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Thesis for M. D.

On Bacteria found in the Human Intestine

by

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The bacterial conditions existing in the human intestine in the various stages of life, & in health & disease, is a most fascinating, as well as an educative one. & for the purpose of this thesis I propose to give the results of investigations & state the views held by many workers in this field of research.

If meconium taken from a child at birth is examined it will be found to be sterile; on the other hand if ordinary faeces are examined, they will be found to be teeming with micro-organisms.

Though the intestinal tract at birth is sterile it is impossible in ordinary conditions of life for it to remain so. From the time the child first opens its mouth, bacteria gain an entrance & find their way into the digestive tract. They are found so soon in the faeces that Moro is of opinion that they enter by way of the anus from the external air.

Be that as it may, it is not long before the intestinal tract swarms with bacteria, & it may be interesting to investigate the various parts of

the intestinal canal inhabited by bacteria.

Distribution of Bacteria.

In the mouth both aerobic & anaerobic organisms are present.

In the stomach anaerobes are few owing to the action of the gastric juice & the presence of air; but where there are large masses of food, or a deficiency of hydrochloric acid, they may develop & set up fermentative & putrefactive changes. We thus see that the gastric juice has a protective action by lowering the vitality of organisms which are injurious to health.

In the duodenum & jejunum we find the fewest number of bacteria, due to the proteolytic action of the peptic ferment & tryptic enzymes. Cushing & Livingstone ("Contributions to the Science of Medicine by the Pupils of William Welch" 1900. p. 543) found that in gunshot wounds of this part of the intestine, the bacteria which escaped into the peritoneum did little or no harm.

In the ileum we find bacteria increasing in numbers until in the region of the ileo caecal valve they are more numerous than in any other part of the small intestine.

In the Large intestine we find the most dense accumulation of bacteria, & the best conditions for the growth of anaerobic organisms, & it is here that we find the most pronounced evidence of putrefaction. There is a gradual fall in the number of living bacteria throughout the caecum & colon, till they are comparatively few in the rectum.

About two thirds of the weight of faecal matter is composed of bacteria, according to Cohenzy, the majority of which are dead. One hundred & twenty six billions are said to be excreted per day! In the lower part of the bowel they undergo a process of disintegration, partly "stewing in their own juice"; in other words, a process of autolysis.

As the digestive tract is so rich in micro-organisms in health & at all ages, the question arises, what are they there for? Pasteur was one of the first to make enquiries on this point, & he expressed the opinion that these bacterial inhabitants are necessary ~~to the~~ in some way to the life of the individual that harbors them.

Are bacteria necessary in the process of digestion?

There is some conflicting evidence on this point:

Nuttall & Thierfelder ("Zeitschr. für Physiol." Chem. 1895, XXI. p. 109; 1896, XXII. p 62; 1897, XXIII. p. 231.) performed some interesting experiments. After delivering young guinea-pigs by Cæsarean section & keeping & feeding them for some days under sterile conditions, they found that they thrived well, & on being killed, the intestinal tract was found to be entirely free from bacteria. They proved therefore, that in the case of the guinea pig at any rate, intestinal bacteria are not essential to normal nutrition & well being.

This view is supported by the observations of Levin ("Skandinavisches Archiv. f. Physiol." 1904 XVI. p. 249.) who examined the intestinal contents of arctic animals at Spitzbergen, including bears, seals, reindeer, ducks, penguins etc. & found that except in three instances they were all sterile.

On the other hand Schottelius ("Munchener. med. Wochensch." 1898. No. 36.) experimenting with chickens; Madame Metchnikoff with tadpoles; ("Ann. de l'Inst. Pasteur". 1901. XV. p 361) & more with the larvae of turtles, came to the same conclusion, viz: that intestinal bacteria are necessary to normal nutrition.

It goes without saying that experiments conducted on animals do not carry the same weight with regard to human conditions, as experiments conducted on man himself, & in connection with the question under discussion I think the following experiment outweighs the former ones already described.

Mac Fadyean, ("Trans. Seventh Internat. Congress of Hygiene." 1892. p 80.) describes some researches made by himself & others at Berne. They had a case which had been operated on for intestinal obstruction, & an artificial anus had been made in the ileum just above the ileo-caecal valve. This condition remained for six months during which time the large intestine was of course completely shut off. & during this period they studied the bacteriological conditions of the faeces & the effect of varied diet on the intestinal flora.

They conclude that bacteria are unnecessary in man for the process of digestion. The decomposition of food in the small intestine is limited to carbohydrates, & the products (succinic, acetic & lactic acids) formed cannot be regarded as necessary to life. Further, any marked decomposition of proteids first takes place

in the Large intestine. This portion of the digestive tract was in their patient shut-off from any participation in the process of digestion, without the least detriment to health.

This, therefore, is strong evidence in favour of the theory that bacteria are not necessary to normal nutrition.

The defensive Action of Intestinal Bacteria.

Probably the most important function of the normal intestinal flora is not connected with digestion, but is that of defending the host against what have been termed the "wild races" of bacteria which have escaped the action of the digestive juices. These normal inhabitants of the intestine are necessary to bacterial foes which cannot be excluded from the intestinal tract.

We may now proceed to examine in more detail the various bacteria found in the intestine. Martin, ("The Lancet." Vol. II. 1909. p 1216) divides them into three groups. - (1) endogenous. e.g. B. Coli: (2) exogenous e.g. B. Typhosus. & (3.) putrefactive. I propose therefore to describe first, the normal intestinal flora, second: The exogenous, or pathogenic bacteria & to conclude with some remarks on bacterio therapy.

I. The Intestinal Flora. (Endogenous)

Certain differences exist in the varieties of Bacteria present in the intestine during the periods of Childhood, adolescence, & senescence.

1. In childhood. Tissier ("Ann. del'Inst. Pasteur." Paris, Feb. 25, 1905) states that in the intestines of nurslings, bacteria which are few in the Stomach are still fewer in the duodenum & jejunum, but progressively increase in the ileum, caecum and rectum where they reach their greatest number. Taking the bacteria found in the intestine from Stomach to rectum, the following is their order:— B. Lactis; B. Coli; Enterococcus; B. Ovidis; B. Acidophilus; & B. Bifidus.

In the Stomach the organisms are aerobic & feebly fermentative, whereas they become more anaerobic lower down, until in the rectum they are strictly so. Their fermentative action ceases proportionately.

The distribution of these bacteria is determined chiefly by three causes. (a) the sterilising action of the duodenal Secretions: (b) the oxidising action, more or less pronounced of the intestinal Contents; (c) the varying fermentative powers of the bacteria.

The bacterial flora in the nursling is only

c Tissier
Inst
1905 p 133

moderately numerous as regards variety, & the bacteria are concentrated in the regions that lie between the lower ileum & the anus. There is a marked diminution of living bacteria in the colon, due partly to autolysis, but many die from diminution of food & lack of moisture.

In bottle fed infants the number of bacterial forms present in the digestive tract is considerably greater than in the case of the nursling, & this is only to be expected when one considers the number of micro organisms present in most specimens of Cow's milk, which apart from specific organisms like B. typhosus etc, contain Streptococci & putrefactive anaerobes.

The flora on the whole is the same as in the nursling but whereas in breast fed infants B. Bifidus is the predominating organism in the large intestine, in bottle fed children B. Coli takes it place. Streptococcus Lacticus (Kruse, "Centrabl. f. Bakt. XXV, P. 737. 1903) is almost always present. also various diplococci, B. Cloacæ, a gas forming bacillus & B. Aerogenes Capsulatus.

2. In Adolescence. Normally most of the above organisms are present, but B. bifidus is not so numerous & there is a greater number of putrefactive organisms.

3. In adult life. At this period there is a greater difference in the habits of persons than in earlier ages. People live at greater stress; there are more variations in diet; they indulge in tea, coffee, alcohol, tobacco, often to excess; their life is often more sedentary than before; & they have more worry. It is also at this period that we find increased putrefactive processes in the intestine. B. aerogenes Capsulatus & even B. putrificus may be abundant.

4. In Senescence the ordinary obligate bacteria are present, but their activity is diminished. B. Coli may not be so numerous & B. aerogenes Capsulatus & B. putrificus are more numerous.

It is therefore clear that there are distinct differences between childhood & old age, the chief one being a tendency towards increasing putrefactive changes. Metchnikoff has often advanced the theory that old age is due to intestinal infections, probably due to putrefactive organisms.

The Intestinal Bacteria may be divided into two classes (a) proteolytic, which act on nitrogenous substances producing putrefactive & toxic products & (b) amylolytic, which act on hydrocarbons. The products of the latter variety are less toxic, & some tend to check nitrogenous putrefaction. The amylolytic organisms

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are found chiefly in the small intestine, the proteolytic in the large. (Jabronski)

The chief products formed by the proteolytic organisms acting on ~~albuminoid~~ alimentary residues are butyric & valerianic acids, leucin & leucein, tyrosin, carburetted & sulphuretted hydrogens, indol, skatol, cresol, etc. (Bouchard)

Some of these products are converted into ethereal sulphates which appear in the urine, & by their presence & amount we can measure the amount of intestinal fermentation

Influence of food on the Intestinal Flora.

Not very much is known on this subject, but some interesting observations have been made. With a meat-diet, (i.e. raw meat) Gram-positive organisms, a good many of which are putrefactive ~~organs~~ anaerobes, are the predominating microbes in the faeces, whereas in herbivorous animals Gram-negative are most numerous. Escherich found in a young dog whose milk-faeces flora was very similar to that of normal nurslings, that after a pure meat-diet the Colon bacilli were greatly diminished, whereas there appeared large numbers of liquefying colonies.

Lembke, (Archiv. f. Hyg. XXVI, P. 325. 1896.) experimented on dogs with meat, fat, & bread diets. Curiously enough he found that a bread diet rendered the faeces much richer in anaerobes than did a diet of meat. The changes induced by alteration of diet were generally

of a transitory nature. He says: "If the diet is changed, there appear on the faecal plates new colonies of the most varied sort. In the course of a few days these are materially reduced, & the colonies of B. Coli again gain the upper hand."

It may be of interest to study in more detail the three chief obligate bacteria of the human intestine viz - B. Lactis aerogenes, b. coli, & b. bifidus

B. Lactis Aerogenes.

This bacillus is found most abundantly in the upper part of the small intestine, diminishing in number till in the Colon there are very few, & usually none in the faeces

There is a close resemblance between this organism & B. Coli; the morphological differences are very slight but the bio-chemical characters show several differences. It seems to require for its growth the presence of milk sugar, hence its absence from that part of the intestine where milk sugar is not found. (Holt: "Diseases of Infancy & Childhood." 1906, p. 322.)

B. Lactis forms gas more readily on Sugar media than B. Coli; coagulates milk more readily (often with Capsule formation): evolves gas from potato starch; grows more luxuriantly on gelatine; & there is a more frequent failure to make Indol.

B. Lactis has greater fermentative powers than B. coli but less putrefactive powers.

Harden states ("The Chemical Action on Glucose of the Lactose fermenting Organisms of Faeces"; Journ. of Hyg. V. 1905, P488.) that there is a constant difference in the action of B. Lactis & B. Coli, when grown anaerobically on Sugar bouillon, in regard to the ratio of alcohol & acetic acid produced.

The chief physiological action of B. Lactis. as before mentioned, is its action on <u>milk Sugar</u>. This it decomposes, with formation of Lactic acid, acetic acid, (Baginsky) carbon dioxide, hydrogen, & methane. This action is not hindered by the bile. The B. Lactis has no action of importance on either the fat or Casein of the milk.

<u>Virulence of B. Lactis.</u>

Little or nothing is as yet known on this subject. It is believed not to be pathogenic, but in Cases of intestinal fermentation, e.g. when over ripe fruit has been eaten, it may add to the fermentative process

The Bacillus Coli Communis

This bacillus was first isolated from human faeces by Escherich. ("Deutsche Med. Wochenschrift" 1885, No. 2.) & it is interesting to note that he then thought it was the cause of Asiatic Cholera

Its characteristics are well given in - H. Escherich & he. Pfaundler "Bacterium Coli Commune"; Kolle & Wassermann's "Handbuch der Pathogenen Mikroorganismen" p. 334. 1902; also "Note on B. Coli Communis & Related Forms." "Amer. Jour. of the Med. Sci." Sept. 1895, by Theobald Smith.

The Bacillus Coli is one of the obligate bacilli; is Gram-negative, & is in all probability the most important micro organism found in the intestinal Canal. It is regarded as a normal inhabitant of the large intestine, & is to be found there in large numbers, except in certain pathological conditions.

In appearance it is a short rod, closely resembling b. typhosus & is motile, due to cilia which may be single or multiple, but not so long or wavy as those possessed by the latter bacillus. It produces thermostabile and thermolabile substances (Conradi & Kurpjuweit, "Ueber die Bereitung der Bakteriellen Hemmungsstoffe für die

~~Beiträge~~ Physiologie und Pathologie des Darms."
"Münch Med. Wochenschr." LII, p.p. 2164, 2228
1905.) which have a powerful antibacterial action
even in a dilution of 1 to 10,000; it is this action
that accounts for the large number of dead alien bacteria
found in the large intestine. These substances are also
capable of destroying the B. Coli itself (autolysis).

The members of the B. Coli group are organisms
characterised by varying morphology: hardy growth
on ordinary media; free production of gas & acid
on sugar: Coagulation of milk; usually form
indol. The fully grown forms have sluggish
motility, but younger groups are more actively
motile. They have an inhibitory action on putrefactive
anaerobes.

The Chief Cultural Characteristics of the B. Coli
are as follows — 1. Incubated on Agar at 37°C for
24 hours, the colonies formed viewed by transmitted
light are denser & more glistening than those
of B. Typhosus, & are of a brownish white Color.
2. On Gelatine & Agar the appearances are the
same as in the case of B. Typhosus, but the growth
is freer, whiter, thicker, & more opaque.
3. A potato Culture in 48 hours shews a brownish
film of growth which rapidly spreads & becomes

thicker, thus differing from a culture of B. Typhosus which forms a colourless film.

Bacillus Coli & the Coagulation of Milk.

In connection with this important function of b. coli: an interesting paper is communicated by Savage "Journal of Path. & Bact." Vol X. 1905. p. 96. His Conclusions are as follows.

1. Curdling of milk by b. coli is due in almost all cases to the formation of acid - presumably lactic acid - by the bacteria.

2. Milk b. coli which curdle only after some days. Lateness in curdling is due to diminished production of acid.

3. Only in a very few doubtful cases can the curdling be ascribed to an enzyme.

4. An enzyme is present in B. Coli, obtained from many varied sources when grown in milk media; but in general it plays no part in the initial curdling, coming into action subsequently, converting soluble Caseinogen into insoluble Casein.

The morphological resemblance between B. Coli & B. Typhosus is so close that it is important to enumerate their chief distinguishing cultural characters.

Virulence of B. Coli.

Since its first description by Escherich, a considerable change has taken place in the views currently held with regard to the rôle that the above organism is supposed to play in human & animal pathology.

Escherich himself, although he had shown that the bacillus could produce a fatal toxaemia in animals, was of the opinion that it was quite harmless to man. Before long, however, evidence began to accumulate to show that the organism was widely disseminated & had pathogenic properties & Since Favel of Berne first reported a case of infection of a gaitre wound by b. coli ("B. M. J." 1887, Vol II. p. 1187) up to the present time, an extensive & formidable list of pathological conditions have been traced to B. Coli.

In 1893. Hurtz ~~found B Coli~~ describes in "Archiv. de Médecine Expérimentale" cases in which he found b. coli to be the causative organism. His list includes (1.) Cholera nostras, dysentery membranous colitis, & other intestinal lesions; (2) peritonitis, (3.) angiocholitis & cholangitis; (4) Cystitis; (5.) various pulmonary affections; (6) endocarditis; meningitis; (8) arthritis. Since then many

more Conditions have been added to the list. Indeed, there are few pyogenic Conditions at the present time in which ~~has~~ B. Coli may not be found. It is capable of producing powerfully poisons, as has been shewn by many observers including Carega ("Ueber die aktiven Substanzen des B. Coli" Centralbl. für Bakt. Aug. 1903.) & in these pyogenic troubles, some of the Symptoms are due to these toxins.

Can the B. Coli produce an actual Septicaemia as distinct from Sepraemia? This is a point that is not quite decided yet. & there are many difficulties in the way. Post-mortem findings are discounted by the differences of opinion held by bacteriologists as to whether the b. coli may invade the body during life from the intestine or not. There are three opinions. (1) The earliest view, that it migrates post-mortem, & it is a fact that it multiplies with extraordinary rapidity after death, & penetrating from the alimentary Canal, may be found in distant organs, such as the Liver Heart, within a few hours of death. (Coats "Manual of Pathology" 4th Ed. 1900.) (2) That the organisms first gain entrance to the body during the so called agonal period which immediately precedes death.

3. That the B. coli may invade the body during life either through healthy or diseased intestines, and either itself producing a Septicaemia modify the course of a previously existing Septicaemia, or prepare the way for a Septicaemia to be caused by some other organism.

It would seem therefore that the most reliable cases are those in which the B. coli has been found in the blood during life. There are some cases recorded which would seem to prove the last mentioned theory. In one recorded by Königer, "Histolog. Untersuchungen zu Endocarditis." ~~[illegible]~~ death resulted from Septic ulceration of the aortic valves. During life the Colon bacillus was isolated from the blood during the early stages of the disease, in pure culture, while Colon Streptococci were also found. Sirodey, in Zieglers "Centrabl. der Path." 1896. P. 771. reports a case of general infection during an attack of influenza. Nowakowski & Moro. in "Klin. Therapeut. Wochenschrift." 1901 report two fatal cases in children where Colitis was found post-mortem. Sittmar & Barlow in "Deutsch. Archiv. für Klin. Med." Bd. 52. Hft-3. 1894, record a case of general B. coli Septicaemia following a local urethral infection. In all these cases

the B. Coli was found in the blood during life.

In experiments on animals, it has been found by various observers that a mixed infection with B. Coli was much more virulent than a pure one & that an organism, harmless by itself, became virulent when mixed with B. Coli. (Widal & Besançon, "Revue Trimis. Suisse d'Histol." 1894.)

Sims Woodhead ("The Lancet", 1896, Vol. I. p. 982) said that he believed that many so called streptococcal infections were really Secondary to Colon infections

If a virulent bouillon culture of B. Coli be injected into a vein of an animal it produces a rapid Septicaemia, with haemorrhages in various organs. If however the virulence is not sufficient to kill, atrophy of the anterior cornual cells takes place causing hypasthenia, then paralysis & atrophy of the muscles.

Although the evidence of the existence of B. Coli Septicaemia in man is on the whole slight, Gillman Woodhead thinks it exists & quotes a case in favour ("The Practitioner." Vol. LXXIV. p. 776) He thinks that possibly its existence in some cases accounts for the inefficacy of anti-streptococcic Serum.

Is the B. Coli capable of becoming pathogenic as long as it is confined to the Intestine?

In the early days of bacteriology, many pathological conditions were placed to the account of B. Coli without sufficient evidence. For example many cases of diarrhoea said to be caused by B. coli, were ultimately found to be due to B. dysenteriae. & even B. typhosus was confounded with it.

MacFarland in his "Text-book of Pathogenic Bacteria." p. 574. says that in infants "Cholera Infantum," may not infrequently be caused by B. Coli, though he qualifies this remark by stating that "probably in this disease, other bacteria play an important rôle."

Cumston, ("International Med. Magazine." Feb. (1897.) made a careful study of Summer diarrhoea in infants & came to the following conclusions: (a.) B. coli seems to be the pathogenic agent in the greater number of cases of Summer diarrhoea. (b) The organism is often associated with Streptococcus pyogenes. (c) The virulence is almost always in direct relation to the condition of the child at the time the culture is taken. (d) The motility of B. Coli is in general, proportionate to its virulence.

It is probable that in these cases B. coli took

on a virulent- action through being a mixed infection.

Lesage ("La Semaine Medicale" Oct-20, 1897) Studied fifty cases of enteritis in infants, due to B. Coli. He found in forty of these cases that the blood of the patient agglutinated the cultures obtained, not only from his own stools, but from those of all the other cases. It is also interesting to note that he found that the agglutinating action only occurs in the early stages & acute forms of the disease.

Sir A.E. Wright has described cases of mucous colitis which were most obstinate & extreme, & which were cured by vaccines of B. Coli, & thinks that they were due to B. Coli infection

Such evidence as the above, supposing that the organisms were real typical Colon bacilli, is in favour of the theory that the B. Coli may cause acute diseases of the intestine.

On the other hand there seems to be plenty of evidence that in Chronic disorders ~~where~~ putrefactive decompositions occur; but even in these cases there must be putrefactive organisms present, because the members of the Coli group cannot initiate active putrefactive of native proteids

Bacillus Bifidus.

This was first described by Tissier. ("La Flore intestinale normale et pathologique du nourrisson." Thèse de Paris. 1900.)

It is a slender Gram positive bacillus of moderate length & thickness, usually with a bifurcated extremity, hence its name. It may occur in three forms, a plain bacillary form, a bifid form, & a capitulated (knobbed) form. It is closely related to B. Coli & was grouped with it by Escherich before Tissier's investigations. It is an acidophile & under certain conditions inhibits the growth of some of the anaerobic organisms such as B. aerogenes Capsulatus of Welch. in this respect also resembling B. Coli.

As has been mentioned before, it is found chiefly in the intestine of nurslings but usually disappears by the fourth year.

Herter however states that in certain cases of infantilism there is a persistence of the flora of the nursing period. In these cases he found in abundance B. Bifidus & an allied organism which he calls B. Infantilis.

II. Pathogenic Bacteria found in the Human Intestine.

Having discussed the normal intestinal flora, we may now turn our attention to some of the bacteria which are hostile to man & which are found in the intestine in pathological conditions of which they are the cause. To describe all the bacteria which are responsible for diseased conditions of the intestine is outside the scope of this work.

The most important group of pathogenic bacteria of the intestine is the Colon-typhoid group which includes

1. B. Coli.
2. B. Typhosus.
3. The Paratyphoid group of organisms.
4. B. Dysentericus & its allied organisms.

All these organisms are linked together by most intimate affinities & in the early days of bacteriology were often confused. Many forms of diarrhoea which are undoubtedly due to B. dysentericus were thought to be caused by B. Coli; even B. Typhosus was confounded with the Eatton bacillus. Thanks however to the progress made in methods of identification, the differences between the various members of this group have been more sharply defined; & though there

is still plenty of work to do in this respect; we know fairly well the effects & limitations of each organism.

We may now take each organism Separately.

1. B. Coli.

This bacillus has been already studied (see pp. 13-21) both as a normal inhabitant of the intestinal tract, & as a pathogenic agent. At the present time there is very little evidence of any weight against B. Coli as a cause of pathogenic conditions of the intestine per se, & it will be interesting to note in the future whether such evidence will accumulate. The tendency has been for it to assume a non pathogenic rather than a pathogenic rôle as an inhabitant of the intestine. Will this continue?

2. Bacillus Typhosus.

This bacillus was discovered by Eberth ("Virchow's Archiv." 1881-1883) & first secured in pure culture by Gaffky. ("Mittheilungen aus dem kaiserl Gisund.")

I do not propose to give detailed descriptions of these bacilli with their cultural & biochemical characters. These are well known & will be found in any text-books of bacteriology.

This bacillus is closely affiliated to the colon bacillus, but differs from it in important biochemical properties & is much more pathogenic to man. What relation it bears to the B. coli in the long process of evolution we do not at present know.

The existence of the intermediate bacilli, - paratyphoid & paracolon - is well established, & the fact that these are transitional forms is suggestive of a descent from a common ancestor.

Lorrain Smith ("Lancet" Dec. 16th, 1905) reviewing the results of recent investigations on the various forms of disease associated with the Colon-typhoid group, came to the conclusion that in each case the disease forms a clinical unity, while the bacilli producing it might belong to more than one type. This conclusion applied to typhoid fever, dysentery, meat-poisoning cases associated with Gärtners bacillus, & Coli infections.

The usual portal of infection in typhoid is the digestive tract, but the bacilli may gain an entrance by the throat. While the bacillus has its primary seat of action in the lymphatic tissues of the intestines, the fever is very largely due to its growth in the internal organs. As Maclagan very well puts it, the action is dual, one a local specific action of the parasite on the glands of the intestine, & a general action of the organisms on the blood & tissues. A single bacillus, as he says, in ten days might produce a billion, & the incubation represents the period during which the bacilli are being

reproduced. (Osler's "Principles & Practice of Medicine" 1904. p.7.) In proof of this it may be noted that B. Typhosus has been demonstrated in faeces during the incubation period by Conradi "Klin. Jahrbuch." Bd. XVIII.; Mayer "Centralbl. f. Bakt." Vol VIII, 1910, p.234.; & Simon, "Klin. Jahrbuch." Bd. XVII.

Not only can the bacilli be found in the stools during the incubation period, but there is evidence to shew that these cases can infect others. Klinger, in the "Journal of the R.A.M.C." Jan. 1910 describes an Epidemic in which, out of 812 Cases of enteric in which Contact infection was proved, 183 had been infected by subjects in the incubation period.

B. Typhosus Can be Cultivated from the blood during the first week of the illness in over ninety per cent of cases, & this fact explains many of the Complications & Sequelae of the disease, - enlargement of the Spleen, Cholecystitis, bacilluria etc. (Coleman & Buxton)

There seems little doubt that the organisms enter the blood & general System via the intestine. Can they enter through an absolutely intact wall? Cases have been described. (Pick, Cheadle, etc) have described cases where after careful Search, no intestinal lesions could be found, but as Osler says, they may have been overlooked, or slight lesions may have healed.

Osler also states ("Practice of Medicine." P.7) that there is no conclusive evidence that typhoid bacilli can ever enter the body, except through the intestinal tract. This is rather a sweeping statement to make, & there are one or two cases recorded which would seem to negative it, though the proof is not substantial enough. Henry & Rosenberger, ("Amer. Jour. of Med. Science." Feb. 1908.) found in a case of meningitis, that both the blood & Cerebro spinal fluid obtained by Lumbar puncture gave Cultures of B. typhosus. There were none of the usual Symptoms of typhoid present, & they consider it a case of primary Lesion due to B. typhosus. Lawenson ("Univ. of Pennsyl. Med. Bull." April, 1908.) records another case, which gave all the Symptoms of meningitis. On the 8th day of the illness the blood gave a positive Widal reaction. At the post-mortem absolutely no Sign of any intestinal Lesion was found but there was a purulent meningitis caused by B. typhosus. He thinks this is a case of primary meningitis, & that the infection was an aerial one by way of the nasal passages.

One curious factor in regard to the B. typhosus is the fact that it may be recovered from the urine & stools of persons who had suffered from the disease for some very Considerable time after the attack. Dean, ("British Med. Jour." March. 7th. 1908.) records

the Case of a medical man in which, twenty nine years after an attack, B typhosus could still be isolated from the stools, & Gregg (quoted in "Amer. Jour. Med. Science" Aug 1. 1908) reports a case in which the interval was forty nine years, & many more instances might be quoted. These persons who harbour B. typh. in their excreta are called "Carriers", & the Germans divide them into "acute" & "Chronic Carriers" according to the length of time they harbor the bacilli many outbreaks of the disease have been traced to these Carriers, & the problem of dealing with such cases is occupying the attention of many workers at the present time.

It is a well known fact that the gall bladder is a favourite habitat of the B. typhosus. Cushing ("Bull. of John Hopkins Hosp." IX. No. 86.) invariably found in the bile in typhoid, clumps of B. typh resembling the agglutination of the Widal reaction. He thinks these clumps probably form nuclei upon which the bile salts are precipitated & Calculus formation is begun, & of course gall stones are a very Common Sequela in persons who have Suffered from typhoid, & typhoid bacilli have been found in gall stones removed at operation. Cushing mentions Six Cases. Sometimes B. coli & other organisms of the group are found in Cases of Cholelithiasis. Blumenthal made an

interesting Study of fourteen Cases of Cholelithiasis, the result of which is recorded in "Deutschen Archiv. fur Klin. Med." Leipzig. 1907. Bd 88. In ten of the Cases he found Organisms of the Colon Typhosus Group. the other four were Sterile. In four of the ten he found B. coli; B typhosus in four; B. paratyphosus A in one; & a modified B. coli in another. He thinks the presence of B. Coli is often accidental & that the importance of it in the Causation of inflammation of the gall Bladder has been overstated, & that of B. typhosus underestimated.

The Widal Reaction, or Agglutination test, is greatly used in the diagnosis of typhoid fever, & a few remarks on it may not be out of place.

It was first discovered by Widal & Grunbaum working independently, in 1896 ("La Semaine Medicale", 1896. p. 295) If the Serum from a patient Suffering from typhoid be added to a culture of Typhoid bacilli, the latter form in Clumps & lose their motility.

Stengel & Kneass ("Amer. Year Book of Med. & Surg." 1908) Collected & tabulated nearly 4000 cases, & found that 96.5 % of the typhoid cases gave the reaction; 98.4 % of non-typhoid cases gave no reaction; in other words the results were correct in 96.5 %; incorrect in 3.5 %.

There are Several fallacies in Connection with the Widal reaction which detract somewhat-

from its action as a diagnostic measure are as follows.
1. Infection with allied organisms (e.g. B. paratyph. B.) may cause the serum to clump B. typhosus.
In general, the <u>casual</u> organism is the one which is clumped in the highest dilution by the patients' serum. But this is not invariably the case, as it has been repeatedly found that the serum from meat-poisoning cases infected with B. Enteritidis Gärtner clumped the B. typhosus in higher dilutions than the <u>casual</u> organisms.
2. The agglutinating reaction does not usually appear for <u>seven days</u> from the onset; sometimes ten, in some cases not until the convalescent-stage is reached. Conradi ("Deutsch. Med. Wochens." Oct: 10, 1907) has shown that in 85 cases of contact infection, 49 were contracted during the first week of the illness. Therefore it does not do to rely too much on the Widal test for diagnostic purposes.
3. A patients' serum may acquire the power of agglutinating the B. typhosus during an infection which is in no way related to it. Wilson ("Brit. Med. Jour." 25th Sept: 1909) has found that the serum of <u>typhus fever</u> cases gives a positive reaction with B. typhosus.

The presence of B. typhosus in the blood & stools is therefore a much more trustworthy method of

diagnosis than the Widal test. In this connection Rémy ("Ann. de l'Inst-Pasteur." Aug. 1900) says that he believes the constant presence of the typhoid bacillus in the stools in cases of typhoid fever, & its absence from them in other conditions is a far more important & valuable method of diagnosis than even the Widal reaction.

Antityphoid serum & vaccines will be considered under Bacterio-therapy.

3. The Paratyphoid & Allied Bacteria.

The importance of this group was first thoroughly studied by Prof. Theobald Smith ("Centrabl. f. Bakt." VII, 1890, P. 504; XI, 1892, P. 367.) By means of careful biochemical studies, agglutination reactions, etc. a large group of pathological bacteria have been discovered. The group includes

1. B. Paratyphosus, A & B isolated from path. conditions in man
2. B. Paracoli.
3. B. Enteritidis (Gärtner), isolated in meat-poisoning cases.
4. B. Botulinus, also found in meat-poisoning.
5. B. Suipestifer (Salmon's B. of hog Cholera)
6. B. Psittacosis, occuring in diseases of parrots.
7. B. Typhi murium, isolated by Löffler in epidemic enteritis in mice
8. Danysz's Bacillus, also pathogenic to mice.

The pathological effects produced by these organisms include general Septicaemic manifestations on one hand, & gastro-enteritis on the other.

Many of these bacteria are the cause of animal diseases, but some are pathogenic for man especially the following.-

B. Paratyphosus.

Of late years many cases of fever running a course like that of typhoid, but as a rule milder, have been put down to the cause of B. paratyphosus.

The first cases were described by Achard & Bensaude in 1896. In their two cases the paratyphoid bacillus was isolated, in one from the urine, & in the other from pus in the right sterno clavicular joint.

Owing to agglutinative & cultural differences, this bacillus has been divided into two groups A. & B. & the latter group appears to be widely distributed.

Clinically, the B. paratyphoid B has the same effect in man as B. Typhosus. It agglutinates in highly diluted sera thus differing from the latter which requires a low dilution.

Yates ("The Lancet." Vol I, 1907, p. 1571.) records two cases, a mother & daughter living together, in which the disease was at first thought to be typhoid, but in both cases agglutination tests were positive with

B. paratyphosus B, negative with B. typhosus, & B. paratyphosus A.

Though paratyphoid fever is usually sporadic it would seem that it may occur epidemically. Hoskins ("Journ. American Med. Assoc.." Mar. 19. 1910) describes an epidemic of thirty five cases clinically resembling typhoid. The blood-serum of sixteen of these cases which were tested reacted positively with B. paratyphosus B. & not with B. typhosus.

F.A. Bainbridge ("The Lancet." Vol II. 1910, P. 555-6.) describes an outbreak of acute enteritis, with pyrexia lasting several days. All the cases recovered but convalescence was prolonged. In the stools of some of the patients B. paratyphosus B was found, while the blood-serum of six of the fourteen cases clumped this bacillus

An out-break of ptomaine poisoning occurred at Wrexham in 1910, affecting 107 persons, with five deaths. The out-break was caused by the consumption of pork pies, which were found to contain the B. paratyphosus B. Several cases gave agglutinative tests with this bacillus, & it was cultivated from blood taken from the heart of one of the fatal cases. Three persons nursing this fatal case caught the disease by contact & one died.

The cause of the outbreak was traced to a "Carrier", one of the Confectioner's staff, who made the pies. The bacillus was isolated & Cultivated from this person who was, as usual in "Carrier" Cases, in perfect-health.

B. Faecalis Alkaligenes.

This is another of the Colon group of organisms. It was first- isolated from faeces by Petruschky ("Centrabl. fur Bakt. u Parasitenk." IXIX. P 187. It- Causes fever which is Clinically inseperable from mild forms of typhoid. Its Cultures are not- agglutinated by typhoid serum.

B. Enteritidis (Gärtner.)

This bacillus was first- described by Gärtner, ("Korrespond. d. Ally. ärzlt Ver von Thüring, 1888. No 9.) who cultivated it- from the flesh of a cow killed because of an intestinal disease, & from the spleen of a man poisoned by eating meat- obtained from it-.

It- is found in diseased meat- & Causes gastro-enteritis in twenty- four hours, but- in Some Cases the effects are immediate, probably due to the presence of a Large quantity of toxin. It- produces an haemorrhagic enteritis & usually a Septicaemia with inflammation of Serous membranes.

Parson ("Lancet" Feb. 19th. 1905. p 430) describes two cases of Continued fever Lasting for fourteen days

& were in some respects like typhoid. On many occasions however, the serum was negative to the Widal test, but gave very definite clumping with Gärtner bacillus. Cultures were made from the urine & faeces but B. Enteritidis was not isolated.

Another organism of the paratyphoid group, & one which resembles in some respects B. aerogenes Capsulatus is the

Bacillus Botulinus.

This organism was discovered by Van Ermengem in 1896 ("Centralblt. f. Bakt. u Parasitenk." XIX. p443) He isolated it from a sample of ham, which eaten raw, had caused an outbreak of poisoning. It acts like the tetanus bacillus, by causing a toxaemia, the toxin being absorbed from the intestine & acting on the central nervous system for the most part.

This particular form of toxaemia is termed botulism. The symptoms include paralysis of the eye muscles ptosis, nystagmus, paralysis of accomodation etc. then swelling & paralysis of the tongue, pharyngeal & laryngeal paralyses, & disturbances of the heart & respiration. Usually there is no local action on the alimentary canal.

Van Ermengem points out that meat may be extensively contaminated with this bacillus & relatively large quantities of its toxin, without any ordinary signs

of decomposition being present. The production of an extra-cellular toxin by this organism ~~with~~ having an extremely potent action on the nervous System is a fact of great Scientific interest & has a bearing on the etiology of other Obscure nervous affections.

4. Bacillus Dysenteriae

This bacillus was confused with the B. coli, until Shiga differentiated it in 1898 ("Centrabl. für Bakt. u Parasitenk." 1898, XXIV, Nos. 22-24) & it is now known to be the cause of wide spread intestinal disorders of temperate & tropical climates which are grouped under the term dysentery, & including true bacillary dysentery.

The organism would appear to have different characteristics in different parts of the globe. Flexner, investigating an out-break in Manila, found an organism allied to Shiga's but differing from it in the capacity of fermenting Sugars, like B. Coli in this respect. Flexner confirmed the opinion that other varieties of the bacillus - Celli, Fisca & Scala are identical with that of Shiga. ("Univ. of Penn. Med. Bulletin." Aug. 1901)

There are said to be five groups of bacteria found in dysentery (Shiga & Hiss) & they resemble the typhoid bacilli in being hemi-parasites; that is, their invasive & destructive properties are only developed

when they have been introduced into the intestine in considerable numbers, or have had an opportunity of multiplying due to feeble powers of resistance on the part of the individual.

Chmo ("The Philippine Journal of Science." Vol I, no. 9, 1906) found in Manila fifteen varieties of the dysentery bacillus all shading into one another but distinguished by fermentative, agglutinative, & other tests.

B. dysenteriae has been found to be the cause of Summer diarrhoea in infants, especially in America

Duval & Bassett ("American Medicine." Sept. 13th. 1902, p. 417.) found it, especially when such diarrhoea were epidemic.

Dunn ("Archiv. Pediat." New York. June, 1905) investigated an epidemic & found it to be the cause of most of the infectious cases.

J. C. Torrey ("Journ. Experiment. Med." N.Y. 1905. Vol VII. no. 4) studied over 100 cultures from twenty-two cases of Summer diarrhoea. It is claimed that bacilli resembling the dysentery organism may be recovered from even the mildest cases of Summer diarrhoea

He divided the bacilli found into two groups:

(a.) the dysentery group giving typical reaction, & the

(b.) pseudo-dysentery group giving atypical reaction.

The points of resemblance indicate a general or family relationship. which may be compared to that existing between the true & pseudo-diphtheria groups. The pseudo forms may be, & perhaps in some ~~[illegible]~~ cases have been mistaken for the true dysentery bacilli, but are probably devoid of active pathogenic properties.

It is worthy of note that the dysentery bacillus in its different varieties resembles the typhoid & paratyphoid organisms in one very important manner; viz- that the severest forms of disease are dependent on the bacteria farthest removed from the Colon bacillus in their biochemical characteristics, - in the first group Shiga's bacillus, & in the other, the typhoid bacillus.

In an interesting paper on Tropical dysentery by Capt. Blackham. R.A.M.C. in "The Lancet" Vol II 1906, p. 1499, he comes to the following Conclusions.

1. That notwithstanding slight cultural differences, the various strains of B. dysenteriae isolated by Shiga, Flexner, Kruse, Vaillard, Harris etc. are simply varieties of the same organism. In addition to these pathogenic strains there are several strains which are non-pathogenic. Whether the latter represent degraded or transitional forms of the true bacillus he cannot say.

2. The specific agglutination reaction with the serum of persons suffering from acute dysentery can generally be obtained within two weeks following onset.

He maintains that the clinical entities which we have hitherto termed dysentery, are not one disease, but a group of maladies of varying degrees of severity, ranging from acute dysentery as found in India, to the simple infective diarrhoeas occurring in infants & adults.

Putrefactive Organisms.

There are several Spore bearing Aerobes found in the Intestine. Of these. B. Aerogenes Capsulatus, & B. Putrificus are perhaps the most important

B. Aerogenes Capsulatus (Welch.)

This a gas producing bacillus described by Welch & Nuttall ("Bull. of the John Hopkins Hosp." Vol. VIII. 1892. July & August.) who gave it that name. It is identical with the B. perfringens of Bissier & Fraenkel's gas-phlegmon bacillus.

It may be found in small numbers in the intestine of the majority of healthy adults. & in fewer numbers in children.

In pathogenic conditions it is often very numerous & Welch & Flexner ("Jour. of Experiment. Med." Jan. 1896. p6.) found it in Cases of gastric &

duodenal ulcer, typhoid ulcerations of intestine strangulated hernia. Dudgeon & Sargeant (The Lancet Vol. I 1905, p 550 found it commonly in appendix abscess.

Tissier ("Ann de l'Inst. Pasteur." XIX, 1905, p. 273.) describes instances of superficial necrosis causing an intestinal affection of children, which he ascribed to the presence of almost pure cultures of B. perfringens otherwise B. aerogenes.

An organism was isolated by Klein ("Reports Med. Off. Loc. Gov. Bd." XXV. p 171; XXVII. p. 210.) from evacuations in an outbreak of diarrhoea following the ingestion of milk containing the bacteria, to which he gave the name B. Enteritidis Sporogenes & which was subsequently found by him in certain cases of infantile & summer diarrhoea; in certain instances in milk; & as a constant inhabitant of sewage. There appears to be some doubt as to whether this organism is not identical with B. aerogenes. Klein's organism however was motile & sporulated much more readily.

We thus see that B. aerogenes is found in many diseases & associated with the intestine. It is certain that there are various strains of the bacillus as regards pathogenicity, & that the different

results obtained by different investigators with respect to that feature are due to this fact.

There are cases of intestinal putrefaction in which the predominating organism is B. aerogenes Capsulatus & it is often found in great numbers in cases of muscular atrophy, pernicious anaemia & other chronic disorders.

Bacillus Putrificus (Cadaver bacillus)

So called by Bienstock. It is like B. aerogenes Capsulatus a spore bearing strict anaerobe. Bienstock ("Ann. de l'Inst. Pasteur." XX. p. 407. 1906.) says there are two organisms B. putrificus & B. paraputrificus; the former decomposing proteids & the latter sugars.

Its part in intestinal putrefaction is difficult to tell, as it is apt to be associated with other microbes especially B. aerogenes & some of the cocci.

Rodella ("Arch. f. Hyg." lviii, 1905. p. 329) says it is a cause of caries of the teeth.

Streptococcal & Staphylococcal Infections of the Intestine.

The human intestinal tract in health is probably normally free from cocci, as they are destroyed in the stomach & duodenum.

Children are more susceptible to these infections

& Booker & Escherich think that some of the severest forms of ileo Colitis in infants are due to Streptococci.

In many of these cases there is little doubt that they are secondary to other infections - viz those of the colon typhoid group.

Cumston ("International Med. Magazine." Feb. 1897) made a careful study of thirteen cases of Summer diarrhoea. He thought that B. Coli was the pathogenic agent, but notes that it was often associated with Streptococcus Pyogenes Congus.

In adults, it is rarely that the intestine is affected by Streptococci, unless they are virulent. It is interesting to note that a chronic Streptococcal diarrhoea often precedes, or occurs during the course of cases of severe or pernicious anaemia.

Steele-Perkins describes a case of mucous Colitis ("The Lancet." Vol. II. 1910.) in which he found Streptococcus Pyogenes Congus, & a bacillus having characteristics between B. Coelis aerogenes & the Bacillus of Friedländer. A vaccine prepared from these two organisms effected a cure.

It is well known that occasionally phlegmonous gastritis is due to Streptococcal infections.

In appendicitis streptococci are often found in large numbers, though their true relationship to the

disease is not quite settled. Dudgeon & Sargent ("The Lancet." Vol. I. March 4th. 1905) studied many cases of appendicitis & found the following organisms present in varying numbers in various cases:—
B. Coli in different strains; Streptococcus pyogenes; the pathogenic Staphylococci; B. aerogenes Capsulatus of Welch; B. pyocyaneus; & the usual intestinal flora.

They found that the most virulent organism was Streptococcus pyogenes, & that cases with which it was associated were almost inevitably fatal.

A case of pneumococcal Colitis has been described by Hale White & others in "The Lancet" Vol. II. 1909. P. 1590.

Very little is known at present as regards Staphylococcal infections. The organisms have been found in abundance in cases of intestinal putrefaction but their significance is unknown.

There are still one or two important organisms which may be briefly alluded to. Amongst them is

Spirillum Cholera Asiatica.

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This, as its name implies is the cause of Asiatic Cholera & was discovered in 1884 by Koch. ("Deutsche Med. Wochenschrift." 1884-1885. Nos. 19-20, & 37-39.)

It is also known as the Comma bacillus. It is not a true bacillus, but really a Spirochaete. In acute cases they do not invade the intestinal wall, but in more protracted cases they are found in the depths of the glands. Koch was unable to find the organism in the internal organs. & Concluded that the Constitutional Symptoms of the disease result from toxins absorbed from the intestine.

Of more interest here in this country is the

Bacillus Tuberculosis.

Tubercular disease of the intestine may be primary, or more commonly, Secondary to disease of the lung. The primary form is more frequent in Children, & may set in with Colicky pains diarrhoea & fever. The Secondary form is very Common in the later Stages of phthisis.

Chronic hyperplastic tuberculosis may exist in the Caecum. giving rise to a tumour like mass in the right iliac fossa. Hall & Simpson. ("The Lancet." Vol. II. 1905. p. 1320) describe a Case affecting the ascending Colon. They believe it to be a Case of primary infection of B. tuberculosis in the mucous membrane of the Caecum.

Can pulmonary tuberculosis be caused by invasion of b. tuberculosis from the intestine?

This is a question that has not yet been decided.

Von Behring states that in adults pulmonary tuberculosis is due to absorption of tubercle bacilli from the intestine in Childhood. But this view is rejected by Calmette & Guérin ("Ann. de l'Inst. Pasteur." 1905. Oct. 25. P. 601.) From the results of experiments on animals, they state that the adult is more susceptible to pulmonary infection by intestinal route than the infant.

On the other hand, in the same no. of the journal quoted above. Prof. de Valée describes experiments on calves in which he gave T.B. by the mouth, & found that they quickly invaded the mesenteric glands & the lungs, without causing any intestinal lesion. He concludes that pulmonary lesions following on absorption of T.B. from intestine are much commoner than supposed, as the tubercle bacilli leave no trace in the intestine.

It may be interest- while describing pathogenic bacteria to glance at some of the organisms which have been discovered in the search for a specific organism for Infantile Diarrhoea.

As we have seen B. dysenteriae has often been associated with it. In these cases it is usually

Flexneri variety that is found. B. Coli, Streptococcus Longus have also been mentioned as a cause of the disease, whilst amongst other organisms are the typhoid bacillus, Gärtner's bacillus, B. pyocyaneus etc.

Among recent observations are those of Morgan, Hc & Sedingham ("Proced. Roy. Society Med." 1909, ii Epidemiological Section, p 133) have found in 63% of cases examined, in stools & intestine an organism non-motile, which has been called "Morgan's no I. bacillus." This is probably another factor in the disease. They found in 50% of such cases that a positive agglutinative reaction was obtained.

Stenhouse Williams & Others in Liverpool have discovered an organism which they term "Bacillus Y." Which differs from Morgan Bacilli, & all others. They say it is closely related to the paratyphoid group.

It is thus apparent that so far there is no one specific organism for diarrhoea, & as I have pointed out ("The Practitioner". Vol. I. 1906. p. 705.). there probably is not one. Most workers would appear to forget the influence of decomposing food in the etiology of this disease.

III. Bacterio-Therapy.

Owing to the genius & research work of Professor Elie Metchnikoff, Bacterio-therapy is now a well recognised method of influencing the nutrition of the body, assisting physiological processes, retarding degenerative changes, & preventing or arresting existing diseases. Yet when all is said & done, this new branch of therapeutics is still in its infancy.

There are three methods by which bacteria or their products can be utilised as remedial agents.

1. Injections of Serums.
2. Injections of vaccines
3. Bacteria given by the mouth.

1. Serum Therapy.

Following on the successes obtained with anti diphtheritic serum, workers began to try the effects in other diseases & with the diseases we are concerned with, most of the work done applies to dysentery & typhoid.

Antidysenteric serum has been used for some years & there is an increasing amount of evidence to show that its effects are beneficial. The dysentery bacillus secretes a soluble toxin so that a true antitoxic serum can be produced.

Shiga says that sub-cultures from the first-generation of bacteria are more effective in the preparation of serum than that ~~obtained~~ prepared from bacilli obtained after passage through animals (Shiga, Osler's "System of Medicine". Vol. II. p. 798)

As in most cases of Serum therapy, the earlier in the disease the treatment is given, the better the result. If 80 c.c. of polyvalent serum is given when the diagnosis of dysentery is made, followed by 80 c.c. of the specific serum, there is improvement in from four to twelve hours.

In Amoebic dysentery it is useless to try serum treatment.

Antityphoid serum. Compared with the serum treatment of dysentery, that of typhoid has so far not given very encouraging results. The typhoid germ invades the blood but does not seem to produce a soluble toxin, & Vaughan who has done a great deal of work in this respect thinks that it is extremely unlikely that any antitoxin comparable to that of diphtheria will ever be obtained.

Stern, ("Zeitschrift für Hygiene." 1894, Bd. XVI P. 458.) found in the blood of persons convalescent from typhoid, a substance which had a protective action upon infected guinea pigs. This observation has been abundantly confirmed by other workers,

notably Vaughan ("Amer. Journ. Med. Science", Sept. 1908) who terms it a proteid poison. This endotoxin, or residue, has been used as a therapeutic measure, & has given better results than serum treatment. Richardson ("Boston Med. & Surg. Journ." 1907. clvii. p.449) gives his experiences of serum therapy in 130 cases of typhoid. He says (1) that an early diagnosis being often impossible, specific therapy is consequently seriously handicapped. (2) Specific therapy seems to increase the tendency to relapse. (3) Anti-typhoid serum is no more effective than residues & much more expensive. (4) The non-toxic residues of Vaughan seem to lengthen the course of typhoid, but render it milder, & are apparently very effective in preventing relapses.

2. Vaccine therapy

Amongst the earlier workers in connection with this treatment was Haffkine who used a vaccine in the treatment & prophylaxis of Asiatic Cholera. His method was followed by a positive diminution in mortality in protected cases. ("Le Bull. Med. 1892. p.1113. "Brit. Med. Journ." 1893. Vol I p.278)

Following on this Wright, at Netley, introduced a similar method of vaccination against typhoid.

Antityphoid vaccine consists of a sterilised bouillon culture of B. typhosus of high virulence. which is injected subcutaneously. Wright was able to show that in the S. African war his method diminished the death rate among those inoculated ("The Lancet." Sept. 6th. 1902.)

This vaccine is used both as a preventative & as a curative agent.

(a) Prophylactic inoculation is largely carried out in the British & American armies.

Capt. Scaife R.A.M.C. ("Journ. R.A.M.C. Aug. 1910.) found that under his charge twenty three cases of typhoid occurred among the uninoculated with three deaths, & four among the inoculated with no deaths. Moreover, in the four inoculated cases there were no complications.

Russell ("John Hop. Hosp. Bull." Mar. 1910) in the American Army used it on 1400 men totalling 3640 doses. & concludes that vaccination undoubtedly protects to a very great extent against the disease, & is indispensable in the case of troops & others exposed to infection. The procedure is easily carried out & no untoward results occurred in the whole series of his cases.

(6). Therapeutic inoculation. There is an increasing amount of evidence to shew, that this method of treatment of typhoid is distinctly beneficial. Waters ("Boston Med. & Surg. Journ." Mar. 24. 1910) gives the result of vaccine treatment in 210 cases of typhoid, as against 70 cases untreated in this way. Vaccination appeared to shorten the duration of the fever by nearly ten days while the number of relapses among the untreated was three times as great as that of the vaccinated.

Richardson ("Journ. Amer. Med. Assoc.", Jan 22. 1910) was not so fortunate in his experiments, but vaccination in his cases seemed to have a distinct reducing action on the number of relapses.

Capt. Smallman R.A.M.C. ("The Practitioner" Sept. 1910) did 36 cases of whom two died, but he noted an unusual freedom from relapse & complication in the remainder.

Capt. H. J. Wilson ("Journ. R.A.M.C. Aug. 1910) records six cases treated with vaccine. The cases were all brought under treatment early & were not severe, & the treatment was decidedly beneficial.

The results therefore of anti-typhoid vaccine as a therapeutic agent are most encouraging.

There are cases of other intestinal disorders

where vaccine therapy has been attended with good results. & Cases of mucous Colitis cured by vaccine are described on p.ps 42. & 21.
L.P. Stephens ("Ind. Med. Gazette." June 1909) records a case of of chronic dysentery subjected to various treatments in the course of five years, which was completely cured by vaccine therapy.

At present the dosage of vaccine is the stumbling block to progress in this form of therapy, & when more accurate dosage is obtained, the results will be more brilliant than they are at the present time.

3. By the mouth.

The method of administrating bacilli by the mouth as a therapeutic agent has been introduced in recent years, chiefly by the advocacy of Metchnikoff. He believes that old age is due to the absorption of poisons, the products of putrefactive organisms living in the large intestine. These organisms require an alkaline medium & he suggested rendering it acid, so that the putrefactive organisms would not be able to exist. As a convenient method of attaining this result he gives lactic acid bacilli, which are non-pathogenic, & easily acclimatised in the intestine. When this is accomplished, the bacilli

flourish & produce Coctic acid.

Tissier. ("Ann. de l'Inst- Pasteur." No 5. Tome XIX.) found that in some cases of infantile diarrhoea of fermentative origin, the B. bifidus disappears & other organisms, including B. perfringens take its place. In recovery he noted that these abnormal forms disappeared & that B. bifidus reappeared. He found that by giving per os. b. bifidus & the Coctic acid bacillus, the development of b. perfringens ceased & a cure was effected.

Moro ("Munchen. Med. Wochenschr." 1906, No 41., Bd liii.) tried Tissier's plan, He found it necessary to give large quantities of B. acidolactici, & thought the results were better when given per rectum.

Moro's plan however has not been followed by other observers.

Dunn. ("Arch. Pediat".) N.Y. April. 1907) tried it also in 35 Cases of fermentative diarrhoea of children with very good results.

The same author in the ("Journ Amer. Med. Assoc. Aug. 21st. 1909) gives details of 120 cases treated in this manner. He used butter milk which was first- pasteurised & then inoculated with pure cultures & ripened. Twelve of his cases were of the irritative type & did not benefit by treatment.

8 were of the infectious type. - 4 benefited & did not. The remaining 100 were fermentative: in 74 the treatment was entirely successful, in 12 it was partially so & in 14 it failed.

Since this method of treatment was introduced it has been taken up & used indiscriminately both by the profession & the laity as a cure-all for all sorts of diseases, & this accounts partly for the pessimistic feeling with which it is regarded to-day.

There are however certain cases in which it does good. Grunbaum ("Brit. Med. Journ." Nov. 19. 1910) finds it useful in three classes of cases: (1) Those in which the irritating micro organisms cannot flourish in an acid medium; e.g. in many forms of mucous Colitis: (2) Where putrefactive toxins are produced too readily, or are excreted too slowly, as in certain cases of intestinal toxaemia, & in disordered renal Secretion: (3) Some cases of "maladie imaginaire".

It is also useful in cases of typhoid & other forms of enteritis. gastric anacidity, chronic intestinal Catarrh, pernicious anaemia, sub-acute & chronic nephritis, rheumatism & gout.

Conclusions.

1. That Bacteriology has made, & is still making, great strides in advancement since Smarts of Edinburgh discovered the 'germ' of rinderpest in 1865
2. That improved methods of technique must soon explain morphological differences in bacteria which biochemical methods prove to be identical.
3. That the function of the normal intestinal flora is not concerned with the process of digestion, but is that of antagonising bacterial foes which gain an entrance to the intestinal tract.
4. That abnormal putrefactions in the intestine are mainly effected through the agency of anaerobic bacteria.
5. That the Bacteriology of the Intestine is now explaining the Cause of many of the so-called "cryptogenetic" diseases.
6. That the severest forms of intestinal diseases are dependent on bacteria which in their bio-chemical characteristics are furthest removed from the Colon bacillus.
7. That there is no one Specific organism which is the Cause of "Cholera Infantum"
8. That Bacterio-therapy, though as yet only

in its infancy, is one of the greatest advances that has been made in recent years, & must in time replace 'eclectic' methods in the treatment of disease; & that vaccine therapy in particular has an immense future before it.