and even effusion into some of the joints being present and producing a considerable resemblance to rheumatic fever. Usually some symptoms very soon occur that show that the case is not one of ordinary rheumatic fever or of scarlet fever or measles, but the fundamental point is that we should not adopt any form of treatment which may be harmful should the case turn out to be one of enteric fever.

Tuberculous peritonitis is a disease that is apt to be very protean in its manifestations, sometimes coming under observation simulating cirrhosis of the liver, in other cases presenting resemblances to malignant growth, in others simulating acute intestinal obstruction under a band.

Again, many very chronic diseases of the nervous system, tabes for example, sometimes may have an apparently sudden onset, in other words the patient quite suddenly becomes ataxic, although it is not very obvious to what this sudden onset of symptoms is due. On examination such patients show well-marked signs of the disease, and very often a history is obtained that points to the conclusion that the malady has really long been present. It cannot be too frequently urged that acute symptoms may occur quite suddenly both in the course of chronic and of latent diseases as well as at the onset of acute maladies.

Errors Dependent on Treatment.

We must also, I am afraid, admit that some of our errors in diagnosis are dependent on our treatment. It is well recognized that some of the most disastrous errors in the diagnosis of abdominal diseases arise from the too-ready administration of morphine to relieve the pain, so that all the symptoms and sometimes even the signs of the underlying condition are masked.

Belladonna is a drug which not uncommonly produces very marked symptoms in the course of its use in the treatment of disease. Thus, meningitis may be erroneously diagnosed in a case of phthisis where the whole trouble is really dependent on the employment of belladonna administered to relieve the cough. Again, in Graves's disease the use of belladonna may produce excitement almost of a maniacal kind and simulating very closely the profound psychical disturbance that is seen in the more serious forms of Graves's disease.

Alcohol is not uncommonly pushed to an extent to produce coma, which is then regarded as dependent on the underlying malady, and sometimes anomalous symptoms may be dependent, as every practitioner knows, on the patient secretly obtaining some variety of alcohol.

The Natural History of Disease.

In order to avoid as far as possible errors in diagnosis, we must not only be cautious in interpreting the value of symptoms and careful in our examinations to detect physical signs, but it is of paramount importance to be familiar with the natural history of disease, and especially to know thoroughly the various modes of onset of particular affections, and the very diverse clinical pictures that are produced by one and the same disease in different individuals. Gastric ulcer, phthisis, malignant endocarditis, general paralysis of the insane, tuberculous peritonitis, and granular kidney are all instances of common maladies which may present very different modes of onset, and it is far more important to recognize the various clinical types or groups of symptoms presented by common diseases than to remember all the various symptoms which may be produced by any given disease. The important point is that these symptoms may in different instances of the same disease be differently grouped. Thus, one patient with gastric ulcer will present symptoms of a haemorrhagic type, another simply those of chronic gastritis, a third perhaps will only present signs of anaemia, and a fourth no signs at all until a perforation occurs. What is true of gastric ulcer is true of many other common chronic diseases, and the importance of studying the natural history of acute or chronic diseases cannot be overestimated if we wish to avoid errors of diagnosis.

DESTRUCTION OF A BRAZILIAN MEDICAL SCHOOL.—The Medical College of Bahia, Brazil, with all its equipment and valuable library, was almost totally destroyed by fire in March. The loss of the reference books and numbers of rare works of the early masters and files of medical journals is irreparable, but the Government is already taking steps to replace the building and to equip it with modern appliances. The official medical journal published there—the *Gazeta Medica da Bahia*—was founded in 1866, and is now in its thirty-seventh volume.

SOME OBSERVATIONS UPON THE MICRO-ORGANISMS OF MEAT POISONING AND THEIR ALLIES.

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THE typical representative of the bacterial flora of the normal intestine is the colon bacillus, its natural habitat being the digestive tract of man and animals. The typhoid bacillus is the most familiar example of those organisms which from time to time invade the intestine of man and produce disease. The colon and the typhoid bacillus, besides this contrast in infective properties, present biological and cultural features by means of which they can be differentiated outside the body. In addition to these established types, there occur in the healthy, and diseased, intestine a large number of organisms of an intermediate character, some approaching to the colon, others to the typhoid type. The colon group, for example, has been found to embrace a number of varieties of undoubtedly the same species. These varieties do not, however, appear to possess any special pathological significance. On the other hand, there occur amongst the intermediate forms, species of micro-organisms with distinct pathogenic properties for man and animals, of which the dysentery, the hog cholera, the meat poisoning and the paratyphoid group have now been identified. It has further been shown that relationships exist between certain of these groups of organisms, as evidenced by the possession of common biological properties. This is particularly the case with regard to the agents of various septicaemias in the lower animals, notably the hog cholera group, and the affinity its members bear to the meat poisoning, and paratyphoid, group of bacteria.

The life-history of such of these organisms as are pathogenic for man and their possible derivation from animal sources—cattle and swine—is a subject that merits careful and prolonged investigation. The problems raised are akin to those met with in other fields of research on the intercommunicability of disease agents—for example, bovine and human tuberculosis, rat plague, and human plague. The refinement of bacteriological methods has enabled a considerable advance to be made in the classification of the septicæmic organisms, whilst the agglutination test has furnished a delicate method of sifting out the homologous species of such pathogenic bacteria. At the same time but little definite knowledge exists as to the distribution of these organisms outside the actual morbid process.

The main object of the present research was to investigate the distribution of organisms of the meat poisoning and paratyphoid groups, more particularly in the intestines of healthy animals. I have endeavoured to determine in how far the organisms isolated from the normal intestine conformed in type to those met with in certain septicaemias of animals, and in meat poisoning, and paratyphoid infections in man.

HISTORICAL.

Meat poisonings are those diseases in man, usually epidemic in character, due to the consumption of meat from unhealthy animals—generally cattle (cow, calf), and more rarely the horse, pig, and goat. The animals commonly suffered from enteric or septic processes. The agents of these diseases in animals produce at times in man a septic or infective enteritis.

Ostertag¹ records from 1880-1903 ninety outbreaks of this form of meat poisoning, with about 4,000 cases. One may assume that the number of unrecorded cases was also considerable.

The symptoms vary in character and severity, and three forms of the disease have been described, namely, a gastro-enteric, a choleraic, and a typhoid.

An important fact to be noted is that such cases of poisoning are not due to putrid meat or its toxins. The meat appears to be healthy, and is without smell or unpleasant taste. The poisoning is due to virulent bacteria present in the meat which invade the intestines and body.

One must differentiate from this another form of food poisoning due to a *post-mortem* multiplication of saprophytic bacteria in a foodstuff, resulting in the production of highly toxic substances. The latter is usually termed allantiasis, botulism, or sausage poisoning. The disease is caused by eating decomposed sausages, or other forms of preserved meat

(hams, etc.). The attack is characterized by nervous symptoms of central origin, disturbances of secretion, motor disturbances, mydriasis, ptosis, etc. The researches of van Ermengem² have shown that this disease is due to the toxins of an anaërobic saprophyte—the bacillus botulinus. The meat comes from apparently healthy animals, and acquires its poisonous properties subsequently. The symptoms are due not to an infection, but to an intoxication with a poison produced by the *B. botulinus* in the meat consumed. In botulism the nervous symptoms predominate, whilst in true meat poisoning the gastro-intestinal symptoms constitute the main clinical feature. The infective organisms in meat poisoning also produce a toxin, as cases are recorded after the consumption of cooked meat or of soup made from it.

The first exact bacteriological investigation of meat poisoning was made by Gaertner³ during an outbreak at Frankenhäusen in 1888. Fifty-eight individuals became ill after eating the meat from a cow which had sickened and been slaughtered. The symptoms were those of an acute gastro-enteritis, with severe general symptoms. Gaertner found in the muscles and spleen of a fatal case a bacillus and also large numbers of the same organism in portions of the meat. This organism he termed the *B. enteritidis*. Its cultures were fatal to mice on feeding, and also on inoculation into guinea-pigs and rabbits. The necropsy showed acute enteritis, hæmorrhages in the serous cavities, lungs and kidneys, and pneumonia. The killed cultures were likewise fatal to experimental animals, and contained a toxin. This toxin, it is stated, may be heated to boiling point without destruction. The *B. enteritidis* thus differs from the colon organism in its marked virulence and in the production of heat-resistant toxins.

Organisms identical with, or closely allied to, the *B. enteritidis* have been isolated by a number of observers in subsequent outbreaks of meat poisoning. Of these a very full account will be found in a paper by Professor Bernhard Fischer, *Zur etiologie der Sogenannten Fleischvergiftungen*, published in the *Zeitschrift für Hygiene*, vol. xxxix, p. 447, 1902.

There is general agreement as to the main characteristics of the meat-poisoning organisms of the *B. enteritidis* type. They are motile short rods, non-sporing, non-liquefying, and decolorized by Gram's method. They differ from typhoid in their colon-like growth on potato and their fermentation of grape sugar, and, on the other hand, from colon in their fermentation of cane sugar, but not of cane and milk sugar. The organisms do not curdle milk, and the majority produce no indol. They further differ from colon and typhoid in their marked infectivity for experimental animals and the property they possess of forming heat-resistant toxins. The *B. enteritidis* is infective per os and penetrates into the blood and organs, producing a hæmorrhagic septicaemia.

The infectivity of the meat-poison organisms and their biological characters point to an affinity with the hog-cholera group of bacteria. I have obtained cultures of many of these organisms and controlled their biological and cultural characteristics.

The study of the meat-poisoning and hog-cholera group has received added importance through the discovery of the paratyphoid infections in man—that is, those forms of disease which, although presenting the clinical symptoms of a mild attack of enteric fever, are due not to an infection with the typhoid bacillus, but with organisms termed "paracolon" or "paratyphoid." These organisms have been isolated directly from many of the cases recorded, and the blood of the patients gives a marked agglutination with their cultures, but not with those of the *B. typhosus*. Attention was first drawn to the paracolon or paratyphoid bacilli by Achard and Bensaude.⁴ These organisms have been particularly studied in Germany by Schottmüller, Brion and Kayser, and others, and in America by Gwyn, Cushing, Buxton, and Coleman, etc. A good summary of the literature is given by Libman in the *Journal of Medical Research*.⁵ These organisms likewise present affinities to the Gaertner and hog-cholera group, and suggest a possible interrelationship of paratyphoid with analogous animal diseases. The mouse typhoid bacillus of Loeffler is another organism that presents similar relationships, and also the *B. psittacosis*. Psittacosis is a contagious disease of parrots, communicable to man, marked by pulmonary disorder and high fever. The organism is fully described by Nocard and Leclainche.⁶

We have, therefore, in meat poisoning, and in psittacosis, diseases derived from animal sources. It remains to be determined in how far the paratyphoid infections have their origin in analogous diseases of the lower animals.

AUTHOR'S EXPERIMENTS.

Morphologically, the bacilli of the enteritidis groups are practically indistinguishable from *B. coli*; they are actively motile, and do not retain the stain by Gram's method.

Their cultural peculiarities were found to be as follows: When grown on peptone beef broth and incubated for twenty-four hours at 37° C., universal turbidity of the broth is produced, with or without the formation of a pellicle. If grown on this medium for five days at 37° C., no indol—or the merest trace—is found to be present. If, however, this five days' old broth be filtered through a Pasteur-Chamberland filter a toxic filtrate is obtained, as can be readily proved by injecting 2 c.cm. intraperitoneally into a guinea-pig, the animal dying within twenty-four hours. Van Ermengem (loc. cit.) states that in the case of the meat poison bacillus he isolated in the Moorseele epidemic, this toxin did not lose its virulence when heated to 100° C., or even 120° C. The growth on agar and gelatine is creamy and moist, resembling that of the bacillus coli, there being no liquefaction of the gelatine. When grown on the various sugar media at 37° C., this group of organisms will be found to produce acid and gas on dulcitol, mannite, and glucose broths, but not to affect lactose or cane-sugar broths. The most characteristic reaction, however, is that on litmus milk, which, incubated at 37° C., becomes acid in twenty-four hours, and then, after a few days, strongly alkaline. No clotting occurs even at the end of a month. The period at which this alkaline reaction takes place varies with the different members of the group, the *B. enteritidis* of Gaertner, for instance, generally completing the reaction within forty-eight hours, whilst the *B. paratyphoid B* of Schottmüller may take from eight to ten days.

The reactions on Petruschky's litmus whey are similar to those on litmus milk, except that the change from acid to alkaline is more rapid in the former medium, taking place in some members of the group at the end of twelve hours.

It will be noticed from the table of cultural reactions that the enteritidis group, with a few notable exceptions, includes most of the food-poisoning bacilli. It includes also *B. typhi murium*, *B. psittacosis*, *B. hog cholera* of Evans, *B. hog cholera* "Maryland" of Theobald Smith, and the *B. paratyphoid B* of Schottmüller.⁷ This latter differs slightly from the rest of the group, producing marked indol when grown in broth at 37° C. for five days.

Some of the organisms under consideration, though nearly allied to the enteritidis group, do not conform to them in their cultural reactions. The *B. paratyphoid A* of Schottmüller, for instance, and the *B. paratyphoid* of Brion and Kayser⁸ have both been isolated from cases clinically resembling typhoid fever. These two bacilli are culturally indistinguishable from each other, and differ from the rest of the enteritidis group in that they produce indol when grown on broth for five days, and when grown on litmus milk the acid reaction is not followed by any alkaline reaction, even at the end of a month, the milk remaining acid without clotting. The other bacilli, from those under consideration, whose cultural reactions do not conform to those of the enteritidis group, are the food-poisoning bacilli of Wesenberg, Grünthal, and Friedeberg,⁹ and the hog-cholera bacilli of McFadyean and the "Arkansas" of Theobald Smith.

The *B. Wesenberg* has practically no resemblance to the members of the enteritidis group; it produces acid on all the sugars, producing gas, however, only on glucose and cane sugar. Litmus milk is rendered acid without clotting; no alkaline reaction takes place, and, when grown on broth, indol is produced at the end of five days.

The *B. Grünthal* resembles the members of the colon group in cultural reactions, being, except for its motility indistinguishable from *B. acidilactici* of Hüppe. It produces acid and gas on glucose, mannite, and lactose, broth, acid and clot on litmus milk, and indol on beef broth when grown for five days at 37° C.

The *B. Friedeberg* differs from the rest of the series in producing no change on any of the before-mentioned sugars, excepting cane sugar, on which it produces acid, but no gas. It creates general turbidity on peptone broth at 37° C. in twenty-four hours, but no indol at the end of five days.

The hog-cholera bacillus of McFadyean differs widely in cultural reactions from the rest of the enteritidis group, as well as from the other hog-cholera bacilli. It produces acid, but very slight gas on glucose broth, no reaction on mannite, or dulcitol broth, acid without clotting, and no alkaline change on litmus milk, and slight indol on broth at the end of five days; in fact, its sole resemblance to the enteritidis group consists

Cultural Reactions of known Intestinal and Food Poisoning Bacilli.

Bacterium.	Morph.	Broth.	Glucose.	Mannite.	Lactose.	saccha-rose.	Dulcit.	Lit. Milk.	Indol.	Agar.	Gelatine.	Litmus Whey.
<i>B. enteritidis</i> , Gaertner, Original A.	B. Motile	G. T.	A. G.	A. G.	Nil.	Nil.	A. G.	A. then Alk.	o	Creamy, raised, moist, translucent	No Liq. Creamy, raised, moist, translucent	4 hrs. A. 8 days. Alk.
<i>B. enteritidis</i> , Gaertner, Original B.	B. Non-Motile	"	"	"	"	"	"	"	o	"	"	"
<i>B. Gaertner</i> , L.I.P.M.	B. Motile	"	"	"	"	"	"	"	o	"	"	"
<i>B. Gaertner</i> , "Guy's"	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. Gaertner</i> , "Van Er-mengem"	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. typhi murium</i> ...	"	"	"	"	"	"	"	"	+ trace	"	"	"
<i>B. Moorese</i> ...	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. psittacosis</i> , Nocard	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. Haustedt</i> , "Fischer"	"	"	"	"	"	"	"	"	+ trace	"	"	"
Food poisoning, Abel	"	J. T. S.	"	"	"	"	"	"	+ slt.	"	"	"
<i>B. Rennfeth</i> , "Fischer"	"	G. T.	"	"	"	"	"	"	"	"	"	"
<i>B. icteroides</i> , Sanarelli	"	J. T. S.	"	"	"	"	Nil.	"	"	"	"	"
<i>B. epidem. jaundice</i>	"	"	"	N.I.	"	"	"	"	"	"	"	"
<i>B. Aertrycke</i> , "Van Er-mengem"	"	G. T.	"	A. G.	"	"	A. G.	"	Trace	"	"	"
<i>B. hog cholera</i> , Evans	"	"	"	"	"	"	"	"	"	"	"	"
<i>B. hog cholera</i> , Maryland, Theobald Smith	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. hog cholera</i> , Arkansas, Theobald Smith	"	J. T. S.	"	"	"	"	Nil	"	o	"	"	"
<i>B. hog cholera</i> , McFady-yeon	"	G. T.	A. G. Slt	Nil	"	"	"	A.	Trace	"	"	A.
<i>B. Breslaviensis</i> ...	"	"	A. G.	A. G.	"	"	A. G.	A. then Alk.	o	"	"	"
Food poisoning, Gunther	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. paracolon</i> , "Day"	"	J. T. S.	"	"	"	"	Nil	"	o	"	"	Alk.
<i>B. paratyphoid</i> A, Schott-müller	"	G. T.	"	"	"	"	A. G.	A.	+	"	"	A.
<i>B. paratyphoid</i> B, Schott-müller	"	"	"	"	"	"	"	A. then Alk.	+ Slt.	"	"	Alk.
<i>B. paratyphoid</i> , Brion and Kayser	"	"	"	"	"	"	"	A.	Trace	"	"	A.
<i>B. moribicans bovis</i> ...	"	J. T. S.	"	"	"	"	"	A. then Alk.	+	"	"	Alk.
<i>B. Wessenberg</i> ...	"	G. T.	"	A.	A.	A. G.	A.	A.	"	"	"	A.
<i>B. pseudo-tuberculosis</i> , "Pfeiffer"	B. Non-motile	"	A.	"	N.I.	Nil	Nil	Nil	"	"	"	Nil.
<i>B. Friedeberg</i> , Gaffky and Paak	"	"	Nil	Nil	"	A.	"	"	o	"	"	"
<i>B. Grunthal</i> ...	B. Motile	"	A. G.	A. G.	A. G.	Nil	"	A. C.	+	"	"	"
<i>B. coli</i> , Escherich ...	"	"	"	"	"	"	A. G.	"	"	"	"	"
<i>B. acid lactici</i> , "Hüppe"	B. Non-motile	"	"	"	"	"	Nil	"	"	"	"	"
<i>B. lact. aerogenes</i> ... [key	"	J. T. S.	"	"	"	A. G.	"	"	o	"	"	A.
<i>B. coli</i> , T. W. F. 6 MacCon-key	B. Motile	G. T.	"	"	"	"	A. G.	"	+	"	"	A.
<i>B. coli</i> , T. W. F. 13 MacCon-key	B. Non-motile	"	"	"	"	"	Nil	"	+	"	"	"
<i>B. cloacae</i> ...	B. Motile	"	"	"	"	"	"	"	o	"	"	"
<i>B. pyogenes foetidus</i> ...	B. Non-motile	"	A.	A.	A.	A.	A.	"	+	"	"	"
<i>B. typhoid</i> , Delépine ...	B. Motile	"	"	"	Nil	Nil	Nil	A.	o	"	"	"
<i>B. typhoid</i> L.I.P.M.	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. dysentery</i> , Shiga ...	B. Non-motile	"	"	Nil	"	"	"	A. then Slt. Alk.	o	"	"	Alk.
<i>B. dysentery</i> , Kruse	"	"	"	"	"	"	"	"	o	"	"	"
<i>B. dysentery</i> , Flexner, Philippines	"	"	"	A.	"	"	"	"	+	"	"	"
<i>B. dysentery</i> , Gray	"	"	"	"	"	"	"	"	+	"	"	"

A. = Acid.
Alk. = Alkaline.
G. T. = General turbidity.
A. G. = Acid and gas.

A. C. = Acid and clot.
A. then Alk. = Acid then alkaline.
S. = Scum.
Slt. = Slight.

in its producing no change on lactose or cane-sugar broth, and in its being a motile bacillus which does not stain by Gram's method.

The *B. hog cholera* "Arkansas" of Theobald Smith differs from the enteritidis group in producing no change on dulcit broth when grown at 37° C. for fourteen days, in which respect it differs also from his "Maryland" culture, as well as by its production of a scum on peptone beef broth at 37° C. at the end of twenty-four hours. In other respects the hog cholera "Arkansas" resembles the rest of the enteritidis group. It produces acid and gas on glucose, and mannite, broths, no change on lactose, or cane sugar broth, acid and subsequently alkaline on litmus milk, and no indol on peptone beef broth at the end of five days.

To recapitulate, therefore: As far as morphological and cultural reactions are concerned, the following bacilli fall into the enteritidis group: The food poisoning bacilli of Gaertner, Aertrycke, Moorese, Hanstedt, Breslaviensis, *B. moribicans bovis*, Günther, Abel, and Rennfeth; also *B. typhi murium*, *B. psittacosis*, *B. hog cholera* "Maryland" of Theobald Smith, and *B. hog cholera* of Evans.

The remaining bacilli that have been experimented with for the purposes of this research differ culturally from the above, and also from each other, excepting *B. paratyphoid* A of Schottmüller and *B. paratyphoid* of Brion and Kayser, which are culturally identical.

Having determined, therefore, that, as regards cultural and biological characteristics, the bacilli of the enteritidis group and of the Paratyphoid A group of Schottmüller include most of the organisms that give rise to food poisoning, and to cases of disease resembling typhoid fever, I proceeded to investigate the question as to whether the bacilli of these two groups were represented by analogous types in the intestines of normal animals.

To this end the following intestinal material was submitted to investigation: The faeces of guinea-pigs, rabbits, sheep, and pigs obtained from a largenumber of the various animals; also the scrapings from the mucous surfaces of the large and small intestines of three pigs, three sheep, two bullocks, one horse, one calf, and of a child that died in Guy's Hospital from bronchopneumonia.

The method adopted was as follows: An emulsion of the substance under examination was made with distilled water, and about ½ c.cm. of the emulsion was added to tubes of bile-salt dulcit broth coloured with neutral-red (MacConkey), and incubated for twenty-four hours at 42° C. Of this culture 4 c.cm. was then injected subcutaneously into a number of guinea-pigs. The guinea-pigs that died within four days were opened, aseptic precautions being taken, and the heart exposed and seared with a hot iron. The heart blood was pipetted with a sterile pipette into tubes of bile-salt dulcit broth, and incubated at 42° C. for twenty-four hours. If at

the expiration of this time acid and gas were produced, neutral-red bile-salt agar plates were inoculated and incubated at 42° C. for twenty-four hours. The colourless colonies were then picked off (the bacilli of the two groups for which the search was made producing no acid on lactose, their colonies are colourless), and from them bile-salt dulcitol-broth tubes were inoculated, and incubated at 42° C. for twenty-four hours. The tubes that gave the acid-and-gas reaction were then used to inoculate the following media: Glucose broth, dulcitol broth, mannitol broth, lactose broth, cane-sugar broth, peptone-beef broth, litmus milk, agar, and gelatin, in order to determine in how far the cultural reactions of the organisms isolated agreed with those of the *B. enteritidis* and Paratyphoid A groups. All the tubes were incubated at 42° C., excepting the gelatine, which was incubated at 20° C.

It will be noted that only those guinea-pigs were tested that died within four days after injection, those dying from a more chronic infection being rejected. This naturally considerably diminished my positive results, but at the same time excluded any possibility of error which might arise through an accidental infection from the sick to the healthy animals, or other causes, though all precautions against such infection were of course taken. The positive results were, however, fairly numerous, and were as follows:

Twenty-one cultures of bacilli, of the enteritidis type, and answering to the characteristic morphological and cultural tests were isolated, namely, motile bacilli of the size and appearance of the *B. enteritidis* of Gaertner, not staining by Gram's method, producing a cream-coloured growth on agar and gelatine, and not liquefying the latter medium, giving acid and gas on glucose, dulcitol and mannitol broths, but not affecting lactose, or cane sugar broths, and rendering litmus milk at first acid and then alkaline, without clotting.

Also ten cultures of the Paratyphoid A type were isolated, which agreed culturally and morphologically with the former, excepting in their reaction on litmus milk, which remained acid without clotting, and in the production of indol on broth at the end of five days.

A. CULTURES OBTAINED FROM FAECES.

- From rabbits' faeces, 3 cultures of the Paratyphoid A type;
- " guinea-pigs' faeces, 1 culture of the Paratyphoid A type;
- " sheep's faeces, 1 culture of the *B. enteritidis* type; and
- " pigs' faeces, 1 culture of the *B. enteritidis* type of organisms.

B. FROM THE SCRAPINGS OF THE MUCOUS SURFACE OF LARGE INTESTINES.

- From 3 pigs, 4 cultures of *B. enteritidis*, and 1 of the Paratyphoid A type;
 - " 2 bullocks, 4 cultures of the *B. enteritidis* type;
 - " 3 sheep, 1 culture of the *B. enteritidis*, and 1 of the Paratyphoid A type; and
 - " 1 calf, 1 culture of the *B. enteritidis* group.
- The results in the case of the child's and horse's intestine were negative.

C. FROM THE SCRAPINGS OF THE MUCOUS SURFACE OF SMALL INTESTINES.

- From 3 pigs, 7 cultures of the *B. enteritidis* group;
- " 2 bullocks, nil;
- " 3 sheep, 1 culture of the Paratyphoid A type;
- " the calf, 1 culture of the *B. enteritidis*, and 2 of the Paratyphoid A type;
- " a child, 1 culture of the *B. enteritidis*; and
- " the horse, 1 culture of the Paratyphoid A type.

It will be noticed from the above tables that the scrapings from the intestines yielded a larger number of positive results than the faeces. This has been observed by other workers in searching for the dysentery group of organisms, and is no doubt due to the fact that the bacilli are parasitic on the mucous surfaces of the intestines. Ford, in his paper,¹⁰ states that amongst other bacteria the *B. enteritidis* of Gaertner has been isolated from the human caecum, and that it is practically never found in any other part of the intestines. Curiously enough the culture I obtained of the enteritidis group was from the small intestine of a child, the large intestine yielding no result. As regards the relative frequency of these bacilli in the large and small intestines it may be noted that in my experiments, both the large and small intestines of the various animals, regarded collectively, yielded nearly the same number of cultures of the enteritidis group, or 9 cultures from the small intestines and 10 from the large intestines. The same also applies to the Paratyphoid A group, 3 cultures being obtained from the small and 2 from the large intestines.

These tests being completed, the cultures of the organisms were tested as regards their pathogenicity, 2 c.cm. of a twenty-four-hours broth culture being injected intraperitoneally into a guinea-pig. This injection, in the case of the cultures of the

B. enteritidis type proved uniformly fatal in a few hours. The cultures of the Paratyphoid A type proved, however, much less virulent, 75 per cent. of the guinea-pigs dying at the end of two to four days, the remaining 25 per cent. recovering. The cultures which did not kill guinea-pigs were therefore tested on mice, $\frac{1}{2}$ c.cm. of a twenty-four-hours broth culture being injected intraperitoneally, and with an invariably fatal result in from one to three days. No difference could be found between these two varieties of the Paratyphoid A type other than that shown by their virulence.

As was previously mentioned when describing the characteristics of the *B. enteritidis* group, a toxin is present in broth cultures of these organisms.

The bacilli of this group isolated by me from the intestines of animals were further subjected to the following test *re* toxicity. Two of the cultures were selected at random and grown on peptone beef broth at 37° C. for five days. The broth culture was then filtered through a Pasteur-Chamberland filter, and 2 c.cm. of the filtrate injected intraperitoneally into guinea-pigs, with the result that the animals died within twenty-four hours. A similar experiment was made with the toxin produced by the *B. enteritidis* of Gaertner (original strain), with the same result, proving that the bacilli of the enteritidis group obtained from the intestines of healthy animals are capable of producing a soluble toxin similar to that produced by other known members of the same group.

From the experimental tests upon the bacilli obtained from the intestines of animals, it will be seen that 21 of the organisms found agree biologically, culturally, and morphologically with the known members of the *B. enteritidis* group, and 10 with the members of the Paratyphoid A group. The sources of the cultures with which comparison was made were quite reliable. I am indebted to Professor Gaertner for two cultures of the *B. enteritidis* of Gaertner, to Professor van Ermengem for a culture of *B. Aertrycke*, to Professor Theobald Smith for cultures of hog cholera "Maryland" and "Arkansas," and to Professor J. McFadyean and Dr. Evans for cultures of their hog-cholera bacilli. The cultures of *B. typhimurium* and *B. psittacosis* were obtained from the Pasteur Institute, and a large number of the food-poisoning bacilli were obtained from Kral.

From the account of the foregoing experiments, it will be seen that bacilli of the *B. enteritidis* type were more frequently met with than bacilli of the Paratyphoid A type, and it occurred to me that this was probably due to the much greater virulence of the former, as proved by inoculation experiments. It was therefore determined to test their relative frequency in the normal intestine of animals by direct cultivation from the scrapings of the intestines without passage through guinea-pigs. By this means the proportionate increase of the more virulent bacilli was prevented, and their relative frequency could be more accurately determined. The colourless colonies were picked off from the plates, planted on dulcitol broth, and incubated at 37° C. for twenty-four hours. Tubes giving acid and gas at the end of this time were put through the various sugar media and litmus milk, as in former experiments. Two experiments were made with pig's intestines. In the first, 1 colony out of the 95 isolated from the plates proved to be of the Paratyphoid A type, and none of the *B. enteritidis* type. In the second experiment, out of 38 colonies 25 were of the Paratyphoid A type, and none of *B. enteritidis* type. This tends to show that, although in experiments where passage through animals was used the *B. enteritidis* type appeared to be more common than *B. paratyphoid* A type, it is nevertheless not so common in the intestines of animals as the latter.

The absence of bacilli of the enteritidis group, in experiments where passage through an animal was not used, is readily explained by the small amount of the culture employed for the inoculation of the plates—namely, a platinum loopful of a broth culture for two plates. In this small amount of material they might easily escape detection, and yet, through their greater virulence, far exceed the others after their passage through an animal. In fact, it may be as difficult to detect bacilli of the *B. enteritidis* type by plating directly from a dulcitol-broth culture as it is to detect the *B. typhosus* in drinking water.

Up to the present the cultures obtained from the intestines of healthy animals have been classified broadly, as of the enteritidis or of the Paratyphoid A type, no attempt having been made to define particular species. In the present state of our knowledge, it seems better to base such classification upon the agglutination reactions of the organisms, for although so-called cross agglutinations may occur, as in the

case of hog cholera, and typhoid, as instanced by Theobald Smith,⁷ they occur, as a rule, only in low serum dilutions. If high dilutions of serums are used—1 in 1,000 or 1 in 20,000—the bacilli generally refuse to react with heterologous serums, but continue to react with homologous serums. These serum reactions have been of great value in grouping the organisms in question, as well as in proving the identity of the bacilli isolated in various food poisoning epidemics, as instanced by Durham¹¹ in his account of the Chadderton outbreak, and again in his account of an epidemic in which 185 persons were affected.¹²

Perhaps one of the most complete classifications of the food-poisoning and paratyphoid bacilli based upon agglutination reactions is that given by Trautmann.¹³

The organisms are found by Trautmann to fall into one or other of five groups—namely:

A. *Enteritidis* (Gaertner).

1. Gaertner (Frankenhausen).
2. Van Ermengem (Morseele).
3. Fischer (Haustedt).
4. Abel (Hamburg).

B. *Breslaviensis*.

1. Kaesche (Breslau).
2. Günther (Prov. Posen).
3. Lochmann (Glessen, "caseolyticus").
4. Trautmann (Düsseldorf).

C. *Hamburgensis*.

1. Schottmüller (Hamburg, Fall Seeman).
2. Bac. *bremensis* febris gastricae Kurth.
3. Hünemann (Saarbrücken-Coblenz).
4. Conradt u. Drigalski und Jürgens (Saarbrücken). Type B of Feyfer and Kayser.

D. *Strassburgensis*.

1. Schottmüller (Hamburg)
2. Brion and Kayser (Strassburg) } Type A of Feyfer and Kayser.

E. *Morbificans Bovis* (Basenau).

Agglutination Table of known Bacilli with—(1) Gaertner Serum; (2) Aertrycke Serum; (3) Serum of Rabbit Immunized with a Bacillus of the Enteritidis Group Isolated from the Large Intestine of a Pig; (4) Paratyphoid A Serum.

These serums caused a distinct reaction with their own bacilli in dilutions of 1 in 100,000.

Bacterium.	Gaertner Serum.		Aertrycke Serum.		B. from Pig's Intestine Serum.		Paratyphoid A Serum.	
	1 in 200	1 in 1,000	1 in 200	1 in 1,000	1 in 200	1 in 1,000	1 in 200	1 in 1,000
1. <i>Organisms of the Gaertner Type.</i>								
B. ent., Gaert., L.I.P.M. ...	3	3	0	0	0	0	—	—
B. Gaertner, Guy's ...	2	2	0	0	0	0	—	—
B. Gaertner, van E. ...	3	3	0	0	0	0	—	—
B. typhi murium ...	2	2	0	0	0	0	—	—
B. Moorseele ...	3	3	0	0	0	0	—	—
B. psittacosis, No-card ...	3	3	3	3	3	3	—	—
	(3, 1 in 100,000)		(3, 1 in 100,000)		(3, 1 in 100,000)			
B. Haustedt ...	3	3	0	0	0	0	—	—
Abel ...	3	2	0	0	0	0	—	—
B. Rennfleth ...	3	3	0	0	0	0	—	—
B. icteroides ...	0	0	0	0	0	0	—	—
2. <i>Organisms of the Aertrycke Type.</i>								
B. Aertrycke ...	2	2	3	3	3	3	—	—
Hog cholera, Evans ...	0	0	3	3	3	3	—	—
Hog cholera, "Maryland" ...	0	0	2	2	2	0	—	—
Hog cholera, "Arkansas" ...	0	0	1	1	1	0	—	—
Hog cholera, "McFadyean" ...	0	0	2	1	2	1	—	—
B. Breslaviensis ...	0	0	3	2	3	2	—	—
Günther ...	0	0	3	2	3	3	—	—
3. <i>Organisms of the Paratyphoid Type.</i>								
B. paratyphoid A ...	0	0	0	0	0	0	3	3
B. paratyphoid B ...	0	0	0	0	0	0	0	0
B. paratyphoid, Brion and Kayser ...	3	2	3	0	0	0	3	3
4. B. moribificans, bovis ...	0	0	0	0	0	0	0	0
5. B. Wesenberg ...	0	0	0	0	0	0	0	0
6. Grünthal ...	0	0	0	0	0	0	0	0
B. typhoid, L.I.P.M. ...	2	2	0	0	0	0	0	0
B. Shiga (dysentery) ...	0	0	0	0	0	0	0	0

N.B.—1 = slight reaction; 2 = distinct reaction; 3 = complete reaction.

The following attempt was made to ascertain to which group, or groups, of organisms the cultures obtained by me from the intestines of animals belonged: Three rabbits were immunized—the first with B. enteritidis of Gaertner, the second with B. Aertrycke (a food-poisoning bacillus of the Breslaviensis and Günther group), and the third with bacilli of the enteritidis group, which I had isolated from the large intestines of a healthy pig. The rabbits were immunized by subcutaneous injection of the respective cultures, and a monovalent serum was obtained, giving an agglutination reaction with its own bacillus in the dilution of 1 in 100,000. These three serums were then used to test the reactions given by the bacilli of the enteritidis and Paratyphoid A type that had been isolated from animals' intestines, the known bacilli of these two groups also being tested individually against the same serums. The results of these experiments are shown in the accompanying agglutination tables.

ORGANISMS ISOLATED BY AUTHOR FROM THE INTESTINES OF HEALTHY ANIMALS TESTED AGAINST THREE SERUMS.

A.—Bacilli of the Enteritidis Type giving no Reaction with Gaertner Serum.

Source of Bacilli.	Gaertner Serum.		Aertrycke Serum.		B. from Pig's Intestine Serum.	
	1 in 200	1 in 1,000	1 in 200	1 in 1,000	1 in 200	1 in 1,000
Pig's faeces ...	0	0	3	3	3	3
Pig's small intestine (a) ...	0	0	3	3	3	3
Pig's small intestine (b) ...	0	0	2	1	3	3
Pig's small intestine (c) ...	0	0	3	2	3	3
Pig's small intestine (d) ...	0	0	2	2	3	3
Pig's large intestine (a) ...	0	0	3	3	3	3
Pig's large intestine (b) ...	0	0	3	3	3	3
Pig's large intestine (c) ...	0	0	3	3	3	3
Sheep's large intestine (a) ...	0	0	3	3	3	3

B.—Bacilli of Enteritidis Group giving a Partial Reaction to Gaertner Serum.

Source of Bacilli.	Gaertner Serum.		Aertrycke Serum.		B. from Pig's Intestine Serum.	
	1 in 200	1 in 1,000	1 in 200	1 in 1,000	1 in 200	1 in 1,000
Pig's small intestine (c) ...	2	2	3	3	3	3
Pig's small intestine (d) ...	2	2	3	3	3	3
Pig's large intestine (c) ...	1	1	3	3	3	3
Bullock's large intestine (a) ...	2	0	2	2	3	3
Bullock's large intestine (b) ...	2	0	2	2	3	3
Bullock's large intestine (c) ...	2	0	2	2	3	3
Bullock's large intestine (d) ...	2	0	2	2	3	3
Sheep's faeces (a) ...	1	1	2	2	3	3
Calf's small intestine (b) ...	1	1	2	2	3	3

C.—Bacilli of the Enteritidis Type giving a Complete Reaction to both Gaertner and Aertrycke Serum, like B. Psittacosis.

Source of Bacilli.	Gaertner Serum.		Aertrycke Serum.		B. from Pig's Intestine Serum.	
	1 in 200	1 in 100,000	1 in 200	1 in 100,000	1 in 200	1 in 100,000
Child's small intestine (a) ...	3	3	3	3	3	3
Pig's small intestine (c) ...	2	2	2	2	3	3

N.B.—1 = slight reaction; 2 = distinct reaction; 3 = complete reaction.

On comparing the agglutination table of the known food-poisoning bacilli with Trautmann's list it will be found that the results as regards the enteritidis or Gaertner group, and the Breslaviensis or Aertrycke group, are identical with my own, and it is with these two groups that the present research is most concerned, as all the bacilli of the enteritidis group isolated from animals' intestines reacted quite as well to the serum of the second rabbit (Aertrycke serum) as to the serum of the third rabbit immunized by one of the cultures obtained from the large intestine of a healthy pig. It is true that about

half the cultures of the enteritidis bacilli reacted to a certain extent to the serum of the first rabbit (immunized against *B. Gaertner*), but in the higher dilutions it was shown that the Aerttrycke serum had a much greater effect. In the same way the Aerttrycke culture itself gave a moderate reaction with the Gaertner serum, and a complete reaction with the Aerttrycke serum, in a dilution of 1 in 1,000.

These results, together with the previously-mentioned cultural reactions, indicate that 18 of the 20 cultures examined belong to the Aerttrycke, or Breslaviensis, species of the enteritidis group. The remaining two cultures of this group, from the small intestine of a pig and from the small intestine of a child, were found to react equally well either to the Gaertner or to the Aerttrycke serum, even in a dilution of 1 in 100,000. This peculiarity was also observed in the *B. psittacosis*, pointing to the conclusion that these two cultures were nearly allied to that bacillus. It will be noticed that the 10 cultures of the Paratyphoid A group gave no reaction with the three serums above mentioned. A fourth rabbit was therefore immunized with a culture of *B. paratyphoid A* of Schottmüller, and each of these cultures tested against the serum. None of the ten cultures, however, gave any reaction, thus giving no reaction at all with the four serums experimented with. It is certain that, according to their cultural reactions, they belong to the Paratyphoid A group, but in their serum reactions they do not agree with two known cultures of the group—Schottmüller's Paratyphoid A and the paratyphoid of Brion and Kayser. They belong possibly to yet another species of the same group.

The agglutination tests furnish one of the best laboratory methods of classifying the different organisms, and are much more delicate than the cultural methods, as is shown in the case of the four organisms of the hog-cholera group "Maryland," "Arkansas" of Theobald Smith, Evans's bacillus, and McFadyean's bacillus, which all differ in their cultural reactions, but, as will be seen on reference to the table, react equally well to the Aerttrycke serum. The agglutination reaction, however, does not necessarily indicate the specific virulence for different animals, the *B. of mouse typhoid*, for example, giving the same agglutinative reaction as the *B. enteritidis* of Gaertner, although the virulence of the mouse typhoid bacillus is, so far as we know, confined to mice and rats. The hog-cholera bacillus of McFadyean is virulent for pigs, but not for guinea-pigs. This specific virulence may possibly be acquired by passage through certain definite animals, but this is a matter for further research.

It will be observed that the cultures of the enteritidis group isolated from animals' intestines agree in agglutination reactions with the hog-cholera bacilli, as they are both agglutinated with Aerttrycke serum; they also agree culturally with the hog-cholera bacilli of Evans, and "Maryland" of Theobald Smith.

It was decided to test, therefore, whether these bacilli from animals' intestines could produce hog cholera in the pig. A broth culture of bacilli of the Aerttrycke type isolated from the large intestine of a pig being selected, 500 c.cm. of this culture, mixed with milk, was given to a young pig 4 months old, that being the most susceptible age. The animal, however, did not contract hog cholera. A second feeding experiment was tried with another young pig, a litre of a forty-eight hours' broth culture being administered. This produced violent diarrhoea and loss of appetite on the following day, which passed off in thirty-six hours, but on the animal being killed a week later no trace of the lesions peculiar to hog cholera was found in the intestines. The *post-mortem* examination was kindly performed by Professor McFadyean, of the Royal Veterinary College. The violent diarrhoea in the second feeding experiment seems a further proof of the relationship of these bacilli with those of the food-poisoning group.

GENERAL CONCLUSIONS.

1. There exist in the intestines of healthy animals organisms conforming morphologically and biologically to the enteritidis and Paratyphoid A types.

2. These organisms, as regards their agglutination reactions, fall into the following groups:

1. *B. enteritidis*, Aerttrycke, or hog-cholera type.
2. *B. enteritidis*, psittacosis type.
3. *B. paratyphoid A*, unknown type.

3. The nomenclature adopted by different observers is unsatisfactory, but is based on the principal differentiating criterion we at present possess—namely, specific virulence.

My best thanks are due to Dr. Allan Macfadyen for many valuable suggestions during this research.

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SPIROCHAETAE IN SYPHILIS.

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IN the number of the German Imperial Health Office Publications just issued,¹ Schaudinn and Hoffmann have a paper (dated April 10th) describing organisms of *Spirochaetae* type which they find constantly present in syphilitic lesions. Of these *Spirochaetae* they distinguish two sorts, one larger, thicker, and more readily stained, the other smaller, thinner, and taking up dyes with difficulty. The former they find mainly in cases of *condyloma acuminatum*; the latter they find exclusively in genuine syphilitic chancres and efflorescences, not only on the surface of the primary sore but also on its deeper aspect (laid bare by excising it). They also find this organism in the secretion of the so-called "mucous tubercles," and in the depth of indolent buboes. This very slender, delicate, stain-resisting organism is provisionally named by Schaudinn, *Spirochaete pallida*.

Through the courtesy of Dr. Pagin Meldon, Surgeon to the Westmorland Lock Hospital, Dublin, I have been placed in a position to verify Schaudinn's statements, and in view of the extreme theoretical and practical importance of any clue to the hitherto mysterious question as to the causation of syphilis, I think it right to at once communicate the results I have hitherto obtained. I may say at once that in every one of the 9 cases of undoubted syphilis in the primary and secondary stage which I have examined, *spirochaetae* were readily demonstrable. In a case of advanced tertiary ulceration of the palate I failed to find the *spirochaete*, and I also missed it in a case of muco-purulent vaginitis, unaccompanied by ulceration and considered by the medical attendant (Dr. Meldon) not to be of syphilitic nature. Admittedly the number of non-syphilitic control cases examined is far too small, but this objection I hope to speedily meet. It is accounted for by lack of time for more extensive examinations.

Method.

The patient (hitherto I have only examined adult females) having taken her position in the examination-chair, thin film-preparations were made on slides from the secretion of any sores, etc. In a few of the cases a trace of the material was suspended in sterile broth, and put up as a hanging-drop, when the movements of the *spirochaetae* could readily be observed. The dried films were (in accordance with the suggestion of Schaudinn) fixed in absolute alcohol for ten minutes and stained for several hours (usually till next day), in very strong Giemsa stain² (Giemsa's azur I azur II eosin, dissolved in methyl-alcohol and neutral glycerine, 3 drops of the compound to the c.cm. of water). The highest powers are required on account of the tenuity of the object and its weak staining affinity. I used an oil immersion $\frac{1}{2}$ th of Leitz.

Description of Spirochaetae Found.

Spirally twisted, extremely delicate organisms, actively motile, with peculiar corkscrew movement in either direction. Length from 7 to about 18 μ , averaging about 12 μ . Thickness too small to measure. Some were equally thick throughout; others, more especially the longer ones, were decidedly thicker in the middle, and tapered, slowly at first, afterwards more rapidly, towards the ends. The coils were often seven or eight in number, not regularly spiral, more open towards the extremities, sometimes nearly effaced. The smaller *spirochaetae* looked like detached flagella of the typhoid bacillus in a Pitfield preparation.

As regards structure, with the magnification at my disposal, I could make out no more than a granular appearance, more highly alternating with less highly refractive dots, in the fresh preparation. In certain specimens I convinced myself that nearer to one end lay a granule larger than the others and