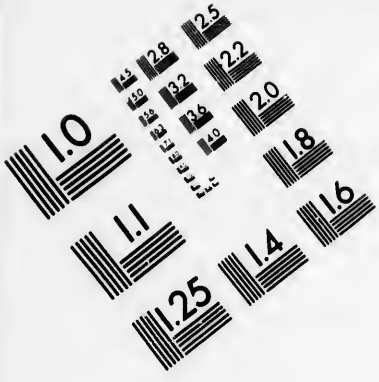
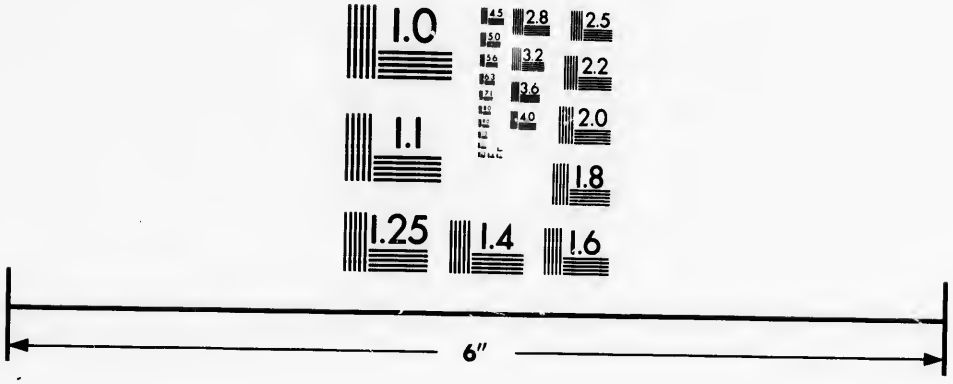
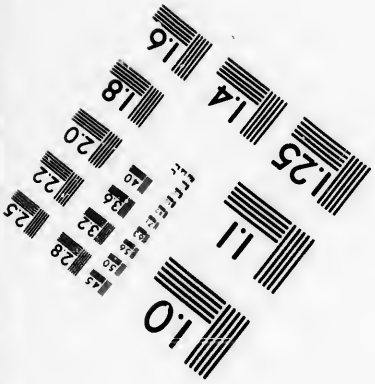
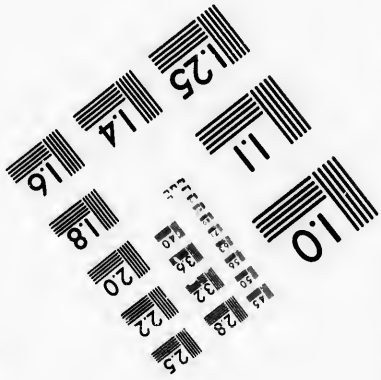


IMAGE EVALUATION TEST TARGET (MT-3)







Photographic Sciences Corporation

23 WEST MAIN STREET
WEBSTER, N.Y. 14580
(716) 872-4503

Technical and Bibliographic Notes/Notes techniques et bibliographiques

The Institute has attempted to obtain the best original copy available for filming. Features of this copy which may be bibliographically unique, which may alter any of the images in the reproduction, or which may significantly change the usual method of filming, are checked below.

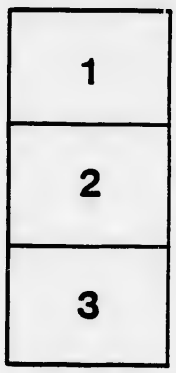
L'Institut a microfilmé le meilleur exemplaire qu'il lui a été possible de se procurer. Les détails de cet exemplaire qui sont peut-être uniques du point de vue bibliographique, qui peuvent modifier une image reproduite, ou qui peuvent exiger une modification dans la méthode normale de filmage sont indiqués ci-dessous.

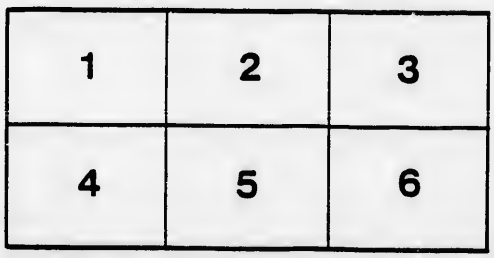
- [x] Coloured covers/ Couverture de couleur
- [ ] Covers damaged/ Couverture endommagée
- [ ] Covers restored and/or laminated/ Couverture restaurée et/ou pelliculée
- [ ] Cover title missing/ Le titre de couverture manque
- [ ] Coloured maps/ Cartes géographiques en couleur
- [ ] Coloured ink (i.e. other than blue or black)/ Encre de couleur (i.e. autre que bleue ou noire)
- [ ] Coloured plates and/or illustrations/ Planches et/ou illustrations en couleur
- [ ] Bound with other material/ Relié avec d'autres documents
- [ ] Tight binding may cause shadows or distortion along interior margin/ La reliure serrée peut causer de l'ombre ou de la distortion le long de la marge intérieure
- [ ] Blank leaves added during restoration may appear within the text. Whenever possible, these have been omitted from filming/ Il se peut que certaines pages blanches ajoutées lors d'une restauration apparaissent dans le texte, mais, lorsque cela était possible, ces pages n'ont pas été filmées.
- [ ] Additional comments:/ Commentaires supplémentaires:

- [ ] Coloured pages/ Pages de couleur
- [ ] Pages damaged/ Pages endommagées
- [ ] Pages restored and/or laminated/ Pages restaurées et/ou pelliculées
- [x] Pages discoloured, stained or foxed/ Pages décolorées, tachetées ou piquées
- [ ] Pages detached/ Pages détachées
- [x] Showthrough/ Transparence
- [ ] Quality of print varies/ Qualité inégale de l'impression
- [ ] Includes supplementary material/ Comprend du matériel supplémentaire
- [ ] Only edition available/ Seule édition disponible
- [ ] Pages wholly or partially obscured by errata slips, tissues, etc., have been refilmed to ensure the best possible image/ Les pages totalement ou partiellement obscurcies par un feuillet d'errata, une pelure, etc., ont été filmées à nouveau de façon à obtenir la meilleure image possible.

This item is filmed at the reduction ratio checked below/
Ce document est filmé au taux de réduction indiqué ci-dessous.

10X	12X	14X	16X	18X	20X	22X	24X	26X	28X	30X	32X
							✓				





TYPHOID FEVER WITHOUT INTESTINAL LESIONS—WITH THE REPORT OF A CASE.

BY

ALBERT G. NICHOLLS, M.A., MD.,

Assistant Demonstrator of Pathology, McGill University ; Assistant Pathologist to the Royal Victoria Hospital.

AND

C. B. KEENAN, M.D.,

Resident Surgeon, Royal Victoria Hospital, Montreal.

(*Reprinted from the Montreal Medical Journal, January*, 1898.)

TYPHOID FEVER WITHOUT INTESTINAL LESIONS—WITH THE REPORT OF A CASE.

BY

ALBERT G. NICHOLLS, M.A., M.D.,

Assistant Demonstrator of Pathology, McGill University; Assistant Pathologist to the Royal Victoria Hospital,

AND

C. B. KEENAN, M.D.,

Resident Surgeon, Royal Victoria Hospital, Montreal.

Formerly typhoid fever could not be diagnosed with certainty in the absence of any of the classical symptoms or the characteristic intestinal lesions. With the increase of bacteriological knowledge, however, and the improvement in technique, we are now enabled to include under the category of typhoid many atypical cases about which we must otherwise have remained in doubt. To this result the discovery of the serum reaction has contributed not a little, and we are now enabled to form a more accurate conception of typhoid processes and to recognise the very various aspects which the disease may assume. The occurrence of typhoid fever with absence of the usual ulcerative lesions of the intestines is now recognised by several observers, notably Chantemesse, Vincent, Vaillard, Sanarelli, Roux and others. A number of such cases are on record, but some are not corroborated by bacteriological investigation, so that they are of no scientific value.

A careful search of the literature for the past 10 years has revealed the existence of only 9 such cases which have been confirmed by the discovery of the bacillus of Eberth.

The time has gone by when we could regard typhoid as an infective process localised to the intestines, producing the general symptoms by the secondary action of its toxin. Rather, have recent researches proved that the disease is an infective one, invading the organism through the lymphatics of the intestine and infecting the system as a whole, the intensity of the lesions being generally but not invariably directly proportional to their proximity to the point of inoculation; the brunt of the disease, hence, may fall upon lymphoid tissue, parenchymatous organs, or at times the central nervous system. From this point

[1] Read before the Montreal Medico-Chirurgical Society, October 29, 1897.

of view, which is abundantly supported by clinical evidence, the intestinal tract merely represents a point of departure for the typhoid germ and not the sole place of localisation for its development. Samarelli is of the opinion that the lesions of the intestine are due to an elective action, not of the bacilli themselves, but their toxins acting from a distance, but this hardly coincides with what we know of the presence of the germs in abundance in the intestinal mucosa. In any case the intestinal lesions should not be regarded as all important, but rather as incidents in the course of a general process. Thus it becomes conceivable that these lesions may at times be wanting. And this is the fact. The prodromal symptoms of the disease, the headache, malaise, anorexia and fever, are to be referred to the nervous system, and the lesions of the intestines may be atypical, delayed, or even absent. Our knowledge, then, of the symptomatology of the disease goes to prove that typhoid is not primarily or necessarily a disease of the intestines any more than variola is merely a disease of the skin. And in support of this view we have the analogous intestinal lesions which are sometimes present in the course of variola, measles, scarlatina, erysipelas and pyæmia. Besides this there is the well known fact that the intestinal lesions bear no relation to the severity of the systemic infection, nor do the objective symptoms referable to the intestine—meteorismus, diarrhœa and the like—bear any relation to the local pathological condition.

Consequently it would be more definite and more accurate to include the typical text-book disease under the term "Enteric Fever," employing the term "Typhoid" in a wider sense to include all pathological processes and conditions resulting from the action of the bacillus typhi or its toxins.

For purposes of comparison the following authenticated cases of typhoid with absence of the usual intestinal lesions may be tabulated as follows:

Case.	Observer,	Clinical Type.	Pathological Condition.
1.	Banti. . . .	Ordinary type.	Intestines normal. Spleen and mesenteric glands swollen. B. Typhi in spleen and mesenteric glands.
2.	Thue	Spleno-typhus.	Slight tumefaction of Peyer's glands. B. Typhi in spleen and kidneys.
3.	Vaillard.. . . .	Meningo-typhus.	Peyer's Patches normal. B. Typhi in lungs, spleen, spinal cord. Streptococci in meninges and spleen.
4.	Karlinski. . . .	Enlarged spleen. Typical symptoms wanting.	No lesions in intestines or mesenteric glands. B. Typhi in spleen. Cultures from other organs and blood, sterile.
5.	Karlinski. . . .	Enlarged spleen. Dark red papules on trunk.	Intestines normal. Two areas of softening on septum of right ventricle. B. Typhi in spleen, liver, kidney and heart.
6.	Vincent	Diarrhœa, purpura, coma.	Peyer's patches normal. Congestion of small intestines. Spleen and mesenteric glands not swollen. Bilateral pulmonary congestion. B. Typhi and streptococci in spleen, liver, kidneys and heart.
7.	Du Cazal. . . .	Ordinary type.	No lesions of intestines or mesenteric glands. B. Typhi in spleen.
8.	Beatty	Jaundice, hæmaturia, coma.	Peyer's patches normal. Mesenteric glands and spleen enlarged. B. Typhi in spleen.
9.	Cheadle	Meteorismus, rose-spots, diarrhœa. B. typhi in urine.	Peyer's patches normal Spleen not enlarged. Liver and mesenteric glands enlarged. B. Typhi in spleen. Partial serum reaction.

The case which we have the opportunity of reporting is in minor points somewhat different from any heretofore described. Unfortunately the history is imperfect on account of the very critical condition of the patient on admission.

For permission to report the case we are indebted to Prof. James Stewart.

Case—W. S., æt. 25, labourer, admitted to Dr. Stewart's wards, Royal Victoria Hospital, on July 8th, 1897 complaining of headache, weakness and constipation.

Personal History.—Whooping-cough, scarlatina and mumps in childhood. Used alcohol to excess until three years ago.

Family History—No inherited taint.

On June 28th, patient came to the out-door department, stating that for some indefinite time, (about two months) previously, he had

been suffering from severe headache, loss of appetite, and general weakness. He had been obliged to give up work several times.

On admission he was found to be a powerful young man, very somnolent and mentally dull. Temp. 103.6°, Pulse 104, Respiration 36. Skin warm and moist. The tongue was coated and dry; abdomen distended, tense and tender. Fading rose spots were visible and spleen was palpable. Bowels constipated. The pulse was dicrotic. Apex beat felt in fourth interspace, half an inch beyond nipple. Heart sounds clear.

Respiratory System.—Expansion, greatest on right side. Some impairment of the note in left axilla. A few moist, crepitant and subcrepitant râles heard in right side. The lungs were not examined posteriorly owing to weakness of the patient.

Urine, sp. gr 1012. No albumen. No sugar.

The blood, as tested by Prof. Wyatt Johnston, gave the typical serum reaction.

From the 8th to the 13th he was semi-comatose and then low muttering delirium set in, with vomiting. At first the bowels were constipated, but after the first week there were involuntary evacuations. The average temperature for the first week was 103° and after that slightly lower. On the day before death it began to rise again and and just before the end reached 106.6°; the pulse 160; respiration 62. Cultures made from the blood the day before death were sterile.

Death ensued on the 21st.

Autopsy.—Eight hours after death (by Drs. J. G. Adami and A. G. Nicholls). Body that of a young adult male with the usual signs of death. Pectorals and recti of fair size and colour. No intra-muscular hæmorrhages or abscesses. Peritoneal cavity dry.

Cranium.—Brain, weight 1250 grains. Slightly hyperæmic.

Thorax.—Bilateral adhesive pleurisy. Trachea reddened and containing frothy mucus. Epiglottis and vocal cords somewhat œdematous. Peri-bronchial glands enlarged. *Right lung*—very œdematous. Lower lobe presented condition of broncho-pneumonia.

Left Lung.—Œdematous. Lower lobes; areas of broncho-pneumonia. Muco-purulent bronchitis.

Heart. Right side contains adherent ante-mortem clot. Valves normal. Muscles of left ventricle pale, cloudy, fatty and friable. Double right coronary. Recent milk spot on right ventricle.

Abdomen.—Spleen. Old perisplenitis. Weight of spleen 375 grms. Numerous infarcts. On section dark red and pulpy.

Intestines.—Mesenteric glands were generally enlarged, congested and succulent, especially about the ileo-cæcal region. Rectum congested and had a distinctly diphtheritic membrane which is most marked in a zone one inch in depth, two inches above anus. The membrane higher up diminished and was present as a dirty greenish layer lying on the rugæ. (Condition probably due to enemata of whisky.) Large intestine somewhat congested and rather slaty with very slight prominence of the solitary follicles. The lowest three Peyer's patches of the Ileum were very slightly raised above the general surface but showed no signs of inflammation. Remaining

Peyer's glands normal. There was no evidence of ulceration anywhere in the intestine, nor any evidence of healed typhoidal lesions. The duodenum showed marked inflammation on tops of rugæ resembling the effects of chlorate of potash.

Stomach.—Moderately small. Posterior aspect greatly congested, extending to lower end of œsophagus. Area of congestion has a characteristically velvety appearance. (Patient had been treated with Yeo's mixture.)

Pancreas.—Pale and glassy looking.

Liver.—Weight 1570 grms. Organ pale, flabby, with moderately obtuse edges. Slight fatty appearance. Bile ducts fairly full of bile. Not specially friable. No focal necroses recognizable. Gall-bladder distended and full of thin greenish bile. Common duct free. Old pericholecystitis.

Kidneys.—Supra-renals cavitated.

Left Kidney.—Weight 210 grms. Capsule peels off with ease. Cortex pale. On section cortex pale and much swollen. Consistency relaxed. Malpighian tufts and straight vessels congested. Fatty change. Sub-acute nephritis.

Right Kidney.—Weight 198 grms. Same as left.

Genito-urinary System—Otherwise normal.

Microscopical Examination.

Lung.—Areas of broncho-pneumonia. Section stained by Gram-Weigert method showed a vast agglomeration of the micrococcus lanceolatus about the pneumonic patches. By Löffler's method a few large bacilli were noted but did not resemble typhoid.

Heart.—Cloudy swelling.

Spleen.—Hyperplastic and congested. Infarction. Stained by Löffler's method, clumps of B. Typhi were seen in pulp. Decolorised by Gram.

Liver.—Severe parenchymatous degeneration amounting in parts to diffuse inflammation with necrosis. Some fatty change. Infiltration of leucocytes in portal sheaths. Proliferation of bile capillaries.

Kidneys,—Sub-acute parenchymatous nephritis. No bacilli seen.

Pancreas.—Slight necrosis of cells.

Thyroid.—Normal.

Mesenteric Glands.—Hyperplasia and acute congestion with commencing necrosis in the centre. By Löffler's method sections show B. Typhi in small numbers, in the characteristic clumps.

Peyer's Patch. A section was made through one of the Peyer's glands which presented the slight swelling. All that could be found was a proliferation of the lymphatic tissue in the sub-mucosa which was very generally infiltrated with lymphoid elements. This affected only the sub-mucosa. The patch was not congested and there was no evidence of necrosis. Stained by Löffler's method, in the deeper parts were found small clumps of bacilli resembling typhoid and which decolorised by Gram's method. On superficial part were numerous bacilli of various kinds, evidently intestinal bacteria which stained by Gram-Weigert method.

Bacteriological Examination.

Cultures from blood taken at autopsy were sterile. Serum gave the typical Widal-Johnston reaction. Cultures from the spleen on agar gave pure growth resembling typhoid. The bacillus was actively motile and negative to Gram. It was grown on gelatin, lactose agar, bouillon, potato and milk, and in every way corresponded to Eberth's bacillus. Litmus agar cultures have in our experience proved fallacious. Tested by the action of typhoid serum a typical Widal-Johnston reaction was produced. From the liver two varieties were obtained. One gave small round transparent colonies and when grown on the above mentioned media corresponded in every way to the B. Typhi, including the typical reaction to typhoid serum. The other presented colonies which were larger and more opaque than the first, and the growth on agar was more luxuriant and opaque in appearance than the typhoid. It however grew otherwise fairly characteristically, except that it curdled milk and did not give the true serum reaction

It may be said here that these tests were made by both of us independently and the results tallied exactly in each case. Parallel cultures of known typhoid germs were made also as controls, so that the chain of evidence should be as complete as possible.

From a study of the cases above referred to, it will be seen that this atypical typhoid is a very protean disease, its toxic power at one time being concentrated upon the mesenteric glands, at another upon the spleen, the liver and gall-bladder, the central nervous system, upon the kidneys, heart, or lungs, as the case may be.

While in typical typhoid the Peyer's patches suffer the most, yet the relative intensity with which the other organs are affected also varies. Thus, variability, while most characteristic in atypical cases, must be regarded as a feature common to typhoid as a whole. Clinicians have long recognized that one or more of the text-book symptoms may be absent, or in the background, and that cases, while they conform to a broad general type, often present minor differences. With respect to the intestinal tract alone, we now know that there may be all grades from a normal Peyer's patch to the most severe ulceration; not only so, but the usual intestinal lesions may be delayed. Cases have been reported recently where as late as the twenty-first day the Peyer's patches presented merely slight hyperplasia without necrosis. We must recognise then great variety in the intensity and course of the process.

Broadly speaking, typhoid without intestinal lesions falls clinically into three main classes.

1. Typical typhoid, minus the ulcerations.
2. Spleno-typhoid.
3. The nervous type, with extreme intoxication.

To the first group would appear to belong the cases of Banti, DuCazal and Cheadle. Diarrhœa may be present in such cases. Cases of this type are very rare.

The second class, spleno-typhoid, presents a more definite clinical entity, and was first described by Eiselt. This form is characterised by an excessively large spleen, often with acute perisplenitis, and fever of a recurrent type. In such cases the plasmodium malariæ and Obermeyer's spirillum are absent. Some of these cases do present ulceration of the intestines, but it is often absent.

Thue's case and Karlinski's first case are examples of this.

The third class, due to a severe intoxication, are characterised by extreme prostration, delirium, coma, sometimes hyperpyrexia, degenerative changes in the vascular system leading to purpura, hæmaturia, melæna. Jaundice is sometimes present. Many of these cases are, no

doubt, examples of secondary septic infection. To this class apparently belong the remaining cases of the table, including our own.

The case here reported at length presented on admission all the signs of an intense intoxication; extreme prostration, somnolence, high fever, muscular twitchings, delirium, coma, and eventually death. The digestive disturbances were decidedly in the background, thus showing that the activity of the process was more directed to the central nervous system. And there is, indeed, some ground for believing that where the intestinal lesions are slight or absent, the nervous phenomena are both relatively and absolutely more intense.

When we come to the etiology of such cases we enter upon more debatable ground. The usual channel of inoculation is, of course, the alimentary tract, but it is abundantly attested by several observers notably Roux and Sicard, that inoculation through the air-passages is by no means uncommon. Sicard, indeed, thinks that at least 10 per cent. of all cases come about in this way. Roux has noted that in barracks, epidemics of typhoid among the troops often coincided with the process of cleaning the walls and floors. Dufand also has reported an epidemic where infection was carried by the dust in a building, and the disease only died out on a thorough disinfection of the building with sublimate. Cases occurring along the line of excavations are also known. In this particular, the experiments of Sicard are suggestive. He caused typhoid patients to exhale into flasks of sterilized water, and in nearly every case was afterward enabled to cultivate the Eberth bacillus from the flasks. The results of such experiments, when they appear to contradict our commonly accepted views as to the infectious nature of typhoid, must be accepted with some reserve, until other investigators corroborate them and place the matter beyond a doubt. It would seem probable at first sight that when the infection was acquired through the respiratory tract atypical typhoid would result, and it is by no means improbable that in such cases the brunt of the disease would fall upon the lungs, and that the intestines might only be slightly affected or not at all. In the absence of further information we are, however, unable to speak with any certainty upon this point. There is no doubt, however, that the B. Typhi have often been found in the lungs. Certainly the action of the B. Typhi at times analogous to that of other germs, notably the micrococcus lanceolatus, the gonococcus, the colon bacillus, and the pyogenic cocci, renders it altogether likely that some of these rare cases may be due to an unusual mode of origin. In our own case, however, we are enabled in all probability to exclude an origin through the respiratory tract, for the pneumonia which was present was clinically

a terminal event, and sections of the lung, stained by the Gram-Weigert method, showed such a massing of the micrococcus lanceolatus about the pneumonic areas that we were forced to conclude that the condition was due to a secondary affection with this germ.

Sections of the Peyer's patches showed, however, bacilli of the morphology of typhoid germs massed in the deeper parts in the characteristic clumps. So that the lowest Peyer's patches may have been the point of origin in spite of the fact that they presented so little divergence from the normal. A further point in favour of this view was the fact that the mesenteric glands were uniformly swollen soft; some beginning to necrose, and others hæmorrhagic. How can we then explain these facts? Observation gives us some information upon this point.

In relapsed typhoid the ulcerative lesions affect those glands which escaped in the [illegible] attack, and are also never so intense as the primary ones. Trou[illegible] indeed goes so far as to say that in the relapse the intestinal lesions are not renewed. However this may be, it seems that the intestinal mucosa having once suffered the action of the typhoid virus can resist the force of a second attack, and thus a local immunity is acquired. So that in these relapses the systemic disease may proceed in the gravest manner and even lead to death, while the intestinal lesions are absent. In the case we record, considering that it was an ambulatory typhoid of six weeks' to two months' duration before admission, it is open to assume that the attack we observed was a reinfection, and that at some earlier period of the illness in the previous attack the Peyer's patches had acquired a local immunity. This primary attack need not necessarily have been a severe one. It is quite probable that in the so-called abortive typhoid the Peyer's patches never get beyond the stage of tumefaction, and yet they will have acquired an immunity for a short time. Cases where a second distinct attack follow shortly after convalescence upon a previous one would, at first sight, appear to negative this view, but we must remember that in experimental animals when this local immunity is attained, it only lasts for a short time, and we have no reason to think that it would be otherwise in the human being. This immunity affects the epithelial and lymphoid elements of the intestine and also the phagocytes, so that the bacilli are carried beyond the first barrier of defence, which remains intact, and are dealt with in the more remote parts of the organism.

We have an analogy to this in the well-known fact that the bacillus of tuberculosis sometimes passes through the intestinal mucosa without affecting the lymphoid elements, and may become localized in the mesenteric glands or in the peritoneum.

Or we may assume that certain ptomaines derived from the gastro-intestinal tract, either circulating in the blood, or present in the intestinal mucosa, act so as to neutralise the local action of the typhoid virus and bring about intestinal immunity. Finally, we may assume that toxins derived from germs other than typhoid may antagonise their virus and a local immunity be thus acquired.

To decide between these hypotheses is an impossible task in our present state of knowledge. As yet they are merely hypotheses, based, it is true, upon experiment, but exactly the degree of importance they possess in relation to the cases here referred to it is impossible to say. Still they are very suggestive. The first assumption indeed explains the process as a partial vaccination of the Peyer's glands and consequent immunity to a second attack. But why should the glands be singled out? Possibly the action of the intestinal mucosa in excreting circulating toxins may have something to do with this, the poison as it were being concentrated upon the enunctories, and thus an immunity is conferred upon the intestinal glands while other organs are not protected.

The last two hypotheses are based upon the theory of a mutual antagonism between the toxins of various germs. This opens up a vast subject in which we are still groping in the darkness of ignorance. The relations of the B. Typhi to the colon bacillus and other members of the colon group, and to the bacteria of the intestinal tract generally, are still unknown, although we are gradually beginning to see the light. But indeed the whole subject is so entangled with the variability in the toxic power of the germs concerned and the question of the resistance of the bodily organism, that the difficulties assume gigantic proportions.

The recent experimental studies of Sanarelli throw considerable light upon this subject.

It may be objected that no proper inferences can be drawn as regards the human organism from a study of experimental animals, but this is not so. The character of the lesions in the lower animals depends very much upon the amount of the toxin inoculated and its virulence. When strong toxins are used, a condition is obtained bearing very close analogies to that which obtains in the case of human beings, including the intestinal lesions.

Sanarelli took two series of guinea-pigs and administered for five days 4 cc. of a typhoid culture in glycerinated bouillon kept for a month in the incubator at 37°C., and then sterilised at 120°. In the first lot of animals the vaccine was introduced into the stomach by means of a sound, and in the second inoculated subcutaneously. The

last series of animals were used as controls to determine the limit of tolerance of the organism. It was found that when the animals which had received the typhoid poison through the stomach up to the limit of tolerance, were inoculated with even small doses of a virulent culture of B. Typhi they died in 8 to 24 hours, and presented neither meteorism, abdominal pain, nor intestinal lesions, while animals which had not been vaccinated died in about the same time, but with the intestines intensely congested and ecchymotic, lymphatic glands enlarged, and mucosa destroyed.

From these experiments it follows that when an organism receives doses of typhoid toxin within the limits of toleration, the intestinal tract acquires a local immunity. A subsequent injection with a virulent growth thus may produce death, largely through the nervous system, while the intestine remains normal.

Sanarelli also discovered the curious fact that subcutaneous injections of sterilized products of the putrid fermentation of beef-broth also conferred immunity upon the intestine, thus opening up the question whether ptomaines derived from abnormal conditions of the digestive tract in man may not have some bearing upon the question of the immunity of the intestinal tract.

This observer also noted the fact that in guinea-pigs suffering from typhoid, the colon bacilli in the intestine increased both in numbers and in virulence, killing out all the other germs, and is inclined to attribute some of the secondary processes in typhoid fever to the invasion of the body by these germs which have thus become pathogenic. An immunity of the organism to typhoid also proved to be an immunity against the action of the B. Coli. Klein's work, too, on the inhibitory action of certain germs, as the Prodigiosus, Komma bacillus, and putrefactive organisms, upon the typhoid bacillus is also very important in this connection.

Altogether Sanarelli's work is the most complete and suggestive one which has yet appeared, and we may reasonably hope for important developments along these lines.

We fear that this paper may appear to some too theoretical and visionary. It was not our intention, however, to lay down hard and fast principles, but rather to draw attention to lines of thought suggested by the newer pathology. Clearly our old views of the pathological processes in typhoid fever will have to be considerably modified, in fact almost replaced by a more adequate and elastic interpretation of clinical facts, and our conceptions, while at present losing definiteness, must acquire greater breadth until further research places the subject on a clearer basis.

That the field is an almost untrodden one, and that the clinical opportunities are so very limited, must be our excuse for bringing forward such an immature and altogether inadequate presentment of the subject. We must emphasize, however, our opinion that the current views upon typhoid fever are far too cramped and stereotyped to convey an accurate impression of the true nature of the pathological processes in this disease.

BIBLIOGRAPHY.

Banti, Archiv. Italiennes de Biol., Dec. 1887.

Thue, Jahresbericht über die Fortschritte (Baumgarten) 1889, p. 196.

Vaillard, La Semaine Médicale, March, 1890.

Vaillard and Vincent, De l'infection par le bacille typhique sans lesions intestinales. Bull. et Mém. de la Soc. Méd. d. Hôp. de Paris, 1890, p. 201.

Coupland, Enteric Fever without ulceration of the Peyer's patches. Middlesex Hosp. Rep. 1889-91, 29.

Karlinski, Wiener Med. Wochenschrift, March 14-21st, 1892.

Eiselt, Gazette Hebdomadaire du Méd. et Chir. de Paris, June 20th, 1892.

Vincent, Annales de l'Institut Pasteur, Feb. 1894,

DuCazal, Le Bulletin Médical, Paris, April 16th, 1894.

Beatty, W., Brit. Med. Jour. Jan. 16th, 1897, p. 148.

Cheadle, Lancet, 1897, ii., p. 251

Sanarelli, Etudes sur le Fièvre typhoide experimental. Ann. de l'Institu Pasteur, 1894, pp. 193 and 353.