On the aetiology of Scarlet Fever.

UNIVERSITY OF EDINBURGH LIBRARY

T. W. McCrae

30/4/83.

With 11 Drawings in packet.

Prefatory Note.

The following Thesis is the result of work done in the physiological Laboratory of the University of Edinburgh, under the direction of Professor Rutherford, to whom I am deeply indebted for the suggestion of the subject, & for the advice & assistance, which he has given me throughout the prosecution of the research.

The notion, that contagious diseases are produced by minute organisms, has prevailed in a vague manner in the minds both of the medical profession, and of the public, from a remote age; but is only within the last 20 years – since the publication of Pasteur's researches on fermentation & putrefaction – that it has assumed the position of a serious pathological doctrine.

During the last 10 years the discoveries of organisms in the blood have given this doctrine the support of actual observation, and its application as a guide in the treatment of wounds by Professor Lister has made it a subject of universal interest to the medical world.

It was but natural that the first steps towards establishing this new theory of the causation of disease should have been taken by a study of the processes of fermentation & putrefaction, which can be done so much more accurately & exhaustively than a study of processes complicated & obscured by the disturbing reaction of concurrent life, as is the case in the contagious diseases.

Accordingly, though perhaps it is not strictly within the lines of the subject

under our immediate notice, it may not be amiss to recall in a few sentences, what has been done in the study of those processes, & of their relation to minute organisms, as it may help us more fully to understand their function in disease, & more especially in that disease with which this paper professes to deal.

Till the purely chemical teachings of Leibig regarding fermentation were overthrown by the vital theory of Pasteur all progress in this study was of course prevented. It was only by Pasteur's discovery that we could realize the position which organic life takes in the process of fermentation; how that minute particles of the yeast plant, when placed in suitable circumstances, can accomplish the fermentation of an unlimited quantity of wort, the reason being that the yeast cell is a living plant, which grows so long as it finds material on which to feed. Nor is this process confined to the ordinary yeast of our breweries. There are many other plants of a like kind, the cells of which have precisely the same powers, namely of appropriating the oxygen, on which they live, from the

sugar around them, which causes a production of CO_2 & alcohol. In fact, quite recently, M. Muntz has professed to shew that alcohol in minute quantities is to be found everywhere in nature, a result of the decomposition of organic matter by the ferments which everywhere exist. As Pasteur says, "The character of ferment presents itself" "to us as a property of the living cell," "a character always ready to manifest" "itself, slight, & of feeble duration if the" "species of life is the same; intense & of" "long duration, when the plant or cell" "can multiply itself with facility under" "the new conditions. Thence all imagin-" "able degrees of fermentation, & thence" "also the existence of ferments of all forms" "& of every different species."

Again he says, "One can imagine with-" "out difficulty that the decomposition" "of sugar should be altogether different" "from that of which we have spoken," "and that in place of alcohol & CO_2" "it should give Glycerine &c, or lactic" "butyric, acetic acid. In a word, &c" "many beings, so many ferments"

And this brings us to the subject of putrefaction.

Putrefaction may be said to be

neither more nor less than "a process of impure or mixed fermentation, the products of which vary according to the species of the ferments which happens to have been sown, the nature of the soil on which they find themselves, & the circumstances in which they are placed." In it the reduction of organic matter to their inorganic elements is effected by the action of several ferments following each other, each being produced by a different micro-organism. And in many of them it is found that whilst the active micro-organism or microbe is extremely delicate & easily destroyed, the germs or spores which produce them are endued with the most robust vitality. This fact will be seen to explain some of the phenomena of disease, especially that one which is under our notice, & will also be found to have an important bearing on the subject of treatment.

It was from a knowledge of Pasteur's discoveries on fermentations, & especially lactic fermentation that Lister by a process of deductive reasoning carried that theory into the domain of Surgery, & grasped the fact of the important part

which micro-organisms play in surgical diseases. The experiments & observations of Lister were confirmed, amongst others, by M. Chauveau in his experiments on sheep, in the operation of castration, by which he conclusively showed that putrefaction was due to micro-organisms.

There are several reasons why attention should have been turned first to traumatic diseases in connection with this study, rather than to the so called infectious diseases of mankind, whether specific or not. This would follow, in the first place, as a natural sequence the fact that Surgery has been the portal through which this new theory of the causation of disease has entered the medical world; also from the fact that these diseases most apparently resemble the processes of fermentation & putrefaction; & also from the very important fact that the lower animals, equally with mankind are liable to them, & therefore we are assisted to a greater extent by experiment in our researches as to the nature of these diseases.

Accordingly, we find that in this field observers & experimenters are by no means limited in number,

Since the observations of Rindfleisch in the year 1866 regarding the occurrence of bacteria in the organs of those who have died of traumatic infection, (Lehrbuch der pathologischen gewebelehre) there has been much labour bestowed on the whole subject.

Koch in his work on "The Relation of Micro-organisms to Traumatic Infective Diseases" (New Sydenham Society Vol. 88), not only gives us the results of his own most careful experiments on the artificial production of such diseases, but also gives a condensed account of the work previously done on this subject, & of the objections raised against the validity both of the facts & of the deductions drawn from them. These objections & his answers will be more suitably considered at a later stage of our paper; here it will be enough to say that his own experiments consisted of the artificial production of

1. Septicaemia in mice
2. Progressive destruction of tissue in mice
3. Spreading abscess in rabbit
4. Pyaemia in rabbit
5. Septicaemia in rabbit
6. Erysipelas in rabbit.

He also produced Anthrax artificially

in animals to judge of the number of the bacteria produced in the body, & of their distribution in the vascular system. Without giving in full the results he arrives at, suffice it to say that the conclusion he draws is that in every case a special bacterium was the cause of each disease, & that these artificial traumatic diseases, as regard their origin, course, & the result of their post-mortem examination, bear the greatest resemblance to human traumatic diseases. He therefore thinks we are justified in assuming that human traumatic infective diseases will in all probability be proved to be parasitic when investigated with like care.

And this leads us now to look briefly at what has been done towards establishing a causal connection between micro-organisms, & those infective (or contagious) diseases not included under the term specific eruptive fevers. Among such diseases are pyæmia inflammations, erysipelas, diphtheria, malaria, gonorrhœa, whooping cough, syphilis, tuberculosis &c. &c. Let us look at each of these in some more detail.

1. Purulent inflammation & catarrh of mucous membranes have been fully shown to be caused by micrococci, i.e.

of spherical bacteria. In various affections of this nature such bodies are found, but it does not yet seem to be proved whether they belong to the same species. Watson Cheyne, in his experiments on gonorhoea shewed that it was due to the presence of a micrococcus, to which indeed its contagiousness, the existence of a period of incubation, & the steady spread of the inflammation, all point. This has been confirmed by Dr. Neisser, who also asserts that the micrococci are larger, & different in appearance from those found in wounds. (Brit. Med. J. 1880 & Centralblatt für Med. Wissenschaft. 1879)

2. Erysipelas, has been shewn by many to be due to the presence of a micrococcus, which spreads by the lymphatics & thence to the tissues. It is found in them to form chains or swarms. Klebs, Koch & others have all agreed in coming to this conclusion. Nepveu has found micrococci in the blood of erysipelatous patients, & those were found in greatest number in that taken from the part. Orth has found micrococci in the contents of the bullae in erysipelas. (V. und V. Jahresbericht 1872) Still more recently Fehleisen in his work "Die Aetiologie des Erysipels" (1883) has demonstrated that this disease is really due to a specific & pathogenic micrococcus.

In all cases examined, thirteen in number, he has found them to be present, has also cultivated them, & successfully inoculated the lower animals & man with the cultivation. In pieces of skin excised from the diseased part, they were found arranged in rows, from which many cultivations were made.

3. Diphtheria

This disease seems to be associated with a micrococcus which is found in the specific membrane deposited in the pharynx & neighbouring parts. All observers seem to be agreed as to the presence of these micrococci, & the latest experiments seem to shew that there is a causal connection between them & the disease. In appearance the micro-organisms of diphtheria & pyaemia are said to be remarkably similar.

4. Whooping Cough

This disease resembles the eruptive fevers in that one attack seems to protect the subject of it against another. That it also is due to the presence of organisms is probable from the investigations of Dr Letzerich, so early as 1871. By an examination of the mucous sputum in the early stage, he discovered the presence of small, elliptically shaped, brownish-red fungous spores, some of which had germinated, and

produced mycelium. These when inoculated into rabbits produced a similar disease, & their lungs were found to contain the fungus. Dr. Mott of New York has lately confirmed Dr. Letzerich's results, & in consequence he recommends quinine as a remedy.

5. Malaria

Through the researches of Klebs and Tommasi-Crudeli it appears that this disease is probably due to the presence of a bacillus, which may be obtained from the soil of the malarious district. They also state that its passage into the air can be observed under favorable circumstances.

6. Relapsing Fever

So long ago as 1872 Dr. Obermeier of Berlin discovered minute spiral organisms in the blood. They are found during the paroxysm, are absent during the apyrexial periods, & disappear at the crisis.

7. Anthrax or Splenic Fever of Cattle has had its causation fully examined by Koch, Pasteur, & Greenfield, who all agree in assigning it to a bacillus, the bacillus anthracis, whose history has been fully worked out by these observers, & by Dr. Cossar Ewart.

8. Tuberculosis

The most recent discovery in this study has been made by Koch, who has found

bacilli present not only in the tubercle, but also in the sputum. He has successfully cultivated the bacillus, & produced tuberculosis by the cultivated bacilli. The exact diagnostic & prognostic value of this discovery is still sub judice.

The number of diseases, which have some connection, probably causal, with microorganisms might be enlarged but enough has been said & shew that such connection seems to be very general. And if we now proceed to consider those diseases which come more immediately under the subject of this paper, namely the specific eruptive fevers, we shall see that the same seems to apply to them also, though perhaps so much attention has not been directed to them, & therefore less progress has been made.

To no class of diseases does it seem more natural to apply the Germ Theory of Disease than to the specific eruptive fevers. For if we remember the connection between fermentation & putrefaction, & the part which microorganisms play in those processes, in considering the causation of the eruptive fevers, we cannot but be reminded of the facts which have been stated in connection with these processes.

The resemblance between a contagious fever, or the action of yeast in fermentation - or of bacteria in putrefaction - is so striking that it is difficult to avoid the impression that there is some real analogy between them. For instance, if we compare the action of yeast with a case of smallpox, the resemblance comes out very distinctly. We see how a bottle of saccharine fluid into which yeast is put after a certain interval begins to rise in temperature, which increase continues for some time, & then subsides to the original temperature with a ~~subsidence~~ formation of a considerable sediment. This rise of temperature in the bottle, or fever as we may term it, resembles smallpox in the following points; A period of incubation intervened between inoculation, & the commencement of disturbance; then followed the period of disturbance, accompanied by elevation of temperature; this was succeeded by a subsidence of the disturbance, & a return to the normal state. Great multiplication of the infectious material or yeast took place during the process, & after its conclusion the liquid was protected from further infection with the same contagion. We likewise see that the contagion of fermentation, like that of smallpox, may take

effect either by direct inoculation, as seen in the above example, or by fortuitous infection through the atmosphere, as shewn by the fact that a bottle of saccharine liquid goes through the same changes after some interval of time, even if it be not charged with yeast.

The resemblance, then, between the action of an organized ferment, & a contagious fever is very striking, & seems to lead us to the inference, that contagium, like a ferment, is something living & organic. There is nothing which exhibits the phenomena of growth & self-propagation except a thing possessed of life, & to state that such is the cause of disease is but to state the doctrine of Contagium vivum, or the theory that disease, or, as far as we are here concerned, the specific exotic fevers, are due to the presence & the propagation in the system of minute organisms. Till of late years this idea has been more or less of an hypothesis, but every day now adds to the number of facts which unite in proving that it is no mere theory.

Before turning our attention to what has already been proved in this connection, it may be as well to look very shortly at the rationale of the theory, as such a

consideration

may assist us somewhat when we come to look at the different points likely to yield further knowledge on the subject. In other words let us see if theoretically germs are competent to produce all the phenomena of the diseases under consideration, & if so, the probable mode by which this is done.

This question has been very fully discussed by Dr. J. T. Maclagan in his work on "The Germ Theory of Disease", from which, of course, it is necessary to give only a few leading features. Dr. Maclagan, after discussing the probable nature of contagium, & he confines himself to the consideration of the specific eruptive fevers, comes to the conclusion that it must be composed of minute solid particles of an organic nature, as being most fitted to explain the different phenomena of these diseases.

Such diseases have several points in common

1) Each has a tolerably definite period of incubation.
2) Each has for its most prominent symptom the existence of that aggregate of phenomena to which we apply the term fever.
3) Each possesses a characteristic local lesion
4) Each has a pretty definite course of duration

5) Each occurs as a rule but once in a lifetime.

The possession of so many features in common can only be due to similarity in causation. The existence of so many definite & distinct diseases proves that the poisons which give rise to them are specifically distinct, whilst the possession by these diseases of so many features in common indicates that these poisons are generically allied.

Dr. Maclagan then goes on to shew how all the phenomena of an eruptive fever can be accounted for by the propagation in the system of such organisms. Thus he brings many facts to shew that, by this theory, the period of incubation, the febrile state, the wasting of the tissues, the thirst, the increased frequency of the circulation, the heat, & other well known symptoms of fever may be, & are all due to this one cause. He also shews that the comparative rarity of the eruptive fevers, the occurrence of local lesions, the different degrees of severity in different individuals, the exhaustion of susceptibility, & the different degrees of contagiousness of the different fevers may all be explained in a similar manner.

While the phenomena common to all fevers are certainly more or less peculiar in each case, in none of them is it so distinct

as to form the leading characteristic of the disease. That which imparts to each of the eruptive fevers its most distinctive feature is not so much any peculiarity of the febrile symptoms, as the occurrence of local lesions. The most characteristic feature of small pox is its eruption; of scarlet fever, its eruption, & sore throat; of measles, the eruption & the accompanying irritation of the mucous membrane of the eyes, & respiratory passages; of typhoid fever the bowel lesion; of typhus, the rash. Now in each of these lesions it is to be noted that it essentially consists in hyperaemia of the part affected, & the question may be asked, What is the pathological significance of this localized hyperaemia? & how is it brought about? That the local lesions form an essential part of the respective maladies, there can be no doubt, they are as constant as the febrile symptoms, & much more characteristic. That a connection exists between them & the specific properties of the contagium seems also certain. Each disease, that is to say, each contagium, has its own special lesion. The presence in the system, of the contagium is doubtless the cause which gives rise to the local lesion.

The question then arises, In what manner

can the propagation in the system of the contagium cause the local lesion characteristic of these maladies?

The primary & essential condition of the local lesion in each of the eruptive fevers is an increased afflux of blood to the part affected, which may go on to congestion, inflammation, suppuration & even sloughing. Now is there any cause capable of giving rise to such localized hyperaemia. This is found in the fact that the organism requires a special medium for its propagation - that the medium is probably situated in the site of the local lesion, & that the hyperaemia & other consequences are due to the hyperaction consequent on the propagation of the contagium at the spot.

From what has been said, it follows that the poisons of the eruptive fevers are most abundant at the seat of the local lesion, & it is there therefore that, if it can be detected at all, the contagium should be found.

The two diseases, diphtheria & erysipelas are so allied to the eruptive fevers that observations made on their local lesions may be utilized in any general investigation into the pathogenesis of the special lesions of those fevers. This resemblance is perhaps more marked between erysipelas and scarlatina, but exists in a greater or less degree

between the others. So much is this the case that Beigel has lately pointed out that in erysipelas, diphtheria + scarlatina certain processes take place in the tissues, nearly allied to those in bacterial putrefaction. He therefore calls the diseases in question putrefactive diseases

The facts noted about the micro-organisms of Diphtheria we have already alluded to. Stated shortly it appears that micrococci are of constant occurrence, both in the local lesion, + in the tissues. Though this is not sufficient to prove that there is a causal connection between the organisms + the disease, yet, when joined to the fact that the extent of the local lesion, + the severity of the general symptoms are in proportion to the extent of the reproduction of the organisms, it is at least highly probable that such a connection exists.

Erysipelas possesses many points of similarity to the eruptive fevers. It is contagious, + therefore results from the reception into the system of a poison derived from without; the onset of the local lesion is preceded by headache, rigors, + general constitutional disturbance. The chief local lesion consists in hyperaemia + redness of the skin, followed by

desquamation of the cuticle over the part affected: The resemblance therefore to scarlatina is considerable, & some writers have even expressed the opinion that it appears, either in sporadic or epidemic form, as a forerunner or companion of scarlatina or diphtheria. We have already stated that in Erysipelas the constant presence of a micro organism has been noted by many careful observers, the habitat of the contagium being specially round & near the local lesion, though also found elsewhere. This organism we have seen to be of the nature of a micrococcus.

Turning now to a study of the specific exanthemic fevers viz Smallpox, typhoid, typhus measles & scarlatina we find that already not a little has been done in this part of the field.

Smallpox. That the fluid of small-pox pustules contains minute organisms was demonstrated some time ago by Keber, (Virch. Arch. Band 42) Cohn (Band 55) & others, whilst Weigert (Centralblatt 1871 - No. 39) found in the neighbourhood of the pustules masses of granular matter, which presents the appearances of the micrococci found in the pustules. Here, as in diphtheria & Erysipelas the local lesion is associated with the development of minute organisms in the affected tissue.

Typhoid Fever has had a considerable amount of attention bestowed on it, & with results of some importance. Klein (Report of Med. Off. of Privy Council No. III) has carefully investigated the changes which take place in the specific bowel lesion. The general result is to shew that the mucous membrane over & around the affected glands is more or less thickly covered with minute organisms, such as found in the Lieberkühnian follicles, in the mucous membrane, in the veins, in the lymphatics, & in the fresh stools. Fischl & Epsinger (Beitrag z. path. Anat. II Pray. 1880), Letzerich & Fitzgerald corroborate Klein, & have also detected micrococci. On the other hand Klebs, Eberth, & Koch agree in finding bacilli both in the local lesion, & in the internal organs. Maragliano of Genoa (Centralblatt für d. med. Wiss. No. 41. 1882) has an important note on the uniform occurrence of organisms in the blood of patients suffering from typhoid. He has found them in the blood of the spleen, as well as in that of the general circulation, which latter was obtained from the tip of the finger. The examination in this way of 15 patients gave the following results. At the height of the disease the blood of the general circulation contained microorganisms, both isolated & grouped, these consist almost exclusively of spherical bodies,

which have a delicate contour, appear to be homogeneous, & are analogous to micrococci. Some of them are mobile. Similar organisms again were seen in the blood of the spleen, & in it, too, were others, rod-shaped, also with delicate outlines. During convalescence these organisms lessen in number in both the splenic & systemic blood. Quinine in large doses caused these organisms to disappear, or to be present in small numbers. By fractional culture a large number of rods ~~were~~ were obtained, similar to those in the fresh blood, some being of great length. Marpmann avoids the expression of any opinion as to their relation to the disease.

Typhus Fever does not seem hitherto to have had much attention paid to its pathogenesis.

Measles. Here the blood has been examined by Coze & Feltz, & found to contain micrococci (Maladies Infectieuses 1872). Bradwood & Sacher have found similar bodies in the breath as well as the tissues (B. M. J. 21/1/82)

Scarlatina as being the most immediate subject of this paper has been reserved to the last.

Before proceeding to give an account of observations made, & experiments

performed, let us look, as in the case of the other fevers, at what has been already ascertained.

There is no doubt, in the first place, that Scarlet Fever is held by all to be Contagious, that is to say it is caused by some peculiar substance which is transferable from the patient to the unaffected individual. The disease breaks out in any district only after the material, which must be looked upon as the cause of the malady has been introduced into the place, either directly by a scarlatinous patient, or through the medium of any substance to which it adheres, the affected persons producing a substance identical in its properties to the one which originally infected them. These facts, together with the fact that the isolation of an affected person prevents all spread of the disease, certainly point to the contagiousness of the disease.

That the contagion is of the nature of a Contagium vivum would be probable, even before experiments + microscopical observations were made, if only we were to reason by analogy from the case of the other fevers, + allied diseases, + also from the fact, as Dr. Maclagan urges, that

possible
Of all causes, ~~that of~~ a contagium vivum
is most fitted adequately to account
for all the phenomena of Scarlet Fever.
As to the possible nature of the contagium
facts seem to lead to the conclusion that
it is possessed of considerable tenacity of
life, as is seen in cases where infection
lingers in clothes &c. long after the
period of the original illness.
As to the locality in the body where the
contagium might be expected to reside,
theoretically we should look for it in
the position where the ~~&~~ local lesions,
special to the disease manifest them-
selves, viz the epidermis, the throat &
tonsils, & the nasal discharge. Again, since
the disease is one affecting the constitu-
tion, one would expect to find in the blood traces
of the causal contagium.
Epidermis. There are several reasons why
one would expect to find the contagion in it.
1) The characteristic eruption followed
by desquamation is well known as the
most marked local lesion of the disease
from which indeed the very name of the
disease is derived. It must be the case,
of course, that this was caused by the presence
in the blood of some extraneous substance,
but that this substance or contagium is
probably in the epidermis itself, is shewn

by the fact of contagion being produced by it.

2) The result of experience has shown that treatment of the disease by frequent sponging & bathing, or oiling of the skin lessens the chance of infection. Such a line of treatment acts mechanically by preventing the scales of desquamation from flying about, & when in addition we add some antiseptic as Carbolic Acid, we, in addition to the mechanical action of the oil, make use of the acid as a germicide.

Dr. Myrtle of Hanogate drew attention to the latter point in Brit. Med. Journ. 21/10/83, where he gives an account of some cases where, by the use of Carbolic oil, the patients were able safely to return to society, when the skin was still desquamating.

The Throat, tonsils, & nasal cavity being the seat of a local lesion ought also to shew traces of the presence of the contagion. A sore throat is usually the first distinctive feature of the disease, caused ~~probably~~ perhaps by the fact that it is the point of entrance of the contagion into the body, though very probably it is due to the fact that like the epidermis it contains the nidus on which the special contagion feeds, the limitation of the lesion being caused by the limited amount of the nidus.

The Tongue undergoes changes peculiar to the disease. At first it is furred and white, in other words, there is an inflammatory redundance of the epithelial covering. Afterward there is a shedding of the epithelium, i.e. a desquamation, producing the well known raw red tongue of Scarlet Fever. As the tongue is the index of the condition of the stomach & alimentary canal, it is but probable that similar changes occur in them, that is to say, inflammation and desquamation; though the process is finished more rapidly than in the skin because of the greater change activity in mucous membranes. It is quite probable then that the contagion may be found in the alimentary canal, since it also appears to be the seat of a local lesion.

The blood ought certainly to yield traces of the contagion, since scarlet fever, being a constitutional disease, must affect the constitution through the circulation. The fact also, that children are sometimes born with scarlet fever seems to point in the same direction. It is probable however that more difficulty will be found in detecting it in the blood than in the special lesions,

1) Because in the lesions one would expect the organisms to be densely aggregated

together, whereas in the blood they are widely diffused.

2) The lesion is the seat of propagation, & therefore the locality in which fully developed organisms most abound, while the blood is the seat of growth, & therefore probably the locality in which germs, prospore so called, are most abundant.
The urine one would suppose, would contain the organism, being probably one of the channels by which it is excreted from the body.
The breath should be examined also, both because it is probably the means by which the organisms enter the system, but also because it is probably one of the means of exit from the system.

Such then, briefly, are the seats in which one theoretically would expect to find the contagion of Scarlet Fever, & that this has been recognized to be the case is shown by the fact that numerous observations & experiments have already been made on these lines.

1. Inoculation has been performed by Mycil upon children with the contents of vesicles from scarlatinal patients, producing an areola like scarlatinal eruption.
He also states that such inoculation furnished protection against a second inoculation, but this is denied by Leroy.
A similar inoculation has been performed

with success by Stoll, though Petri Nadel has failed in a like attempt.

2. The blood of scarlatinal patients has been examined by Coze & Feltz who found a peculiar aggregation of the red blood corpuscles, so that their contour was lost, & the margins of the majority of the isolated corpuscles were indented. Both of these facts however by the coagulation of the blood examined, with ~~en~~ cremation of the corpuscles. In the blood the same observers found punctate & rodlike bodies.

According to Hallier the blood of Scarlatinal patients contains micrococci in great abundance, either single or in colonies, within the blood corpuscles or on their external surface; ~~occasionally~~ occasionally they are found also as short chains & germinating.

Riess examines the blood freshly drawn from the vein in the arm of a patient dying from Scarlet Fever & found that "the serum was filled with an infinite number of small rapidly oscillating bodies, which under a magnifying power of 500 diameters appeared as dark spots between the groups of blood corpuscles. In addition there were also rodlike formations, which at many places were recognized as being composed of 3, 4 or more of these minute bodies disposed in rows.

The blood of a scarlet fever patient has been injected into rabbits, with the result that almost all die the others only recovering after intense fever.

The Pharynx, tonsils & nasal discharge have lately been examined by Dr Crookshank in which he describes a bacillus which he states is to be found in these parts. (Lancet 3/3/83) The urine was also examined by him, but not with much success.

All these observations & experiments though very fragmentary would lead one to expect that the contagious principle, whatever be its nature, enters the body through the mouth, throat, lungs. Hence it may enter the circulation through the stomata in the alveoli of the lungs, is disseminated through the system by the blood, & thus reaches the seats of the rash where it causes the special local lesions to which reference has already been made. Taking for granted that the contagion is found in the skin, it is possible that the local lesions of the skin is not a necessary result of the process of excretion, in other words it is nature trying to get rid of the poison. This view is rendered the more probable when one considers the bad effects produced by the failure of a rash to "come out," in other words, of the poison to be eliminated from the system;

& the benefits produced when it is brought to bear by hot baths or other means. Of course the want of a copious rash may also be due to the slightness of the attack, owing, as Dr. Maclagan's theory is the slight amount of the virus present in the body.

Having now given a slight sketch of what has already been done in the field, we are now in a position to give an account of the observations made & experiments performed for the purpose of more fully investigating the nature of the contagium of Scarlet Fever, the account of which forms the essential of this paper.

Naturally these observations & experiments ran very much in the lines of what had been done before, that is to say the blood, urine, & local lesions were the chief objects of enquiry. Besides, however, merely examining these structures, we endeavoured by the method of cultivation to arrive at a correct result. Of course, the difficulty we here encounter is that many of the objects which we wish to subject to cultivation are of necessity full of obvious extraneous matter. The epidermis, for example, to which attention was chiefly directed could not be obtained in a "pure" condition, & of course this ~~resulted in~~ produced

a difficulty in discriminating between what was essential & what foreign. The mine, also, presents great difficulties of a somewhat similar nature, whilst the nasal discharges obviously are even worse to deal with.

Before, however, we go on to the account of the observations &c. themselves, it will be well to describe the mode in the cultivations were made, & the fluid employed.

The first method employed was that of putting in an ordinary cultivation flask a suitable quantity of meat solution & in the proportion of 1 gramme meat extract & 200 c.c. of water. This was then plugged with cotton wool, & sterilized by boiling it twice or thrice for a few minutes at a time, allowing it to partially cool between each boiling. The epidermis was then inserted & it was then again plugged & put into an incubator at a temperature of about 90° & 95° F. For several reasons however this mode of cultivation did not suit. The flasks were too large & it was found to be difficult to abstract some of the contents for examination. This was especially found to be the case when a piece of epidermis was wanted, as it seemed often to sink to the bottom, & or if floating, to evade the means taken to take it out.

the depth & shape of the flask presented great difficulties also in the way of obtaining specimens of the sediments so often produced in cultivations, & which are so important in a full examination of such fluid. It was found also that every such examination, which of necessity must be made frequently, involved the great risk, in fact almost certainty, of contaminating the fluid in the flask, so that all these reasons combined made me change my method of cultivation to one which I shall now describe.

The fluid used was aqueous humour, obtained from the perfectly fresh eyes of bullocks. The method of putting up this fluid was as follows; A piece of glass tubing of the calibre of an ordinary pencil was calcined thoroughly & after cooling was melted at a point about two inches from one end; here it was drawn out & a capillary tube of say four inches in length, & broken across in the centre of the capillary portion. We then set a tube of about 4 inches in length, half being of the original calibre, & half of capillary size. If not required immediately the capillary end was closed up, & it was then put into an ordinary test tube, capillary end first, into this test tube there being put

another smaller calibre, enveloping the the piece of glass tubing which was then enclosed in two test tubes, both of which, I may mention, were also calcined. In this condition they were kept till they were wanted to be charged with aqueous humour which was done in the following manner. Having obtained some fresh bullock's eyes, a small incision was made through the cornea with a thoroughly cleansed knife, into this opening the capillary end of the tube, opened if necessary, was inserted, when the capillary action of the tube caused the fluid to ascend. When a sufficient quantity had entered the tube, it was taken out of the orifice in the cornea, sealed up at the capillary end, & returned to the test tubes. Pieces of epidermis, nasal discharge, or blood were inserted, when wanted, through the open extremity of the tubing, & the specimen labelled accordingly. The cultivation was carried in an incubator at a temperature of from 90° to 105° F.

Though probably from the nature of the objects cultivated it was not absolutely necessary to have a cultivating fluid perfectly pure in some cases, yet as in the case of the blood such a fluid was necessary, I resolved to test the adequacy of this mode of cultivation

To prove this I adopted two tests;

1. I kept such a tube, charged with aqueous humour only, in the incubator along with the other tubes for more than two weeks, at the end of which no organism of any sort could be observed in it by the microscope. This I did on two different occasions.

2. To test the efficiency still more thoroughly, I charged two such tubes from the same eye. Into the second of the tubes thus charged I put nothing, but placed it in the incubator along with the other tubes charged with epidermis &c. The contents of this tube I examined almost daily, under the precautions which I shall presently mention, & the result was that although it was so examined for about a fortnight there was at the end of that time absolutely nothing to be seen in the fluid on microscopical examination. This, I think, may be held to prove that, after charging such a tube with epidermis, blood &c, all that is observed in the fluid subsequently, is entirely due to the products of such foreign substance introduced.

Then a word must be said as to the manner in which examinations of the

cultivation fluid were made. When a specimen was wanted for microscopical examination a long German vaccination tube with a small bulb in the centre was taken; it sealed ends were broken off, & it was thoroughly calcined; when cool it was thrust into the charged tubing, which for the moment had been taken out of the 2 test tubes, & speedily returned. Owing to the capillary size of the vaccination tube, it only required insertion of its point into the fluid & fill it with the fluid; by deeper insertion one was able to catch solid particles, or sediment.

I may here mention that for general examination ~~high power~~ 1/4 inch Hartnack, & Zeiss F were the objectives used. For more careful examination 1/14 in. oil immersion lens, & 1/25 in. Powell & Lealand were employed.

As to the staining agents employed, at first, for a short time a dilute solution of methyl aniline was used, but this speedily gave place to a dilute solution of Magenta, which I continued to use to the end. This I found to stain the objects under observation most clearly, much more so than the methyl aniline which if its stained deeply was too dark, & if not so deeply did not produce such a precise definition as the Magenta.

So much then for the methods employed in cultivation, & in the examination of the result. Let us now look at the account of a systematic examination of the blood & structures forming the local lesions in Scarlet Fever, namely epidermis & nasal discharge, & the urine.

I The Blood

In a general constitutional disease like Scarlet Fever, which affects the whole system & produces special local lesions so far apart as the throat & the entire surface of the skin, it is but natural to expect that the blood, at some stage or other of the disease, should contain traces, at least, of the contagion germ, if there be one. At the outset of our enquiry however, we are met with the difficulty that, as Koch says, "A considerable number of investigators have advanced the statement that the normal blood & tissues of man & of the lower animals always contain micro-organisms. From this some infer that these organisms are not the cause of the infective disease, but that an abnormal increase in their numbers follows the morbid process, because the fluids of the animal body, when altered by disease, present conditions less favorable for their development. We need not consider these views, which have as yet never been experimentally

proved, but which are advanced on ~~the~~ theoretical grounds alone. Were it, however, true that ~~the~~ bacteria do occur in normal blood, & that the same bacteria e.g. micrococci, are found, though in unusual numbers, in organs altered by disease, then the possibility of proving that these micrococci were the cause of the disease would be rendered much more difficult, perhaps indeed quite hopeless. We must therefore enquire how far the assertion in question is correct.

Koch then proceeds to this enquiry. On the one hand he mentions Lostorfer, Nedvetzki & Beckamp as having discovered small moving particles in normal human blood, called by Beckamp "haemococci" Lüders, Bettelheim & others believe that they have seen bacteria in normal human blood. Siegel & Billroth attempted to prove the existence of bacteria in normal animal tissues by introducing with precautions fresh portions of muscle &c. into melted paraffin. These, when examined after the lapse of some time were found to contain bacteria. But as Koch points out, paraffin when cool, cracks, & does not form a protection against the entrance of bacteria.

On the other hand, Pasteur, Burdon Sanderson,

and Klebs after testing normal blood as to its power of causing development, by methods excluding all sources of error, obtained negative results. Also, opposed to the alleged direct observations of bacteria in normal blood are the statements of trustworthy microscopists such as Reinhardt & Ruess, who distinctly assert that the normal blood is free from bacteria, but that on the other hand, as Ruess more especially points out, it contains small round bodies, more or less numerous, which are most probably debris arising from the disintegration of the white blood corpuscles, & which on account of their resemblance to micro-cocci, have been confounded with them.

Koch comes to the conclusion, after very careful examination of normal blood & tissues, that bacteria do not occur in the blood, nor in the tissues of the healthy living body of man, or of the lower animals. To verify, if possible, this conclusion, I have examined not a few cases of normal human blood, under a Parkes' microscope of 750 magnifying power, & if anything suspicious like a micrococcus was seen, under a still higher power. In no instance was a micro-organism to be seen, but in most cases, the debris of white corpuscles was found, though as a rule & to a less extent than was

was found in the blood of scarlatinal patients.
Such being the facts as regard normal blood
what do we find in the case of scarlatinal
blood? The previous observations of Hallier
Riess &c. have already been noted.
On January 24 the blood from a scarlatinal
patient was examined, & a very few micro-
cocci were observed in distinct active vibratory
motion. In a malignant case observed on the
same day the White corpuscles seemed to be
increased in number, several of them being
large, with included particles of doubtful
nature, many probably fatty, but it is
possible that one might be included seems.
It is doubtful whether any micro-organisms
were seen in this specimen in the liquor sanguinis.
Subsequently to this, specimens of blood
from patients at all stages of the disease &
the number of 15 or 20 were examined from
time to time, till it was found that the
presence of micro-organisms in the liquor
sanguinis was invariable at some stage
of the disease. The presence of the debris
noticed above was also invariable, & added
much to the difficulty in detecting with
certainty the presence of the micro-organisms.
In the end of February I began systematically
& made almost daily ~~observations~~ examinations
of the blood of all the fresh cases which entered
the Children's Hospital, & continued this for

several weeks. The result of this examination quite corroborates my former ~~results~~ results, & enables me, I think, to draw some conclusions. These conclusions will be most clearly understood if put in the form of general statements, instead of giving the daily account of the microscopic examination.

1. In all the cases of scarlet fever under observation, about a dozen in number, the blood was found to contain micro-organisms, at some stage of the disease.
2. These micro-organisms were of the nature of micrococci, & were never found to be very numerous, as often only one or two are seen in a field of the microscope, & not unfrequently none.
3. As a rule, the more severe the case, the more numerous are the micrococci.
4. The appearance presented by the micrococci was that of small, spherical, bodies, with a delicate contour, apparently homogeneous, with a vibratory motion, & under a power of 700 diameters appear as small black specks. Occasionally they were seen of dumb-bell shape & wriggling violently. Besides bodies of this appearance bodies were also seen of somewhat larger size, & oval in shape, with a more distinct contour, & possessed of an active wriggling motion. These seemed to be present at a later stage of the disease than the former, which seemed

to be found co-incident with the disease. As there seemed to be gradations between the two, probably they are merely different stages of the same organism.

5. These organisms generally were found up to the 3rd or 4th week, but in malignant cases were observed up to the 5th or 6th week.

6. Besides these bodies there is always present a considerable quantity of debris, apparently the fragments of broken white corpuscles. This is not found to such an extent in normal human blood.

7. This debris was most marked after the first week, & disappears about the 6th week.

8. The white corpuscles seemed to be increased in number, though this was never accurately tested.

Specimens of Scarlatinal Blood were put up in aqueous humour on January 23., February 3, & March 11 & 28 & cultivated in the manner already described. The blood was obtained from the tips of the fingers, & received into purified vaccinator tubes with all precautions.

The results of these 4 cultivations agree in showing that micrococci are the only organisms produced. The following are the notes of the 2 last cultivations, the two former agreeing in every particular.

March. 11/83. Put up one specimen of Scarlatenal blood.

13/3/83. Blood corpuscles, & a considerable quantity of vibrating micrococci similar & those in fresh blood.

14/3/83. Contents of blood corpuscles effused in many cases, & appears as debris, also micrococci

15/3/83 Blood corpuscles - micrococci - single double - rows - & groups. also debris of blood corpuscles.

16/3/83 - 17/3/83. - 20/3/83. - 31/3/83, - on which days the specimen was again Examined, gave the same results.

& March 28/83. Put up one specimen of Scarlatenal blood.

29/3/83. Blood corpuscles - some beginning & crenate - micrococci in active motion some double - a few in rows.

30/3/83. Blood corpuscles. numerous small micrococci - single. double - & in rows & groups.

31/3/83. A few blood corpuscles - quantities of micrococci - in rows - & zooglea.

3/4/83. Blood corpuscles - debris - micrococci single & double.

6/4/83. Quantities of micrococci - single. double - rows & small groups.

II The Epidermis.

Passing now to the examination of the epidermis, we shall first consider the result of the examination of the epidermis itself & then pass on to that of its cultivation.

Whatever be the nature of the scarlatinal contagion, whether it belong to the bacillus order, or be included under the genus micrococcus, if it exist in the epidermis at all one would expect to find traces at least of its germs. Whilst in the cultivation fluid one would expect the fully formed contagion, in the fresh epidermis the original germs should probably be found.

With this end in view specimens of epidermis were carefully examined on several occasions after having been placed in KHO (dilute) for some time, in order to swell, & clarify the cells, thus making it more easy to observe the contents. The results certainly were not distinctly satisfactory. No trace of spores was seen, & nothing clearly indicative of minute germs appeared. On staining, some parts of the epidermic scales stained more deeply than others, & a faint indication of granular matter was to be seen in the stained portion. It is not improbable that this was due to the presence of a zooglœa of germs as seen & figured on Feb. 11 in Fig. 10. It is true that the figure is taken from Ordinary Epidermis but it seems probable from it that the origin

of micrococci may be seen extremely minute germs. And though the germs seen in the Scarlatinal Epidermic scales seem to be morphologically similar to those seen in ordinary Epidermis, there is no reason why they should be physiologically alike.
That there must be germs of some sort in the scarlatinal epidermis is shewn by the production of various organisms in the cultivation fluid, no such organisms appearing in simple aqueous fluid, though kept in the manner described for some time. But if we are asked the question - Are these germs distinguishable clearly from mistaken for those found in ordinary epidermis we must answer that they are not.

We now come to the subject of the cultivation of epidermic scales.

If it is the case that the epidermis contains the germs of Scarlet Fever, & it is highly probable that such is the case, then by the cultivation of these scales in a suitable fluid we ought to obtain the organism in its most highly developed form.

According in December last I began to investigate this part of the subject, & have continued the observations down to the present time.

It will perhaps be most advantageous if first I give an account of my investigations & then attempt to point out the essential results.

Results of cultivating Scarlatinal Epidermis

5/12/82.

Obtained some desquamated scales from the leg of a boy in the Sick Children's Hospital. The case was mild, & in the third week.
From this 2 specimens were put up in aqueous humour on Dec. 6 called respectively I A & I B, also 3 specimens in peptone solution as already described, called respectively, Ia, Ib, Ic.
On Dec. 7 two specimens of healthy epidermis from a healthy individual were put up in aqueous humour = II A, & II B, & two specimens in peptone solution = II a, & II b.
The results of these cultivations were as follows.

I A = scarlatinal epidermis in aqueous humour

6/12/83. Put up

13/12/83. Epidermic scales, numbers of micrococci many arranged in a sarcinous form - & skein deeply with methyl-aniline.

15/12/83 Sarcinæ still apparent in quantity - often grouped together irregularly - ordinary micrococci

19/12/83. Full of sarcinous micrococci - among epidermic scales.

20/12/83. Epidermic scales - sarcinous micrococci & ordinary micrococci - some in beaded rows.

18/1/83. Sarcinous micrococci are still present, also beaded rows of micrococci

I B = scarlatinal epidermis in aqueous humour

6/12/82 = Put up.

19/12/82. Not examined this now. Sarcinous micrococci are the predominant feature - ordinary micrococci - & epidermic scales also seen.
20/12/82 - Sarcinous micrococci still seen not so large as in I A

II A = Ordinary epidermis in aqueous humour
7/12/82 - Put up
12/12/82. The fluid is turbid + is found to contain torulae + micrococci - no rod shaped bacteria to be seen.
13/12/82 Full of small micrococci & torulae forms - epidermic scales.
20/12/82 - In addition to the above there are now some rodshaped bacteria to be seen.
16/1/82. Sarcinous micrococci are now to be seen as in I A.

II B. = Ordinary epidermis in aqueous humour
7/12/82 = Put up.
The result of several examinations showed that it resembles I A in most particulars. No torulae forms were seen.

I a = Scarlatinal epidermis in peptone solution.
6/12/82 = Put up.
11/12/82 - Fluid is quite clear, but the pieces of epidermis are surrounded by whitish fungus. On microscopic examination an epidermic scale is found to be surrounded by a mycelium

in the form of a dendritic fungus growth, branching like a tree, enclosing some micrococci in its meshes. It is ~~somewhat~~ similar to penicillium with conidia, single or in clusters, their relation to the filaments being not quite clear.

12/12/82 - Tubes - contains bacteria & micrococci

14/12/82 - an epidermic scale is found to be surrounded by a mycelium of large size in which are found many buds, which look like spores in formation. In the surrounding fluid are many rod-shaped bacteria.

15/12/83 - Epidermic scale - mycelium - is evidently in a more advanced stage. It is now not hyaline, except at the free ends. More deeply among the older mycelium, it is either granular, the granules being collected into irregular masses of a round oval or elongated shape, or it full of oval refractive spots - probably vacuoles. Groups of zoogloea are also seen.

^

I b, & I c. were not opened till 16/12/82. & were found then to contain micrococci & rod-shaped bacteria.

II a & II b = Ordinary epidermis in peptone solution

These were examined at various times & the result was that they showed as a rule micrococci - & bacteria.

The first result from these experiments was to shew that the fittest fluid in which to conduct the cultivations was aqueous humour. This was due partly to the fact that it could most easily be introduced in a pure condition into a small tube, & also because during cultivation some of the fluid could be abstracted more easily, & with less risk of putrefaction than from the large cultivation flask of the peptone solution. The sediment, also, so often produced during cultivation was more easily obtained from the former mode of cultivation.

I therefore decided, in the future, to employ aqueous humour in my experiments, & all the specimens that are described in the following pages are to be understood as being put up in aqueous humour.

I may here mention that, the purpose of these experiments being to see if the cultivation of Scarlatinal epidermis ~~anything special~~ any organism was produced which could not be produced by a similar cultivation of ordinary epidermis, of necessity a considerable number of specimens of both had to be cultivated & examined, & probably the best mode of comparing the two kinds is first to give the results of the scarlatinal epidermis, & then those of the ordinary kind.

I find that the following specimens of Scarlatinal Epidermis were put up & examined.

January	5.	one Specimen	
"	10	two	"
February	1	one	
February	7.	eight	"
January	29	two	"
February	19	three	"
"	21	three	" ~~from the~~
March	15	three	"
March	24	~~three~~ two	"
"	22	one	"
"	28	six	"
April	5	two	"
"	11	one	"
"	14	two	

The following specimens of Ordinary Epidermis were put up & examined.

January	23.	Five Specimens	
February	1	Four	"
"	8	Seven	"
"	20	one	"
"	21	one	"
March	15	three	"

Occasionally from some of these cultivations other cultivations were made, but these will be mentioned along with the results of the primary cultivation.

Cultivation of Scarlatinal Epidermis

5/1/83. Put up one specimen

12/1/83. Epidermic scales, micrococci & rod shaped bacteria

15/1/83. Presents the same appearance as before

10/1/83. Put up two specimens, both from the same individual, an ordinary case, in about the 3rd week.

12/1/83. A few micrococci

15/1/83. Epidermic scales, surrounded by a mycelium with spores in it.

16/1/83. The same appearance was presented, as is shewn in Fig. 1. The mass of Epidermic scales was surrounded by a dense mycelium, thickest in its deeper parts. The filaments composing it were hyaline for the most part, but contained at regular intervals bright oval spots, probably conidia or spores. Between the spores were marks across the filaments of transverse segmentation, as seen in the figure, each segment containing a spore.

Besides this fully formed mycelium, there was seen numerous filaments in an earlier stage (Fig. 2) when apparently the protoplasm in the interior of the filament had only just begun to divide transversely, as shewn of the transverse segmentation

The granular contents of each segment thus made has not yet been gathered into a spore, but that it has begun & do so is shewn by the rounded appearance assumed by the protoplasm at each end of the several segments.
There were also seen in other fields of the microscope, from the same specimen, quantities of free spores as in Fig. 5
They are bright refracting oval bodies, those figured in this plate being motionless, evidently elongating, & about to form new filaments & mycelium by segmentation.
They are thus older than the actively moving spores of recent origin, to be afterwards described.
In another field from the same cultivation were found filaments, as in Fig. 4.
Here we have a filament where the division of the spore by constriction has commenced inside the filament. The free Sporidia figured there shew the same process at slightly different stages going on outside the filament.

19/1/83. On examining the same cultivation again, the appearances shewn in Fig. 3 were seen. The filaments there figured ~~through~~ though observed three days later than the mycelium of 16/1/83, shew some appearances which belong to an earlier stage in the development of the bacillus.

The structures shewn in this figure serve in fact to connect Fig. 2 with Fig. 1.
In a we see a stage in the history of the filament slightly more advanced than the stage shewn in Fig. 2. Here we find the ends of each segment of protoplasm (coloured by magenta) have become more rounded than in Fig. 2, & owing to the greater concentration of the protoplasm each segment is now separated by a distinct interval. The centre of each segment is now observed, as is shewn in the figure, to be swollen, & broader than the ends, & whilst the rest of the segments stains with magenta, it is found to remain unstained, clear & refractive. Each segment thus formed, is still connected by the faint sheath of the filament.
In c we have another filament, which apparently is in a further stage of development than a. In it we have some segments at the same stage as a, whilst we also see some segments in which the spores are fully formed, the surrounding granular matter having totally disappeared.
This condition leads us to b, where we get a filament with nothing but spores in it, similar therefore to the filaments composing the mycelium of Fig. 1. The resemblance is apparent, though seen under different powers.

In Fig. 6 a is shewn a filament resembling that shewn in Fig. 3 a, though seen under a lower power. Here we have the division of the protoplasm into segments, with a swelling of the centre of each, denoting the position of the future spore. In the same specimen were seen spores in different shapes, some being similar to those in Fig. 5 Thus d is a young active spore, of oval shape, highly refractive, & in active vibratile motion, owing to the possession of a flagellum at one end, which was distinctly observed, & figured in the drawing.

c shews a later stage, when the flagellum disappears, & the spore becomes pear shaped, elongated, & constricted, till at length it assumes the figure of rod shaped characters as seen in b

20/1/83. Some of the appearances seen today are shewn in Fig. 7. Here we have an epidermic scale with myriads of micrococci, single - double - or arranged in a sarcinous form, all staining deeply with magenta.

29/1/83. Put up two specimens of Scarlatinal Epidermis.

31/1/83. One of these specimens when examined shewed the appearances given in Fig 9 (I)

Here a shews a segmented filament with vibratile motion, the probably being the same as that shewn in Fig. 2, only stained with magenta. b shews an earlier stage when the segments are shorter, & perhaps forms of fission, as they seem to be arranged in pairs. At c we have an epidermic scale with filamentous stained objects, probably a still earlier stage in which segmentation & growth of the filament has not yet occurred. d is probably the same as b, & in e, e we have a more advanced stage of a where the segment is beginning to swell in the centre, but as yet with no signs of the clear unstained spore at that ~~spot~~. In f we have a drawing shewing a further stage. Here each segment is all but occupied by an oval clear spore, having at one or both ends a minute particle of stained protoplasm, whilst in g we see each segment free, consisting of the clear spore, & the protoplasm at ~~each~~ one or both ends. These little bodies are actively motile, & probably have already at least the elements of one or two flagella becoming developed at their extremities. At j we see the spore alone, the protoplasm at the extremity of the bodies shewn at f having developed into a flagellum, as shewn in the figure. h is a spore developed into a figure of 8

body, prepared & it elongating into a segmented filamentous body as in a.

3/2/83. - Some of Fig. 9 was drawn from a specimen observed today, but the description of the appearances seen has been joined & that of 31/1/83. for the purpose of simplifying it.

5/2/83. Epidermic scales on which many gonidia are arranged in rows, & many lying in the fluid are a few bodies as at g Fig. 9.

1/2/83. Put up one specimen

5/2/83. Epidermic scales - mycelium - spores sarcous elements as at g Fig. 9. single - double, or 3 or 4 attached. Apparently it is commonest for such a sarcous segment to have protoplasm at only one end of the spore.

7/2/83. Put up ~~6~~ 8 specimens of Scalp Epidermis, being two cultivations each of ~~4~~ specimens from 4 different individuals They are respectively I a, II a, III a & IV a I b, II b, III b, IV b.

I a

9/2/83. Epidermic scales with micrococci

10/2/83. Epidermic scales with myriads of micrococci - with zoospores - & ~~&~~ rods shaped bacteria. No filaments, no spores, no sarcous segments

11/2/83. Epidermic scales - myriads of short bacteria darting across the field - zooglaea beaded filament of micrococci which stain with magenta.

12/2/83. Epidermic scales - bacteria - micrococci filaments ~~cocci~~ of micrococci - sarcinae

13/2/83. Epidermic scales - bacteria in active motion - micrococci - single & in pairs - a few short filaments - fragments.

14/2/83. Epidermic scales - bacteria - micrococci single - figure of 8 - & in rows.

15/2/83. Same as yesterday with zooglaea

16/2/83. Same as yesterday with sarcinae.

II a -

9/2/83. Epidermic scales - micrococci - single double - & sarcinous. also segments filaments of 2 or segments.

10/2/83. Epidermic scales - micrococci in myriads adherent to the scales - & bodies resembling figure of 8 bacteria - moving with vibratory motion - they dart short across the field. sarcinae - the young sarcinae when dumb-bell-shapes are larger than the micrococci & than the figure of 8 bacteria - a few short filaments quite similar in size & appearance to the elongated bacteria seen in ordinary epidermis

11/2/83. Epidermic scales - micrococci -

sarcinae - some micrococci in chains - which don't wriggle - they may contain be seen is faint vibration in the rest & double micrococci. Tonloid forms shown - oval & spherical in shape - some with one bud - they are larger than the sarcinae.
The filament seen unsegmented & similar to Fig. 8. When stained magenta it assists sarcinae stain deeply - tonloid bodies not at all.

12/2/83. Epidermic scales - micrococci - single & in rows. sarcinae - & filaments of 2 segments.

13/2/83. Epidermic scales - micrococci - single & in rows - figure of 8 - sarcinae.

14/2/83 Same as yesterday

15/2/83 } no change observed.
16/2/83. }

III a.

9/2/83 Quantities of figure of 8 micrococci

10/2/83. Micrococci in mycaid - no bacteria no filaments.

11/2/83. Epidermic scales - attached & thick on mycaid & micrococci - some are also free, single - double & in short chains - with vibratile motion. no bacteria - no filaments - no sarcinae - no tonloid forms.

12/2/83. Epidermic scales - micro-cocci - single & fig. of 8.

13/2/83. Same as yesterday - with some unsegmented filaments as in fig. 8.

14/2/83. Epidermic scales - micrococci - figure of 8 - in rows - some unsegmented filaments some ~~bacilli~~ bacilli of putrefaction with terminal spores.

16/2/83. Epidermic scales - micrococci - figure of 8 - & in rows & chains

IV a.

9/2/83. Epidermic scales - micrococci - figure of 8 - in rows

10/2/83. The micrococci in rows are more abundant - & move in a wriggling fashion.

11/2/83. Epidermic scales - unsegmented filaments as in ordinary epidermis - micrococci in chains - ~~bacteria~~ & not a faint vibration.

12/2/83. Epidermic scales - micrococci - single double & in rows.

13/2/83. Similar to yesterday.

14/2/83. Similar to yesterday

15/2/83. Epidermic scales - micrococci - zoogloea - a few short segments filaments.

The other series were not examined for 6 or 8 days after being put up, but unfortunately the records of some of the examinations have been lost.

I b

11/3/83. Epidermic scales - micrococci & zoogloea

13/3/83. The same with chains of micrococci

II b

6/3/83. Epidermic scales - micrococci - zooglaea sarcinae - & chains of micrococci

14/3/83. Epidermic scales - micrococci - sarcinae

13/3/83. Epidermic scales - micrococci -

14/3/83. Epidermic scales - micrococci - double & in chains.

III b

11/3/83. epidermic scales - micrococci sarcinae

13/3/83. epidermic scales - micrococci - double & in chains

14/3/83. The same as yesterday.

IV b

6/3/83. Epidermic scales - micrococci - filaments somewhat similar to mycelium of Fig. 1 with spores in the filaments

14/3/83. Maynard's well defines oval micrococci = spores.?

19/2/83 - Put up three specimens of Scarlatinal Epidermis viz. I, II, III.

21/2/83. Epidermic scales, micrococci - double & in chains - some sarcinae - & all moving in a vibratory manner.

22/2/83. Epidermic scales - micrococci - double & in chains - zooglaea - some sarcinae - a few short segmented filaments - similar to Fig. 9

23/2/83. Present the same appearances as yesterday

24/2/83. The segmented filaments ~~seemed & have~~ are still present.

26/2/83. The same appearances as yesterday - except that II shows some bacterial forms.

28/2/83. I. Epidermic scales, micrococci & the scales - quantities of forms of 8 - also chains a few filaments

II. Epidermic scales - micrococci - single double & groups.

III. Epidermic scales - micrococci - & a few bacterial filaments.

29/2/83. Same as yesterday

1/3/83. I Epidermic scales - micrococci - forms of 8 - & in rows.

II Epidermic scales - micrococci - forms of 8 - & in rows.

21/2/83 - Put up three specimens from a semi-malignant case - rash still out.

22/2/83. Epidermic scales - micrococci - single forms of 8 & in rows - some of the rows grow from the scale - from brush spots on them Are these spots spores?

23/2/83. Epidermic scales - myriads of micrococci - single - double & in rows or chains which are seen in some quantity.

24/2/83. Presents the same appearances.

26/2/83. Nothing new to note.

28/2/83. Epidermic scales - quantities of micrococci - with a wrapping membrane - many are in chains - zoogloea are also seen.

II Epidermic scales - quantities of micrococci many are in the scales figures of 8 + rods.
III Same as II, with some sarcinæ.

6/3/83. Present no new appearance

11/3/83. I Epidermic scales - micrococci - double chains - zoogloea - a few segmented filaments, with clear spots in them
II Similar to the above - fewer zoogloea - no staining the segmented filaments - spots & bodies resembling the sarcinous segments of Fig. 8 g. are seen.

13/3/83. I Epidermic scales - micrococci - figures of 8 - chains + some groups.
II Epidermic scales - imperfect micrococci - figures of 8 - rods.

14/3/83. I + II same as yesterday - micrococci - figures of 8 & in chains.

15/3/83. Put up three specimens of Epidermis

16/3/83. I Epidermic scales - micrococci figures of 8 - chains
II Epidermic scales - micrococci - figures of 8 - chains + some groups.
III Epidermic scales - micrococci - figures of 8 - chains - + some groups.

17/3/83. II Epidermic scales - micrococci - figures of 8 - chains + some segmented filaments
III Similar to II, filaments long & unsegmented longer.

19/3/83. I. Epidermic scales - micrococci - figures of 8 - chains - some groups.

II. Epidermic scales - micrococci - figures of 8 - chains - some filaments.

III. Epidermic scales - micrococci - figures of 8 - chains - some groups.

21/3/83. I - apparently putrid with bacterial filaments

II - Epidermic scales. micrococci - some in chains.

III - Same as II with some zooglaea.

24/3/83 I. Epidermic scales - micrococci - bacteria - no chains

II. Same as yesterday - scales - micrococci - some in chains.

~~21/3/83~~.

24/3/83 Put up two specimens of Epidermis from different cases. I was from a semi-malignant case in which the desquamation occurred very soon. II was from a mild case, desquamation also early.

I

26/3/83. Epidermic scales - micrococci - figures of 8 - round scales in a mycelium of beaded rows of micrococci

27/3/83. Same as yesterday - mycelium seen

28/3/83. Epidermic scales - micrococci - some in mycelium of beaded rows round the scales

as seen in Fig. 10.

24/3/83. Epidermic scales - mycelium of beaded rows of micrococci is very dense round the scales.

31/3/83 - 3/4/83. 10/4/83. & 13/4/83. all show the same results as before.

II

26/3/83. Epidermic scales - crowds of micrococci between cells - groups - no mycelium.

27/3/83. Epidermic scales - ~~mycelium~~ of micrococci between cells - groups. & chains

28/3/83 - 29/3/83. 31/3/83. when examined show the same results.

22/3/83. Put up one specimen of Epidermis - 5th day of disease

26/3/83. Epidermic scales - micrococci - rows of micrococci, & groups which look extremely like a densely packed mycelium.

27/3/83. Same as yesterday.

29/3/83. Epidermic scales - simple - double - rows & groups.

31/3/83 - 2/4/83. No change observed.

28/3/83. Put up six specimens of Epidermis all from diff different cases - & all from early stages of the disease

29/3/83. I - Epidermic scales - micrococci - figure of 8 - & groups

II - Scales - micrococci - beaded rows

III - Scales - quantities of micrococci - some in rows.

IV - Scales - micrococci - fig. of 8 - in rows

V - Scales - micrococci some in rows.

VI - Scales. micrococci - a considerable number being in rows.

30/3/83. I - Scales - micrococci - in rows & groups.

II - Scales. micrococci - in rows - & mycelium also some zooglaea.

III Scales - micrococci & mycelium

III & V - Scales - micrococci - some in rows

VI Presents the same appearance

31/3/83. I - Epidermic scales - micrococci - zooglaea & rows. Zooglaea looks as if formed from a mycelium of rows.

II Injected into rabbit.

III Epidermic scales - micrococci - figure of 8 - rows & mycelium.

IV Scales - micrococci - some in rows - a few rod shaped bacteria with spores - of putrefaction?

VI Epidermic scales - micrococci some in rows.

3/4/83. I - Epidermic scales - micrococci - zoo-glaea - no rows to be seen.

III Epidermic scales - some rows -

IV V Quantities of filaments with spores - probably of putrefaction.

III - Epidermic scale - micrococci -

10/4/83. III - Micrococci - simple chains + in zooglea.

13/4/83. III - Same as yesterday.

5/4/83. Put up 2 specimens of Epidermis I & II

I

6/4/83. Epidermic scales - a few micrococci - numbers of short segmented mobile filaments.

7/4/83. Epidermic scales - micrococci - groups of 8-rows & small groups. Segmented filaments still seen - some arranged in slight mycelium.

9/4/83. Epidermic scales - micrococci - groups of 8 + in rows. some filaments

10/4/83. Same as yesterday

16/4/83. Epidermic scales - bundles of crystals - micrococci + bacteria

II

6/4/83. Epidermic scales - micrococci - short indistinct segmented filaments.

7/4/83. Same as yesterday - some of the filaments being in a mycelium.

9/4/83. Epidermic scales - micrococci & filaments

10/4/83. Epidermic scales - micrococci - filaments some segmented - others with concentrated points of protoplasm in them.

13/4/83. Epidermic scales - micrococci - single double - & in rows. some filaments.

11/4/83. Put up one specimen of Epidermis.

12/4/83. Epidermic scales - quantities of micrococci - double & in rows

13/4/83. The rows are now in the form of a mycelium

14/4/83. Micrococci in rows - & mycelium which when $\frac{1}{25}$ in. lens is used shows the sarcous segments of Fig. 8. g.

16/4/83. Micrococci - sarcous segments - filaments with spores in them.

18/4/83. No change is observed.

14/4/83. Put up two specimens of Epidermis.

I

16/4/83. Epidermic scales - a few single micrococci - & several long filaments of micrococci in rows.

17/4/83. Exactly the same as yesterday - except that the rows are more abundant.

18/4/83. Epidermic scales - micrococci - fig. 8 - great quantities of beaded rows - some of considerable length.

21/4/83. Epidermic scales - micrococci - fig. 8 - rows forming a mycelium.

II

16/4/83. Epidermic scales - a few micrococci some of which are in rows.

17/4/83. Same as yesterday - rows more numerous.

18/4/83. The rows are now seen of greater length.

21/4/83. Epidermic scales. micrococci. in rows of some length. those at one end of the row being more clearly defined & moving more actively.

From II 14/4/83 a tube was inoculated on 21/4/83 which the following result.

23/4/83. Epidermic scales. micrococci. figures of eight. rows from the scales.

24/4/83. Micrococci. figure of 8. a quantity of rows. free & a mass of mycelium rows. Zooglea.

From the preceding another tube was inoculated on 25/4/83.

27/4/83. Epidermic scales. micrococci figure of 8. some rows.

27/4/83. Put up 2 specimens of Scarlatinal Epidermis 28/4/83.

I. Epidermic scales. micrococci. free & on scales, dumbbells. & sarcinæ as in Fig. 7. some in rows.

II Epidermic scales. micrococci. dumbbells & in rows.

Cultivation of ordinary Epidermis.

23/1/83. Put up four specimens: I, II, III, IV(M), II 7

25/1/83. Have examined 4 cover S & certain micrococci + bacteria of S.

30/1/83. The four specimens have examined & there epidermic scales - micrococci - tetrad cells

1/2/83. Put up four specimens - I M, II, III, IV, (7)

3/2/83. Examined all the specimens of + ve II 7 discovers micrococci in masses, + groups of segments of a fungus - mycelium — & somewhat like that of the bacillus in Sea-Natural Epidermis. No spores have seen either amongst them, or in the centre of the segment. Some filaments are composed of 2 segments, others of more up to six.

5/2/83.

I 7. Epidermic scales - micrococci by. of S + in groups

II 7. Epidermic scales - micrococci by. of S - sarcinae

III 7. Epidermic scales - rod shaped bacteria & micrococci - sarcinae.

III M. Epidermic scales - micrococci & bacteria

I M. Micrococci - rod shaped bacteria

6/2/83.

I 7. Epidermic scales - micrococci - simple type of S - some rod - bacterial filaments

II 7. Epidermic scales - micrococci - sarcinae & groups

III 7. Epidermic scales. micrococci - sarcinae zoogloea - a few rodshapes bacteria.

III M. Epidermic scales. micrococci & zoogloea.

IV M - The same.

7/2/83. T

II 7. The same as yesterday - only fewer filaments

II 7. Epidermic scales. micrococci zoogloea

III 7. Epidermic scales. micrococci zoogloea - a few rodshapes bacteria

III M. Same as yesterday

IV M. Epidermic scales. micrococci in zoogloea. some rods.

8/2/83. Put up seven specimens - I, II, III III, I, VI, VII.

I

9/2/83. Epidermic scales. micrococci - bacteria

10/2/83. Epidermic scales. micrococci - bacteria + sarcinae.

11/2/83. Epidermic scales. micrococci - Fungus of 8 - some rods. bacteria.

15/2/83. Present thus same appearance.

II

9/2/83. Epidermic scales. micrococci. a dense network of filaments, apparently structureless - dont stain with magenta - filaments branch - now amongst the

epidermic scales - stick out from the margins of clusters; much fewer than mycelium + are probably due to precipitation of some substance. They resemble a network of fibrinous threads.

10/2/83. Epidermic scales - micrococci bacteria, & the clear filaments of yesterday

11/2/83. Epidermic scales - micrococci bacteria - active & moving - some of considerable length - sarcinae & long filaments as on 9/2/83. Zooglaea & filaments as in Fig. 8. g.

12/2/83. Epidermic scales - micrococci - some in rows. sarcinae - bacteria - some of considerable length - & moving in a worm like fashion - also some bacilli of putrefaction with spores at the end.

13/2/83. Epidermic scales - bacteria - bacilli of putrefaction - zooglaea - + a few sarcinae

14/2/83. As before, in all essentials.

III

9/2/83. Epidermic scales - micrococci - sarcinae bacteria.

10/2/83. Epidermic scales - micrococci - sarcinae bacteria & a few filaments similar to dl

11/2/83. Scales - micrococci - zooglaea - sarcinae segmented filaments - some of great length viz. long & short Zeisi E, & similar to Fig. 8. f.

12/2/83. Epidermic scales - micrococci -

staff + in rows. long segments of filaments + sarcinæ

18/2/83. As before.

IV

9/2/83. Epidermis scale - micrococci - in zooglaea. bacteria in active motion

10/2/83. Epidermis scales - micrococci - bacteria

11/2/83. Scale - micrococci - bacteria - a few filaments of precipitation - zooglaea

12/2/83. Scales - micrococci - bacteria - sarcinæ zooglaea

14/2/83. Epidermis scale - micrococci - groups of 8 - some rows - sarcinæ - zooglaea - bacteria

18/2/83. As before in all essentials.

V

9/2/83. Epidermis scale micrococci - sarcinæ bacteria

10/2/83. Scales - micrococci - + filaments - segments - some similar to c others to e others to f, others to g of Fig. 8. - in one part of the field a filament like g unstained - was found at one end swollen + stained like f

11/2/83. Scales - micrococci - segments filaments similar to e g f d of Fig. 8. sarcinæ.

12/2/83. Scales - micrococci - zooglaea - filaments as in g.

18/2/83. Filaments are not seen in fields - otherwise - as before

VI

10/2/83. Epidermic scales - micrococci.

11/2/83. Scales - micrococci - filaments similar to g. minute masses (a) of apparently young zoogloea found sticking to epidermic scales - (Fig 10.). Very minute dim particles could be detected in them much smaller than ordinary micrococci (c'). On the general surface of the epithelial scale there were many minute dim particles, unstained, without zoogloea - as at b. : c = large micrococci.
Query. What are the germs in the case of the zoogloea masses a? Are they not merely excessively minute particles of protoplasm, that would present nothing but the appearance of extremely fine particles.

12/2/83. Scales - micrococci - zoogloea - filaments as in g.

14/2/83. Scales - micrococci in myriads of large sarcinæ - rolling about.

VII

9/2/83. Scales - micrococci - zoogloea - filaments of which drawings are made in Fig. 8

10/2/83. Scales - micrococci - some filaments

11/2/83. Scales - bacteria in myriads filaments as in c d & g. zoogloea.

12/2/83. Scales - micrococci - bacteria filaments as seen in g & d.

19/2/83. Same as before.

20/2/83. Put up one Specimen Ordinary Epidermis

22/2/83. Scales. micrococci single & double - & some filaments

23/2/83. Same as yesterday - with filaments & spores of putrefaction

21/2/83. Put up one Specimen

24/2/83. Epidermis scales - a few micrococci

28/2/83. Scales - a few micrococci - figures of 8 bacteria running across the field.

15/3/83. Put up three Specimens

16/3/83.

I - Scales - micrococci - figure of 8.

II - Scales - micrococci sarcinae - long segmented filaments wriggling across the field.

III Spi. scales - micrococci - figure of 8.

17/3/83.

I Scales - long filaments with spores in them forming a mycelium round scales.

~~IV~~ free spores - few or no micrococci

II. Micrococci - figures of 8

III Scales - short filaments - a few micrococci

19/3/83.

I Scales - quantities of spores - filamentous mycelium with spores & a few micrococci

II Scales - micrococci - figures of 8 & zooglaea

III Scales - micrococci - figures of 8, & a few narrow filaments.

Before any comments are made on the results of these cultivations, we will now give the result of an examination of the other great local lesion - viz - nasal discharge + sore throat - with an account of the cultivation of the former.

Unfortunately the type of cases at present prevalent is so mild that I have only been able to get 3 cases in which I examined the discharge - the 2 of which I have also cultivated. The discharge from these 2 I examined with care, staining it with methyl aniline & also with magenta, + found among the débris of mucous corpuscles &c. several micrococci single + double or dumbbelled. I thought that in one specimen I was able to see filaments with spores inside, but of this I was by no means sure.

After the death of one of the cases I examined some of the pharyngeal discharge, + was able to make out a few micrococci - single - double + some in rows - also a few segments filaments

On March 7. 83 I put up 3 specimens of fresh nasal discharge - with the following result.

I

11/3/83. Mucous Corpuscles - micrococci - figures of 8 - + in rows

14/3/83. Same as yesterday

16/3/83. Micrococci - figures of 8 - groups.

17/3/83 No change seen

19/3/83. Mucous corpuscles + micrococci in rows

21/3/83. Same as yesterday.

II

8/3/83. Mucous corpuscle - many bacl. micrococci with vibratg motion - figures of 8 - & beaded rows - sarcinous groups.

9/3/83. Mucous corpuscle micrococci - figures of 8 - & in rows. In one field were seen filaments with what seemed to be spores

10/3/83. Mucous corpuscle - débris - micrococci single & in rows. groups of very distinct oval micrococci

11/3/83. Mucous corpuscles - débris - micrococci - figures of 8 - rows.

13/3/83. Micrococci - figures of 8 - rows

14/3/83. Same as yesterday with some zoolaea.

15/3/83. The Same - no filaments

19/3/83. Myriads of micrococci - single - double - rows & groups.

21/3/83. Mucous corpuscle - débris - micrococci in rows.

III

11/3/83.

Micrococci - figures of 8 - zoolaea segments filaments probably bacterial

17/3/83. Rodshapes filaments present - few micrococci

16/3/83. Same as yesterday.

17/3/83. Fewer rodshapes bodies - more micrococci

single - double - in rows - a few zooglaea.

21/3/83. Same as yesterday?

The Urine was examined very regularly in a considerable number of cases - but very little result of a positive nature was obtained. As a rule there was a copious deposit of urates during the first week - of the amorphous kind, + occasionally other deposits were seen.

Not living organisms - a few simple micrococci were sometimes obtained, but whether they were due to external causes is not easy to say. The urine, of course, was fresh, + as soon as it was obtained some was put into a test tube, which had been cleaned in boiling water, + then closed with a plug of cotton wool.

On several occasions I injected the results of the cultivation of both scarlatinal epidermes + ordinary epidermes into rabbits + guinea pigs without any effect - as shewn by the thermometer - except on one occasion when I injected some of 28/3/83 II ~~4/4/83 I~~ into a rabbit whose normal temperature was about 100.5 - The result was as follows

2nd day	101.5	after this his temperature was normal. As well as a rise in temperature - there was diminution for food.
3rd "	103.2	
4th "	103.5	
5th "	102.	
6th "	101.	
7th "	100.8	

On 17/4/83. I inoculated ~~injected~~ a mouse with some of 14/4/83 I the result being that it died on 20/4/83.

The blood when examined contained a considerable number of vibrating micrococci - + then when cultivated gave as follows

21/4/83. Large growths of micrococci - some free micrococci - double + in rows. - also some segments of filaments

23/4/83. Micrococci - single - double. + in rows.

So much space has already been occupied by the account of these different observations + experiments that but little will be said on the possible conclusions to be drawn from them.

Even apart from the question of the cause of Scarlet Fever, several interesting results have followed the cultivation of Scarlatinal + ordinary epidermis.

In the earlier cultivations one was struck by the frequent appearance of sarcinous micrococci, which in some cultivations were extremely abundant, of large size + perfectly shaped. This form of micrococci, which was first discovered by Goodsir in 1842 as much uncommonly found in the human body. The sarcina ventriculi is of frequent occurrence in the stomach in cases of dilatation, sometimes in ulceration & catarrh. They are then associated with an acid fermentation of the gastric contents, & have been supposed by some to reach the stomach from the blood & transudation through the walls of the stomach. A sarcina urinæ is also said to occur, though perhaps developed after boiling of the urine, + they are also said to be found in cholera stools, the bronchi of the brain, & a few other parts of the human body.

That a sarcinous form of micrococcus is to be regarded as the ultimate cause of Scarlet Fever is entirely improbable, not only because it does not appear in any very large proportion

of the scarlatinal cultivations, but also because it was frequently present in those of ordinary Epidermis. It must also be remembered that it was never found in any of the other structures examined or cultivated. We must therefore look upon its presence as being entirely accidental.

Much more interesting, however, than the presence of the saprophytic micrococci, was that of the organism of the "bacillus" type, of which a tolerably full life-history has already been given, & from which most of the figures accompanying this paper have been taken. As Professor Greenfield says in his Lectures on the Pathology of the Infective & Contagious Diseases "There seems to be a sort of glamour about the very name bacillus."

Since the discovery by Cohn of a bacillus in boiled hay infusion, the number of new bacilli have been largely increased, & as the discovery by Koch of the bacillus tuberculosus has brought this type of organism still more prominently before the medical world, one felt inclined to jump to the conclusion that the bacillus scarlatinæ might be added to the list. The test, however, of corroboratory cultivations seems to indicate that its presence in the epidermic cultivations is by no means constant, & also I have been unable to find any trace of it in the blood, urine, nasal discharge, nor have I found it in any of the cultivations

of these structures. Any organism which lays claim to be the cause of a disease must surely be constantly found in that disease, as seems to be the case in tubercle, but here our bacillus does not stand this test, & therefore it is difficult to see that it can stand in any causal relationship to the disease. Also we must remember that in cultivation 15/3/83 I of ordinary epidermis there was found on 17/3/83 a mycelium resembling in all particulars that in Fig. 1, which goes far to shew that its presence is merely an accidental occurrence, however interesting it maybe.

Of course it may be urged that the non-presence of the bacillus in many of the cultivations is due to the (under the circumstances) unavoidable presence of other organisms, such as bacterium termo &c., which have been shewn by Professor Ewart in his "Life History of Bacillus Anthracis" to stop all active life in bacilli, causing the filaments to become granular & gradually to disappear. This might be the case in some cultivations, but there were by many in which no bacterium termo appeared, & yet there was no sign of any bacillus. The presence, however, in some cultivations of epidermis, of many organisms was unavoidable, as, owing to the nature of the object cultivated, a pure cultivation could not be obtained. This would, of course, not occur in the human body, where very few of the bodily

of the tissues, accidental organisms such as bacterium termo would not find a pabulum on which to prey, thus leaving the specific organisms free to spread in the system.

Apart however from the question of the part it plays in the causation of scarlet fever, the presence of a "bacillus" in a not unfrequent proportion of cultivations of scarlatinal epidermis is, to say the least, very interesting, & it may not be amiss to say a few words as to its similarity or otherwise to already known bacilli.

The bacillus anthracis is undoubtedly the one whose history has been most fully worked out, Professor Ewart by his paper on "the life-history of bacillus Anthracis" having left little more to be done in this connection.

According to him, the spores begin to escape from the filaments on the third day, only the débris of the filaments being visible on the fifth day. In the bacillus produced from the epidermis either owing to a lower temperature being maintained or from some other cause the spores do not usually appear till the sixth & the ninth day, & the filaments been entirely visible till after the latter date. The spores of bacillus anthracis grow at once into rods according to Koch & others, the rods being formed from the capsule. According to Ewart, however, the spores first elongate & become dumb-bell shaped, & then separate, forming two bright round bodies surrounded by a thin capsule, developed from the original spore. Each of these then go through the same

process, then forming four spores at first adherent to each other, but soon becoming free. A similar process is sometimes seen in a number of spores, & then a colony or zooglaea is formed, similar & but easily distinguishable from a group of micrococci. These spores germinate by sending a process out from one of the extremities, which pushes the capsule before it, till it finally disappears. By this means rods are formed, which when cultivated grow in length, become segmented, & then pass into spore-bearing filaments. These are sometimes formed into a mycelium, at first hyaline, but rapidly granular in appearance. This granular contents divide & sub-divide & in these subdivisions clear spots or spores begin to be formed. The filament now is made up of numerous segments each of which contains a spore at the adjacent ends of the several segments. To free the spores, one of two changes occurs. Either the gelatinous-looking envelope which surrounds the spores may swell so that the filament gives way & the spores escape; or the filament may break up into long & short pieces, the spores for some time remaining in the detached segments, or the filaments may remain entire retaining all the spores in situ. Whatever happens, the filament as it disintegrates, first gets granular, & then almost entirely disappears. Prof. Ewart adds that when the filaments break up into

short segments, in many cases containing a spore at one end, they may be easily mistaken for terminating spores. Young rods, however, as long as the remains of the spores are visible in them, are rounded at both ends; whereas pieces of filaments containing spores have always square or angular ends. When the filaments remain entire, their position sometimes through time can only be inferred from the spores remaining in exactly the same position as they occupied when first formed.

As to the bacillus under our consideration, its history seems to be somewhat as follows; The spore when young are general actively vibratile, possessed of a flagellum (Fg.6.D) they soon begin to elongate & become constricted, dumbbell-shaped + finally figure of 8 (At first of B&C Fg.6 a bright clear appearance they are now granular, & stain with magenta, which previously they would not do. (Fg.9.h) Each of the halves of the figure of 8 now elongate + subdivide again, till a segmented chain is thus formed (Fg.9.a+d.) Gradually these segments separate + we get a number of rods then formed (Fg.9.c) These, under favorable circumstances elongate & form filaments, hyaline at first, then full of granular contents, which are divided transversely forming segments. In the centre of each of these segments spores are formed by the concentration of the granular contents after which their development may occur in different manners.

In the first place (Fig. 3) all the surrounding granular protoplasm in the segment may be absorbed by the spore, & finally nothing is left but a hyaline filament full of clear spores at regular intervals. These escape either by disintegration of the filament then causing them to become free, or they may remain in the same relative position to each other & form a colony or zooglaea, the only remains of their origin in filaments being the manner in which they are formed & lie, viz. in lines, circles, & sinuous curves. It is very probable that the mode of freeing the spores is the same in both cases, but in one case it occurs in a fluid, & therefore the spores can move about, while in the other case it occurs in a solid, perhaps of a jelly nature, which glues them together. Both these modes of development were frequently noticed.

Besides this mode of development of filaments from the rods (Fig. 9 c) there seems to be another mode, in which the segmented filament (a a a Fig. 9) does not break up, but remain together. Soon the centre of each segment swells (c, c Fig. 9), & gradually a clear spore is developed (b Fig. 9), with some protoplasm at one or other extremity. Here, instead of waiting till the spore absorbs all the protoplasm, each segment separates, & thus are formed the sarcous segments (Fig. 9. g). These are actively motile, & gradually by the absorption of formation of a flagellum from the granular protoplasm, we get a spore formed (Fig. 6. D.

These filaments seem to differ from those of the bacillus anthracis mentioned by Prof. Ewart, as he expressly states that their distinguishing feature is the fact that they have square sharply cut extremities

So much for the bacillus found in the epidemic cultivations. The above will serve to show how similar in many points it is to the bacillus anthracis. The history of the bacillus tuberculosis has not yet been so fully made out as to admit of a comparison being made, but from specimens I have seen, there seems to be a stage very much resembling the saccous segment stage (Fig. 9. g)

As it seems from the evidence of the observations, & experiments already described, that the bacillus cannot be said to fulfil the requirements of the cause of the disease, we must try to see if any other organism seen in the cultivations &c. seems to do so.

It will be remembered that it was stated, that in a constitutional disease like scarlet fever, one would expect to find the cause of it, if it be due to a germ, existing in the blood. Accordingly the blood was most carefully examined microscopically with the result, as has been stated, of showing that the presence of a micrococcus in it was constant during the fever, several other conclusions being also drawn from these examinations, all of which have also been already stated. It has been seen also that the cultivation of the blood

produces nothing but micrococci - sometimes in rows. And if we look at the results of the cultivations of epidermis we find that micrococci are constant, some, I think, being always present in rows, sometimes short, but often of great length, and unfrequently forming a regular mycelium (Fig. 11.). The drawing of the mycelium does not fully give an idea of the great thickness of the mycelium, which sometimes almost covers the scale, on which it grows.

It is true that micrococci were also present generally in the cultivations of ordinary epidermis, but they were rarely found in rows, nor as of any small size, short in length, & were never found as a mycelium. The fact, however, of them being found is no argument against them being the cause of Scarlet fever, any more than against them being the cause of Erysipelas, or Diphtheria, or against them being the cause of pyaemia because they are found also in variola.

This theory that they are the cause of Scarlet Fever is also supported by the effects of inoculation. The Blood which contains them has been proved & held an immense proportion of rabbits inoculated with it. A cultivation in which they were found when inoculated ~~into a rabbit~~ into a mouse killed it, & after its death the blood was found to contain micrococci. A rabbit when inoculated with a similar preparation was ~~for~~ made highly feverish, but in fact nearly died. As to whether either of these inoculations

really produces Scarlet Fever in the mouse or in the rabbit is not easy to prove. It is quite possible, & very probable that it is a disease which cannot be produced in the lower animals, in which case verification of the discovery of its cause is of course made difficult.

Again the examination of the fresh epidermic scales, seems to favor the idea of the causation of the disease. As has already been stated, micrococci seem to spring from the most minute germs, hardly distinguishable from of the highest power of the microscope. It is quite possible therefore to examine epidermic scales & not make out anything definite beyond some dirt particles, as are seen in many scales, if examined.

And then if we argue from analogy, it is highly probable that such a theory is the correct one. We have already alluded to the fact that such diseases as Erysipelas & Diphtheria are due to micrococci, & we have pointed out the great similarity from a clinical point of view there is between Scarlet Fever & Erysipelas, & also that pathologically they have been collectively called the "pulrefactive diseases" Now Erysipelas has, as has been stated, very recently been shown to be caused by micrococci in the form of beaded rows.

What is more natural, then, than to suppose with all these facts before us, that a similar cause, that is to say, a different species of the

same germ should be the cause of Scarlet Fever. Positive proof of this, however, can never be reached until we find that the ~~product~~ disease can be produced in the lower animals by inoculation of a perfectly pure cultivation, often repeated by constantly inoculations. This of course I have not been in a position to perform. At the same time it must be kept in mind that failure in producing the disease by inoculation does not necessarily mean failure in discovering the germ causing the disease. This failure may be due either to the fact that the animal has already had the disease, a factor, I think, too too often left out of account, or to the fact that the animal is not liable to take the disease.

In conclusion, I would say that if the foregoing has assisted in any measure the further elucidation of the germ theory, I am well repaid for the months of work I have devoted on it, & fully aware as I am how much more yet must be done, I intend as suitable cases reach my notice to endeavour to place the subject on a still surer basis.

Finis.

— ·· —

Explanation of Drawings.

Figures 1, 2, 3, 4, 5, 6, 7 are all taken from the same cultivation (in the same tube of aqueous humour) of Scarlatinal Epidermis, of 10/1/83.
Figure 8 is from a cultivation of Ordinary Epidermis of 8/2/83, a b d & e being drawn from IV on 9/2/83, whilst f & g are from II, drawn on 10/2/83.
Figure 9 is taken from the cultivation of Scarlatinal Epidermis of 29/1/83, a b & c being drawn on 31/1/83, the rest on 3/2/83.
Figure 10 is from the cultivation of Ordinary Epidermis of 8/2/83, VI, being drawn on 11/2/83.
Figure 11 is taken from two cultivations; A being of Scarlatinal Epid. drawn from 24/3/83 on 26/3/83, & B from 14/4/83 & drawn on 28/4/83.

Figure 1. (made on the sixth day of cultivation) Zeiss 7
Mycelium of filaments containing ~~fila~~ gonidia, projecting from the margin of a mass of epidermic scales. g = gonidium a = filament with septa indicating transverse segmentation, each segment containing a gonidium.

Figure 2. (made on sixth day of cultivation). 1/25 in.
Earlier state of filaments. Fissure & concentration of protoplasm have occurred, but gonidia are not yet formed in the segments.

Figure 3 (made on ninth day of cultivation) 1/25 in.
Although this was drawn later, it is in reality

an earlier stage than Fig. 1.

a = formation of gonidia in the segments. One gonidium is formed in the centre of each segment. It does not stain with magenta. Its outline on each side is strong + sharp. The protoplasm in the remainder of each segment stains faintly with magenta. The free extremity of the protoplasm is of deep tint, + slightly knobbed.

b = A similar filament, gonidia fully formed. No stained protoplasm remains.

c = Filament with 2 fully formed gonidia, + 3 segments in which gonidia are being produced.

Figure 4 (made on sixth day of cultivation). $\frac{1}{23}$ in

a = Filament containing gonidia, one undivided, two ~~each~~ constricted, three divided.

b = A free gonidium divided, two halves clinging closely.

c = Free gonidium at a more advanced stage. A slightly greater separation between the two halves, resembling a figure of 8.

Figure 5 (made on sixth day of cultivation) $\frac{1}{18}$ in. oil immersion

a = Epidermic scales

b = Free spores lying on the scales - some oval, others pearshaped, others constricted, + others transversely marked, according to the stage of development. All are highly refractive, + bright.

Figure 6 (made 8 on ninth day of cultivation) Zeiss F

A = Filament with segmentation of the contents, somewhat similar to a Fig. 3, only it is unstained, & under a lower power. The position of the undivided condition in each segment is indicated by the swelling in the centre. The filament is motionless.

B = A condition in the form of a figure of 8, also motionless & about to elongate & form a filament.

C = Conidia, not so far advanced as B, one is pear shaped, some constricted, & some approaching figures of 8. Similar to those in Fig. 5.

D = A young motile active spore with a flagellum at one end.

Figure 7 (made on tenth day of cultivation)

Epidermic scales, with micrococci resting on them, some of them of saccinous form. Stained with magenta.

Figure 8 (made on second & third days of cultivation) 1/25 in.

a = micrococci stained with magenta.

b = Figure of 8 bodies - moving

c = A chain of figure of 8 bodies, with a fine filament, uniting each pair of segments. undulating motion.

d = Filament, faintly segmented.

e = Filament, no sign of segmentation - motionless

f = Filament, with some of the segments are swollen

g. = a segmented unstained filament.

Figure 9 (made on second & fifth days of cultivation) $\frac{1}{25}$ in.

a = Segmented filaments - vibratory motion. precisely the same as that shewn in Fig. 2.

b = Segmented filament - segments arranged in pairs.

c = Elongated bodies lying on an epidermic scale. Probably an earlier stage of a & b.

d = Segmented filament as at a

e = Segmented filament, where the segments are beginning to swell in the centre, no signs of the gonidium yet apparent.

f = Segmented filament, with gonidium beginning to appear in the centre of each segment - with stained protoplasm at one or both ends.

g = Free segments, with central gonidium, & stained protoplasm at one or both ends. Motile.

h = Free gonidium developed into a figure of 8 body, preparatory to its forming a filament

i = Free spores with flagella at one extremity, as in D Fig. 6.

~~Note that~~

Figure 10. (made on third day of cultivation) $\frac{1}{25}$ in

Epidermic scales of healthy epidermis.

a = zoogloea, stained magenta

c' = Very minute particles in the zoogloea - stained

b = Very minute particles - unstained

C = ordinary micrococci - some dumb-bell shaped.

Figure 11. (made on second fourteenth day of cultivation) 1/2 in.

A = Beaded chains of micrococci stain slightly with magenta

B. = An epidermic scale with dense mycelium of beaded rows growing from it.