastro-Intestinal symptoms, Dysenteric in type. The motions contain blood and mucus, tinged with bile; with great distress and prostration.
A Peritonitic type may be included here.

Therefore it should be again emphasised that no organic Brain lesion should be diagnosed in the Tropics, however obvious the symptoms be, without a careful blood examination.

(cf. Castellani & Chalmers, Tropical Medicine 2nd. edn; pp. 882 - 885.)

SECTION VII. AMOEBIC INFECTION OF THE LIVER AND OTHER ORGANS.

PART 8. COMPLICATIONS & TERMINATIONS OF LEFT LOBE LIVER ABSCESS: AND ABSCESS OF THE SPLEEN.

Complications and terminations of Left Lobe Liver abscess.

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1. Abscess of the Spleen secondary to Left Lobe Liver abscess.

Amoebic infection of the Spleen occurs but rarely as a complication. The routes of such infection may be:-

i. A direct spread from the liver.
ii A direct invasion from the Splenic flexure of the colon.
iii A metastatic spread by the blood stream secondary from the liver.
iv. A metastatic abscess from the colon by the blood stream.

Not many cases of infection are on record. W.C.Brown in his work on Amoebic Dysentery ( p.192 ), records the following case of Preston Maxwell of Amoy, of abscess in the Spleen of a young Chinaman a month after the first symptoms of Dysentery ( Maxwell * ).

* Maxwell -" Society of Tropical Medicine & Hyg: Transactions ". July 1909.

"The swelling completely filled the left half of the Epigastrium, and projected over to the right of the mesial line; there were daily rigors which simulated a double benign Tertian temperature, and in the dejecta which were dysenteric in character Ent: Histolytica was found. The Spleen was incised through the abdominal wall, and 80 ozs. of yellow pus and blood were evacuated- the patient making a good recovery. Large numbers of Amoebae were present in the contents of the abscess-cavity- the liver was healthy ".

Rogers details the following case of Splenic abscess which was cured by aspiration and Emetin injection ( Rogers Dysenteries, p.241 ).

* c/f. P.112, Diagram & Chart.

" A native male aged 32 was admitted with marked enlargement of the Spleen to 2 inches below the left costal margin and a tender prominence of the lower ribs with redness of the skin over it; 8 ozs. of thick reddish pus were aspirated. Three days later this refilled and a second aspiration drew off 4 ozs. of pus, and Emetin Hydrobromide was now injected ( 1 Grn.) into the cavity. Amoebae were found in the pus. He had two more injections during the next two days ( half grain subcutaneously ), but the temperature rose, and six days after the second aspiration there was again slight bulging which was aspirated for the third time, drawing only a little pus and blood. One grain Emetin was again injected into the cavity and two more half grain doses were given subcutaneously. Two days later the temperature was normal, the abscess did not again refil and complete recovery ensued. The interest of the case lies in the fact

Rogers'Spleen abscess case - continued

lies in the fact that Splenic abscesses heal very slowly and leave obstinate sinuses. The Emetin employed and given direct into the cavity produced the fortunate results."

Splenic suppuration therefore secondary to Liver abscess is distinctly uncommon - the number of cases recorded appear to be Primary abscess.

Clinical Pathology.

As in the group of the pre-suppurative hepatitis there appears to be the pre-suppurative Splenitis. These solid, hard Spleens with some pain or diffuse feeling of uneasiness, caused by their weight, and perhaps adhesions are exceedingly difficult to diagnose in patients with a history of chronic Malaria and Dysentery accompanied by a Hepatitis. Are these cases due to chronic Malaria or may they be some kind of Splenic inflammation secondary to Dysentery, not necessarily going on to suppuration? The soft condition of the Spleen is no criterion to go by to differentiate between Splenic enlargement caused by chronic Malaria and that due to dysentery; for I myself, have seen many cases where the Spleen has been massively enlarged crossing the middle line and quite hard and firm, almost like a Splenic Tumour. These cases are apparently common in the badly nourished natives. Slight fever 99 -100 degs: with a few B.T. rings and some pain over the Spleen with an attendant liver enlargment, will indeed by very difficult to differentiate from a chronic Malaria in which there is some Cirrhosis of the liver. In such cases Emetin injections must always be employed along with Quinine administration. Such a case has been personally noted and described under the Hepatitis group-type. *

These patients with massively-enlarged spleens associated jaundice, and some enlargement of the liver, often present a complex association of symptoms; in which obvious Splenic enlargement continued low fever and often a deep yellow discolouration of the "whites" of the eyes (jaundice), without any accompaning dysenteric symptoms but with history of dysentery, may be three weeks ago,-are the outstanding features. Examination of the blood is negative generally for parasites: a Widal gives no result when the serum is tested against the whole Enteric Group ie. Typhoid,& ParaA. & B. The patient is generally so well saturated with Quinine that it is not a remarkable thing that no parasites are found; and the Widal cannot be explained by defective reaction in the development of specific agglutinor Group- Agglutin to the Typhoid & Paratyphoid Bacilli-as W idal is constantly negative. The Splenic enlargement reacts best to good food, and tonics of Arsenic and Iron. The Jaundice is however very persist-

* c/f. P. 112, Diagram & Chart.

-continued-

-ent, such medicines as Salines, Hydragr. Subchlor Soda Salicylate, Bismuth, Salol, and freshly-made Chlorine mixture of Burney Yeo, do no good. Some of these cases clear up under Emetin. The temperature however is very curious-and gives inconstant results to different kinds of treatment. In some of the more Chronic cases which are resistant to a continuation of QUININE or appear to be made worse by it, the mere o stopping of Quinine reduces the temperature to normal. It would seem as if prolonged Quinine administration had upset the Thermogenic CENTRES In some cases Emetin subcutaneously brings about some improvement for a time but the low fever relapses. Two such cases will be found detailed under the Hepatitis-Group of cases with a curious Jaundice-temperature. (P. 112; 113).
In one case, * also recorded in that section, the Spleen totally disappeared under Emetin * Such persistent temperatures are known to occur in Latent Amoebic or Chronic Amoebic Dysentery. One case showed symptoms of proufound anaemia, suggestive of Myelocythemia, of the Spleno-Medullary Type. Blood-examination was however negative. In cases in which reduction of the Spleen occurred, such reduction in size was more marked in the antero-posterior, rather than in the lateral direction; this perhaps may be explained by the fact that Splenitis was "tacked" on to an already enlarged and cirrhotic chronic Malarial Spleen, which had originally crossed the middle line and could be felt descending towards the Umbilicus; such already -diseased Spleens being more easily affected than a previously healthy one. In two cases the liver and Spleen dulness vanished entirely under Emetin after six days injections of one grain given intra-muscularly. These series of cases all occurred in coolies from Mesopotamia, averages ages being 35 - 45; and the duration of their stay in Mesopotamia was never more than three months. They all gave previous history of dysentery; some contracted while on War service, others who had had previous attacks in India, long- antecedent to their departure overseas. At present I am treating all blood-diagnosed Malarial cases with Emetin, who have no history of dysentery and no hepatitis as a control to the above series of cases. Enough experience has not been obtained to testify precisely the meaning of the reduction of enlarged Spleens when treated by Emetin, in which there is no associated hepatitis; and a second series of cases where there is hepatitis. IF Emetin be the sole means we have to judge and correct such diagnosis then undoubtedly such clinical cases must be justly labelled Acute Splenitis, and although Splenic suppuration is very uncommon, Acute Splenitis on the other hand, considered purely as a pre-suppurative type failing to materialise, is in comparison more common and not so rare a condition as one would think. Emetin should therefore be employed in treating all massively enlarged hard Spleens giving a history of dysentery; and probably it is wise in such chronic enlargments attended with a low type of temperature -

* ANOTHER CASE of Emetin controlling Acute (Malarial) Enlargement of the Spleen - with Diagrams & Temperature Chart is published over-leaf.

## A CASE OF TYPICAL TERTIAN (BENIGN) MALARIAL FEVER & ENLARGED SPLLEN TREATED SOLELY WITH EMETIN.

A Temperature-Chart is attached for reference. This man a Sepoy from Mesopotamia, aet.20, was admitted to the Annexe-Hospital on 11/Jan/17, with history of Chronic Malaria. He had no fever at the time of admission but developed an attack on the 14th.* Blood-examination showed a heavy infection of Benign Tertian & the Spleen became enlarged. Emetin Injection of 1 gr.daily begun. He had no fever on the 15th, but on the 16th. the temperature again rose to 105F. but not so high as on the first occasion. Parasites were still present in the blood. The Spleen was still enlarged. The temperature fell to normal on 17th.morning but did not rise again on the 19th. continuing normal till the 23rd.evening. The size of the Spleen is shown on the 20th.in the Diagram, after 6 grs.Emetin. Emetin was discontinued after the 20th. He had thus received 7 grs.Emetin (total). On the 23rd.evening*he had another attack of what we must regard as Malarial, as fever reappeared on the 25th.evening.* The blood showed no Parasites on the 26th. No Emetin had been given after the 20th. to be able to judge as to the effectiveness of the drug. The Spleen remained Normal throughout the "relapse" and afterwards. He has continued normal in temperature after the 25th. and is well at the time of writing ( 8th.Feb/17.).

The case is worth consideration; and the rapid decline of Splenic dulness & control of the high fever, are both remarkable.

* The temperature rose to nearly 106.F.

* The temperature never rose beyond 100.2 F.

* The temperature did not rise higher than 99.6 F.

Diagram.

**A Case of Typical Tertian Malarial Fever with Enlarged Spleen, in whom numerous Benign Tertian Parasites were found. Treated solely with EMETIN**

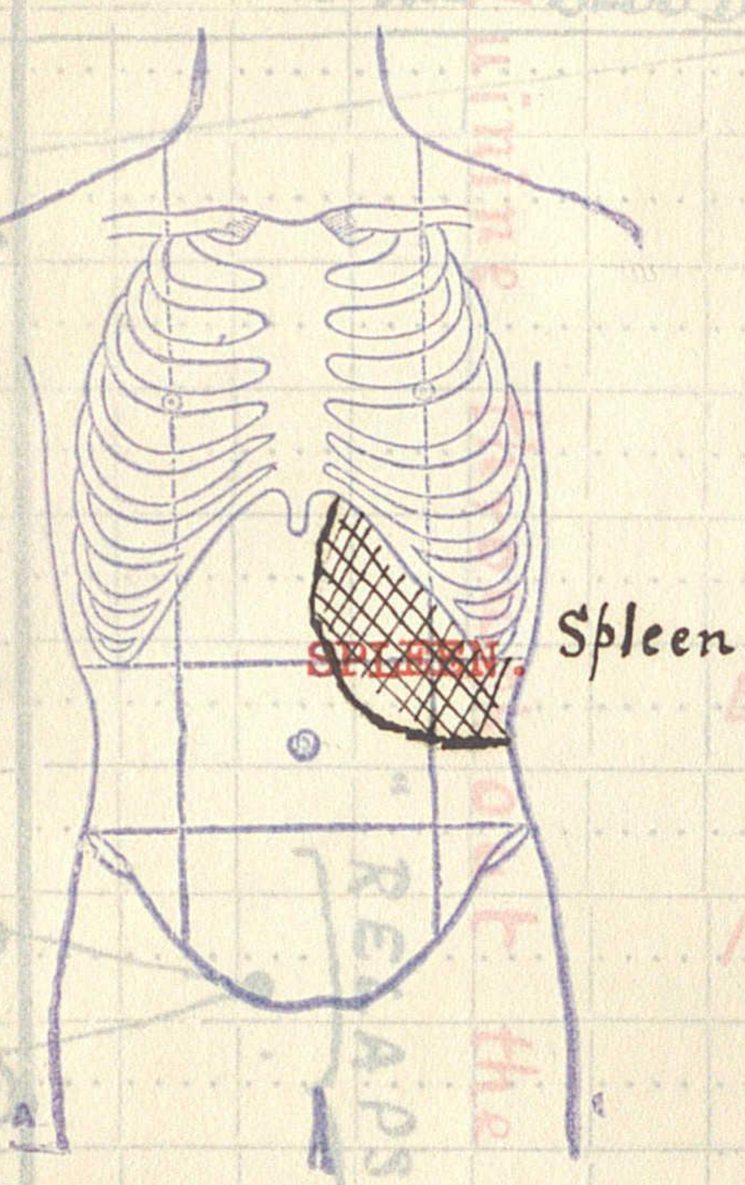


Fig.1. Size of Spleen before Treatment. on 14/1/17.
EMETIN INJECTION - 1 gr. daily begun. Numerous Typical Benign Tertian Parasites seen.

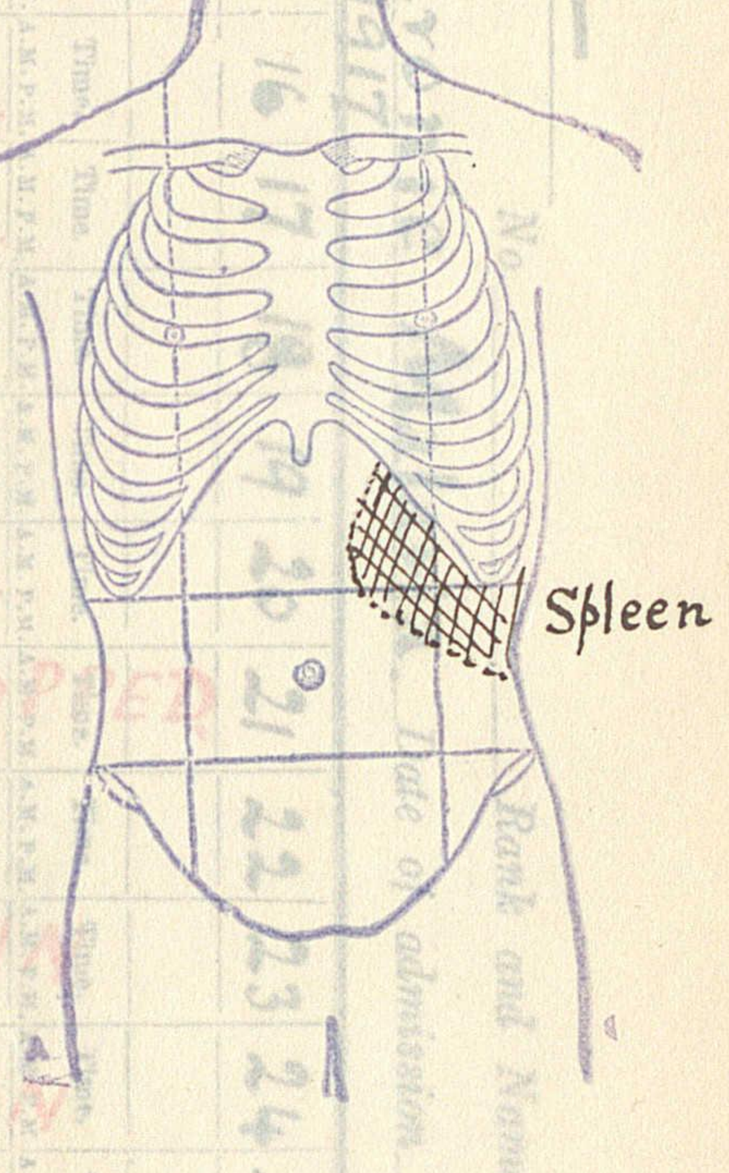


Fig.2. Size of Spleen on 17/1/17. Has had 3.grs. Emetin (total).

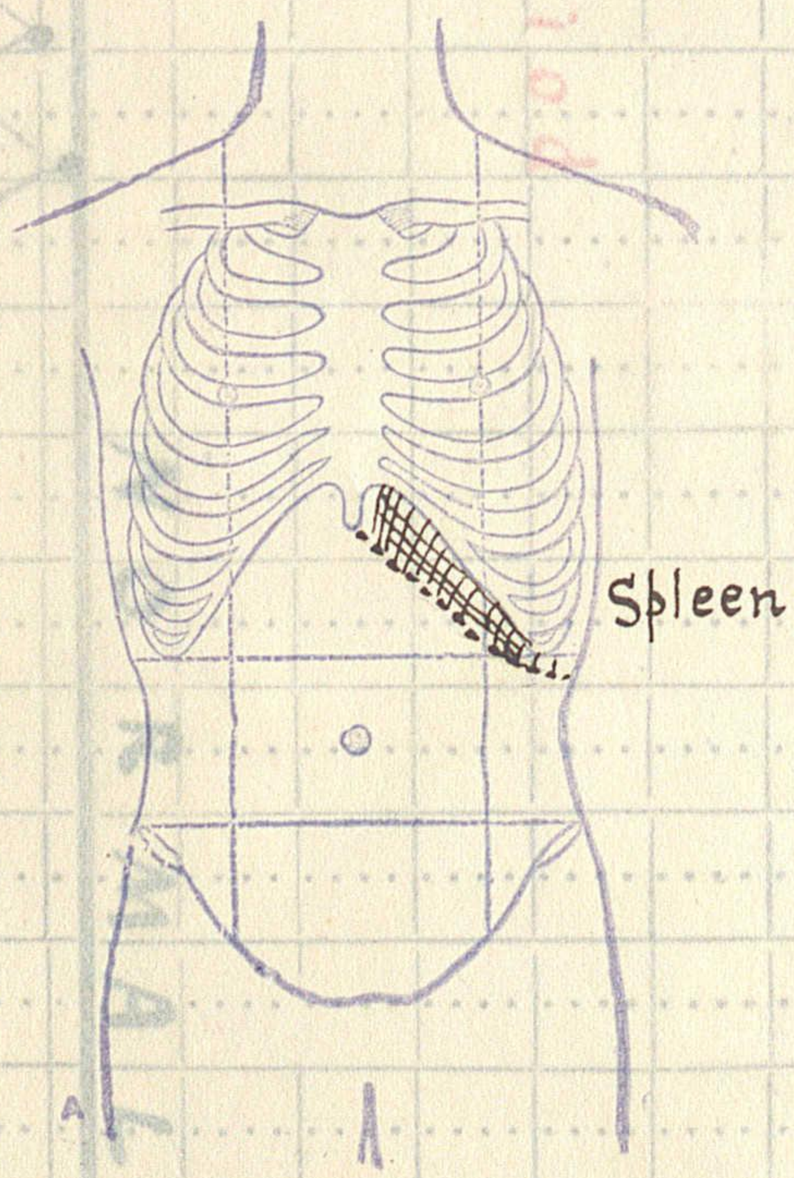


Fig.3. Spleen on 20/1/17. 1.gr.Emetin Injected. Emetin to be discontinued as no Fever since 16th.

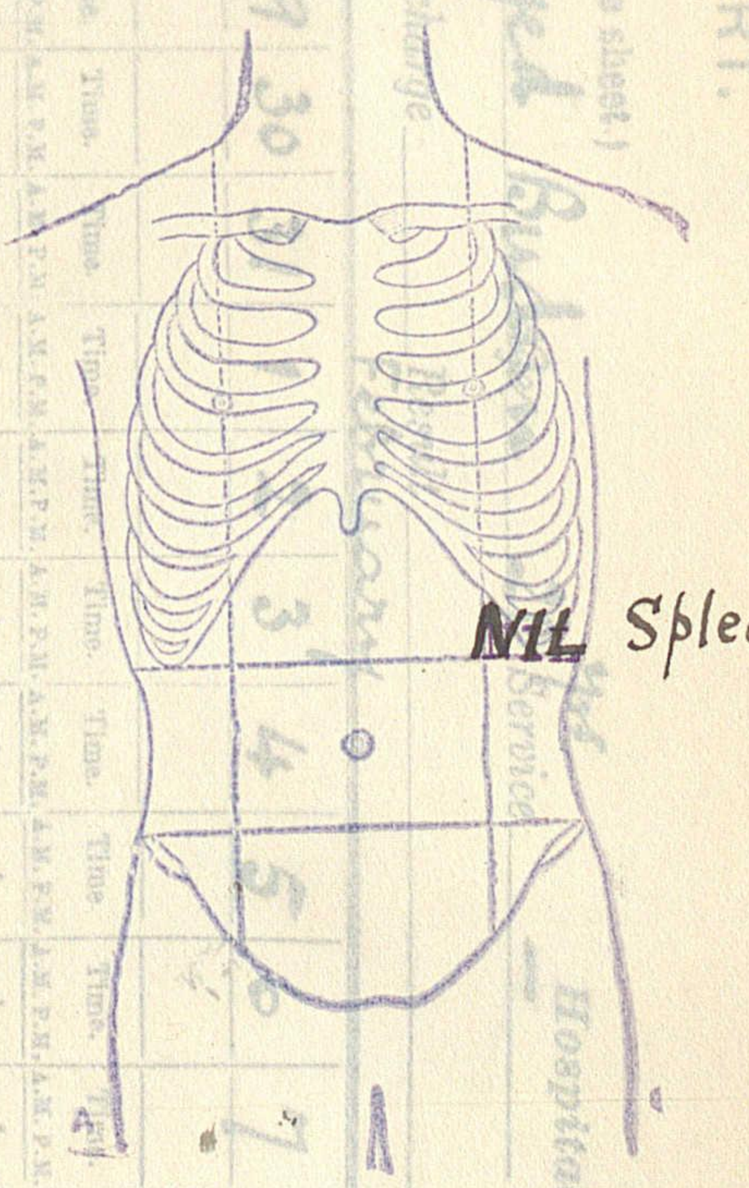


Fig.4. Size of the Spleen on 25/1/17; although a rise of temperature on 23rd. and 25th. No Parasites however seen. Has been given no Emetin since 21st

4.

# CLINICAL CHART.

A. F. B181
Gratis.
15-2-10.

(To be attached to the case sheet.)

Corps — No. — Rank and Name Sepoy Syed Budgen 20 yrs Service — Hospital Station Karachi

Disease Chronic Malaria. Date of admission — Date of Discharge — Result —

JANUARY. 1917 February

| Dates of Observation. | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Day of Disease. | | | | | | | | | | | | | | | | | | | | | | | | | | |
| Temperature, Fahrenheit. Time. A.M. P.M. | | | | | | | | | | | | | | | | | | | | | | | | | | |

RIGOR
EMETIN Hydrochlor 1 gr.
after DIAPHORETICS
EMETIN 1 gr.
EMETIN 1½
EMETIN 1½
EMETIN 1½
EMETIN 1½
EMETIN STOPPED.
NO EMETIN
NO EMETIN
NO EMETIN
NO PARASITES

Numerous BENIGN TERTIAN PARASITES in the BLOOD.

No Quinine throughout the Whole period

"RELAPSE"

NORMAL

J. O. Moses

temperature, to stop all Quinine administration for generally such patients are saturated with it.

## The Pathology of Acute Splenic Suppuration.

When the condition is brought about by amoebae solely; and occurring as a metastases, resembles the acute liver condition in its pathology and mode of production. The "modus operandi " passes through the successive stages of thrombosis, hemorrhage and softening of the Splenic pulp by amoebic infection, and the final necrosis and disintergration, just as in the liver. The paths of amoebic infection of the Spleen have already been detailed. The necrosis may be massive. Such an " acute abdomen " may resemble the condition of Acute Splenic Infarction, when the abscess is primary or metastatic. The Infarct does not however, correspond solely with passively-produced Acute Infarction, for in addition to the blocking of the circulation by the amoebic masses in the coagulated capillaries, there is the further action of living amoebae to accentuate and extend this necrosis, also probably due in part to some toxin elaborated during the process, either specific or derived in part from the katabolism of the tissues. Finally a huge abscess cavity is produced in the affected area, both by many areas of Infarction breaking down and the extension of the abscess cavities into each other by the amoebae. From published cases it appears that there is really single large abscess produced.

## The Differential Diagnosis of Splenic Enlargments

Causes of Splenic Enlargment.

I. Chronic Enlargment of the Spleen.

(a) Very great enlargment:

Splenomedullary Leukaemia.
Lymphatic Leukaemia.
Leukanaemias( mixed types).
Hodgkin's Disease ( nodular type ).
Chronic Malaria
Kala-Azar
Pseudo Kala-Azar or Tropical Febrile Spleno-Megaly.
Splenomegalic Cirrhosis.
Splenic Anaemia
Pseudo-Leukaemia Infantum ( Von Jasch ).

(b) Moderate enlargment.

All conditions mentioned in group (a) will at some stage exhibit a Spleen that has not yet become enormous; and besides these, chronic and moderate enlargment of Spleen may be exhibited in cases of -

- continued -

I. (b) Pernicious Anaemia
Congenital Syphilis
Hodgkin's Disease
Cirrhosis of the Liver
Lardaceous Disease
Thrombosis of the Portal Vein or)
pressure upon the Portal Vein by)
adjacent Tumours. )

II. Acute enlargment of the Spleen, the enlargment as a rule being slight.

(a) Acute infective fevers, viz -
(especially)
Typhoid
Para-Typhoid
Relapsing Fever
Malaria
Erysipelas
Septicaemia.
(And less often in)-
Smallpox
Typhus Fever
Pneumonia
General Tuberculosis

(b) Embolism in Ulcerative Fungating Endo-Carditis.

(c) Injuries and accidents, such as Torsion of the pedicle

III Wandering Spleen( Splenoptosis ).

IV. The enlargment due to abscess.

The largest of all Spleens are those due to Spleno-Medullary Leucocythaemia. The complete blood changes will be found under the section in the Differential Diagnosis of Blood Diseases under " The Blood in Hepatitis and abscess of the Liver ( dysenteric ) ". Here it may be noted that if there is an extreme degree of Leucocytosis and if in the differential count, from 20 to 50% of Leucocytes are Myelocytes, with in doubtful cases the occurrence of a positive Indophenol-Oxydase re-action, the disease is certainly of the Spleno-Medullary type

- continued -

If the Small Lymphocytes yield a count of 90% or more, the disease is Lymphatic Leukaemia of the Lymphocytic type; there is less pronounced Leucocytosis compared with Myeloid Leukaemia. The Lymphoblastic type of a Lymphatic Leukaemia is characterised by the following clinical features :-

1. Rapidly fatal course
2. Fever weakness and Hemorrhages
3. Moderate glandular enlargment - in children the Spleen may reach the largest size observed in other Leukaemias.
4. Progressive Anaemia of secondary type.
5. Extreme rarity of Granular Leucocytes.
6. A Leucocyte formula mostly made up of primitive Lymphoid cells.

Splenomegalic Cirrhosis. Affects children and young adults. There is more or less jaundice anaemia, lack of developement, and ultimately ascites, as well as considerable enlargment of the Spleen. It is generally Familial. The cases exhibit more or less fibrosis, or cirrhosis of the liver. What relationship this disease has to the ordinary cirrhosis of Hanot, and to Splenic Anaemia or Banti's disease, is not clear. The blood changes are merely those of a simple Chlorotic Anaemia.

Splenic Anaemia . The characteristic features are, primary splenomegaly and progressive secondary anaemia, with leucopenia. The Spleen is often considerably enlarged and tender. Epistaxis is often one of the earliest symptoms, and of frequent occurrence. The diagnostic value of the blood in this disease, consists in the absence of special characteristics.

The Differential Diagnosis of Splenic Enlargments, Acute and Chronic.

- continued -

Splenic Anaemia

The Cachexia, as in Hodgkin's disease, is out of all proportion to the degree of Anaemia.

The Spleen is intimately connected with the Etiology of the disease since Splenectomy is curative. Its further stage, with Ascites & Cirrhosis of the liver, and Jaundice, constitutes Banti's disease.

Hodgkin's disease - the nodular form

A very good account will be found in the Medical Annual for 1913. It first appeared in one of the numbers of the Quarterly Journal of Medicine in 1913 ( I forget the exact ref:)* There is of course associated considerable and progressive Lymphatic Glandular enlargments. The blood changes in it are not pathognomonic even when they are severe.

* cf/- P. 215 THESIS.

Waxy disease. The Spleen is not always enlarged, but may be palpable, and the liver is generally enlarged at the same time. It occurs in two chief types -

I. The Sago waxy in which the changes involve the Malpigian bodies and the Arterioles of the Malpigian bodies." The main changes is in the Adenoid Reticulum and perithelial connective tissue of the capillaries of the Malpigian bodies..... the Venous Sinuses of the pulp usually show associated chronic venous congestion, leading to extensive compression atrophy of the pulp cells. " (cf. Beattie & Dickson, Special Pathology, p. 143.)

II. The Diffuse Waxy is the less common type of the two. There is extensive affection of the Splenic pulp. In this variety the waxy change occurs in the "supporting reticulum and the perithelial connective tissue of the venous sinuses of the pulp which are thus sharply outlined by the change .... The endothelial lining of the venous sinuses, do not undergo the waxy change. The pulp cells are compressed & usually show extensive atrophy.... the Malpigian bodies may, or not, be affected." (cf. Beattie & Dickson, ibid, p. 144.).

- COntinued -

Lardaceous disease results from long continued suppuration or from Tertiary Syphilis. If considerable enlargment of the Spleen is associated with any of these conditions, it is probably due to Lardaceous disease. There is generally diarrhoea on account of the affection of the intestines in the general waxy change; and polyuria and albuminaria, owing to renal changes. Blood counts exclude Leukaemia, and indicate more or less severe anaemia of the Chlorotic type.

The Acute Infective Fevers.

Typhoid Fever, is the best known febrile disease in which moderate enlargment of the Spleen occurs. The organ is usually soft. If in a case of obscure fever in which a continued Pyrexia is associated ( especially during the first 10 days ) with a relatively slow pulse-rate, the Spleen is found to be enlarged, the diagnosis of Typhoid Fever is very lightly, especially if there is a history of a gradual onset, lassitude, headache, sometimes epistaxis, and a gradual rise of temperature. Widal is not positive generally before the 7th. to the 10th. day. Earlier confirmation of the nature of the fever may be obtained by the blood count, there being No Leucocytosis - indeed, sometimes Leucopenia- and if there be a relative increase it is not in the polymorphonuclear cells, but in the Small Lymphocytes. Such blood changes are in themselves almost pathognomonic, and they are obtainable more frequently in the early stages of the disease than any other sign, including Widal.( Gennari ) (cf. Haemocytes & Haemic Infections, F.W.E.Burnham, lst.edn; 1913, pp. 38; 210 - 212. ).

Malaria. Apart from the chronic enlargment of the Spleen, due to recurrent attacks of malaria, the spleen becomes enlarged and soft as a result of active hyperaemia during acute attacks. When the patient has more or less chronic enlargment of the spleen as the result of preceding attacks, each acute febrile paroxysm is associated as a rule with an additional swelling which passes off after the attack. It is in these cases where there is associated history of dysentery that greatest difficulty attends the diagnosis. Blood examination for parasites must be made. As regards the type of anaemia and changes in the blood, full reference has been made in the section of the diagnosis of blood diseases. Here it may be mentioned that the leucocytes are diminished, with a relative increase in the Large Hyaline Lymphocytes, up to even 15 or 20%.

Ulcerative (Fungating) Endocarditis.
Fungating Endocarditis is nearly always associated with palpable enlargement of the spleen, and sometimes the organ attains a considerable size. Except in children, enlargement of the spleen in a heart case, should always arouse serious suspicion of infective Endocarditis. The enlargement may be due to Embolism and Infarction. Sometimes it is due less to actual Infarction than to the general toxaemia. There may be a history of acute pain low down on the left side

- continued -

Fungating Endocarditis, continued.

of the chest, accompanied by a definite rub due to perisplenitis over the infarct.
Fungating Endocarditis sometimes developes without there being any bruit at all; the diagnosis is then exceedingly difficult unless the patient suffers from Multiple Emboli.
Sometimes such an Embolus may be followed by the development of an acute aneurysm, esp. cerebral - death resulting from the rupture of the aneurysm. Progressive anaemia of the chlorotic type, without much leucocytosis is another feature of these cases. Of course there is fever of a septic type.
Thrombotic Infarction may cause acute splenic enlargement in almost any of the Blood diseases, particularly in Lymphadenoma and Leukaemia.

Hereditary & Familial forms of Splenomegally.

i. Variety with marked constitutional disturbances , e.g, dwarfing, infantilism, pigmentation of the skin, etc. -the Collier - Bovaid - Brill - Taylor type.

ii. Minkowski type - with associated Congenital Acholuric Jaundice; but the health of the patient is not disturbed. ( cf. Principles & Practice of Medicine, Osler, 7th. edn; p.762.).

Tropical Splenomegally ( Kala-Azar ).
The initial fever attending Kala-Azar, may be intermittent or remittent, and may be accompanied by Rigors. During its progress the spleen and liver enlarged, increasing and decreasing in harmony with the fluctuation of the fever. Then comes a period of Apyrexia and general improvement to be followed later by fever, splenic and hepatic enlargements; and perhaps tenderness. Profuse sweats are common. When the disease is thoroughly established, emaciation and anaemia become noticeable, oedema of the legs appear, and the patient assumes a typical appearance. (cf. Manson, Tropical Diseases, 5th. edn, p.209 ).
"The irregular high remittent fever which may early show two remissions per day in a four-hourly temperature chart, is considered by Rogers to be almost diagnostic of the disease."( cf. Castellani & Chalmers, Tropical Medicine, 2nd. edn.p. 955 ).
Intestinal disturbances in the form of diarrhoea or disenteric attacks are common, and may be due to the actual disease or to complication with true dysentery. The only certain method of diagnosis is to find the parasite. In early stages it may be found in the peripheral blood ( Donovan & Patton ); aided perhaps by exciting artificial pustulation of the skin ( Major Cummins R.A.M.C ); failing this, by liver or splenic puncture so as to withdraw pulp.- the surest means of diagnosis is by spleen puncture; liver puncture is the safer method of the two, on account of possible haemorrhage.( cf. Burnham, Haemocytes & Haemic Infections, 1st.edn; p. 376.)
The disease itself has to be diagnosed from Leukaemia, Chronic malaria; in the early acute stages from Typhoid and acute malaria, Typho -

- continued -

Kala-Azar, continued

Typho-Malaria, and mixed infection of Kala-Azar and Malaria.

The Histological lesions of Leishmania- Donovani are summed up by Makkas of Athens as follows:-

" 1. The spleen, liver & bone marrow are, during the course of the disease, and prior to the terminal cachectic stage, the only organs infected with Leishmania.

2. The occurrence of Leishmania, in other organs before the final stage, is thus rather the nature of an accident.

3. The organ first infected with parasites is the spleen, and it is only later that they instal themselves in the liver and bone-marrow. The more serious lesions of the liver are only produced after the lapse of some time from the commencement of the disease.

4. The fact that the parasites, whether in the spleen, liver or bone-marrow, are always in one kind of cell, the MONONUCLEAR cell,

5. The chief lesions of the splee n are due directly to the organisms themselves.

6. The lesions in the liver are due to toxins generated in all probability, by the Leishmania.

7. It is the same toxins that bring about the enormous destruction of red corpuscles, which takes place in the disease.

8. The alterations in the bone marrow are merely an exaggeration of the normal physiological function of this organ. "

(cf. Burnham, ibid. p. 368. ).

The Blood in Leishmania-Donovani.

The most remarkable change in the blood, is the great and constant reductions in the number of the leucocytes. There is a most marked leucopenia, and Rogers reports that in 42.1% of his cases, the leucocytes were 1000 or less; in 30.3%, 1000 - 2000; and in 22.6%, 2000- 3000. The proportion of white to red, according to the same Author, is less than 1: 1,500 in 67.9% or if inflammatory cases are excluded in nearly 90% of the cases he examined. The reduction is most marked amongst the polymorphonuclear variety, and in the Eosinophiles; and a relative increase in the mononuclear leucocytes and lymphocytes; which may reach 70 or 80%, but the differential lymphocyte percentage varies from time to time in the same individual. There is marked anaemia - 54.2% of Rogers cases giving from 4,000,000 to 2,500,000 corpuscles per c.m. The haemoglobin is reduced, but nearly always in proportion to the reduction in the red cells; the colour index deviates but little from the normal. Poikilocytosis and Polychromatophilia are observed; Normoblasts and Megaloblasts are

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The Blood in Kala-Azar.- continued

present in severe conditions.
The anaemia associated with Kala-Azar is said to vary with the degree of infection. The diminution of the polymorphonuclear leucocytes is thought to explain the tendency to bacterial infections.
Localisation of the parasites after splenic puncture. The parasites are included in hypertrophied, endothelial cells of the blood-lacunae. They are contained in the Mononuclear cells, up to 50 or 80 in each, or in the debris of the cells The parasites may be extra cellular, in groups or single, but are never in the red corpuscles. In heavy infections they are contained in the polymorphonuclears.
After liver puncture, parasites are found in the liver cells.
Bone-Marrow. They are found in Mononuclear cells

Kala-Azar can easily be differentiated from Ankylostomiasis by the fact that there is a high and persistent Eosinophilia, which is never observed in Kala-Azar.

Cf. The Kala-Azars
in
Tropical Medicine
Castellani & Chalmers.
2nd. edn, pp 952-965.

Pseudo- Kala-Azar (Febrile)

This is a form of Febrile Splenomegally of unknown causation, characterised by splenic hypertrophy and gastro-intestinal disturbance followed by emaciation; resembling Kala-Azar but the typical parasites can not be found either during life or after death. There is absence of leucocytosis. The Febrile attacks distinguish it from Banti's disease; and splenic removal does not affect a cure.

Pseudo- Kala-Azar-( Afebrile ).

This is a chronic Afebrile disease characterised by Splenomegally severe anaemia, absence of gastro-intestinal disturbances, and absence of parasites from the blood or other organs. There is also absence of leucocytosis.

Infantile Kala-Azar, or Ponos (Nicolle)

This is a sub-acute or chronic specific disease clinically closely resembling Indian Kala-Azar, but occurring in childhood, and due to Leishmania Infantum Nicolle. There is always associated gastro-intestinal disturbances of acute character, e.g, diarrhoeic and dysenteric attacks, ulcerative stomatitis. There is progressive anaemia marked wasting; enlargement of the spleen and liver in the later stages and a peculiar white tinge of the body as the disease becomes fully established. There is a rapid pulse rate even in the apyrexial interval. The characteristic clinical symptoms are the enlarged spleen, irregular fever, and the pallor occurring in a child. Splenic, liver or bone-marrow puncture must always be resorted to for search of the parasites, which can then be cultivated on the so-called N.N.N. medium. The disease can also be successfully inoculated into dogs. The leucocytic formula is mononuclear, 70 to 80%. The polymorphonuclears making up the remaining 20- 30%. There is absence of leucocytosis

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Liver abscess bursting into the Stomach.

The spontaneous bursting of a hepatic abscess into the stomach is infrequent. Rogers can only detail two such cases. These abscesses empty themselves through the muscular coats. Adhesions occur between the gastric area of the stomach and the liver ( the stomach bed ). Often there is hepatitis as well with Peri-Hepatitis. The clinical symptoms will be intense boring pain in an acute rupture, feeling of nausea and faintness and cold sweat; and directly as the abscess ruptures, violent vomiting. Death is often due to the tearing of adhesions by the violent gastric efforts. In chronic rupture the symptoms will be more insidious. There may be severe hematemesis, especially when one of the big arteries supplying the stomach, such as - the Right Gastro-Epiploic, the Coronary, and even the Superior Mesenteric. Unless free drainage to the outside is established at an early period, practically every case proves fatal. For some reason or other, large hemorrhages are rare; " blood-vessels often show remarkable resistance to ulcerative processes ( W.E.Brown, Amoebic Dysentery, p. 194 ). "

Liver Abscess opening into Bowel.

"1% of abscesses open into the small intestine especially into Duodenum; 10% into the Colon, generally the Hepatic Flexure." (cf.Brown, ibid, p. 186 ). Such cases may recover spontaneously; the abscess apparently draining through the Gut. When the contents of the abscess are evacuated into the Gut, it is rapidly expelled per rectum. " Herbert Milton, has recorded a case in which an abscess opened into the Gut and discharged completely by this path; the patient had been operated on a few days before for a Liver abscess, and was practically moribund, but under the use of Ipecacuanha he recovered. "
(cf.Phillips, Amoebiasis & The Dysenteries,p.48 ).

Liver abscess opening into the Pericardium.

This also is a rare complication. In one of Sambuc's cases, the pericardium was found to be in direct communication with a Left Lobe Liver abscess, from which 150 c.c's of pus was removed. (cf.Phillips, ibid, p.48 ). The pericardium may be infected by a Pleuro-Pericardial rupture, that is - a secondary Empyema infecting the pericardium. A Pleuro-Pericardial rupture would at least give the signs of Empyema with an added on sudden embarrasment of the Heart, unless it resulted from chronic perforation. Adhesions between the Pleura & the Pericardium, might be shown by the alteration of the lie of the Heart or by its adhesions with the chest wall. The signs of pus in the pericardium will then be merely the clinical condition of a Pyo-Cardium. X-Rays may be helpful.

Rupture into the Inferior Vena Cava, is the direct result of an adhesion between the liver and the Inf: Vena Cava lying in the Portal Fissure. Death of course would be instantaneous.

Rupture into the Peritoneum;-General Peritonitis.

Sambuc's Tables give two such cases. In Rogers collected series, 39 cases giving 6.9% are noted. Acute general Peritonitis, was more often caused by operation than spontaneously. It is analaguos to the production of a Pulmonary abscess sine Empyema and Empyema secondary to hepatic abscess sine Pulmonary abscess in the first instance.
The whole question is a matter of adhesions.
As a rule the base of an amoebic ulcer rests on the circular muscular fibres, and tissue destruction seldom extends beyond the submucosa.
It occasionally happens that the muscular coat is invaded; and when the Peritoneum is weakened by infiltration and effusion, perforation may take place. Although this sometimes occurs at the base of an ulcer following coagulation-necrosis, it is more frequently seen as a result of suppurative burrowing. When there is unusual tension in a submucous abscess, it may point downwards as well as upwards and the pus, as if endeavouring to find an exit in both directions has thrust aside the dense bundles of muscular fibres and reached the Peritoneum ( Visceral ).
The comparative rarety of perforation is due to the strength of the Serous Coat, and also that the inflammation is of an unusually plastic and adhesive type. This, therefore, is one type of case, where there is coincident acute ulceration of the Intestine going on to separate perforation, and the abscess in the Liver by hydrostatic pressure, bursts through the Peritoneum.
This may therefore be classified as a Peritonitis complicating acute amoebic dysentery, and a rupture of abscess of the Liver into the Peritoneum, This class of case is the gravest.
A second type of case may result from secondary burst from the Stomach by the violent vomiting attending a Primary rupture into this organ from the Liver--death resulting from the tearing away of adhesions, and allowing the amoebic pus to flood the general peritoneal cavity.
The next most frequent complication after rupture of an abscess into the Lung is, opening of the abscess into the colon or Duodenum, which has already been described; hence, it is rather rare to meet with Primary rupture of a Liver abscess into the Peritoneum, either by a burrowing of the pus through the Liver, or a burst caused by pure hydrostatic pressure within the Liver.

## SECTION VII. AMOEBIC INFECTION OF THE LIVER.

### PART 9. SPECIAL POINTS IN THE DIAGNOSIS OF TROPICAL ABSCESS.

## 1. The value of X-rays, & Shadow Interpretation.

An excellent resume of this is given by Rogers, in his "Dysenteries" p.201.
"On the whole, X-rays do not give quite as much assistance as might be expected, and some experience is required in drawing reliable conclusions from the appearances seen. The absence of any increased density of the liver-shadow, does not negative the presence of a collection of pus; whereas a shadow may also be seen at the base of the Right Lung, in cases of Subacute Hepatitis, which yields to Ipecacuanha, thus proving its exact nature!" Shadow-diagnosis seems to be more useful in Left Lobe Abscess, where the liver tissue is thinner; also in debilitated patients with lax & thin abdominal walls, e.g. in an advanced state of the disease; and in localised Chronic abscesses, with thick fibrous walls, or where the abscess has undergone encapsulation.
Nor must one forget Riedel's Enlarged Lobe, an innocent Congenital condition.
Other pathological conditions, e.g. enlarged glands due to Hodgkin's Disease, Lympho-Sarcomas & other Neoplastic processes, be forgotten; and also all precautions must be taken not to read a collection of inspissated bowel-contents as a liver-shadow.

## 2. The Causes of Recurrent Rigors.

The occurrence of a series of rigors are of much greater importance than a Single or merely a 2nd. for it is seen in but a comparatively limited number of Local or General Infections, most of which have some characteristic or localising signs. In themselves these rigors are no more than evidence of the severity of the Infections in which they are seen, and of the extent toxins have been absorbed into the blood, & have upset the Thermotactic Centres. The following is a list compiled from "The Index of Differential Diagnosis of Main Symptoms"- ed. by French, 1912, p.p.648-651.

Malaria - all types, but the character depends on the Parasite or Hemameba.
Relapsing Fever. - but Obermeir's Spirillum is found in the blood.
Acute Leukaemia. - occasionally, but the Diagnosis is clear on blood-examination.
Acute Blood-Infections, including:-
Portal Pyemia) Special forms of which are known as
Pyemia ) Malignant Endocarditis, Suppurative
SepticoPyemia) Phlebitis, Acute Osteomyelitis, etc.
Septicaemia )

Acute Inflammations, such as:-
Pyelitis
Pyelonephritis & Charcot's Hepatic Intermittent
Cholecystitis Fever,
Empyema of the due to Chronic Cholangitis.
Gall-Bladder.

Abscess-Formation:-
Hepatic Tropical Perinephrenic
Hepatic Septic Cerebral
Subphrenic Septic Sinus Thrombosis.
Appendicular

Advanced Pulmonary Tuberculosis & Bronchiectasis

Special Points in Diagnosis of Tropical Abscess.

- continued -

2. The Causes of Recurrent Rigors.- continued -

Portal Pyemia, or Suppurative Pylephlebitis, is seen in patients with various Acute inflammatory intra-abdominal lesions, and is due to the spread of Bacterial Infection to the Portal Vein. The commonest precursor is mild appendicitis. The blood in the portal vein clots, becomes infected and the clots soften, break up and are carried as infective emboli & distributed throughout the liver Multiple Hepatic Abscesses result, with pain & liver enlargement; jaundice is present in less than half the cases, & there is hectic fever with diarrhoea. Pyemia is characterised by the formation of abscesses- Metastatic - in any of the organs, but more especially in the Lungs.

Multiple Rigors occur in a number of Acute Inflammatory Infections . If the Gall-Bladder & Bile-ducts are the seat of the inflammation, jaundice & pain are common with fever & rigors, and perhaps a history of gall-stone colic. It is in these cases that greatest difficulty wii be found in the exclusion of suppuration, only a blood- examination will be found decisive. Charcot's Hepatic Intermittent Fever is due to Chronic Cholangitis, with intermittent biliary obstruction due to a ball-valve stone lying in the Ampulla of Vater.
The occurrences of rigors in a child recovering from a Pneumonia or Acute Infective Fever, is suspicious of Empyema. A leucocytosis occurs in Pneumonia, and this has to be borne-in mind when examining the blood.
Acute Tropical Liver Abscess bears a close resemblance to all these Acute Diseases, and each case must always be considered on its merits. The diagnosis from Infective Cholangitis must be made where jaundice is more marked & often intermittent, and enlargement of the Gall-Bladder can be made out.

3. The Characters of Amoebic Pus.

I. Liver-Pus.

Typical (sterile) liver-pus is a soft creamy liquid material, usually coloured reddish-brown . There is no other pathological substance that has been so thoroughly compared with table-delicacies, than this misnomer. Thus it has been described as resembling Anchovy-sauce; treacle ; Gooseberry Jam; and Chocolate; and a characteristic feature about it is its mawkish odour, like semen or fish. Occasionally it may be yellowish or even greenish, when bile-stained. When newly-evacuated it is so thick & viscid that it does not soak into the dressings, but lies on the surface of the gauze "like Treacle on bread". It is not pus, but is best described as Liver-Purulage, consisting of liquefied liver-tissue mixed with red blood-corpuscles. Microspically it contains degenerate Liver & connective-tissue cells, with Red blood-cells, some leucocytes, chiefly Mononuclears, Amoebae, oil-globules, Hemoidin crystals, debris & occasionally Charcot-Leyden Crystals.
Sometimes, owing to the advancing Lobular disorganisation, portions of necrotic tissue break off from the walls, and float free in the interior of the cavity. These sloughs are generally a notable

Special Points in Diagnosis of Tropical Abscess.

- continued -

3. The Characters of Amoebic Pus - I. Liver Pus.

notable constituent of the pus contained in Tropicl Abscess, and indicates extensive & rapid destruction of the tissues, with abscence of definite limits of suppuration. The pus is usually sterile, but it may get infected, when it becomes yellow & foul - smelling. When contaminated with B.Coli it comes to have a fecal odour, and the same is noticed when the abscess is situated near the Colon, probably for the same reason. When it is evacuated in the fresh condition, here & there, little islands of 'laudable' pus, may be made out in the brown mass. In rare instances, the pus , insteading of possessing the typical chocolate-colour & viscid Consistency, is yellow or creamy. This is particularly the case where the abscess becomes encysted. In time it becomes cheesy, and ultimately calcified.

II. Characters of Expectorated Pus.

It is of the same dark-brown colour & viscid consistence as ordinary Liver (amoebic) pus. It may be streaked with blood; or sometimes it is almost pure blood, as an ordinary haemoptysis, for which indeed it may be mistaken. Under the microscope it has the same characters as Liver pus.

III. Characters of Amoebic Brain Pus.

The contents of a Brain-abscess sometimes resembles those of Liver-abscesses, being reddish in colour. At other times it resembles 'Gooseberry' Jelly; but it may be grumous, yellowish-grey, or blackish, from altered blood. Just as in Liver-abscess, we sometimes find necrosed portions of abscess wall, so here necrosed portions of Brain-tissue may be either found free in the cavity, or still attached to the abscess-wall by thrombosed vessels. Septic infection alters the typical appearances, and the abscess then comes to resemble ordinary Brain abscess, due to Intra-Cranial disease.
When the abscess becomes encysted - generally only a partial process - the contents turn rusty-coloured due to altered blood-pigment (Haematin).

4. The Evidence of Anti-Dysenteric Measures.

Ipecacuanha or Emetin, specific for Amoeba Histolytica, has no controlling action on Amoeba Coli, on Flagellate or Ciliate Dysentery or Diarrhoea , or on Bacillary Dysentery. Although A.Coli dissapears during treatment with Emetin, it reappears after discontinuation of the Drug.

5. The Duration of Symptoms before Liver Abscess becomes Clinically evident.

The earliest premonitory symptom is Acute Hepatitis. When however Abscess has developed, any symptoms of localising or diagnostic value, depends upon the depth & character of the Abscess. It has already been shown, that there exists a Latent or Insidious Type of abscess. The more deep-seated the abscess, the longer will be the period before it becomes clinically evident, and the larger is this abscess likely to be; and the reverse

## Speecial Points in Diagnosis of Tropical Abscess.

- continued -

5. the reverse is equally true.

The following Table of Rogers is very instructive:-

| Time | Multiple | LEFT-LOBE | RIGHT-LOBE pointing through the :- i Abdoml:Wall | ii Ribs | iii Lung | Total | %% |
|---|---|---|---|---|---|---|---|
| Under 1 week | 2 | - | - | - | 1 | 3 | 5.2 |
| 1-2 wks: | 1 | 2 | 1 | 2 | 2 | 8 | 13.4 |
| 2-4 wks: | 2 | 2 | 4 | 8 | 3 | 19 | 32.9 |
| 1-2 mths: | - | - | 2 | 5 | - | 7 | 11.9 |
| Over 2 " | - | 1 | 3 | 8 | 6 | 18 | 30.5 |
| Time ?? | - | 2 | 1 | 1 | - | 4 | 6.7 |
| TOTALS ... | 5 | 7 | 11 | 24 | 12 | 59 | below |
| %%s ... | 8.4 | 11.9 | 18.6 | 40.7 | 20.8 | - | |

### Analysis of Table.

1. Multiple abscesses have the shortest course, and are clinically evident from the reaction they inevitably cause.

2. Next to these come Small abscesses in the Left Lobe. These rapidly produce local swelling in the Epigastrium, within 1 - 4 weeks of the first symptoms.

3. As regards the Right-Lobe Abscesses. They ar are always more deeply-situated & are also larger. Those which ultimately pointed through the Abdominal Wall, i.e. in the Right Epigastrium, had a variable time-interval; but the majority took about 2 - 4 weeks; but 3 cases were evident only after the symptoms had lasted over 2 months.
The time-interval in those that took the RIB-Route, was certainly the longest. This is simply because these abscesses beneath the Thoracic Wall, are deeply-placed. According to the Table they may appear either fairly early or take over 2 months to show themselves, & there is also a fairly large Intermediate Group, of some 1 - 2 months duration. Only in a very few cases is early appearance noted. "In one of these 2 cases was the condition diagnosed by blood & X-Ray examinations." (Rogers).

Special Points in Diagnosis of Tropical Abscess.

- continued -

5. Duration of Symptoms before Liver Abscess is clinically evident.

- continued -

Analysis of Table.

4. Lastly, come the Lung-Group of cases. Half of these had a history not exceeding one month, including the case with less than a week duration. This is not altogether true, for as,has been alreadypointed out, this class of case has always an element of doubt & surprise attached to their appearance, as to when they really formed; and often an Insidious Abscess takes this route to proclaim that original suppuration existed in the Liver. Perhaps a certain number of these cases under review were of this complicated nature. In the remaining ½ of the cases, there were histories of over 2 months'duration. These cases therefore are perhaps illustrative of the most Chronic Forms of all,

5. "Taking all the Varieties together, only 1/5th. had a history not exceeding 2 weeks; 1/3rd. from 2 weeks to 1 month; and nearly ½ a duration of over 1 month. It is impossible to say in each case the length of time which elapsed before actual Suppuration took place, and consequently , how long an abscess had been present before it made its presence felt." (Cf/Rogers'Dysenteries pp.191-193 ).

Acute Amoebic Hepatitis usually occurs after an attack of Dysentery, but the interval between the two may be very variable. In one of my own cases there was an interval of something like a month, In many cases, however, there is no history of dysentery, the lesions being entirely Latent, as has been shown by Clegg & Musgrave* . The onset of the Hepatitis is usually gradual. The various aberrant Types of Hepatitis will be found in that particular Section of the Thesis.

* Musgrave - "Intestinal Amoebiasis Amoebiasis s without diarrhoea 50 fatal cases" Phi;ippine Jl.of Science, Sec,B. 1910, Vol 5, p.229.

6. The General Symptoms & Co-related Clinical Types of Tropical Liver Abscess.

1. Types of Abscess-Temperature.

When an acute attack of Dysentery complicates symptoms of Liver trouble, it becomes necessary to read the temperature-chart rightly & draw correct inferences. In Amoebic Dysentery, in Balantidium, & Flagellate Dysentery, although the onset may be sudden & acute, there is little or no fever; only in Bacillary Dysentery, does the thermometer rise & often sharply sometimes. Any fever appearing in an associated & microscopically-diagnosed Amoebic Dysentery, with Hepatic Symptoms

Special Points in Diagnosis of Tropical Abscess.

- continued -

6. The General Symptoms & Co-related Clinical Types of Tropical Liver Abscess.

1. Types of Abscess-Temperature.

is certainly due to the Hepatic condition. As a rule the thermometer affords the earliest and most reliable indications of suppuration. Not infrequently, there is a rigor or series of rigors; blood-examination excludes Malaria not only because there is absence of Parasites but principally because there is a leucocytosis; and the temperature, which after the Acute stage of the dysenteric attack, usually remaining below normal, rises suddenly to 103-104°F.

i. In well over 50%, the temperature is of the Low Remittent Type, - falling below 100°F. in the morning, & rising to 103-104°F. in the evening - the daily exacerbations ascending, during the development of the abscess, by ladder-like increases of one or two degrees, until t the temperature reaches a maximum of 105 which corresponds to full development of the abscess. Each access of temperature lasts but a short time, and subsides with copious sweats within a few hours. These copious sweats may produce two or more depressions in the temperature curve within the 24 hours. These sweats may be so copious as to soak through the bed clothes.

ii. In about 20%, fever may be of a more severe character, the Higher Remittent Type, not falling below 100°F. for several days together. FULMINANT MULTIPLE Abscess cases, often exhibit such temperature

iii. In about 15%, there is High Continued fever, i.e. the temperature keeping above 101°F. & not varying more than 2°F, in the 24 hours. In such cases the NERVOUS System is apt to be more seriously affected, especially in alcoholics. Although the onset of NERVOUS complications occur often after an attack of acute Dysentery, e.g. Chorea, Peripheral Neuritis, & even Epilepsy, yet when the Abscess is relieved or spontaneously relieves itself, all Mental or other Nervous complication, also spontaneously disappears. Intense headache or even Acute Mania, Disorientation, etc. may occur. W.C.Brown, in his "Amoebic Dysentery", (p.182), records a case of Acute Mania in a case of unsuspected abscess, in a man whose temperature remained up to 104.5°F. for over a week. Acute Mania developed on the 8th. day. An unsuspected abscess burst through the lung, on the 10th. day, with immediate relief to all Mental & other symptoms.

Special Points in Diagnosis of Tropical Abscess.

- continued -

6. The General Symptoms & Co-related Clinical Types of Tropical Abscess.

1. Types of Abscess-Temperature.- continued

iv. Very rarely, in 3% of cases, the Insidious Normal Type, of temperature, may exist for a few days before the abscess is opened. Rogers has met with with cases, especially among Natives, who have walked into hospital with a large bulging Liver abscess, and in whom the temperature was normal. These cases often continue like this so long as the abscess is unopened by the Open Operation. When however this is done, septic Infection invariably occurs and the temperature begins to rise. This Normal Temperature Type, is explained by the fact that the degree of pyrexia is highest in actively-enlarging deep-seated abscesses; whilst in the more Chronic Type, or in the fully-developed abscess, esp: when tension is reduced, as when it has bulged through its Capsule & is making its way towards the surface, whatever fever there was is less, & may even entirely subside.

The Co-related Clinical Types of Liver Abscess are

I. FULMINANT MULTIPLE ABSCESS. The clinical features of this very fatal type, & fortunately the rarest, are very pronounced. In almost every case, there is a clear history of dysentery, generally within a short time previously, & frequently during the development of a Hepatitis. Hence it can be recognised at an early stage. The fever is of the High remittent Type, with rapid rises & falls of the temperature-curve, frequently with RIGORS, accompaning the exaccerbations; and very copious sweats during the decline. The Liver rapidly enlarges & becomes so acutely painful & tender, that even the weight of the bed-clothes turns unbearable. A slight degree of Jaundice is more frequent in this Form than in the less-acute varieties. Such cases linger from six to at most fifteen days. Post-mortem, the Liver is found riddled with abscesses breaking down, one into another, & ofcourse there is no limiting membrane.*

II. ACUTE Abscess of the Liver. In this variety of suppuration, the symptoms are generally acutely developed, and depending on the position of the abscess. The fever may be of the Hectic Type, or of the High Remittent variety, and there is nothing very special to be said concerning them. Very often they go on to the Fulminant type, if there be sepsis superadded.

III. The SUBACUTE & usually SINGLE ABSCESS. These constitute the most frequent & typical

* "The Dysenteric Symptoms are seldom influenced by the development of an abscess; but in cases of a marked Septicaemic character, severe & even fatal attacks of Choleriform Diarrhoea are not unusual."
(Brown - Amoebic Dysentery p.184.)

The Co-related Clinical Types of Liver Abscess.

III. typical condition. The temperature is of the Low Remittent Type, hardly rising above 104°F, & being more commonly 103°F. There are copious sweats. Jaundice is not a common feature. This Subacute Acute Type often resembles the

IV. **The INSIDIOUS CHRONIC TYPE**.* In this there may be irregular fever, sometimes of the Low Continued Type, and sometimes of the Low Remittent Type, there being nothing diagnostic in the case. Such abscesses frequently reveal themselves, by spontaneous rupture; or they may be only found at the autopsy. It is often associated with Latent Amoebic Dysentery, because that condition is generally unrecognised & untreated. The Insidious abscess may become Acut when there will occur rapid oscillations in the fever & perhaps more definite symptoms will have developed.

* The Clinical Pathology of Chronic Insidious Abscess will be found detailed after "Haemic Changes & Their Significance". (P. 219.)

7. The FACIES. This is characteristic, often pathognomic. "The expression is one of intense weariness, anxious & pinched, and the complexion sallow or mud-coloured." The conjunctivae are described by Castellani as possessing a peculiar bluey-whitish colour. Sometimes there is an icteric tinge, but deep Jaundice is not common.

8. JAUNDICE. This has already been mentioned. In the more slowly-developing Abscess it is usually totallyabsent. I have however seen a case of Acute Hepatitis, which undoubtedly would have gone on to abscess-formation, had Emetin been witheld, in which there was the most intense Jaundice present and the conjunctivae deep-yellow. In a case of Intense Jaundice, in a case of Abscess, there was suppuration involving the Neck of the Gall-Bladder; the case ended fatally.

9. The TYPES of PAIN. There are several types of Pain - local and referred or sympathetic.

1. Visceral Pain. There is always a sense of weight & discomfort in the Region of the Liver. Liver Visceral Pain may be further subdived into the Pain which accompanies Perihepatic Inflammation. This is to be suspected when tenderness on pressure is complained of. Although most marked in and along the margin of the Costal Arch, in the Mammarry Line, it is sometimes widely distributed; and palpation between the Ribs causes intense pain all over the Liver area. Perihepatitis results from the Infiltration & infection of the enveloping membranes of the Liver with pus; therefore it more likely results when Suppuration is Multiple & Septic and seldom when the abscess is Single & Sterile. As it is really a Peripheral phenomenon it occurs as a late symptom.

Special Points in Diagnosis of Tropical Abscess.

- continued -

9. The TYPES of PAIN.- continued

2. Regional Pain. This is usually acute & subcostal, and independently of the position of the abscess, it is generally most intense in the Mid-Axillary Line, at the level of the 9th.rib. In many cases however, there is dull aching pain over the whole of the Right Hypochondrium, wiyhout there being any localised pain or tenderness.
Pain in the Lower end of the Œsophagus, has been noted by Manson in a case of Hepatic Abscess, the patient being a medical man.
This pain was excited by the immediate taking of food, the bolus as it passed the lower end of the Gullet, caused pain.

3. Sympathetic or Referred pain. When the abscess is Large & Solitary, the pain is often referred to the back of the Right Shoulder, & often, curiously, enough to the very tip of the Acromion Process,- a purely reflex phenomenon, but hardly ever seen in MULTIPLE Suppuration.
Among Reflex Pains, are to be included the sharp shooting pains, radiating over the Chest and down the right flank & Right Hypochondrium.
Pain in the Right Shoulder. Manson's description is so complete and descriptive, that I quote it in extenso.
"This symptom is present in about 1/6th. of the cases. It may be persistent or it may intermit; it may radiate to the side of the Neck, or to the region of the Scapula, or down the arm; or it may be limited to the shoulder-tip and Clavicular region. In some instances it is of a dull, gnawing, aching character; in others it is more acute; and in some it may be represented by a burning sensation, as if the skin had been flayed by a blister. This reflex reflex is transmitted from the Hepatic terminals of the Phrenic, through the IV.Cervical N: to the branches of the Cervical & Brachial Plexuses." (Cf/Manson, Trop. Med, 1914, p.578).

10. The Hemic Changes & their Significance.

This, the last & most important of all tests, will be here described, in detail, and the Differential Diagnosis from Blood-Diseases, will be considered.
Two chief elements of White-Cell study are come up for description, as on them depends correct diagnosis; they are
I. POLY-MORPHONUCLEAR Leucocytes
II. The EOSINOPHILE CELLS.
The leucocytosis, which was always looked upom as pathognomonic of Liver-abscess, was described by Rogers to apply equally well in its Pre-suppurative stage, viz. in Amocbic (Acute) Hepatitis
Even such high degree of leucocytosis, as 28,500 cells, subsided entirely under Anti-Amoebic treatment, without abscess-formation.
The following are the chief points in a test:-

i. The Differential

Special Points in Diagnosis of Tropical Abscess.

- continued -

10. HAEMIC CHANGES & their Significance.- continued

i. The Differential White count is of greater value than the Total estimation. The characteristic feature of Amoebic Leucocytosis, according to Rogers, is the less-marked increase of the polynuclears, than is usual in secondary Pyogenic Infection. This is equally true of both Hepatitis & Abscess. In the majority of cases, the Polymorphs make up from 70-80% of the whole, but in Chronic Liver Abscess, they may be below 70% Sometimes in the very Acute cases, esp: when there are Multiple Abscesses or when secondary Bacterial Infection occurs, they may rise to 80-90%.

ii. Even in cases where there are marked degrees of Anaemia, the Leucocytes invariably show a relative increase to the number of Red Cells - sometimes as much as 1 to 332, as actually occurred in one of Rogers'cases; so that a relative leucocytosis certainly exists. Such Inferential or Relative increase does not exclude actual Suppuration; indeed Rogers observed the significance of relative increase "several times" in actual abscess.

iii. The Total Count of the Leucocytes, has little bearing on Prognosis, unless the count reaches very high figures, e.g. over 30,000.
Two rapidly-fatal fatal cases, Rogers investigated, gave counts of 35,000 & 38000, respectively. Multiple Liver Abscesses were found after death.
In a series of Abscess-cases, Rogers obtained the following Total Counts & noted the Results:

| Cases | Leucocytosis of | Recovered | Died. |
|---|---|---|---|
| 6 | 11 - 15,000 | 2 | 4 |
| 10 | 15 - 20,000 | 4 | 6 |
| 3 | 20 - 30,000 | 1 | 2 |
| 1 | of 35,000 | - | 1 |
| 1 | of 38,000 | - | 1 |

The average of cases yield 15-20,000.
Khouri & Legrand found in Alexandria that out of 22 cases of Liver abscess, there was a leucocytosis in 14 cases of 16-32,000 per c.mm; that in 7 cases there was no leucocytosis; and in 1 (cachectic) case there were only 5000.

iv. A Leucocytosis of a peculiar type occurring in Tropical Cirrhosis of the Liver has been described by Rogers. About 93% of cells are Polymorphs, esp. if the case is going to end in Cholemia.

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10. HAEMIC CHANGES & their Significance.- continued.

iv. As regards the Differential White count, V.Schilling Torgau* has shown that the state of the development of the Nuclei should be noted as of direct importance - especially the younger members of the series, to what corresponds to Classes I & II of Arneth's * Nuclear Index. In many Acute cases of Amoebic Abscess, a large number of the cells are immature, the Nucleus being Single & undivided, horse-shoe shaped, or only exhibiting slight twistings; and the same author shows further, by a consideration of cases, " that where the number the number of Immature Polymorph cells is relatively great, the case is a severe one, & that sometimes after an abscess has been opened and the blood-picture does not improve, another abscess is also present; conversely, in cases doing well the immature cells diminish in number." (cf/Phillips,"Amoebiasis & Dysenteries" p.51).

* V.Schilling Torgau "In Mense, Handbuch der Tropenkrankheiten (the blood-changes in Dysentery & Liver Abscess,)1914, Bd.2, p.103 et seq.

* Arneth's Index - The basis of the test is that Polymorphs with only one or two nuclei, are considered immature whilst those having 3 4, or 5 or more nodes, possess greater phagocytic power. They are grouped as follows :-

| | Classes I. | II. | III. | IV. | V. |
|---|---|---|---|---|---|
| % | 6 | 35. | 42 | 16 | 1 |

To obtain the Index, add to the sum of the Polymorph %, of cells containing 1 or 2 nodes, ½ of the % of those with 3 nodes. In the above the Normal Index is 62.

NOTES.

In Chronic Encysted Abscess, the blood-picture may be almost normal - yet this abscess may suddenly extend or rupture into some vital organ, and death result.

&

The leucocytosis of an Acute Hepatitis under Emetin, may disappear in a few days.

v. The Eosinophile Cells. In Hepatitis the percentage of these cells may be normal, but when it comes to abscess-formation, the number of Eosinophiles usually diminishes & this Hypoeosinophilia may pass into Total disappearance. An Eosinophilia may be present due to Helminthiasis; but even then in Liver abscess it may disappear. Mathis quotes a case of Liver abscess in the Right Lobe, in which the day before operation, there were 79% of polymorphs, with only 1% of Eosinophiles. The patient steadily improved and on his discharge, showed 56% of Polys: & 11% of Eosines - Ascarides & other Intestinal Vermes were found in the stools. (Phillips). In 10 out of 15 cases (Mathis) in which Multiple Abscess occurred, there were no Eosines at all.
If in a suspected case of Liver-abscess there be an Eosinophilia, examine the stools; it may be from Parasites or an Acute attack of Dysentery (amoebic). In Intestinal Amoebiasis there may be a local Eosine increase & some may pass over into the blood.
This question of associated Parasites is of real practical importance, for in Egypt, where Ankylostomasis is so common, cases may be found of the two diseases combined.
Moreover there is Entozoal Dysentery.
Therefore stress is being laid on all these points, and the question of Eosinophiles becomes of Differential importance.

10. HAEMIC CHANGES & their Significance.- continued-

v. The Eosinophile Cells. Carnegie Dickson in his work on the"Bone-Marrow", emphasises the absolute distinction between these cells & the Members of the Neutrophil Series of Polymorphs and traces three sets of Eosin-cells, viz: The Eosinophile Myelocyte, the Intermediate Myelocyte, & The Polymorph,"which never attain the same complexity of shape & structure as shown by the Neutrophil Leucocyte" (p.49). Therefore in a blood-estimation these two elements must be carefully differentiated from each other.

"In certain conditions, there exists some peculiar relationship between the occurrences of Lymphocytosis & Eosinophilia, e.g. Tubercular conditions in children." (Ibid, p.51).
This therefore must be borne in mind in Chronic Malarial conditions.
The Group of the Infectious Diseases generally are associated with a reduction of the Eosines especially in Typhoid.
More attention will be found devoted to this Question in the Section of "Haemic Changes in Amoebic Dysentery & their Significance".(P.65).

vi. Inflammatory Leucocytosis. In Acute cases of Liver Abscess, some difficulty may be found in excluding other Acute Surgical Conditions, and hence it is advisable to clear up the subject. Sometimes there is co-incident Amoebic Appendicitis & abscess-formation.
Burnham in his book "Haemocytes & Haemic Infections" (pp.72-76) summarises the state of affairs as follows:-

"Leucocytosis in Suppurative Apprndicitis.
Curschmann has found, in 60 cases of Appendix that the number of White Cells, in the blood, is a reliable indicator of the presence of pus. If the exudation is serous, the number is increased but little,if at all. If however there is pus or tendency to pus, then the number of leucocytes are 20,000 - 30,000..... Sill emphasises the importance of a Differential Count, and the enumeration of Polymorphs, in purulent infections. If both the Leucocyte & Polymorph counts rise together, the infection is growing more severe, but also is the resistance of the patient rising. If they both fall together, it means the body has overcome the infection, and the latter is on the decrease. If the leucocyte count falls & the Polymorphonuclears remain high, or even rises, it indicates that the infection is spreading, with diminution of resistance; and the outlook is unfavourable. The leucocyte count is only of value to the surgeon, if positive" ( ibid, pp.74-76).

"Hewitt expresses his opinion on the value of the leucocyte count, in acute surgical diseases, as follows.

vi. Inflammatory Leucocytosis.- continued-

1. The TOTAL count is an Index of the patients resistance to the infection.

2. The relative Polymorphonuclear count, is an Index of the degree, or severity, of the infection.

3. A percentage of Polymorph-cells, from 75 - 80 %, means that infection is probable; if from 80 - 85 %, infection is usually found; & this regardless of the Total Leucocytic numbers.

Dacosta has collected a series of observations, on the blood, in Appendicitis cases, & his result may be summarised as follows:-

1. Moderate leucocytosis may occur, both in the abscence of, & in the presence of, an abscess and its consequences.

2. It accompanies about 35% of non-puralent, & 90% of purulent cases.

3. Leucocyte counts, ranging from 10,000 to 17,000, cannot be depended upon to reflect the nature of the local lesion, since this degree of increase may be found, both in mild catarrhal, & in purulent cases. Counts of 20,000, or more, almost invariably indicate the presence of pus, gangrene, or General Peritonitis, one or all.

4. Leucocytosis may be absent in Trivial, Catarrhal, & in Fulminant cases, as well as in forms of Circumscribed Abscess.

5. In Operative cases, thorough evacuation of the abscess is followed by, within a few days, the decline to normal, in the number of leucocytes, provided that the recovery of the patient is uneventful. Persistence of the leucocytosis, after the third day, or the fourth day, following the operation, may usually be attributed to either undrained pus-pockets, to general peritonitis or to both of these factors." Cf/Ibid-pp72&73

SUMMARY.

If therefore, the blood shows alteration of & in the Polymorphs, & a hypoeosinophilia, it may indicate Multiple foci, improper drainage, (if Liver-abscess has been operated upon), the formation of another abscess, or insufficient protective reaction, & then the prognosis is serious. In Chronic encysted Abscess, the blood-picture may be almost normal. Repeated examinations are absolutely necessary, as a guide to Prognosis; for a single count is only the record of the blood-state, at the time of the examination.

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## Concise SUMMARY of the HAEMIC CHANGES.

Rogers looks upon such high Leucocyte-counts in Hepatitis, Abscess & Amoebic Dysentery, as of PROGNOSTIC importance, equal to the finding of numerous Malignant Tertian Parasites in Malaria, in every field of the microscope, for it enables early recognition even when the clinical signs are not alarming.
Finally, there remains the complicated question of how much we are to attribute to associated lesions or extra-complications of Dysentery, the occurrence of definite leucocytosis, when there is merely inflammatory signs (early) in the Liver. Such a case came under my own observation, & which has been detailed under "Amoebic Appendicitis" In these cases vigorous treatment with Emetin is recommended, & at the same time the Liver condition must be carefully watched.

## The DIFFERENTIAL DIAGNOSIS of BLOOD-DISEASES.

It now alone remains to give an account of the Blood-Diseases which either from the pathological changes induced in the Liver or in the elements of the blood, may cause them to resemble early abscess or Amoebic Hepatitis, which perhaps has resulted from Latent Amoebic Colitis, & hence the causation of the Liver condition is not clear.
Moreover, in chronic cases of Amoebic Colitis, & in prolonged chronic Suppuration there are secondary Anaemic changes induced in the blood, which rather confuse the direct changes alluded to above.
cf. THESIS. P, 66.
These diseases may be classified into :-

I. Those in which the main pathological changes fall upon the RED-CELLS, or in which these are more characteristically changed or influenced.
II. Those in which the WHITE-CELLS are principally concerned.

### I. "Red-Cell Diseases".

1. PERNICIOUS ANAEMIA. The Liver is sometimes enlarged, but not painful, & their are often Gastro-Intestinal attacks, with diarrhoea, & owing to the marked tendency to haemorrhages, blood may appear in the stools & there may be haemorrhages into the Liver. Sometimes there are Nervous Symptoms, & there may occur Sub-Acute Combined Degeneration of the Spinal Cord It is difficult to put this as a separate Clinical entity by itself, for the characteristic blood-picture of a Primary Pernicious Anaemia, may be induced in patients in Malignant Disease; and the clinical symptoms & blood changes may be also induced by repeated haemorrhages, as occur as Complication to Amoebic Dysentery; and by Intestinal parasites, notably in Ankylostomasis, which disease is often associated with Amoebic Dysentery, at least in Egypt Therefore Addison described this Anaemia"as one with an insidious onset, arising without discoverable cause, characterised by progressive reduction in the Red corpuscles, & high C.I. "

## Special Points in Diagnosis of Tropical Abscess

- continued -

## The Differential Diagnosis from Blood-Diseases.

- continued -

1. PERNICIOUS ANAEMIA.

The most notable feature in this Disease is the remarkable rapidity with which the blood changes are established & its obdurate permanency. The age is generally over 25, and the severity of the change & the progress towards a fatal termination, (hence the term'pernicious') are also characteristics of this condition. It may however be marked by remissions, during which the Colour-Index, drops to normal, with improvement in the Cell-elements. Excessive haemolysis is a constant feature - the red corpuscles entering the circulation are predisposed to early disintergration. The final clinical picture results from excessive disintergration within the blood-paths.
The blood - phases herein described, are applicable to All forms of so-called Primary &r Cryptogenic & Secondary Anaemias. Hence , for the Purpose of the THESIS it is sufficient merely to indicate how far in any direction Specific Blood-Diseases are linked up with gross morbid changes which occur in Amoebiasis & are the direct result of Chronic Intoxication or are produced by special aberrations, such as profuse haemorrhages in Amoebic Dysentery, accompanying a Liver Infection.

### The Phases of Anaemias- Primary & Secondary.

#### I. The Normocytic Phase.

This is the first stage in all anæemias, whatever be the cause.
It begins with the reduction in the number of the red cells; gradual in Chlorosis, sudden in hemorrhages.
In Pernicious Anaemia, the oligocythaemia is more profound in degree than in any other form of anaemia wherein the decrease in the number of corpuscles is more marked than the decrease in the percentage of the Haemoglobin - the C.I. being usually over 1.
Loss of strength is often the first symptom to bring the case under observation, when the red cell count yields 1,000,000 - 2,000,000 corpuscles per c.mm.
The cases with fewest corpuscles are not necessarily the most severe, nor those with more numerous corpuscles milder in type.

#### II. The Poikilocytic Phase.

It is also not characteristic of any particular type of anaemia, and begins with the appearance of Poikilocytes in the blood.
When Pernicious anaemia generally comes under observation, the blood is already in this condition.

i. The distinctive feature of this Phase is the great irregularity in both the size & shape of the corpuscles; in Pernicious anaemia they are oval or pear-shaped.
ii. Microcytes are also a product of this Phase, and are said to result from Schistocytosis or Fragmentation.

- continued -

## The Differential Diagnosis from Blood-Diseases.

- continued -

## The Phases of Anaemias - Primary & Secondary.

### III. The Normoblastic Phase.

This is most marked in the Acute anaemias, except in Aplastic Anaemia; and characterised by the appearance of Normoblasts. A sudden increase is a regenerative phenomenon.

i. A periodical increase of Normoblasts in Chlorosis, lasting 4 to 6 days, and accompanied by a marked increase in the number of red cells, has been described by V.Noorden as " A Blood Crisis ". In the remissions of Pernicious anaemia they usually disappear from the blood.

ii. Microblasts & Poikiloblasts are also products of this stage.

### IV. The Megalocytic Phase.

This is marked by the appearance of Giant Reds in the blood - is pathological and indicative of exhaustion of the Bone-Marrow, and characterised by its persistence when once established.

i. It is responsible for the high Colour-Index in Pernicious anæemia; but this high C.I. descends in periods of remission. It is justifiable to class as Pernicious anaemia, cases in which any considerable number ( 10-33%) of red cells are Megalocytes, with increased Hg.Index.

ii. In Chlorosis the Hemoglobin is reduced out of all proportion to the reduction of the Reds.

iii. In post-hemorrhagic anaemia, the C.I. remains unaltered and the percentage of colouring matter corresponds with the number of the corpuscles present.

### V. The Megaloblastic Phase.

This is the final stage and characterised by the presence of a preponderance of Megaloblasts over Normoblasts. It is indicative of pathological changes in the Bone-Marrow, and hence is the Final stage of pathological blood-production.

" Though Normoblasts are found in all grave anaemias, and are known to be regenerative in function, practically in no condition other than Pernicious anaemia, do the Megaloblasts so constantly out-weigh numerically the Normoblasts. This is regarded as a distinctive feature of Pernicious anaemia and a point of Differential Diagnosis from Secondary Anaemias. The histoligical picture of Pernicious anaemia is often of the Megaloblastic Phase, more often of the Megalocytic ". (cf.Burnham p.122 " The Blood Phases of Anaemia " ).

Megaloblasts appear in the blood of severe forms of Secondary Anaemia especially in Ankylostomiasis, & also in chronic chemical poisoning e.g, Acetanilid.

The Leucocytes are markedly diminished in numbers esp. the Polymorphs, but increase may occur from intercurrent infections. A relative Lymphocytosis is the rule in Pernicious anaemia.

- continued -

## The Differential Diagnosis from Blood-Diseases.
- continued -

### Polychromatophilia.

It is classed as a degenerative phenomenon, and occurs in Pernicious Anaemia, Leshmaniasis, and also in severe secondary anaemias. I have noted this also as a marked feature in the Megalocytes, which are found in Chronic Malaria, with enlarged Spleen, in which when found I regard as Diagnostic of the condition; and also there are absence of Parasites in the blood & cachexia, which is generally marked. Some writers believe that they are actually the youngest cells of the blood, and instance there abundance during the active haemogenic process, following severe haemorrhage.

### Post-Haemorrhagic Anaemias.

Every cause which can produce anaemia, may produce either mild or a severe form: haemorrhage is no exception to the rule. Continued small losses of blood, as occurs in an Acute Dysentery, lead to a much more profound anaemia, than a single large haemorrhage. After complete restoration, a normal blood count with diminished Hg. Index is found; or reduced blood count with haemoglobin approximately normal. Poikilocytes & later normoblasts are constant features of post-haemorrhagic anaemia. In profound post-haemorrhagic anaemia, Megalocytes and Megaloblasts are also found resembling very closely that seen in Pernicious Anaemia, with this distinction that in various Secondary anaemias, the blood-phase is not distinctive of any particular form of Anaemia, but is solely an Index of the severity of the condition.

### Malarial Anaemia.

The cause of the Anaemia in Malaria is quite apparent, in the destruction of the red corpuscles, by the Specific Parasites. Anaemia in the Fourth Blood-Phase, in which there was a preponderance of Megalocytes, with increased haemoglobin, has been observed in severe infections. The Fifth Blood-Phase of Anaemia is also found, as a sequel of Malaria; the Megaloblasts having the same unfavourable Prognostic significance, as in other severe anaemias Polychromatophilia has been alluded ti above.
The enormous blood-destruction resulting from severe infection, is equivalent to a large periodical haemorrhage. There is usually a big increase in the Mononuclears, as a differentiating point.

### Ankylostomiasis.

The Ankylostoma Duodenale frequently complicates Amoebic Dysentery, or expressed in another way, it is frequently met with in Egypt, where Amoebic Dysentery is also prevalent, and the two diseases may occur in the same case. The blood-changes are rather characteristic & may complicate the blood-picture in Amoebiasis, in which there is the outstanding Leucocytosis, which occurs whether there happens to be Dysentery, Hepatitis, or abscess.
As a factor in the production of anaemia, in the Tropics, the Ankylostoma, is second only to Malaria

## The Differential Diagnosis from Blood-Diseases.
## - continued -

### Ankylostomiasis.

The anaemia is mainly toxic, and only secondarily due to small haemorrhages. The blood in the majority of cases is of the Chlorotic Type. In other cases, the blood-cells may sink below a million, with a low colour-index, & marked Poikilocytosis. As in Chlorosis, the average C.I. is found to be 0.5. Normoblasts are common, and, in the severe grades, the blood enters the Megalocytic & Megaloblastic Phases. An ever-present Eosinophilia serves to distinguish the blood-condition, in this infection, from Pernicious Anaemia. The number of Eosinophiles varies from 5 -72%. The latter percentage was found by Leictenstern, in a very anaemic patient. Boycott & Haldane found the highest percentages in recent cases, and the lowest in Chronic cases. They also noted that a fall in Eosinophiles with no improvement in physical signs, was unfavourable. Eosinophilia is so constant in Ankylostomiasis, that it has been recommended by Boycott, as the most important sign, next to the presence of Ova in the faeces, in endemic areas. The Liver is very often enlarged, and a low Intermittent type of fever is commonest, but is due to Bacteria. *

* "Three types of Pyrexia have been described.

1.
The Low Intermittent and in which the fever rises to only 100.

2.
An irregular type, either Intermittent or subcontinuous.

3.
Undulating - very uncommonly observed. The fever is bacterial, as it often continues long after the patient is thoroughly cured.
' Agchylostoma Fever ' is therefore not quite appropriate."

Castellani & Chalmers Trop:Medicine 2nd.edn. p.1309.

### II. " White-Cell Diseases ". - The Leukaemias

These group of Diseases probably afford greatest difficulty in the Differential Diagnosis of Liver-Abscess, and it is only by careful blood-examination that they can be recognised. Greater difficulty apparently lies in the obscure cases of Lymphatic Leukaemia and in the so-called Leukanaemias or Mixed Types. Herbert French in the " Index of Differential Diagnosis of Main Symptoms ", p.32, writes upon this subject as follows:-
" The chief difficulties that arise in the diagnosis occur in two ways:

i. that there are a few instances in which Lymphatic Leukaemia has run its course without any actual increase in the number of Leucocytes, per c.mm. of blood, the diagnosis being afforded only by the enormous relative increase in the Small Lymphocytes; and,

ii. from the fact that children normally have a relatively high Leucocyte count from which it happens, that Lymphatic Leukaemia may sometimes be suspected when it is not really present at all, unless there are Lymphatic enlargements, esp. the Spleen."

It is not safe to insist upon a diagnosis of Lymphatic Leukaemia unless there is either a very large increase in the TOTAL number of Leucocytes, or a relative increase in the Small Lymphocytes up to 90% or over, or both these changes at the same time.

- continued -

## The Differential Diagnosis from Blood-Diseases.

- continued -

### II. "WHITE-CELL DISEASES or The LEUKAEMIAS.

(A). MYELOGENOUS LEUKAEMIA. The typical pathological changes in the organs are

1st. Enlargement of the Spleen & sometimes very markedly so.

2nd. The Liver is usually considerably enlarged, but not so markedly as in Lymphocythemia.

3rd. The Lymphatic Glands do not exhibit any enlargement, though this is said to occur in Intermediate Forms.

4th. Haemorrhages, especially from mucous surfaces, are not so common as in the other variety.

5th. Blood-Changes which are practically pathognomonic of the disease.

Two Types of the Disease are recognisable viz. A Chronic Myelocytic Type, & The Acute Myeloblastic Type, and in addition Intermediate & Mixed Types.

The Spleno-Medullary or Myelocytic Type.

The essential point in the diagnosis is the occurrence of a very great increase of the TOTAL number of the leucocytes, not uncommonly to 200,000 or 500,000, in association with which there is a large relative number of the Myelocytes. There is only one other condition which can produce so extreme an increase in the TOTAL number of Leucocytes, and that is Lymphatic Leukaemia. The two are immediately distinguishable as in the Myelocytic type there is a large number of Myelocytes present, whereas in the second variety it is the Small Lymphocytes are relatively increased.

The variety of White Cells specially increased are those of the Granular Series as follow

(a) The Polymorphonuclear Neutrophil Leucocytes, & themarrow-cells from which they are derived,

(b). The coarsely granular Eosinophile cells which form one of the most notable characteristics of this condition. The Eosinophile Myelocyte - the ancestral form of the Eosinophile Leucocyte - is found regularly in Myeloid Leukaemia.

(c). The Neutrophile Myelocytes make up from 20-60% of the White cells, with an average of about 35%.

(d). The Basophilous leucocytes or Mast-Cell are increased up to 18%, with an average of about 5%. This increase is a very constant phenomenon, and is more marked in this condition, than in any other known condition.

The TOTAL Leucocyte count is so high that the diagnosis is unmistakable. In Liver Abscess it seldom goes above 30,000 - an acute difference.

- continued -

## The Differential Diagnosis from Blood-Diseases.
- continued -

### II. "WHITE-CELL DISEASES or The LEUKAEMIAS.

#### The Myelocytic Type.

Intermediate and mixed types of the disease occur and all transitions are known amongst the Leukaemias;-

1. The Leukanaemias, which partly resemble Pernicious anaemia & partly Myelogenous Leukaemia.
2. Multiple Myelomata & the Nodular Type of Leukaemia.
3. Pseudo-Leukaemia Infantum of Von Jasch in children with massive enlargement of the Spleen with no Leukocytosis but symptoms of severe anaemia.
4. Mixed forms in which both Myelocytes and Lymphocytes are present in large numbers and specially characteristic of early childhood. Fowler believes that this is the form that Myelogenous Leukaemia takes in early childhood.
5. Sometimes the Myelocyte-cell is so immature that it is difficult to differentiate it from the Lymphoid-cell. For this purpose the Oxydase reaction is employed. A brief account may be here given, but full particulars will be found in The Journal of Quarterly Medicine, Apl. 1913 pp 298-299. The films are fixed in 1% Osmic Acid for 5 seconds by immersion. It is washed thoroughly in running water for 5 mins, and then treated for periods varying up to half an hour with a mixture of in equal parts:-
   i. Dimethyl-para-phenyl-endiamin, 1/5th.% Aqueous Solution; & 
   ii. Alpha-Naphthol saturated Aqueous Soln.
   It is re-washed in running water for 2 - 3 mins, and mounted in a mixture of equal parts of commercial water-glass & tap-water. Normal blood-films treated by this method, show a deep blue staining of the Polymorphs due to formation of Indophenol in their protoplasm, occurring in virtue of the oxydising ferment or Oxydase in these cells.

Attention has already been called to a case which showed symptoms of Myelogenous Leukaemia in the Section of "Acute Splenitis of Amoebic origin." - P. 185.

- continued -

## The Differential Diagnosis from Blood-Diseases.
- continued -

### II "WHITE-CELL DISEASES or The LEUKAEMIAS.

#### The Myeloblastic Type.

This according to Burnham is the Acute form of Myeloid Leukaemia. It is recognised by the presence in the blood of large numbers of Myeloblasts, which is the ancestral form of the Myelocyte. The separation of Lympho-blastic & Myeloblastic Leukaemia is a diffi-cult one. " The primitive Leukocytes, which are poured into the circulation, in Lympho-blastic Leukaemia, are of Lymphoid origin, while in Myeloblastic Leukaemia they are of Myeloid origin".(cf.Burnham,Haemocytes & Haemic Infections, p.174). A very inter-esting paper by Panton & Tidy on Myeloid Leukaemia - Chronic & Acute, appeared in the Lancet of May 18, 1912, pp.1328-1333.,* to which reference has been made in draw-ing this difficult subject up from a prac-tical point of view. It is not my object to expound at length on the views held but merely to call attention to the more diffic-ult cases which are atypical & which have every now & again turndup & confusedthe Blood-diagnosis of Liver-abscess; & alsohave appeardrather as some Special Type of Blood Condition, than a complicating feature of an ascertained Dysentery, with Liver or Spleen symptoms.

This Acute Type is, then, characterised by cells which vary between "a non-granular looking myelocyte" & "a hyaline (Large) of normal blood" ; but there is a close relat-ionship between these Hyaline cells, the Myelocytes & the Polymorph Neutrophiles.

The Myeloblast is a spherical cell, with a large nucleus, almost filling the entire cell The nucleus is finely-reticulated, stains feebly, & often contains two or three white-looking Nucleoli. As the cell develops the nucleus turns excentric & reniform.

Schultz & Winkler's Oxydase Reaction would be very helpful here.

Panton & Tidy discovered a "Leucoblastic Failure"in their 10 cases, characterised by

(i). A fall in the out-put of Leucocytes, &

(ii). A failure on the part of the leucocyte to develop, thus accounting for the numbers of non-granular cells found, which has led to the inception of an apparent conversion of a Myelaemia into an Acute Lymphaemia.

The most frequent type of non-granular cell is the Myeloblast. Such a blood-picture has to be carefully differentiated from the rare condition of Lymphatic Leukaemia in which the lymphocytes are of the Large Var-iety. Sometimes in Acute Myelaemia there is leucopenia, in which the "Whites" are down to 2000, or more; in these cases there is also absence of palpable Spleen emlarge-ment, as occurred in Case V of Panton & Tidy Series, but even then there was a very high percentage of Mast-cells, a large number of

* The article is illus-trated by 10 figures, & Leishman's Stain was used in all cases.

## The Differential Diagnosis from Blood-Diseases.
- continued -

### II. "WHITE-CELL DISEASES" or the LEUKAEMIAS.

#### The Myeloblastic Type of Myelocythemia.

of Amphophilic Myelocytes, together with the presence of every other variety of Myelocytes and Myeloblasts, " make up a blood-picture seen in no other disease".(Panton & Tidy).
The Large Type of Myeloblast can be differentiated by Leishman's Stain from other NON-GRANULAR cells; as also the SMALL type of Myelo**blast.**
The abscence of marked Splenic Enlargement in these Acute cases suggest a failure of any protective action of the Spleen.

#### (B). LYMPHATIC LEUKAEMIA or LYMPHOCYTHEMA.

The typical pathological changes in the organs are as follows:-
1st. Enlargement of the Spleen but only moderately so, and never so enlarged as in the Myelogenous type.
2nd. Enlargement of the Liver and much more so than in the Myelogenous type.
3rd. Rapidly progressive anaemia with Asthenia & Hemorrhages from mucous surfaces.
4th. Blood changes which are practically pathognomonic of the Disease.
5th. Glandular Enlargements, visceral & peripheral, and sometimes in addition the Salivary & Lachrymal.

Two forms of Lymphoid Leukaemia are distinguished, viz -
i. Lymphocytic Leukaemia
ii. Lymphoblastic Leukaemia.
& in addition, there are mixed types.

##### The LYMPHOCYTIC TYPE

The White Cells are enormously increased in numbers, reaching from 20,000 to 80 or 100,000 and sometimes rarely from 200 to 800,000.
Whatever the total number of Leucocytes, the most striking feature is the enormous relative increase in the number of Small Lymphocytes in the differential count, averaging from 90 to 98% so that there is an enormous relative and sometimes absolute reduction in the other corpuscles of the blood. The increase of Lymphocytes is both relative and absolute. Myelocytes, Normoblasts & Megaloblasts are usually not seen.
While mostly the Small Lymphocytes make up the Leucocyte-Formula, cases occur in which the Large Lymphocytes predominate, with every gradation from the smallest to the largest.
In instances in which excess of polymorphonuclear Leucocytes has been found, there is a complicating infection. A fall in the number of leucocytes or "leucocytolysis" may occur when Lymphemia is complicated by some intercurrent disease.
In most cases the C.I is less than 1, but curiously sometimes this has been found to be greater than 1, as it is in Pernicious anaemia, esp. as the case is approaching a fatal termination.

##### The LYMPHOBLASTIC TYPE.

The Spleen is normal in size or moderately

Special Points in Diagnosis of Tropical Abscess.

- continued -

The Differential Diagnosis from Blood-Diseases.

- continued -

II. "WHITE-CELL DISEASES"or the LEUKAEMIAS.

The LYMPHOBLASTIC TYPE.

The Spleen is normal in size or only moderately enlarged.
This Lymphoblastic Type is the Acute condition and is relatively infrequent as compared with its more Chronic form or Lymphocytic Type. The following are the special Clinical features.

1. A rapidly fatal course, with Pyrexia, and weakness.
2. Hemorrhages constitute a most striking feature seen on post-mortem; they occur in mucous membranes, the Pericardium, Peritoneum Pleura, Genito-Urinary Tract, Intestines & Brain.
3. Moderate Glandular Enlargements. Lymphoid tissue, wherever situated may take on abnormal activity, as in the whole alimentary Tract, the Intestinal lesions often simulating the lesions of Typhoid. There is no organ in which Lymphomas may be found wanting.
4. There is prggressive anaemia of Secondary type, and of the 1st. & 2nd.Phases.
5. Extreme rarity of Granular LLeucocytes and the Leucocyte Formula is mostly made up of primitive Lymphoid Cells. The suppression of the Myeloid elements in the Marrow, accounts for the absence of the Granule Cells from the blood.

What has hitherto been described are Anaemias with positive blood pictures. Liver Abscess (Amoebic) can hardly be confounded with the classical blood picture which has been so fully described in each condition. The diseases in which the red cells are characteristically affected have a negative white cell element and in those conditions that give rise to characteristic changes in the white cells, the red cells are similarly unaffected except perhaps secondarily. The degree of Leucocytosis has throughout been pointed out, and the total count indicated in each case. The differential points of importance should be compared with what obtains in Amoebic Dysentery uncomplicated & complicated. A concise synopsis will be found in the last section of the Thesis - " Summary and Conclusions ".

The Clinical Pathology of Chronic Insidious Abscess of the Liver.

So far the Acute morbid condition has been studied, but there remains an exceedingly important clinical type known as the Chronic Insidious abscess. Whether this should be regarded as an aberrant clinical form of abscess of the Liver, or as an actual clinical and pathological variety is difficult to determine. What percentage of Liver abscesses manifest themselves by acute symptoms, or form in a Chronic Insidious manner, cannot be gathered from the statistics. There is always a personal or pre-disposing factor to be considered, a sort of anaphylactic condition of the liver whereby it readily becomes a nidus, and undergoes acute changes; there is always the degree and virulence of the original infection to be taken into account with the intensity or otherwise of specific medication; and finally the resistance of the individual to an acute infective process. Studying it from a distributional point of view, it cannot be stated precisely whether it is more common in Right Lobe or Left Lobe infections ipse se; one can only infer that as Right lobe abscesses are commoner, this modified clinical expression of its existance will probably correspond with this simple pathological distributional fact. Another point which has certainly more association with the above is that Right lobe abscesses are generally deeper than the Left, and therefore obvious clinical objective signs will not be so readily appreciated. This will account for a certain number of the cases, and the fact that it be slow forming, will probably go hand in hand. There is, however, an entirely different class of case, which will not be due to the fact that because a deep liver abscess has taken some considerable time to form and show itself symptomatically and objectively, but, will have certain special characteristics which will classify it as an Insidious abscess of the Chronic type. In this class of very slowly forming liver abscess which present great difficulties in recognition, and is sometimes only diagnosed on the post-mortem table, there are the usual insidious symptoms of chronic ill-health. Low irregular fever of 100 ? general malaise, sometimes diarrhoea alternating with constipation, and often no history of definite dysenteric attack, will cause the symptoms to be referred to cachectic fever of chronic malarial origin; or a run-down condition so common in the Tropics; or resembling early and indefinite ambulant cases of enteric; or even perhaps, T.B.

" Golden rules in Tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature. "

(cf.Manson, Tropical Medicine, 5th.edn, p.585.)

The further history of such cases is progressive deterioration of health, in definite symptoms of pain in the lower part of the chest and mental depression. Finally the patient suddenly develops some acute and startling condition e.g - a Pneumonic consolidation at the base of the lung, and the coughing up of typical amoebic pus; or the condition may reveal itself in a pronounced enlargement of the liver, a break out of an acute

dysenteric attack, a rise of temperature, and all other phenomena indicative of acute suppuration. Rogers details two such cases of chronic insidious abscess in which the condition was revealed by the coughing up of amoebic pus. (cf. Rogers Dysenteries, p.198.)

It is in such chronic hepatitis cases, that we possess in the blood changes the readiest means of a diagnosis from other chronic Tropical Fevers. (Rogers, ibid - p. 198.)

There are six possibilities of practical impor - tance to be always taken into account in cases of obscure low fever in Tropical Countries; they are -

Chronic Malaria,
Typhoid or Para-Typhoid.
Typho-Malaria.
Tuberculosis.
Kala-Azar.
Amoebic Dysentery.

It is well-known that an amoebic liver abscess may arise when there has been no history of an antecedent dysentery, and yet the gut may be the seat of amoebic ulceration. These abscesses therefore correspond to what may be termed "Chronic Intestinal Amoebiasis of a Latent Type". Negative history of dysentery often complicates the diagnosis or clouds the mind from appreciat- ing such cases may in reality be amoebic abscess.

# SECTION VII. AMOEBIC INFECTION OF THE LIVER.

## PART 10 CLINICAL POINTS OF INTEREST FROM THE TREATMENT OF RECORDED CASES.

Clinical points of interest from the Treatment of Recorded Cases.

1. The most advanced cases are quite suitable for treatment by Aspiration & Quinine Injections. A case from whom 6 pints of pus were aspirated had a history of one year's illness. A second aspiration yielded 36 ozs of pus, and into the cavity 40 grs of Quinine Bihydrochloride was injected - followed in time by complete recovery.

2. After a single injection in 8 cases, the temperature fell finally, all the symptoms disappeared and weight rapidly gained.

3. More frequently the effect is temporary; after use of Quinine solution; aspiration and re-injection with Quinine or Emetin should be performed in a week after the lst tapping. The study of the temperature chart is important. In very large abscesses in two cases four such aspirations were necessary.

4. " If in a case an originally-present leucocytosis completely disappears, little or no pus will be present at the second aspiration, and an uninterrupted convalescence ensues. The continued presence of even a slight leucocytosis persisting after aspiration, calls for a second aspiration.

5. In the chronic fibrous walled Single abscess there is no danger of Cinchonism from the use of as much as 60 grs. of Quinine. In the acuter cases, some absorption takes place.

6. With proper precautions primarily-sterile abscesses almost invariably remain so through out. When no bacteria are found microscopically, the occurrence of a very few isolated colonies on culture indicates only accidental contamination, and not an infection of the abscess. Such a condition requires no drainage. If, however, numerous bacteria are found on microscopical examination, drainage must be carried out. Such cases clinically manifest themselves by a discharge of thin abundant greenish-yellow pus with putrid odour, and sometimes with foul-smelling gas-production, instead of the typical thick reddish pus of a purely amoebic abscess; the temperature chart assumes the hectic type, and symptoms of toxaemia are evident. Such abscesses may go on to the Multiple Pyemic variety.

7 Cases with a thin watery fluid discharge, followed by the typical thick reddish pus, usually do well.

Clinical points of interest from the Treatment of Recorded Cases.

- continued -

8. Aspiration & Quinine Injection often fail in the very acute Large abscesses with softening and widespread disintegration of the liver tissue; but they do equally badly on Open Operation - the aspiration method being the less exhausting.

9. The Open Operation often merely localises and deals with one collection of pus for which it is undertaken. Often symptoms of a second abscess manifest themselves after the first has been successfully dealt with. Such abscesses may be tapped by the aspiration method in the first instance; and secondly when such a further abscess is diagnosed, aspiration is the better method of treatment of the two.

10. Rupture of the abscess into the Pleural cavity of Peritoneum or Pericardium, demands Open Operation.

11. Operative procedures in an abscess opening through the lung should be avoided."If the expectorated discharge is becoming less, there is little or no fever and the patient is not losing weight, it is better to watch events. Under the reverse circumstances the abscess in the base of the lung and vault of the liver, must be drained through the chest wall without delay..... When it appears clear from the first that the patient's strength will not suffice to allow him to cough up a liver abscess, it should be opened as soon as possible after pus appears in the sputum, and before its cavity has contracted and become difficult to find." (cf.Rogers, p. 224.).

12. Hemorrhage as a complication after exploratory puncture of the liver. This condition generally results from performing it in the acute hepatic congestion of the pre-suppurative stage. The patient should invariably be treated first with a course of Emetin or Ipecac. The risks arising from Hepatic Phlebotomy is small in comparison with the risk of allowing an hepatic abscess to remain undiscovered and unopened. Phillips calls attention to certain danger zones of puncture - they are more especially the under surface of the liver, and the neighbourhood of the Hilum; and in general the Left Lobe. Some obvious large swellings in the Left Lobe may be punctured with great caution. Sambuc, who has had an enormous experience of puncture in Tonkin, has never had an accident, and has found it yield a positive result in about 80 - 90% of cases.(cf. Phillips, p. 31. ).
Syncope, and Collapse may result after rapid evacuation of a huge abscess by relief of pressure, allowing Sympathetic dilatation of the intra-abdominal vessels.
Troublesome return of dysentery occurs sometimes after a liver abscess has been opened (cf.Phillips, p. 50 ).

- continued -

13. Hemorrhage may be caused in the following ways after puncture.

(i) The puncture of an acutely congested liver in its pre-suppurrative state; or what has been termed " Tropical Liver ".

(ii) Sudden relief of pressure from evacuation of an acute abscess of large dimensions.

(iii) The actual perforation by the Trocar of an important or large vessel, Venous Sinus; or the accidental tapping of a Congenital Hemangioma of the liver.

(iv) From tapping an erroneously diagnosed abscess when the condition is a Kala-Azar infection of the liver; or enlargement produced by the Anaemias.

(v) In those acute cases where liver substance is disintegrating, the passage of a large Trocar may cause fatal hemorrhage.

(vi) In pathological conditions of the blood - such as diminution in Coagulability, due to Pernicious Anaemia or Leukaemia.

(vii) In so-called Idiopathic states. e.g - Hemophilia, Alcoholism, and Opium-Eaters, and in secondary Hemorrhagic conditions, e.g - Purpura, Scurvy, and Infectious Jaundice due to Spirochaetosis Icterohaemorrhagica ( Weil's Disease ). (cf. The Journal of Experimental Medicine, Novr.1st, 1916, pp 485 - 496; & ibid, Apl. 1 1916, pp 557 - 562; B.M.J's , Apl 1st, 1916 p. 491; Apl.29th, p. 627; Sept.23rd, pp 413 to 417. ).

(viii) In the chronic Venous Congestion of the liver due to co-existent Heart Disease.

14. " I have seen the peculiar brownish fluid resulting from the action on blood of the Carbolic Lotion that has been used to sterilise the exploring syringe mistaken for pus. To obviate so grave a mistake the exploring syringe should be washed out with boiled water before use ". ( cf. Manson, p. 588. ).

15, "A point to note in exploring is that when the instrument enters the liver, an up & down pendelum-like movement will be communicated to the outer extremity of the needle, in harmony with the rising and falling of the organ in respiration. If the needle does not exhibit this movement, its point may be in an abscess cavity, but this abscess is not in the liver. " ( cf.Manson, p. 586 ).

16. Perforation of adherent Intestine may occur.

Further complications of Liver abscess; After operation.

1. Infection of the Ribs. This is generally in connection with an operation for the evacuation of liver pus by the trans-pleural route or the drainage of an Empyema. Lecomte* quotes four cases which occurred as complication of liver abscess. It generally occurred after hepatotomy, without resection of a rib. Eight such cases of necrosis of the rib without resection, are on record. It may also result in cases where the abscess opens spontaneously or when it pursues an extra-pleural course. The osteitis spreads forwards and invades the Sternum, and it also spreads to other ribs. Legrand considers these cases as true amoebiasis of the chest-wall.

* Lecomte,- " Carie costale consecutive aux Abces du Foie. " Ann. d'Hyg. et Med. Coloniales, 1913, vol.16, No.1, pp 17 - 48.

2. The Skin. Carini * records two cases of Phagedenic cutaneous amoebic infection of the skin after drainage of the liver abscesses. Similar observations have been made by Daghorn & Heymann *; Menetrier & Tourrain; and Basseres. Gaducheau * has found a short fine bacillus associated with the amoeba. Some observers think that there is a special variety of amoeba responsible for this gangreno- phagedenic action and have called it " Amoeba Phagacytoides ". Similarly , Maxwell * has reported from Formosa and Southern China, a " Fistulous disease of the buttocks ", discharging pus in which amoebae were demonstrated. Castellani has also reported such cases from Ceylon. Brown states that "although the rectum itself is seldom affected in amoebic dysentery, most of the large Ischio-Rectal abscesses, which are so common in the Tropics, originate in penetration of the Intestinal wall by the specific organism of dysentery ".(cf. W.C.Brown, Amoebic Dysentery, p. 189.). These two groups of cases show that skin infection may occur either as a sequel to abscess of the liver, or as in the case of the Ischio- Rectal abscess by the blood-stream. A pure blood-stream infection case complicating acute dysentery, has already been detailed under the"Complications of Acute Dysentery".

* Carini - "Phagedenismo Cutaneo Amebico " Rev.Med. de S.Paulo, 1912.vol.15 No.16, pp 315 - 316.

* Daghorn & Heymann- "Abces Amibien du Foie" suivi de Phagedenisme de la Plaie Operatoire, et d'Abces Cutane Amibien." Bull. Soc.Med. Chir. de l'Indo-Chine.1912 vol 3. No.8 pp 518-524.

* Gaducheau - "Observations sur Quelques Entamibes (Ent. Amoeba Phagocytoides) ". Ibid. p.525.

* Maxwell - "Fistulous Disease of the Buttocks - a clinical entity ". Trans. Soc. Trop.Med. & Hyg. 1912, vol 6. No.2. pp 50 - 53.

## I. Treatment with Emetin

Aspiration & Emetin or Quinine Injection can only be persisted in so long as the pus is free from marked secondary bacterial infection. When, however there is contamination, the abscess must be opened and drained.

Case 1. **Epigastric liver abscess cured by Aspiration & Emetin Injections after failure of the Quinine Treatment.**

A native boy aged 15, was admitted for liver abscess bulging in the Epigastric Region. Aspiration removed 6 ozs. of liver pus, & 10 grs. of Quinine Bihydrochloride in Saline solution was injected into the cavity. The cavity refilled within 4 days attended with intermittent pyrexia. A 2nd. aspiration removed 8 ozs of pus & 1 Gr. Emetin Hydrobrom: dissolved in 2 ozs of sterile Saline was injected into the cavity. Emetin Hydrobrom: was also used subcutaneously for 4 days. In addition, 10 grs of Ipecac: was given by the mouth every evening; after 2 days the temperature fell to normal, and never [illegible] cavity steadily contracted, & the patient was discharged cured just under 1 month [illegible]

Commentary. This case might have done quite as well under Open Operation as the abscess was a comparatively small one, but the rapid subsidence of the fever and cessation of pus-formation under Emetin was very striking.

Case 2. **Right Lobe Liver abscess cured by Aspiration & Emetin Injection.**

A native male aged 30, admitted for liver abscess following dysentery 6 mths before. Aspiration withdrew 8 ozs typical liver pus & 1 gr. of Emetin Hydrobrom: dissolved in 2 ozs N. Saline was injected into the cavity. ½ gr. doses of Emetin were injected subcutaneously on each of the 4 following mornings, & 25 grs. of Ipecac given in the evenings; the temperature rapidly fell to normal, but on three occasions in the next 13 days, reached 100° in the evening. At the end of this time the liver was normal in size, and a 2nd. Aspiration yielded a negative result.

Commentary. The simultaneous employment of Emetin & Ipecac: used in this case were not tested experimentally" as the supply of Emetin was limited " & the Emetin was therefore supplementary to the use of Emetin. Emetin Hydrobrom: gives as good results as the Hydrochloride or Bi-Hydrochloride. This case like Case 1, was throughout sterile.

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SECTION VII. AMOEBIC INFECTION OF THE LIVER.

PART 11. THE TREATMENT OF TROPICAL ABSCESS.

## I. Treatment with Emetin

Aspiration & Emetin or Quinine Injection can only be persisted in so long as the pus is free from marked secondary bacterial infection. When, however there is contamination, the abscess must be opened and drained.

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Commentary. This case might have done quite as well under Open Operation as the abscess was a comparatively small one, but the rapid subsidence of the fever and cessation of pus-formation under Emetin was very striking.

Case 2. **Right Lobe Liver abscess cured by Aspiration & Emetin Injection.**

A native male aged 30, admitted for liver abscess following dysentery 6 mths before Aspiration withdrew 8 ozs typical liver pus & 1 gr. of Emetin Hydrobrom: dissolved in 2 ozs .N.Saline was injected into the cavity. ½ gr. doses of Emetin were injected subcutaneously on each of the 4 following mornings, & 25 grs. of Ipecac given in the evenings; the temperature rapidly fell to normal, but on three occasions in the next 13 days, reached 100° in the evening. At the end of this time the liver was normal in size, and a 2nd. Aspiration yielded a negative result

Commentary. The simultaneous employment of Emetin & Ipecac: used in this case were not tested experimentally" as the supply of Emetin was limited " & the Emetin was therefore supplementary to the use of Emetin. Emetin Hydrobrom: gives as good results as the Hydrochloride or Bi-Hydrochloride. This case like Case 1, was throughout sterile.

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Cases 3 & 4. Amoebic liver abscesses cured by Aspiration and Subcutaneous Emetin Injection.

In one case, pus was aspirated and Emetin injected subcutaneously, but not into the abscess cavity.

In the second case Emetin Injections were commenced two days after the aspiration of liver pus.

Commentary. In the first case the Emetin Injections were given for acute hepatitis in the first instance, but as leucocytosis persisted, the liver was explored, and pus withdrawn. There were no Emetin Injections made into the abscess cavity.
In the second case, the Emetin Injections were commenced after the aspiration, with an equally happy result; and no Injections were made into the abscess cavity.
In both cases, only a single aspiration was necessary. As a single aspiration so rarely cures such cases that the credit of the recovery is due to the subcutaneous injections of Emetin - so that it may eventually prove unneccessary to inject it into the abscess cavities; although this procedure aseptically carried out is harmless, and Emetin will certainly kill the active parasites it comes in contact with.

Case 5. Amoebic Abscess of the Spleen cured by Aspiration & Emetin Injections.

A native male aged 32 was admitted with enlargement of the Spleen and redness of the skin over a tender prominence of the lower ribs. 8 ozs of typical Amoebic pus was withdrawn. Three days later the cavity refilled, and a second aspiration withdrew 4 ozs. But this time 1 gr. of Emetin Hydrobrom: in 2 ozs. of water, was injected. The pus contained amoebae but was sterile. On each of the next two days, ½ gr. Emetin was injected subcutaneously, but the temperature rose again, and 6 days after the 2nd. aspiration, there was again some bulging. A 3rd. aspiration withdrew only a little pus and much blood, and 1 gr. of Emetin Hydrobrom: was again injected into the cavity, and two more ½ grs. doses were given subcutaneously. The temperature fell to normal two days later, & final complete recovery ensued.

Clinical cases of interest from the Standpoint of Rogers' Methods of Treatment, in Hepatic Suppuration.

- continued -

Commentary on Case 5.

The case is of interest both on account of the rarity of the amoebic abscess occurring in the Spleen, and of its successful treatment by this method. For when opened these abscesses are liable to heal very slowly and to leave obstinate Sinuses It was to obviate this, that a repitition of the Emetin injection into the cavity was carried out with completely satisfactory results.

Cases 1 - 5, cf. Rogers Dysenteries, pp 238 - 242.

Commentary on cases treated by Emetin Injection in preference to the use of Quinine Solns: into the abscess cavity.

Taken as a whole, the cases detailed treated by Emetin Injections are full of promise. The direct introduction of Emetin in Solution into the abscess cavities will destroy the causative parasite, especially in the superficial parts of the lining membrane, after very thorough evacuation of their contents by Aspiration. Combined with subcutaneous injections which will kill the organism in the deeper layers of the abscess wall by way of the blood stream, besides benefitting any latent amoebic ulceration in the Large Bowel; this method has indeed opened up a new vista on the past more dangerous method of Open Operation. Quinine Solution has been shown in strength of 1 in 500 to destroy amoebae.* Many cases are on record by Rogers, where the earlier method of aspiration & Quinine Injection into the abscess cavity are followed by complete recovery. Emetin, however, has been more recently used, and is said to be more specific in this direction. The results of cases treated by Aspiration & Quinine Injection Only, has already been noted in Mortality Table No.3.

* In Sept. 1902, Rogers recorded that a 1 in 500 Solution (either a soluble salt or Quinine Sulph: dissolved in very weak acid), would readily destroy Amoebae in the wall of such an abscess in Vitro.
Cf. Rogers Dysenteries, p. 229.

## II. With Quinine Solution.

Some cases have already been noted in "clinical points of interest from the treatment of recorded cases" and the "comments upon the General and Surgical Mortality from Liver abscess." To these the following are appended:-

Case 1.

A man aged 24 was admitted to the Calcutta European Hospital under Dr. J.G.Murray, I.M.S. He had suffered from dysentery recently and presented well marked signs of liver abscess beneath the right lower thoracic wall. 10 ozs of pus was aspirated, only partially emptying the cavity, and then siphon-drainage was employed. The pus was sterile; an attempt was made to run in Quinine Solution through a funnel, but little entered.

- continued -

Treatment with Quinine Solution.

Case 1.* On the second day the discharge was less and only a few drachms of pus could be aspirated. Qunine Solution was injected. On the 3rd. day some shreddy pus had drained, and only a few drops could be removed by aspiration. The cavity had already contracted so much that only ½ oz Quinine Solution could be injected. Within a week, no pus could be obtained by aspiration. The drainage cannula was left in for a week longer by way of precaution. 3 days after its removal the 4 inch Sinus left by it had filled completely to the surface.

* Case recorded by Rogers in Dysenteries, p.221.

Commentary. This case was treated with the Flexible Sheathed Trocar & Siphon drainage. The case was observed from time to time for upwards of a year by X-Rays, and his liver remained throughout quite normal. It is noteworthy that his stay in Hospital after operation was less than half the shortest time of that of any liver abscess case in which the Open Operation through the Thoracic Wall had been performed in the Hospital during the previous 9 years. The instrument employed allowed sterile drainage & Quinine irrigation to be carried out efficiently. This case was therefore drained. The simpler method of merely aspiration & Quinine injection without drainage, has proved very effective in the last few years. The value of drainage lies in the fact that where repeated aspirations fail to complete the cure, or when the abscess cavity is secondarily infected, drainage should be resorted to.

Case 2.* A European patient was admitted to the Calcutta European Hospital with a history of having been four times operated on for liver abscess in 4 months. A large fresh one was opened at the last he had still high fever & severe pain, and was steadily losing ground. He was put on Ipecac: and the wounds washed out without Quinine Solution. The next day he was free from pain and soon after the fever subsided, the discharge grew less and in time he made a full recovery.

* Rogers' case recorded in his Dysenteries, p. 228.

Commentary. This case illustrates the value of the more conservative method. Although the patient was a powerful man, he had nearly given up all hope of recovery. It is noted above that he had just had a large fresh abscess opened in the last (4th.) operation. It took some weeks after the man was convalescent for the extensive incisions to heal.

Case 3.* A sepoy developed fever when an opened liver abscess had nearly healed. The sinus was dilated, but no collection of pus was found, and the temperature continued to rise higher. Ipecac: was administered in accordance with Rogers advocacy. The fever declined rapidly and the patient made a good recovery.

* Case of Captn.Foster-Reany, I.M.S,recorded by Rogers in his Dysenteries, p.228.

Commentary. This case is of interest in showing the value of Ipecac: in arresting the process of an undoubted second abscess formation - amoebic hepatitis in its pre-suppurative stage. This case was entirely treated by oral administrations of Ipecac: without any further attempt on the treatment of the abscess cavity although the sinus was opened up from a diagnostic point of view. This case, as Rogers says, was treated by his earlier method of Ipecac: by the mouth, in hepatic inflammations; as Captn. Reany, I.M.S had just then read his advocacy of Ipecac: in amoebic hepatitis

Cases 4 & 5.* In 1906, Roger P.Wilson, I.M.S, carried out the procedure in two patients with deep-seated Right Lobe liver abscess with the most striking success.

* Cases 4 - 8, detailed by Rogers, in his Dysenteries, p. 230.

Cases 6 & 7.* In 1909, Prof.G.C.Spencer of the R.A.M. College, Millbank, London, recorded two cases both of which were cured by a single injection of 15 - 20 grs. of Quinine Hydrobrom:

Case 8.* This occurred in the same series as cases 6 & 7 above detailed. The patient was a greatly emaciated subject from whom 50 ozs of pus were removed at the first aspiration, and 40 grs of Quinine were injected. Symptoms of Cinchonism developed, but were of short duration. A fortnight later 53 ozs of pus were evacuated, and 20 grs of Quinine injected. After another week, a further 40 ozs of pus were removed, and the injection of 20 grs of Quinine repeated. There were no symptoms of Cinchonism on the last two occasions. From this time he steadily recovered and put on several stones in weight.

Commentary. As a result of his experience, Spencer advises that this method should first be tried in every case, as even when unsuccessful, it gives temporary relief and may place the patient in a better position to stand open operation.

Clinical cases of interest from the Standpoint of Rogers' Methods of Treatment, in Hepatic Suppuration.

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Case 9. Major D.G.Marshall, I.M.S.( Lecturer in Tropical Medicine, in Univ: of Edinburgh) had a case of liver abscess, which was admitted into Prof. Caird's ward in the Edinburgh Infirmary. As members of the class of Tropical Diseases, Summer 1911, we were shown the case, which was being treated by washing out the abscess cavity with sterile Quinine solution, after the liver abscess had been opened. The case was that of a soldier who was at the time at the Castle, where he was seen and diagnosed as suffering from liver abscess. I do not remember full details of the case; butthe man made a perfect recovery. Here then is another case who recovered under Quinine irrigations. There was abundant typical discharge present, and had the characteristic fishy odour, which permeated the atmosphere of the whole ward, when the man was dressed.

All these cases were treated with Injection of Quinine Solution. All authorities,* however, are not in complete agreement. Thurston * has shown in his paper that with the use of Emetin subcutaneously, the injection of Quinine is not necessary. Moreover, the amoebae are in the wall of the abscess cavity, and may not be reached by the Quinine. The absorption of Quinine from the walls of the abscess cavity, does not occur, as has already been stated above. He further found that re-aspiration was required more often after Quinine Injections than if simple aspiration had been alone employed. In many cases the aspiration may have to be repeated two or three times, and some cases may even require the Open Operation. In all cases, the use of Emetin greatly adds to the chance of recovery. A dose should be immediately given after the aspiration, as with the flow of serum into the abscess cavity after aspiration the Emetin which has just been injected subcutaneously may be carried in as well and kill the amoebae. This treatment was quite successful in one of Thurston's cases, from which 92½ ozs. of pus were withdrawn at one aspiration.( Thurston quoted by Phillips, p. 72.).

To avoid the chances of Hemorrhage occurring after aspiration, especially where there is acute hepatitis - Chloride of Calcium or Calcic Lactate, should be administered for a day or so in advance, and the patient be kept on subcutaneous injections of Emetin. Chloride of Ammonium used to have a great reputation in cases of Hepatitis but it has been entirely supplanted by the introduction of Emetin.

* Thurston; "A series of 101 cases of abscess of the liver" Indian Med.Gaz, 1914, vol.49, No.3, pp 88-96.

*"A case has been recorded of a patient who refusing operation, was completely cured by Emetin Injections - 21 grs. being administered altogether.
In another case in which the abscess burst into the lung, all discharge stopped on the administration of Emetin."
cf.Manson, Trop.Med. p. 595.

Hypochlorous Acid
or
Eusol.

Newer Antiseptics have been introduced into the Practice of Surgery - especially the Hypochlorites by Prof. Lorrain Smith of Edinburgh, Drennan, Rettie & Campbell and named Eusol. It is claimed for this, that it is at once extraordinarily powerful, non-toxic, non-irritating, and extremely inexpensive. Its non-toxicity is well borne out by the fact that it has been administered by Intra Venous Injection in a hopeless case of Septic Endocarditis followed by recovery; and as used for the toxemia of Gas-Gangrene by Fraser & Bates. (cf. Septic Endocarditis; Intravenous Injection of Eusol: recovery by J. Allman Powell, B.M.J. Sep. 23, 1916, p. 422.)- (cf. Captns: Fraser & Bates R.A.M.C B. M. J. Jan. 15th. 1916 ).
Two preparations of the Hypochlorites are recommended.

1. "Eupad" - a powder consisting of equal parts of Bleaching- Powder, finely ground and intimately mixed with powdered Boric Acid.

2. "Eusol" - a solution of free Hypochlorous Acid which may be prepared by two methods

   i. 25 grms. of Eupad are shaken up with 1 litre of water, allowed to stand for a few hours , then filtered.

   ii To 1 litre of water add 12.5 grms: bleaching-powder (or 1 oz. of acid in 40 of water ), then add 12.5 grms: (1 oz.) Boric acid powder, and shake vigorously. Allow to stand for some hours, preferably over night, then filter off, and the clear solution is ready for use.

This solution contains Hypochlorous Acid 0.54 %; Calcium Biborate 1.28 %; Calcium Chloride 0.17 %; total 1.99 %. (cf. B.M.J, 1915, ii, 129 ).

For other preparations of Sodium Hypochlorite cf. Dakin, Lancet 1915, i; and The Medical Annual 1916, pp. 683; & 656.

Although this has so far not been used in any recorded case of Liver abscess - there is no reason why it may not be substituted for the Quinine Injections. It is strongly deodorising liberating nascent Chlorine; and is non-toxic & non-irritating. It should certainly exert a more lethal action than Quinine Solution. For this reason it may perhaps have a greater future in the treatment of Hepatic Amoebic Suppuration. In septic processes it has been found to diminish the formation of pus and clear up wounds in a surprisingly short time. I have had ample opportunity on H.S "Letitia" to use it on septic cases received at Alexandria from the Dardanelles. All of the cases in the early part of the expedition were received with septic nauseating suppuration from ground-organisms which produce a characteristic odour & greenish yellow pus. The deodorising action of Eusol was most marked. In the use of it for Amoebic Suppuration besides exerting this action

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action, it may perhaps have some specific action on the amoebae in the superficial parts of the abscess wall; and by causing a flow of Serum into the abscess cavity after aspiration, it may like Thurston's cases, allow of the introduction of specific Emetin given subcutaneously beforehand, into the contents of the abscess cavity.

Iodine Solution.

The ordinary Tincture of Iodine diluted so as to give a definite yellow solution, may be used to wash out the abscess cavity. Solutions may vary in strength from a pale yellow to a reddish color. These solutions must be freshly made up before use, as it rapidly deteriorates on keeping.

Permanganate of Potash.

Rogers recommends the use of 1 in 1000 solution for daily irrigation when the discharge becomes foul smelling from bacterial infection. It is said to rapidly reduce the amount and improve the character of the pus.

## The Treatment by Ipecacuanha & Its Alkaloid Emetin.

The action of Ipecacuanha was understood in the most ancient times. It was used by Pringle in 1774 during the Walcheren Expedition. It was recommended by Annesley in 1828 in India, in what he termed as Hepatic Dysentery; it was further used by Twining in 1835 which he considered the best remedy in Dysentery. In 1860, Morehead in Bombay regarded Ipecacuanha as the best remedy and gave it in small doses according to Twining's Formulæ. Parkes in 1846 advocated it in doses of 30 - 60 grs at a time. Docker, however, is generally credited with having re-introduced large doses of Ipecac: in 1858, using 20- 30 grs after Opium. In 1886, Norman Chevers advocated it in full doses in India, recognosing its influence in preventing serious Hepatic complications ending in Liver abscess. A fuller account will be found in the Treatment of Amoebic Dysentery.
The treatment with Emetin is firmly established as a reliable specific for Hepatitis & Abscess of the Liver due to Amoebae. The dose of the Emetin should be ½ to 1 gr. injected subcutaneously or intramuscularly twice per day or oftener, according to the severity of the case. Not more than 3 injections are recommended daily, until about some 20 grs have been given. The drug often produces pain and a sterile abscess may form. Emetin may be combined with Ipecac. in 20 gr. doses by the mouth once daily, probably with Opium to diminish vomiting. Emetin alone is curative, however. Ipecacuanha sine Emetin is useless.

The Treatment by Ipecacuanha & Its Alkaloid Emetin.

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The Statistics by which alone judgement can be based on the universally successfully treatment by Ipecacuanha & its alkaloid Emetin, have to be gathered from a series of cases, in which results can be compared before & after the introduction of the Brazilian Root into the systematic treatment of Dysentery & its Complications; and inferences of its Prophylaxis in the prevention of the resultant sequelae in cases of Amoebic Dysentery. Accordingly the Indian Statistics of "THE REDUCTION IN DEATHS FROM LIVER ABSCESS IN THE BRITISH ARMY IN INDIA, SINCE THE REVIVAL OF IPECACUANHA TREATMENT OF HEPATITIS. 1894 - 1911. Rogers.- is appended.

Up to 1907 it was the second largest cause of death in the British Army in India.

| Year Periods | Admissions per 1000 | Deaths per 1000 | NO. of Cases | NO. of Deaths |
|---|---|---|---|---|
| 1894-1903) (average)) | 2.39 | 1.39 | 157.5 | 92.5 |
| 1904 | 2.6 | 1.36 | 184.0 | 96.0 |
| 1905 | 2.1 | 1.17 | 152.0 | 83.0 |
| 1906 | 2.6 | 1.52 | 183. | 107. |
| * 1907 | 2.4 | 1.01 | 165. | 70. |
| 1908 | 1.7 | 0.80 | 115 | 55 |
| 1909 | 1.4 | 0.48 | 100. | 34. |
| 1910 | 1.0 | 0.48 | 75. | 35. |
| 1911 | - | - | 71. | 33. |

* In 1907 Rogers published his papers on the Treatment of Pre-Suppurative Hepatitis. The immediate reductions both in the number of cases admitted for liver abscess & the reduction in the death-rate have been recorded above in red.

" Moreover Lt-Col.Pilgrim, Superintendent of the Calcutta European General Hospital, has recorded that during the 4 years subsequent to the introduction of Rogers' Methods , out of an average of 200 cases of Dysentery, not a single case developed Hepatitis -& out of an yearly average of 82 Hepatitis treated in the same way none developed a liver abscess; while admissions with suppuration already estabd: had fallen to about one-third of the previous number."
Cf/Rogers Dysenteries-pp. 151-153.

Prophylaxis.

Thus, from a prophylactic point of view the Ipecacuanha treatment (&more recently its active principle Emetin) has stood the tests of time, &is unrivalled by any other drug in the whole domain of Therapeusis.

The Treatment by Ipecacuanha & Its Alkaloid Emetin.

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In place of preparations of Ipecacuanha e.g - Dover's Powder - administered orally, the recent preparation of the double Iodide of Bismuth & Emetin - Emetin Bismuthous Iodide, introduced in 1914 by Du Mez of the School of Pharmacy of the University of the Phillipines, may be used by the mouth. Recent literature in the treatment of Carrier Cases of Amoebic Dysentery, which recurred after Emetin Hydrochloride subcutaneously shows the drug to be most powerful in killing not only Amoebae but even the Emetin- resisting Cysts. Details of its preparation will be found in the Section of Treatment of Carriers. (cf.B.M.J. Nov.4th. 1916, pp. 612 - 616; & 626 ). Three grs of the double salt containing about 1 gr. of Emetin, seems to be a good average daily dose, and 12 such doses may be given in succession The vomiting if it occurs, usually does not come on until some time after the dose has been taken. The dose should not be diminished when vomiting occurs, for if persisted with, the patient gets accustomed to the drug. It is recommended that the dose should be given after a full meal, when the stomach contents will be certainly acid. Tolerance is usually established in a couple of days.

The Operative Treatment.

The Operative treatment of liver abscess consists of two main methods; the Open method & Aspiration. The Open method consists in incision over the abscess and free drainage. In the case of an abscess in the Left Lobe, this is usually very simple. In the case of abscess in the Right Lobe the abscess is localised by first puncturing with an aspirating needle as a guide and the abscess is opened. In draining an abscess after Open Operation, it is a great mistake to begin shortening the tube before it has been pushed out, or so long as there is any appreciable discharge. Delay in remedying imperfect drainage, is a serious it may be a fatal error. The Open Operation is substantially the one described by Sir Rickman Godlee, in the B.M.J. of Jan.11th, 1890 - cf. Manson, Trop. Med.p. 589, for details.
The first modification of the original Open method was Manson's Method of Drainage, he advised puncture of the abscess with a large bore Trocar, through which was passed a large drainage tube; the Trocar was withdrawn and the tube left in. Rogers introduced a flexible Sheathed Trocar for Sterile Siphon drainage & Quinine injection. This lead on to the treatment by aspiration. At least 6 punctures should be made before the attempt to find pus is abandoned. ( Manson ) If pus be not struck the needle must be slowly withdrawn, a good vacuum being maintained the while in case the abscess has been transfixed, and the point of the needle lodged in the sound tissue beyond. The up and down pendulum movement of the extremity of the needle in harmony with the rising & falling of the organ in respiration will denote that the needle has entered the liver.

## The Treatment of Liver Abscess opening through the Lung.

These cases often present considerable difficulty in knowing how to deal with them. The treatment has been referred to at some length in the estimation of the Mortality rate General & Surgical. Abscess of the Lung is best treated by general anti-amoebic treatment; if the abscess be purely one of the Lung, rapid improvment is the rule. Chauffard * has published a case of recovery under Emetin after 18 months; so has Phillips * When, however, a large liver abscess continues to discharge through the lung, this may not be sufficient. These abscesses are very hard to find and drain. X-Ray examination will be of great help in many of these cases; if the discharge be intermittent the period should be chosen when the abscess cavity is full. Intra-Thoracic collections of pus such as an Empyema secondary to Dysenteric liver abscess, must be dealt with as in Empyema cases - by rib resection & drainage. Major Whitmore, I.M.S has published a case of liver abscess opening through the lungs at Rangoon which was treated by aspiration & injections of Quinine, the fluid being introduced under low pressure, with the result that the expectorated pus rapidly became reduced and recovery ensued. Cf.Rogers, Dysenteries, p. 223.

* Chauffard; "Etat hemoptoique chronique, consecutif a l'Ouverture dans les Bronches d'un Abces dysenterique du Foie Guerison parl'Emetine" Bull.et Mem Soc.Med. des Hop de Paris.1914 3e Ser.30e Ann.No.2 pp.29- 34.

Idem -"Les Rechutes de la Dysenterique ambienne et leur Traitement ".Jl.des Practiciens,1914 vol 28.No.3,pp 39-40.

* L.P.Phillips. The treatment of liver abscess discharging through the lung. St.Bartholomew's Hspl. Journal,1913,vol.20 pp 158 - 159.

## The Treatment of Abscess of the Brain.

The treatment is in the main surgical; but energetic treatment should always be carried out with Emetin. The cases hitherto operated upon have all proved fatal. Early diagnosis is the key to success. A thoroughly treated liver abscess or a known amoebic dysentery with Emetin will remove all chance of this condition developing by killing off the amoebae before they have passed into the blood stream. Bromides & Morphia may be necessary for the relief of the headache which is always a marked feature.

## The After-Treatment of Abscess of the Liver.

A course of Emetin treatment should always be persevered with after recovery from Liver abscess. From time to time X-Ray examinations of the liver should be made to note its condition. Like all Protozoal diseases, it is apt to relapse. Stimulating foods, rich spices, hot curries, etc, and Alcohol should be avoided, and the patient warned against chills. A Cholera-Belt should always be worn so as to protect the liver. A damp hot climate should be avoided if possible. The question of return to the Tropics after recovery from liver abscess is frequently raised. If possible the patient should remain in a temperate & healthy climate, and a long change to England may be undertaken.

The anaemia which follows this debilitating condition, must also be treated by Iron tonics Strychnine, Arsenic etc.

The General and Surgical Mortality from Liver Abscess.

L. Rouis in Algiers observed a mortality of 80% in 203 cases. In Rouis's 162 fatal cases, the causes of death are stated as follows:-

| | | |
|---|---|---|
| i. | Severity of the local disease or through the associated dysentery | 125 cases. |
| ii. | Bursting of the abscess into the Peritoneal cavity | 12 cases. |
| iii | Into the Pleura | 11 cases. |
| iv. | Pericarditis | 3 cases. |
| v. | Hepatogenic form of ulcer of intestine | 3 cases |
| vi. | Septicaemia | 2 cases |
| vii. | Septic Pleurisy | 2 cases |
| viii. | Septic pericarditis | 1 case. |

SECTION VII. AMOEBIC INFECTION OF THE LIVER.

PART 12. THE GENERAL & SURGICAL MORTALITY OF LIVER ABSCESS,

AND THE PROGNOSIS.

The General and Surgical Mortality from Liver Abscess.

L. Rouis in Algiers observed a mortality of 80% in 203 cases. In Rouis's 162 fatal cases, the causes of death are stated as follows:-

| | | |
|---|---|---|
| i. | Severity of the local disease or through the associated dysentery | 125 cases. |
| ii. | Bursting of the abscess into the Peritoneal cavity | 12 cases. |
| iii | Into the Pleura | 11 cases. |
| iv | Gangrene of abscess wall | 3 cases. |
| v. | Peritonitis | 3 cases. |
| vi. | Pneumonia from effusion of liver-pus into the lung | 3 cases |
| vii | Rupture of adhesions | 2 cases |
| viii | Pneumonia | 2 cases |
| ix | Rupture into the Pericardium | 1 case. |

(cf.Manson " Abscess of the Liver ", Trop.Med. 5th, end, p. 584.)

II. "Since operative measures have come into more common use, the mortality has decreased according to Dujardin Beaumetz, from 82% to 32%".
(cf. Castellani,& Chalmers, Trop.Med, 2nd edn. p. 1411.)

III. Megaws analysis at the Calcutta Medical Hospital from 1895 - 1905 period, 292 total cases yielded 60% mortality.

IV. Rogers in 1907 at the same Institution quotes the mortality among all cases he could find records of, was as high as 73% among 52 cases; the open operation being in general use.
" During the last few years better results have been obtained, especially in the formerly very fatal deep seated Right Lobe liver abscesses by the adoption of .... repeated aspiration and injection of Quinine ( and later Emetin ) without drainage ", (cf.Rogers Dysenteries, pp.205 - 206 and p. 180.).
The mortality is apparently influenced by the following general considerations:-

1. The class of patients and state of the disease at the time they are first seen; and the position of the abscess.
2. The numbers of abscesses present.
3. Early diagnosis especially of the preceding hepatitis in its pre-suppurative stage.
4. Mortality from the different forms of Liver abscess.
5. Mortality after operation and drainage and
6. Treatment by aspiration & Quinine injection with or without drainage.
7. From complications of the abscess arising spontaneously.

## The General and Surgical Mortality from Liver Abscess.

- continued -

### Mortality in different forms of Liver Abscess.

Rogers gives the following tables from a series of Calcutta Medical College Hospital Cases.

**Table No. 1.**

I. Opened through Abdominal Wall.

| Left Lobe | | | Right Lobe | | | Total | | |
|---|---|---|---|---|---|---|---|---|
| cases | deaths | % | cases | deaths | % | cases | deaths | % |
| 33 | 4 | 12 | 51 | 30 | 59 | 84 | 34 | 40.5 |

II. Opened through Chest Wall.

| cases | deaths | % |
|---|---|---|
| 79 | 58 | 73.4 |

III. Through Lungs.

| cases | deaths | % |
|---|---|---|
| 13 | 6 | 46. |

The Total mortality becomes nearly 60% (53.3%).
(cf. Rogers Dysenteries, p. 207. ).

**Table No.2**

General mortality - causes of uncomplicated liver abscess after operation ( in weeks.) - Rogers European series.

| Nature of Termination | 1st. week | 2nd.week | 3rd.week | 4th week. | Total |
|---|---|---|---|---|---|
| Shock & Exhaustion .... | 4 | 1 | 2 | -- | 7 |
| Hemorrhage .... | 2 | -- | -- | -- | 2 |
| Dysentery .... | 1 | -- | -- | -- | 1 |
| Fever ? Septic Infection, | 1 | 2 | 2 | 2 | 7 |
| Complications .... | -- | 2 | -- | 1 | 3 |
| Totals | 8 | 5 | 4 | 3 | = 20 |

(cf. Rogers' Dysenteries p.203).

- continued -

Table No.3.

Series of cases of Liver abscess treated by Rogers'Method by Aspiration & Quinine injection with or without drainage.

| Method of Treatment | | Cured | Died of other diseases | Died of Liver-absc |
|---|---|---|---|---|
| 1. Aspiration& Quinine Injection only | (a). Cured cases .... | 16 | - | - |
| | (b). Liver-abscess cured;died later of dysentery. | - | 1 | - |
| | (c). Liver-abscess cured;died later of Pneumonia. | - | 1 | - |
| | (d). Died of Liver-Abscess. | - | - | 3. |
| | Total ..... | 16 | 2 | 3 |
| 2. Ditto- && Opened later. | (a). Cured ..... | 3 | - | - |
| | (b). Died ..... | - | - | 3. |
| Grand Total ... | | 19 | 2 | 6. |
| 3. Abscess evacuated through the Thoracic Wall. | ... | 24. Cases. | | |
| 4. Abscess evacuated through the Abdominal Wall. | .... | 3. Cases. | | |

(Cf. Rogers' Dysenteries p.231).

Table No.4.

Liver Abscess treated by Aspiration & Quinine-Injection-Without Drainage.

| Site of Puncture | Cases | Cured | Died | %Mortality by Open Operation. ( Percentages.) | Estimated Mortality of these cases by Open Oper |
|---|---|---|---|---|---|
| 1. Through Chest Wall | ... 16 | 13 | 3 | 73 | 11.68 |
| 2. Below Right Ribs | ... 1 | 1 | - | 59 | 0.59 |
| 3. Epigastrium | ... 2 | 2 | - | 12 | 0.24 |
| Totals | . 19 | 16 | 3 | .. | 12.51 |

(Cf. Rogers' Dysenteries p.234.).

## The General and Surgical Mortality from Liver Abscess.

-continued-

### Comments on Table No.1.

The following are summarised from Rogers' Statistics, and form a compendium of them.

(i) The small early Left-Lobe abscesses have only 1/5 th. the average mortality.

(ii) The Abdominal Route of Evacuation yields 2/3 rds. of the whole Tabular rate; and just over ½ of the large deeply-seated abscesses opened through the Thoracic Wall

(iii) Abscesses of the Right Lobe have a much higher rate than Left Lobe -because
(a) they commonly reach a much larger size before they are opened; and
(b) they are much the commoner.

(iv) "Those opening spontaneously through the Lungs have a lower mortality than in any other form excepting Left Lobe abscesses this mortality further, being far lower in cases not operated on, than in those in which the abscess is opened, partly due to the former including less severe cases. " (Rogers).

(v) The highest rate obtains when abscesses are opened through the Chest Wall.
A greater case-incidence of Empyema resul from operation; (cf. Tables of Frequencie Rogers).

(vi) "Some low mortalities given by individual operators may in part depend on a certain selection of cases; either conscious or accidental". (Rogers).

(vii) A convincing contrast is afforded by a comparrison with Table No.4. Rogers' Methodof Aspiration & Quinine Injection without drainage becomes the operation of choice.

The General and Surgical Mortality from Liver Abscess.

- continued -

## Comments on Table No.2

This table shows the causes of death in a series of fatal Liver abscesses, together with the period after operation at which it occurred.

(i) During the first week shock and exhaustion were the most frequent.

(ii) The two fatal Hemorrhage cases occurred on different days within the first week- one on the day of the operation, and one on the fourth day. ( The cause of the Hemorrhage in each case is unstated - but Phillips remarks that a troublesome return of Dysentery occurs after a Liver abscess has been drained ).

(iii) Septic Complications. Although the records are marked under " Fever ", Septic Complications were the cause of this, for the clinical symptoms are those of Septicaemia. The temperature generally rose only about the third or fourth day, and continued till death, the discharge assuming a yellow creamy colour, and having a putrefactive odour. This fact alone would distinguish such cases from an Acute Hepatitis, secondary to unhealed amoebic ulcers in the Large Bowel, which often causes rise of temperature, controlled by Emetin... general primary sterility of amoebic abscesses uncomplicated are emphasised by all authors.

(iv) Complications, shown under the second week are not given by Rogers, i.e - although two cases are recorded, what the complications are, are not stated. In the fourth week, one such case is recorded. Out of a total of 20 cases, complications were only met with in 3.

(v) In analysing the figures Shock & Exhaustion caused the greatest number of Mortalities, within the first week, and Hemorrhage yielded the next highest. The aggregate totals of Shock & Exhaustion and Septic Infection are alike ( 7 in each case ) - these two accounting for ¾ of the total Mortality. There is progressive diminutio in the Mortality rate from the 1st.week, being lowest in the 4th. The middle weeks are approximately equal; the death rate in the 3rd.week, is ½ that of the 1st.week.

(vi) Hemorrhage as a cause of death, always occurred within the first week, and the is true for Dysentery as a complication. The missing links in the analytical table are caused by insufficient clinical data of the precise nature of the cases considered and the intensity of the terminal disease.

- continued -

## Comments on Tables Nos. 3 & 4

Both these tables are based on Rogers' point of view, that repeated Aspiration & Quinine or Emetin injections direct into the cavity of the abscess without drainage will of itself, cure liver abscesses. The following cases are likewise detailed by Rogers showing the efficacy of repeated Aspirations & Injections. ( cf Rogers Dysenteries, pp 238 - 242; and p.180 ). These will be referred to under " Treatment ".
The following points are emphasised :-

(i). 70 - 80 % of Liver abscesses are sterile. Aspiration treatment has therefore a rationale to recommend it.

(ii) In 1902, 1 in 500 Quinine solution was advocated for usè. In Table 3, out of 18 cases treated by Aspiration and Quinine Injections, 16 were completely cured; two were cured of the Liver abscesses, but subsequently died of other diseases.
Three were totally uninfluenced and died of the Liver abscess. The clinical facts concerning these three cases are set forth at some length by Rogers.
" As all but 3 of these cases were evacuated through the chest wall, which class when treated by the open operation has a Mortality among native patients ( who formed a large proportion of the whole ) of over 70%, these are very encouraging results, which are enhanced when we consider the nature of the three cases it failed to save. One was admitted in a very bad condition, for whom only very temporary relief was possible. From another, no less than 112 oz. of pus were aspirated at the first operation, when he was in an extremely critical state. He rallied, however, and a week later 20 ozs were removed, while after another 7 days only 10 ozs. could be got..... He suddenly died of heart failure due to over-exertion
The 3rd. was a very acute case with extreme jaundice due to the neck of the Gall-Bladder being completely dissected out by the suppuration, and he had a destruction of most of the Right Lobe with very large sloughs, which prevented complete evacuation. He could be said to be even beyond the pale of Surgical interference. " ( cf Rogers Dysenteries pp 231 - 232.).

(iii) The two cases dying of other diseases after cure of the Liver abscess, have a remarkable clinical history. One succumbed to Dysentery nearly 3 months after his abscess had dried up. The second died of Acute Left Pneumococcal Apical Pneumonia quite unconnected with the Liver trouble, after thé abscess had ceased to form pus.
"He had been admitted inan extremely debilitated condition with a huge Liver abscess from which 86 ozs of pus were aspirated.

- continued -

Comments on Tables Nos. 3 & 4, continued.

(iii) aspirated and 15 grs Quinine Bihydrcl: were injected into the cavity. By repeated injections after aspirations he lived for 24 days, but died of Pneumonia. At the autopsy, the Liver substance beyond the encysted abscess was quite healthy. The cavity in the Liver which had held 4 pints of pus, 4 weeks earlier, contained now only 2½ ozs. of clear bile but no pus, and its inner surface was free from amoebae and sterile on culture. Some recent scars with a few slit-like depressions of almost healed dysenteric ulcers were found in the Caecum. The case illustrat es the value of this method of treatment even in very large chronic abscesses in debilitated subjects, in whom open operation would almost invariably be fatal" (cf.Rogefs, ibid, p 232. ).

(iv) Out of 21 cases treated throughout by Aspiration & Quinine Injections, 3 died of Liver abscess ( 14% ). 19 of these cases belonged to the deep-seated Right Lobe class, the mortality of which by open operation is 70% or more ( Rogers ).

(v) Subsequent operation after Aspiration & Quinine Injection - the mortality per-centage rises from 14 to 22%.

(vi) Table 4, is given for comparison of the open operation mortality with that of the mortality after Aspiration & Quinine Method of Treatment. The last column in this table, gives the estimated death rate in the particular cases, in accord-ance with the previous rates by the open operation in each class of case. The reduction in deaths in this series by the Method of Aspiration & Quinine Injections is shown to be fourfold.

(vii) In the treatment of Liver abscess opening through a lung, Rogers European Series show that out of five cases operated on, three recovered and two died; while of 7 cases not operated on, 5 recovered and 2 died. In Rogers Native Series, out of 8 cases operated on, 6 died, while 5 not submitted to surgical measures, all recovered.

" Operative procedures in this complica-tion are of a very serious nature and to be avoided whenever possible .... They are often rapidly cured without operation by Ipecacuanha or better by Emetin given subcutaneously ".

The General & Surgical Mortality from Liver Abscess.

- continued -

## S U M M A R Y

The Prognosis of Liver abscess cases, either with or without attendant complications, self-induced or otherwise, therefore depends almost entirely upon the Method of Treatment employed. As has been mentioned before, and which the detailed cases emphasise, the clinical condition of the patient is sometimes less important than the measures employed for their alleviation. The most important consideration is the exhibition of Ipecacuanha in full doses or its alkaloid Emetin subcutaneously, in the pre-suppurative stage of an Acute Hepatitis. Other factors which will influence the Mortality rate e.g, the presence of complications when the case first comes under treatment, the number of abscesses present their position, size & sterility, will be described under Prognosis. The Tables arranged have been chosen to illustrate the mortality aspect from every point of view, and though the Commentary Notes appear rather as a criticism of post-operative treatment, than actually reviewing the gross mortality rates, yet mortality rate is essentially wrapped up with the question of Open Operation, and the less heroic procedures. Evacuation through the three routes have been compared and contrasted as influencing profoundly the mortality rate. Such clinical facts as have been presented by Rogers, have been gathered together and re-quoted; so that the gross figures themselves should be co-related with the clinical state of the patients, so that some index may accompany the dull recital of bare figures, and have a direct bearing upon what has been termed " The General & Surgical Mortality following Liver Abscess ". In some cases of spontaneous evacuation taking place into the Bowel or through the lungs, spontaneous cure results, so that Nature's methods of evacuating amoebic abscesses of the liver, are frequently entirely successful in curing the patient, while they are far less often accompanied by the extension of serious inflammation to the Pleura or Peritoneum, or septic infection of the abscess cavity, than are the Surgeon's attempts in the same direction ( Rogers ). Any method of treatment must always be governed by the clinical condition and an appreciation of the pathological state, combined with the reaction of the system against such state.

## Prognosis of Liver Abscess.

(1) The number of abscesses present.

This perhaps is the most essential element in the Prognosis.
Sambuc's Table of Mortality is based upon the number of the abscesses present.

| | |
|---|---|
| One abscess ..... | 23% |
| Two " ..... | 45% |
| Three " ..... | 90% |
| More than 3 ..... | 100% |

Many types of cases come up for consideration,

(i) A Liver may be so riddled with rapidly extending collections of pus and be accompanied by a hopelessly advanced amoebic dysentery as to make the prognosis hopeless. These cases are rare.

(ii) Cases with a small number of localised abscesses give a worse prognosis than where there is only a single cavity however large for they are more difficult to locate and evacuate.

(iii) The Single Acute abscess. Fortunately 70% of all cases are Single abscesses. The frequency of Single & Multiple Liver abscess has already been tabulated.

(2) The condition of the abscess cavity.

Gangrenous condition of the wall has already been noted. The great majority of Liver abscesses have sterile contents in the first instance. Septic infection will produce Multiple abscesses of a pyemic nature. Bacterial infection secondary to the open operation is a far more important factor than mere size in rendering the prognosis unfavourable. " The chief cause of high mortality due to this, apart from the presence of more than one abscess, or extreme debility of the patient before operation, is undoubtedly infection through the open wound..... The patient does well for the first few days after operation, then infection occurs, the temperature goes up again, and death from Septic poisoning slowly but surely follows. " (cf. C.G.Spencer, exProfessor of Military Surgery, R.A.M.College, Millbank, London ).- is quoted by Rogers, p. 211.
If the abscess however is a small one, the patient may ultimately recover, in spite of the secondary infection; but healing will be delayed, and there may be recurrences of chronic suppuration.

(3) The position of the abscess.

Anatomical considerations furnish difficulties where the abscess is deep-seated. Abscesses of the Right-Lobe have a worse prognosis than Left- Lobe as they are generally so deep-seated. The Left Lobe is primarily affected in about 10 %; and becomes involved by extension of suppuration from the Right Lobe in about 15% of all cases. The Lobus Spigelii is occasionally (3%), and the Quadrate Lobe

-continued-

(3) The position of the abscess- continued

more rarely (1%) the seat of suppuration.(Brown). Moreover it has already been pointed out that mortality varies in different forms of liver abscess (cf.Table No.1, Mortality ).

(4) The size of the abscess

Large abscesses will presumably destroy a greater amount of liver substance than a smaller one. This however, applies rather to very acute and often Multiple collections containing large sloughs than to single more chronic abscesses, which almost invariably have thick fibrous walls completely localising them from adjacent liver tissue which is surprisingly healthy. As recovery has taken place even in these large single amoebic liver abscesses often containing more than four pints of pus when properly treated by Emetin, it is clear that they do not commonly destroy sufficient liver tissue to make recovery impossible.

(5) Chronic suppuration and discharge of pus will ultimately lead to Waxy Degeneration which may involve both Intestine and Kidney, and carry off the patient. Evidence of these changes will be clinically revealed by chronic Uremia & terminal diarrhoeas. Moreover, such patients are apt to develop some intercurrent malady e.g, Tuberculosis or Pneumonia which proves fatal.

(6) The presence of active dysentery.

When this occurs or perhaps recurs, it renders it more likely that Multiple abscesses are present in the liver, or that further ones will continue to develop. It may be directly the cause of death after the liver complication has been successfully dealt with.
Active dysentery may also be the terminal factor in an advanced case of Sprue or Kala-Azar.

(7) Other complications, such as Empyema, Pericarditis, and more especially Cerebral abscess, may prove fatal. Cerebral abscess has hitherto been invariably fatal.

(8) Much emaciation, Chronic Malaria and Alcoholism, are of serious prognostic import.

(9) An abnormal amount of immature Polymorphonuclear Leucocytes ( the youngest members in Arneth's Index) after an operation offers a bad prognosis. A marked degree of Anaemia indicated by marked oligocythaemia & poikilocytosis; Normoblasts, Megalocytes & Myelocytes in the blood, indicate a somewhat acute phase of toxaemia, especially seen during the later stages of amoebic dysentery - a secondary anaemia induced by absorption of Toxins.

(10) Specific Therapy. Hitherto Emetin Hydrochloride has been the one specific that was known to profoundly modify amoebic disease. The recent introduction by Du Mez of Emetin Bismuthous Iodide, offers the fairest prospects of attaining Ehrlich's conception in "Therapia Magna Sterilisans" Amoebae.

## I. ETIOLOGICAL RELATIONSHIPS.

1. The final & ultimate establishment of Amoebic Dysentery as a definite pathological unit, with a specific cause, is largely due to Kartulis' pioneer work in Egypt in 1885. His researches were corroborated by Osler in 1890, and later by Councilmann & Lafleur, who introduced for the 1st. time, the distinctive Title "Amoebic Dysentery".

2. It was Schaudinn's researches in 1903, that laid the foundation of our present knowledge of the disease, for he investigated its Life-History & biological relationship, and established the Ent.Histolytica as the causative organism, & acquitted the Ent.Coli of any harmful tendencies. Two main species have therefore been established.

3. The Ent.Histolytica has a definite life-History and definite structural appearances which mark it out from all other species. Although it has been proved, Non-Pathogenic, can only be cultivated by Symbiosis with Bacteria, neither Ent.-Histolytica or Ent.Coli can be so cultivated. There does not appear to be any proportional relation between the Endemic Index of Non-Pathogenic Amoebic Infection, and the Case-Incidence of Amoebic-disease, - these may vary actually in all degrees ranging from Temperate Climates, the Endemic Index of Non-Pathogenic Amoebae is often as high or higher than in the Tropics.

4. Specific function has been established on the ground of constant association of the organism with the Clinical condition; on Experimental evidence, notably of Sellard & Walker's who infected Prisoners in Manila, and on the reaction to Emetin. Musgrave & Clegg's work is open to the great objection of contamination, for they assert that all Amoebae are potentially pathogenic. Lesage has proved that his organism (E.Tropicalis) contaminated Musgrave & Clegg's results. However some of the results are undoubtedly due to Anaphylactic Reaction. Variations occur more especially in the Non-Pathogenic Species and their Cysts, but this is not enough reason to create New Species as has been almost definitely

## SECTION VIII. SUMMARY AND CONCLUSIONS.

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Ent.Africana (Hartmann); Ent.Minuta (Elmassian); Ent.Tetragena (Viereck); E.Nipponica (Koidzumi); Ent.Noc; Ent.Phagocytoides (Gauducheau);
are all forms in the life-history of Ent.Histolytica, or have similar biological relationship.
E.Tropicalis (Lesage); E.Hominis (Walker); E.Williamsi; E.Brasiliensis; E.Hartmanii, (Prowazek), are all variations of Ent.Coli.

5. The case for the Pathogenicity of Ent.Histolytica, has been summarised on Page 13, Thesis.

6. Amoebic Dysentery is not essentially a Tropical Disease, though it is most common in the Tropics. It is particularly common in Egypt and in India. 14 Autochthonous cases have been reported in France by Laudouzy; in England and Scotland; in Germany; Russia; Austria-Hungary, & The Balkans. It does not seem to be common either in Japan or Northern China. Australian Records are not available.

ETIOLOGICAL RELATIONSHIPS (Cont.).

7. It has curious Epidemiological features, as it is intimately associated with the Rainy Season or Monsoon - probably as moisture is required for the developement & survival of Cysts, & also because at that time, sewage-pollution of Wells & drinking water is more apt to occur.

8. Accessory factors are undoubtedly necessary -
   i. A lowered resistance.
   ii. Habits & idiosyncrasies of the individual, more especially in relation to Alcohol.
   iii. Non-acclimitisation & Climate, living in a continuously raised temperature, and subject to chills by the sudden lowering of such temperature by atmospheric disturbances.

9. The distinctive differences between Ent.Coli, & Ent.Histolytica as two main types are:-
   i. Ent.Histolytica has a definite refractile ectoplasm, and a definite granular endoplasm - little vacuolated & greenish in color - E.Coli has only a uniform protoplasm, much vacuolated; greyish colour.
   ii. Ent.Histolytica always contains blood-corpuscles - E.Coli, never.
   iii. Size is not a distinctive feature. Generally speaking E.Histolytica is larger than E.Coli.
   iv. E.Histolytica has a nucleus eccentrically placed, generally not rich in Chromatin, a small central Karyosome which is responsible for Cycle growth. A large Karyosome is held to occur in E.Tetragena.
   E.Coli has a nucleus, rich in Chromatin, excentrically placed, and a large Karyosome.
   v. E.Histolytica is a much more resistant organism, exceedingly active, and its pseudopodia are long & sharp, very clear and refractile, & the concentration of protoplasm is posterior polar -i.e, away from the scene of activity. E.Coli has delicate pseudopodia, sluggish movement, & a concentration of protoplasm which is anterior polar, so that this readily flows into the pseudopial-cavity till nothing is left behind.
   vi. Variations occur more in the Non-Pathogenic Species & Cysts, than in the Pathogenic Variety (Wenyon).
   vii. Ent.Coli has a definite Schizogony and Sporogony cycle with the formation of 8-nucleated Cysts. Ent.Histolytica has only a Sporogenous cycle reproducing 4-nucleated Cysts in its typical form. The budding off of portions of Ent.Histolytica described by Schaudinn, is a degenerative phenomenon. Simple Conjugation of two apparently similar forms in both Species has been described by Craig. No complete evidence is at hand on this point.

10. A Summary of the Reproduction process is given on pps. 84 -85, Thesis.

## II. MORBID ANATOMY OF AMOEBIC DYSENTERY.

1. Three main types of the disease exist, & have corresponding different Pathological appearances. The most typical form is in the more Chronic lesions alternating with Acuter patches.

2. Membranous conditions result more from Bacillary infection.

3. In the more Acute Varieties, the disease is limited to the Caecum or Ascending Colon. It practically never extends beyond the Ileo-Caecal valve. In the more Chronic cases, the Transverse & Descending Colon may be affected, with the Sigmoid & the Rectum. Often there is definite localisation in the Sigmo-Rectal Pylorns of Cantlie - it is in these cases that great suffering is induced.

4. There is always marked thickening of the Colon. Perforation rarely occurs, except in the Malignant Form, when it may be so rapid, that even blood may not appear in the Stools, & the whole Gut resemble the consistence of wet blotting-paper. The Microscopical changes & Distribution are absulutely distinctive from what occurs in any other Intestinal lesion. It is, however, exactly similar in Experimentally-produced lesions by Amoebic Infection.

i. The mucous membrane is not universally affected but patchily - the intervening area being quite healthy.

ii. The primary lesion is always sub-mucous and always marked in that structure.

iii. The typical ulcer is characteristically undermined, and has a definite Fawny-yellow color, due to infiltration of its floor. The superficial mucosa may be practically intact with a submucous abscess underneath. The ordinary ulcer has been described picturesquely as the Florence Flask Type. When a submucous abscess bursts into the lumen of the Gut, it may burst through a minute opening the so-called "ulceres en bouton de chemise". Different types of ulcers have thus been described, depending upon the variations of cell-death, and extent of the same.

iv. Cell-death is rather due to Vascular obstruction caused by small round-celled infiltration than the activity of the Amoebae. A powerful secondary factor is the specific Amoebic Toxin.

v. Invasion of the submucosa is practically always through the Follicles of Lieberkühn, though Dopter considered that the route lay t through the intact mucosa by the pushing-aside of the Epithelial Cells, and that the Follicles were attacked from behind.

vi. Extension towards the Peritoneum is always by necrosis caused by Vascular obstruction and stasis, with a small round-celled infiltration, the elements of which strangle the blood-supply; and the elements of which are themselves liable to death from Amoebic Toxaemia.

vii. Bacterial Toxins & Bacteria do not play any part in the Morbid process. The Bacteria themselves are probably kept out of the lesion by the Amoebae themselves or the Amoebic Toxins.

viii. Repair may be complete or incomplete. The

- continued -

formation of permanent structures is incompatible with the continued development of Ent Amoebae. In the Malignant Variety, the glandular tissue may be almost completely destroyed & replaced by a fibrinous & cellular exudate (Flexner).

ix. The typical ulcer is trans-Axial. Other smaller rounded or oval separate ulcers may occur, produced by secondary changes in the mucosa, e.g - the "Harris Ridge Ulcer".

x. Characteristics of Amoebic Abscess of the Liver is definitely governed by the characteristics of Intestinal Ulceration and its distributional variations (Rogers).

xi. The number of Amoebae in the stool; and the presence of blood, or other characteristic evidence of Amoebic Ulceration or their absence, form no guide to the severity of the lesions. Black sloughs however, in the stools, are always prognostic of Malignant changes.

xii. Goodeve's Method of washed stools & examination of the residue, are important clinical guides to the character of the pathological process; and a definite pronouncement on the character of the sloughs.

## III. CLINICAL ASPECTS OF INTESTINAL AMOEBIASIS.

i. The most practical Classification is into:-
   a. Very Acute & Malignant -sometimes like Cholera.
   b. Acute Simple.
   c. Chronic.
   d. Latent.
   e. Mixed Types.

ii. The Latent cases are especially interesting. No symptoms of Dysentery or Diarrhoea occur, yet there may be the most widespread ulceration (Musgrave). Two types are common, viz - the Suppressed Latent & the Non-Diarrhoeal Type.

iii. Fever is usually absent or very low. When high, it may result from some Complication, e.g - T.B, Pneumonia or Typhoid.

iv. Jaundice is apparently uncommon.

v. A Diarrhoeal Group of cases occur. Trichomonas is often a common cause of this. Some cases are undoubtedly Sprue. The Monsoon-Diarrhoeal Type is most often Amoebic.

vi. The Carrier Group of cases are essentially Latent. A common characteristic is Anaemia, due to Chronic Amoebic Toxaemia. It is exceedingly important to remember that Amoebic infection may be present in conditions other than Intestinal. Dobell's work in this direction is especially convincing. Repeated Examinations of the Stools are absulutely essential.

## CLINICAL ASPECTS OF INTESTINAL AMOEBIASIS

- continued -

vii. A Practical Classification of The Carrier-Problem is presented on pps. 54 -55 Thesis.

viii. The prognosis depends essentially upon Early Diagnosis and energetic "Emetinisation" of the patient. The presence or absence of complications, more especially due to other causes than Amoebic, is important. Blood-examination is very helpful - a Leucocytosis of over 30,000 in a Dysenteric case being grave. Information may be obtained also by washing the Stools by Goodeve's Method.

ix. A General Amoebemia may result. There is no organ in the body which is exempt from Amoebic invasion, except perhaps the Small Intestine. Thus, Arthritis, Phagadenic Cutaneous Abscess (Carini); Appendicitis (Wooley & Musgrave); Pyorrhoea; Salpingitis; Parotitis,&c.
Scurvy-Gums are generally not due to Amoebae, The question of Pyorrhoea due to Amoebae is denied. Recently, Entamoebic Tonsillitis has been described the toxaemia being held to be due to Amoebae.
Dysentery may occur as a Terminal complication notably in Kala-Azar & Chronic Sprue. It may, however complicate, or be complicated by other diseases, e.g - Typhoid.

x. The subject of Typhoid & Dysentery is a complicated one - many symptoms of Typhoid in the Tropics being misleading and often absent.

xi. The Incidence of Nervous Disease due to Amoebae is undoubted. It is especially apt to occur in a Liver-abscess before rupturing through the Lungs.

xii. Intestinal Haemorrhage is uncommon - blood vessels being remarkably resistant to ulcerative processes. It is especially apt to occur in Blood-states & Diseases with Hemorrhagic tendencies, e.g -Hemophilia, Pernicious Anaemia etc.

xiii. Perhaps the most common accompaniment is Indigestion & pain, akin to Gastric Ulcer, more marked in the period of convalescence.

xiv. Diagnosis chiefly rests on the observation of a Total or Relative Leucocytosis, with or without Eosinophile changes - increase or normal %. The Leucocytosis is generally over 15,000 - this figure being held to be diagnostic. Leucocytosis of 10,000 is more often seen in Chronic Amoebic Dysentery or Acute Bacillary Disease with high fever. Blood-Diseases may occur which alter the clinical picture. The finding of Specific Ent.Histolytica or its 4-nucleated Cyst in the discharge, absolutely clinches the diagnosis A Saline purge should always be previously given. Positive Widals on Typhoid & Paratyphoid and on the Bacillary Dysenteric Group are distinctive. A negative Widal may or may not differentiate. The clinical condition must then be read along with this Serological result.

## IV. TREATMENT OF AMOEBIC DYSENTERY.

1. It is through Vedder's work in 1910 that the Treatment of Amoebic Dysentery & Amoebic States by Ipecacuanha was re-introduced into Medicine; and the application of his researched to practical therapeutics by Rogers, has revolutionised Treatment. "How this remedy almost deserving the name of a specific, came to be superseded by Calomel & Opium in the treatment of Dysentery in the East, is one of the most curious questions of Tropical Medicine" (Maclean, 1886). The following are the Conclusions of the use of Emetin in Dysenteric States:-

i. Emetin often acts rather as a charm than a true specific - this is, it controls Dysenteric symptoms, induces a rapid convalescence, & favours the early incidence of comparative quiescence of the Entamoebae themselves. It may hasten Cyst-formation on the other hand.

ii. It has no action on Cysts, but only kills the Ent.Histolytica in the Intestinal Walls. It does not cause death of the Ent.Histolytica lying free in the Intestinal contents because it does not reach them.

iii. It is <u>essential</u> in Malignant & Gangrenous Amoebic States. It is the only drug which may pull a serious case through, because of its rapid absorption & simple method of administration (injection).

iv. It requires no Adjuvant Treatment, beyond perhaps the administration of Ipecacuanha. Bismuth alone in large doses may be harmful. It is not a specific.

v. It is remarkably beneficial in all Chronic cases, and has revolutionised its treatment. It has replaced the Surgeon's Knife, and the era of appendicostomies for relief, beyond that of saving life, has passed. The indications for Appendicostomy is given on pps.99 -100, Thesis.

vi. It is especially valueable, nay, a specific, in preventing Visceral complications - notably Liver Abscess.

vii. It has no effect upon Ent.Coli or its Cysts which through temporary disappearing during Treatment, reappears on stopping the drug. The same applies to Lamblial Infection. In fact Emetin is of Diagnostic value.

viii. It apparently fails in the treatment of Carriers, in as much as it fails to kill the Cysts (Dobell) - even 24 grs of Emetin have been found inefficient.

ix. The double Iodide of Emetin & Bismuth (Du Mez) is more lethal to Cysts, but is more troublesome than Emetin. A full & practical <u>Discussion</u> on this question will be found on pps.103 -104, Thesis.

x. Emetin may be given by the mouth. It then produces Vomiting, It is efficacious, however. Emetin has been intravenously (1 gr) given, without toxic effects (Rogers). Emetin is usually given by Intramuscular injections of ½ -1 gr.daily for six doses, smaller doses are given to children (1/5th.grs). It is non-poisonous, but may cause pain.

2. Other Indigenous Drugs have been recommended, e.g - Kho-sam; Siamaruba; Bael; Chaparro, Amargosa. The last is a recently investigated drug.

2. -continued -

They sometimes appear to do good, especially in refractory cases.

3. Synthetic Compounds & derivaties of the (Organic) Chromaffin System (Adrenalin) have been recommended. There is no indication for their use.

4. Dietetetic treatment is of more importance in this disease than in the Bacillary Type. The best food is undoubtedly "Yaghurt" made with specially prepared "Leben Zibad" cultures (Willmore & Savage). The use of pure milk is to be condemmed as it leaves a large residue.

5. Enemata have been advised. There is no special indications for their use. Rectal & Sigmoidal ulcers have been watched healing under Emetin Treatment by the Sigmoidoscope. Either Quinine Sulphate 1/1000; or Pot, Permangate 1 in 2000; or Tannin (0,5%) as originally introduced by Kartulis are the best. Some have advocated Creosote (½%). (Chantemesse & Rodriguez). Enemata of Saline are of use in treating post-Dysenteric Constipation.

6. Saline treatment should always be adopted. It washes out dead Amoebae & toxic products.

7. Mixed Entamoebic & Bacillary cases should be treated by a combination of Emetin; Polyvalent Sera & Salines.

8. Emetin in Amoebic Dysentery most nearly approaches Ehrlich's standard of "Therapia Magna Sterilisans".

Amoebic Dysentery is an Endemic & not an Epidemic Disease.

## V. ACUTE HEPATITIS.

1. It is essentially a Pre-suppurative Stage of Suppuration. It is impossible often to tell the difference between the two, especially if the suppuration be Small & Localised.

2. The same-blood picture exists for Amoebic Dysentery, Hepatitis, & Liver-Abscess; with the exception of a hypo-Eosinophilia or totally absent Eosinophile cells in the blood. The Leucocytosis of a Hepatitis may entirely disappear under Emetin in a few days.

3. Several Types of the disease undoubtedly exist. In many cases there is no history of antecedent Dysentery, although it is always secondary to this, the organism invariably coming to the Liver. The fundamental difference between Amoebic & Bacillary Dysentery is the liability of the former to Liver Infection.

4. The Clinical Types of greatest interest are, by reason of their diagnosis -
   i. Chronic Hepatitis with non-antecedent history of Dysentery - Type V.

4. -continued-

ii. Latent Hepatitis with non-antecedent history of Dysentery, but with fever - Type VI.

iii. Latent Hepatitis of the Jaundice-Diarrhoeal & Pseudo-Sprue Types - Type XI.

5. There is an "Infectious Jaundice Group" of cases sometimes hard to distinguish. The characteristics of Infectious Jaundice caused by Spirocheta Icterohaemorrhagica - are given on p.111, Thesis.

6. Two cases of clinical interest are published by me under Hepatitis -cf. p.112 & Charts; p. 113 & Charts, and Comments, pps.112-114, Thesis.

7. Infectious Jaundice is a distinctive disease from Amoebic Hepatitis - though the two may exist together.

8. Emetin is absolutely curative & remarkably effective. It may really be claimed as a therapeutic triumph in curing Amoebic states of the Liver, and in being their absolute prevention.

## VI. AMOEBIC ABSCESS OF THE LIVER.

1. It is the gravest complication of Intestinal Amoebiasis, & one that is most easily preventable by use of Emetin.

2. It is the great barrier of Generalised Infection; consequently Abscess of the Brain, Lungs, &c, are all Secondary from the Liver.

3. It has specific relationship to Antecedent Amoebic Dysentery, though this may not always be easy to prove. In Bahr's cases in the Fiji Epidemic, the disease was essentially Bacillary. Only 11 Amoebic cases occurred. Amongst these, Liver-Abscesses developed but not a single case of Liver-Abscess amongst the Bacillary cases.
The relationship between Abscess of the Liver & Dysentery, from a clinical point of view, is discussed on p.118 -Thesis.

4. There is definite relationship of the Type of Liver-Abscess with the Character & Intensity of the Dysenteric lesions in the Bowel. The complete Pathological findings of the Distribution of Dysenteric ulcers in the Bowel, when there is an associated Liver-Abscess , is given on pp.121 - 132, Thesis. The Cases are Rogers.

Table I. Amoebic Dysentery & Small Liver-Abscess 24 cases.
Table II. Amoebic Dysentery & Multiple Large Liver-Abscess - 12 cases.
Table III. Amoebic Dysentery & Multiple Small Abscess - 5 cases.
Table IV. Post Colic Abscess, complicated by Perforation & Liver-Abscess -1 case.

My Analysis & Conclusions of these results are published on pps. 129 -132.

- continued -

5. The Paths of Amoebae to the Liver is generally by the Portal Blood-Stream. Marshall found Amoebae in a branch of the Portal Vein. Lymphatic-carriage is more common than is thought. Amoebae have been demonstrated in the Mesenteric Glands.

6. Liver-Abscess are primarily Sterile. In Roger's Series, 86% were so. Cantlie has made similar observations.

7. Accessory or Predisposing Factors are considered necessary, given the presence of Amoebae in the Liver. These are chiefly -

i. Age- Sex & Race.- the female rate is astonishingly low. An analysis of the Age-Sex & Race Incidence will be found on p.139 -Thesis.
Habits are undoubtedly Racial - especially the indulgence in Alcohol.

ii. Climate & Duration of Residence (Acclimatisation).

iii. Chills are an important factor.

iv. So-called "Tropical or Congested Liver" is a definite pathological & clinical Status, induced especially by Alcohol, lack of exercise, and over-eating, and having a special relationship to Liver Infection (Amoebic).
A Summary will be found on P.144 (Thesis).

8. The Single Large abscess is the Typical Type, is the commonest, has a tendency to form a "lining limiting membrane", and although Large, may leave large areas of Liver-tissue apparently healthy.

9. The Multiple Type is essentially Pyemic and rapidly spreading. In the more Chronic Type, definite Cirrhosis of the Liver results. There is a type of Infantile Tropical Biliary Cirrhosis of unknown Etiology, probably Kala-Azar, The Varieties of Multiple Abscess are given on pp. 152 -154.
"Rarer Types" on p.158, Thesis.

10. The seat of Election is the posterior part of upper portion of the Right Lobe. These Right-sided abscesses are always deeper & more Insidious than the Left-sided ones.

11. The changes are always produced by the following sequence of events. At first, thrombosis of the small vessels occurs, & Amoebae may be seen within them; then liquefaction of the thrombosed area occurs, & the Amoebae escape. The Amoebae are most readily found in the walls of the abscess.

12. A Summary of the Multiple & Single Abscess Types is given on p.156, Thesis.

13. The commonest complication is rupture through the Lung, being about 10% of all cases. It is more common on the Right than on the Left side. Spontaneous evacuation into the Colon is ten times more common than into the Duodenum or Small Intestine.
A Summary is given on p.161.

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14. The (Clinical) Differential Diagnosis of Liver Abscess in relation to Anterior Abdominal Wall is a complicated one. Full details are given on pps. 165 -166. The chief Method of Diagnosis is by Blood Examination; and by effects of Emetin Treatment. No Exploratory puncture should be attempted till a thorough trial of Emetin is given. It may be purely Hepatitis. X-Rays readings require a considerable amount of practice. Shadows may be given indicative of pus, yet this has been known to clear up under Emetin (Rogers).

15. Invasion of the Lung is generally a direct process; Empyema is uncommon and more readily induced by operation. In some cases the original Tract between the Liver & the Lung cicatrises, leaving only the active Lung condition. Primary Lung Abscess is rare.

16. Sometimes the Liver condition is so Insidious that it only reveals itself by spontaneous evacuation through the Lungs. Such cases may recover Spontaneously. Insidious Liver-abscess often results from insufficiently or untreated Dysentery.

17. Lung cases often give distinctive symptoms; notably exaccerbations of cough, & temperature and pain followed by a paroxysm of cough, & the expectoration of typical anchovy-pus.

18. Insidious Lung cases may be mistaken for T.B, & Chronic Pneumonias. Hemoptosis may then occur. In all cases of obscure Lung Disease, an eye should always be kept upon the Temperature Chart and body-weight.

19. Brain-Abscess is not common. They are always secondary to Liver suppuration & the seat of election is Cerebrum. They are almost always fatal. Abscence of Meningitis and optic Neuritis are features. Intense headache is a characteristic. Four Varieties have been described by Legrand. Encystment is generally partial. In its differential Diagnosis the Cerebral Type of Malignant Malarial Fever should be borne in mind & the blood examined.

20. Abscess of the Spleen is rare. Acute Splenitis (like Acute Hepatitis) may be more common than is suspected. Difficulties arise in enlarged Spleen & Liver (due to Malaria) with antecedent or recent history of Dysentery. Emetin often controls Enlarged Malarial Spleens. One case is published by me -(cf. Thesis p.185* Note.-Charts & Diagram).

21. In its Differential Diagnosis,
Kala-Azar
Blood-Diseases
Malaria
should be excluded by a study of the Blood.

22. Involvement of the Stomach occurs only by rupture through it. Spontaneous cure may result, or the patient die from Peritonitis caused

- continued -

by adhesions being torn through by the violent Vomiting efforts.

23. Rupture into Inferior Vena Cava has been known to occur. Death is instantaneous.

24. "Hydrostatic pressure" Rupture into the Peritoneum is uncommon.

25. Liver-pus has special characteristics. It is not pus, but liquefied degenerated Liver-tissue & dead Mononuclear-cells. It is an instance of "Mononuclear Pus". It has a distinctive small. Its special characteristic is its colour and consistence described variously as Anchovy-sauce; treable; Gooseberry Jam & Chocolate. In encysted cases it may be creamy or yellow.

26. Multiple abscesses have the shortest course, and are clinically evident from the reaction they inevitably cause. Next to these come Small Abscesses in the Left Lobe. They rapidly produce local swelling in the Epigastrium within 1 -4 weeks of the first symptoms.

27. Types of Abscess-Temperature vary.
i. The commonest is the <u>Low Remittent Type,</u> with ladder-like increases up to 2 degrees, followed by rapid defervescence in a few hours & profuse sweats. These copius sweats may produce two or more such depressions in the temperature-curve in 24 hours. Such temperature specially occurs in the Subacute and usually Single Abscess.

ii. The Fulminant Variety is characterised by a High Remittent Type of Fever.

iii. Acute Abscess of the Liver has a similar High Remittency.

iv. High Continued Fever is very apt to be complicated by Acute Nervous complications subsiding on the evacuation of the abscess.

v. Very rarely a Normal Temperature is shewn especially when the tension is reduced by a bulging of an abscess through its capsule.

28. The type of pain specially characteristic is -
i. <u>Sympathetic pain</u> to the Right Shoulder - often to the very tip of the Acromion Process. This is transmitted from the Hepatic terminals of the Phrenic, through the <u>iv</u> Cervical, to the Cervical & Brachial Plexuses.
ii. Regional pain in lower end of Oesophagus excited by the passage of food, may be present. (Manson).
iii. Visceral (Liver) pain is common enough in abscess, especially if complicated by a Hepatitis.

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29. Blood-Examination is by far the most important
A Leucocytosis is invariably found, sometimes manifested by an Absolute, sometimes only by a Relative increase. The Differential Count is more important than the Total. Attention has been directed to the large number of Immature Polymorphs & alterations in the nucleus. In Chronic Encysted cases, however, the blood picture may be normal.
The Eosinophile cells are always diminished and may totally disappear. Hydatid Disease is thus easily differentiated. Until cure is established, the blood shows a definite Leucocytosis & the alterations described above.
A Summary is given on p.208, Thesis.

30. Anaemias of a Secondary Type may complicate
the blood picture, both in Dysentery and in Abscess. Ankylostomiasis is another complication of considerable importance.
The Leukaemias are distinctive enough generally.
Golden rules in Tropical practice are to think of Hepatic Abscess in all cases of progressive deterioration of health; & to suspect Liver Abscess in all obscure abdominal cases associated with evening rise of temperature.

31. A Series of observations have been given on
pps.221 -224, Thesis, on "Clinical Points of Interest from the Treatment of Recorded Cases". These sum up the Treatment & Dangers.

32. Emetin Injection is the main method of prevention and Treatment. Liver-Abscess should only be aspirated, and their contents washed out with a solution of 1/500 Quinine Sulph. or other Salt, and Emetin given subcutaneously. In place of Quinine, Emetin solution may be so used, and the Emetin continued by Injection. This conservative Method is undoubtedly the best. Thurston, however, disagrees as to the use of Quinine & recommends only Emetin Injection & Aspiration. Other solutions recommended in lieu of Quinine are "Eusol", prepared according to Prof.Lorrain Smith's formula; Iodine Solution; or Pot.Permang.
The Ipecac.Treatment has notably reduced the Case-Incidence of Liver-Abscess in the British Army in India, and the death-rate.
Operative measures should only be undertaken when General Peritonitis has occurred. Free Drainage should always be employed. Amoebic Phagadenic Cutaneous Abscess as a Complication in the edges of the wound, should be remembered.
Lung-Abscess, even Chronic, can be cured by Emetin-Injections & Aspiration. They should not be primarily operated on. The risk of Empyema resulting is greater with, than without operation.

33. The General & Surgical Mortality rates are
discussed in Tabular form, pp.237 -238, Thesis. An Analysis & Comments are given on pps.239 -242 . The Salient point is that Open Operation has higher death-rate than the more Conservative Method advocated. Moreover, it deals with one Collection of pus. In Multiple collections it is out of the question. If, however, Septic Infection occur, only then should an abscess be operated on.

AMOEBIC ABSCESS OF THE LIVER.

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34. i. Sterile Abscesses should always be Aspirated and energetically treated with Emetin.

ii. Infected Abscesses must <u>always</u> be opened & drained. Aspiration in this case will fail.

iii. Infection more readily occurs in the Open Operation Method than in Aspiration.

35. A <u>Summary</u> is given on the General & Surgical Mortality from Liver Abscess, on p.243, Thesis.

The Pathological Role of Ent.Histolytica is undoubtedly a great one; and Emetin its most potent Curative & Prophlactic Antagonist . It has come to stay; it may perhaps be modified and rendered Cyst-Destructive. It has robbed Amoebic Dysentery of all its terrors; it has brought another Tropical scourge under Therapeutical control.

AMOEBIC ABSCESS OF THE LIVER.
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" STUDIES IN

THE LIFE-CYCLE OF HUMAN AMOEBIASIS:

FROM ITS

PROTOZOOLOGICAL, MORBID, & CLINICAL

ASPECTS."

(Illustrated)

Being a

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BY

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