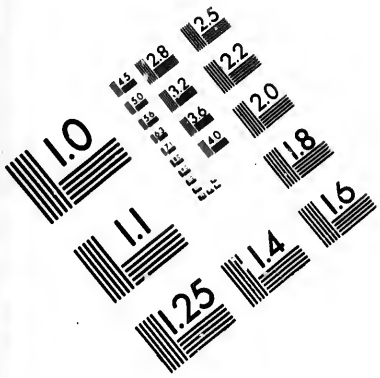


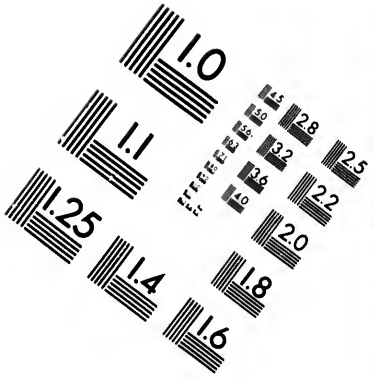
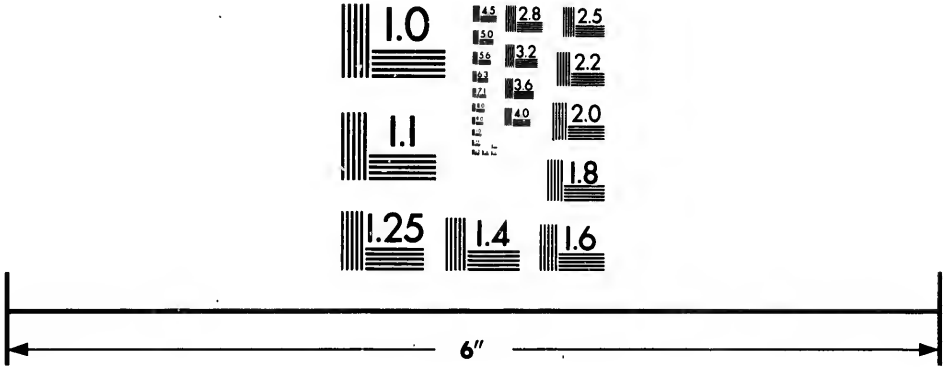
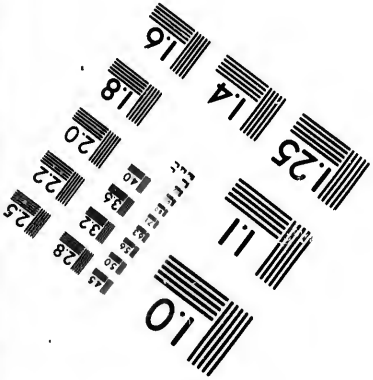
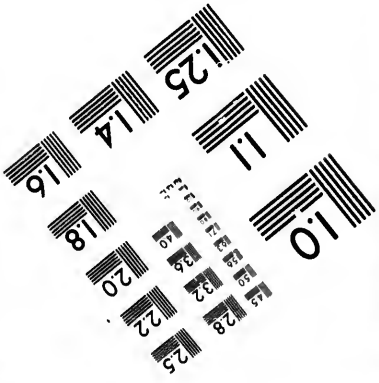


IMAGE EVALUATION TEST TARGET (MT-3)







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.

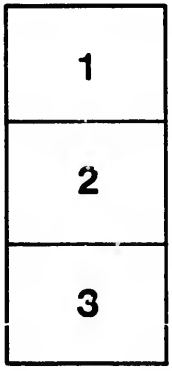
- ☐ Coloured covers/ Couverture de couleur
- ☐ Covers damaged/ Couverture endommagée
- ☐ Covers restored and/or laminated/ Couverture restaurée et/ou pelliculée
- ☐ Cover title missing/ Le titre de couverture manque
- ☐ Colcured maps/ Cartes géographiques en couleur
- ☐ Coloured ink (i.e. other than 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 distorsion 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:

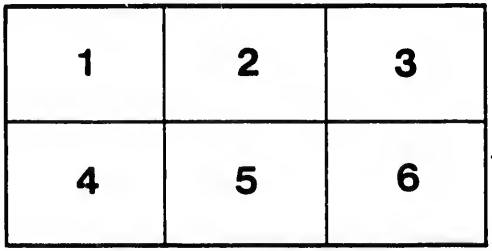
L'Institut a microfilmé le meilleur exemplaire qu'il lui a été possible de se procurer. Les détails de cet exemplaire qui sont peut-être uniques du point de vue bibliographique, qui peuvent modifier une image reproduite, ou qui peuvent exiger une modification dans la méthode normale de filmage sont indiqués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

- ☐ Coloured pages/ Pages de couleur
- ☐ Pages damaged/ Pages endommagées
- ☐ Pages restored and/or laminated/ Pages restaurées et/ou pelliculées
- ☑ Pages discoloured, stained or foxed/ Pages décolorées, tachetées ou piquées
- ☐ Pages detached/ Pages détachées
- ☑ 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
			✓								





Hae

HAMILTON - W. F. 27

THE HÆMORRHAGIC DIATHESIS IN TYPHOID FEVER AND ITS RELATIONSHIP TO PURPURIC CONDITIONS IN GENERAL.[1]

IT is a matter of common observation that in certain infectious and presumably infectious diseases like typhus fever, scurvy, Werlhoff's disease, and peliosis rheumatica, hæmorrhagic eruptions develop in the skin and mucous membranes. That which is the primary and cardinal train of symptoms in these diseases may be found exceptionally as a complication in certain others, like variola, scarlet fever, measles, enteric fever, cholera, yellow fever, sepsis, and acute atrophy of the liver.

In the course of typhoid fever or enteric fever a number of examples have been recorded during the past two decades where hæmorrhagic complications have supervened. Of course, minor hæmorrhagic manifestations, like epistaxis which so frequently ushers in the attack, or like intestinal hæmorrhage which is present in a considerable proportion of ordinary cases, are common enough, while either of these conditions may, under certain conditions, be part and parcel of a general hæmorrhagic tendency and represent its first symptom. This does not in itself constitute the hæmorrhagic diathesis. This term should be restricted to those cases where multiple hæmorrhages take place and which are evidenced clinically by purpuric eruptions into the skin, oozing of blood from the mucous membranes, epistaxis, hæmoptysis, hæmatemesis, melæna, or metrorrhagia. All of these symptoms, of course, may not be present simultaneously, since very varying grades of the condition exist. Most authorities are agreed that such occurrences are very rare, though their possibility has been recognised for many years.

[1] We desire to express our thanks to Dr. W. F. Hamilton of the Royal Victoria Hospital, Montreal, for the opportunity of recording this case of hæmorrhagic typhoid fever.

Some hesitation has arisen in our minds in regard to the proper expression which should be used to designate this interesting form of typhoid fever. The term "hæmorrhagic diathesis" is possibly open to criticism, since to many minds it connotes the idea of some pre-existing constitutional deficiency or dyscrasia of the blood or some congenital weakness of the blood-vessels. With the single exception of certain of Wagner's cases, to be referred to later, such inherited defects can usually be excluded in the type of disease under consideration, and yet it is clear that there is at work some serious disturbance of the blood. Further, the term "purpura hæmorrhagica" is not altogether suitable, since it has not been settled between clinicians and pathologists what conditions are properly to be included under this designation. Litten, for instance, restricts the term to Werlhoff's disease, Schönlein's disease, and some others, and would deny it to the purpuras which occur in variola, typhoid fever, sepsis, and mineral poisoning. We must, however, dissent strongly from Litten's view, for the trend of recent pathological research, as we shall see, is to prove that the prime factor underlying the vast majority of cases is some systemic intoxication, either bacterial, chemical, or animal, and there is no sufficient reason for believing that Werlhoff's disease and the group of so-called "idiopathic purpuras" differ essentially from the others in this respect.

That circulating toxins, bacterial or otherwise, do produce marked alterations in the quality and composition of the blood and lead to degenerations of the blood-vessels may be regarded as proven. Since, then, we have to admit a serious qualitative vitium in the blood, even though it be acquired, and since we are unable entirely to exclude the presence of some inherited defect, it would seem fairly scientific and at the same time less liable to misapprehension if we use the designation "hæmorrhagic diathesis" for these cases in preference to any other.

We in Montreal have had the unusual experience of meeting with four cases of a more or less hæmorrhagic type in a series of about 200 cases of enteric fever from the clinic of Professor James Stewart at the Royal Victoria Hospital. These were recorded by one of us (Nicholls[2]) in 1896, but at that time little attempt was made to analyse the clinical symptoms or to determine pathological conditions.

In the present communication we are enabled to report an

[2] Hæmorrhagic Typhoid Fever, Montreal Medical Journal, June, 1896 (Bibliography).

additional most extreme example of enteric fever with the hæmorrhagic diathesis, which has been very carefully worked out and which will, we hope, help to place the subject on a more satisfactory basis.

The hæmorrhagic type of enteric fever has for years been recognised as a clinical entity and was first brought into notice by the earlier French school, notably Trousseau, who referred to it under the name of "*fièvre putride hémorragique*." Liebermeister in Von Ziemssen's Cyclopædia notes the occurrence of hæmorrhages from the nose, gums, stomach, bowels, lungs, kidneys, ecchymoses into the skin, and extravasation of blood into the various organs and serous cavities. He further remarks that hæmorrhages into the skin, true petechial vibices, are most likely to occur in patients of a hæmorrhagic diathesis, but occasionally appear in others. Murchison[3] had occasionally observed hæmorrhages into the muscles. Wilson and Loomis mention hæmorrhages from mucous surfaces and in the skin. Wood and Fitz[4] state that "hæmorrhagic typhoid fever is a very deadly complication of the disease, especially prone to occur in debilitated subjects suffering from scorbutus, alcoholism, &c. There is in it a rapid alteration of the blood with profuse hæmorrhage from the nose, mouth, intestines, and kidneys—indeed, from all the mucous membranes, the formation of abundant ecchymoses, blotches, and suggillations, &c. In these cases the adynamia is extreme from the beginning, the fever is high, the pulse very rapid and small, heart's action greatly enfeebled, tongue and mouth loaded with a brownish deposit, the breath very fœtid and even ammoniacal. Death usually occurs before the tenth day in these cases and has been recorded as early as the third."

Osler[5] says of hæmorrhagic typhoid fever: "This is excessively rare. ..... Hæmorrhages may be marked from the outset, but more commonly they develop during the course of the disease. The condition is not necessarily fatal." Hare[6] in his admirable monograph on "The Medical Complications of Typhoid Fever" states that "hæmorrhagic eruptions may occur in the course of typhoid fever, and, as a rule, they appear in the neighbourhood of the joints, when the exudation may be small or quite large."

[3] Continued Fevers, 1873, p. 609.
[4] Practice of Medicine, 1897.
[5] Practice of Medicine, 1899.
[6] Medical Complications, Accidents, and Seque'æ of Typhoid or Enteric Fever, 1899.

It is somewhat singular that the cases of hæmorrhagic enteric fever published during the past four or five years have been regarded chiefly as clinical curiosities and no attempt has been made to study the condition fully or to ascertain its cause. Indeed, in most even the clinical features are very inadequately described, and in a very few where a post-mortem examination has been made the investigation has been, to say the least, very superficial. After a careful study of the recorded cases we have been obliged to conclude that they are of little scientific value and do not materially advance our knowledge of the intimate nature of this process. In the case herewith presented we have endeavoured to make a minute examination of the various organs in the hope of arriving at a more adequate conception of the processes involved. The case was as follows.

A female, unmarried, aged 21 years, a school-teacher, was admitted to the Royal Victoria Hospital under the care of Dr. W. F. Hamilton on June 19th, 1900, with headache, anorexia, and pain in the back. Her history was as follows. She was born in Canada. She had had measles eight or nine years previously, but no other illness; her habits were regular and her food and clothing were satisfactory. Her father was subject to asthma; her mother was weakly and "bothered with her kidneys"; and two sisters were dead (one from diphtheria). Careful questioning failed to elicit any evidence of hæmophilia or rheumatism. The patient first felt ill six days before admission, but kept at work for two days. The illness began with chill, pains in the back, and following this some fever. The condition persisted and gradually got worse until she applied for admission to the hospital. On admission the patient was a well-nourished girl of medium size. Her face was flushed, her eyes were dull, and her lips were dry and sore. The temperature was 100° F., the pulse was 98, and the respirations were 22; the mucous membranes were pale. The pulse was regular and of good volume; tension was slightly *plus*. The apex beat was visible in the fifth intercostal space, two and three-quarter inches from the mid-sternal line. Cardiac dulness was normal. On auscultation the first sound at the apex was rather muffled; at the base the pulmonary second sound was extremely accentuated. With regard to the respiratory system expansion was good; a few fine crackling râles could be heard over the base of the right lung posteriorly; the lungs otherwise were normal. The tongue was dry and caked; it was moist at the edges.

The teeth were covered with sordes; anorexia was marked; the bowels were regular. The abdomen was slightly prominent below the level of the umbilicus. There was no rigidity; general tenderness was present. The percussion note was tympanitic throughout. The spleen was doubtfully palpable. The liver was not palpable and dulness was normal in extent. The skin was hot and dry. Numerous rose-spots were present upon the abdomen. The muscles were small and flabby. The lymphatic glands were not palpable. The intelligence and memory were good; there was no headache; the patellar reflexes were increased. Menstruation began at 14 years of age and was normal. On June 7th, 14 days from the onset of the first symptoms, a hæmorrhagic area made its appearance near the umbilicus following the application of an ice-bag. There was distinct ecchymosis of the skin of a dark purple colour which did not disappear on pressure. On the 20th the abdomen was still distended but less tender. On the 29th the patch on the abdomen was fading. During the night the patient had two intestinal hæmorrhages and multiple hæmorrhages were present over the left half of the trunk posteriorly. On the 30th, during the night, there were profuse epistaxis and hæmorrhage from the lips and gums and effusion of blood into the conjunctivæ, and during the day there was hæmaturia. A blood count gave 13,000 leucocytes. Widal's reaction was present. On July 1st subconjunctival hæmorrhages of the right eye had partially disappeared, but now there was hæmorrhage below the right lower eyelid. The urine still contained blood, but there was no vaginal bleeding. There were a few subcutaneous hæmorrhages upon the trunk. During the night there were epistaxis and hæmorrhages from the back of the throat. On the 2nd ten ounces of saline solution were injected below the mammæ. A few subcutaneous hæmorrhages appeared upon the lower limbs. The patient was much weaker. A blood count gave 1,540,000 erythrocytes and hæmoglobin 35 per cent. On the 3rd the patient did not sleep and became gradually weaker and died at 8.40 A.M. The treatment adopted was as follows. Cold baths, 18 in all, were given until the hæmorrhagic tendency developed. Spirit of turpentine and liquor calcis chloridi were given internally; applications of suprarenal powder in glycerine were made to bleeding mucous surfaces.

This case may be described as one of typhoid fever of moderate severity occurring in a young person in previously good condition. The course was typical except that the disease set in with a chill and the spleen was at no time

definitely discoverable by palpation. The abdomen was not particularly distended and the bowels were regular, moving generally once daily; during the last three days of life the bowels were constipated. The highest point which the temperature reached was 104·3° on the day of admission. During the following four days the temperature kept about 103° or 102·2°, being reduced about two degrees by the tubs. During the next three days the temperature averaged about 101·2°. On June 29th, when the hæmorrhages from the bowels took place, the temperature in the course of seven hours dropped from 103° to 100·2°, but rapidly returned to 102·3°. On the 30th the incidence of the submucous hæmorrhages led to a more decided fall, the temperature coming down to 98·2°; the return was almost immediate to 101·3°. On July 1st the average was 100°, on the 2nd 99·2°, and at death on the 3rd the thermometer fell to 95·2°. The character of the temperature curve at no time suggested the idea of any septic infection, nor was it affected by the development of the hæmorrhagic diathesis in any other way than is usually seen in enteric fever where there is considerable loss of blood.

Necropsy.—A post-mortem examination was made two hours after death by Dr. W. W. Ford. The body was found to be that of a well-developed young female presenting the usual signs of death. The skin and mucous surfaces were pale. The breasts were well developed, the genitalia were normal, and the rectum was normal. In the left eye hæmorrhage had taken place into the sclerotic at the internal canthus. There was also slight hæmorrhage into the conjunctiva of the right eye in the neighbourhood of the inner canthus. The skin below both lower eyelids was discoloured. The mucous membrane of the lips showed small ecchymoses; the pharynx was apparently normal. There was subcutaneous discolouration below the right breast at the site of the saline injection. There were a few dark areas of subcutaneous hæmorrhage over the left buttock. Petechial spots were scattered rather plentifully on the skin of the trunk in front together with some irregular ecchymoses; one most striking feature was a large ecchymosis, roughly oblong in shape, about 12 centimetres across, which was situated near the umbilicus and represented the site where the ice-bag had been applied. A few petechial spots and small ecchymoses were present on the left thigh just above the knee and above the left internal malleolus. The cranium was not touched. The diaphragm reached to the height of the fifth rib

in the right side and the fourth on the left. The right lung presented a few old adhesions posteriorly and to the diaphragm. The pleural surface of both lungs showed numerous punctate hæmorrhages. The right lung weighed 460 grammes. The bronchi were filled with frothy fluid; the mucous membrane was normal. The tissue on section was congested and œdematous and numerous indefinite patches of hæmorrhage, some of them of the size of small peas, were present throughout the substance. The edges of the lung were emphysematous. The left lung weighed 450 grammes. On section it was found to be congested about the posterior surface; in other respects it was similar to the right. The heart weighed 190 grammes. The right ventricle was filled with red blood-clot; all the valves were normal. The tricuspid orifice admitted the tips of two fingers. The edges of the mitral valves were a trifle thickened; the mitral orifice admitted three fingers. The left ventricle was filled with blood-clot. The heart muscle was pale and contained a few pin-point hæmorrhages. In the abdomen there was a fair amount of subcutaneous fat of a normal deep straw colour except at the umbilicus, where it was discoloured by free extravasation of blood into the tissues. On opening the abdomen the intestines were found to be slightly distended. The great omentum lay coiled up on the left side below the spleen. The peritoneum was smooth and glistening. The appendix lay on the brim of the pelvis pointing upward and inward; no fluid was found in the peritoneal cavity. The retro-peritoneal tissues over almost the whole of the lower part of the abdominal cavity were occupied by a large recent hæmorrhage which spread over the whole surface of the pelvis, over the top of the bladder to the front, and towards both sides. The spleen weighed 90 grammes; the surface was smooth and the capsule was rather wrinkled and showed a few minute subcapsular hæmorrhages. On section it was rather friable but was not congested or juicy. Except for the points noted it was practically normal and was far removed from the appearance of the ordinary typhoid spleen. There was nothing special in the stomach. In the duodenum, one inch below the pylorus, there was a minute pale scar as if from a healed peptic ulcer. The peritoneal surface of the small intestines showed numerous areas of a dark red colour. The serous coat, however, was smooth and showed no signs of exudate. At these points the intestinal walls were thickened and the patches evidently corresponded to hæmorrhages into the

inflamed patches in the bowel wall. The mesentery was occupied by a large hæmorrhage which was dark red in colour. On cutting into this the blood was found to be coagulated. The lymphatic glands of the mesentery were enlarged and succulent. In the ileum the Peyer's patches were only slightly swollen, showing marked hyperplasia of the lymphoid elements. One of these patches showed hæmorrhage into its substance. In the lower part a few shallow serpiginous ulcers were present. The peritoneal surface of the rectum and the meso-rectum were occupied by a number of hæmorrhages. Numerous hæmorrhages were also present in the appendices epiploicæ of the sigmoid flexure and the rectum, dark red in colour. The mucous membrane of the large intestine was congested and catarrhal throughout. The solitary follicles were numerous and somewhat swollen. Many shallow and some deep ulcers were present in the cæcum about the ileo-cæcal valve and in the first part of the colon. The bases were somewhat indurated. The ulcerations were fairly characteristic of typhoid fever at the end of the third week, except that they appeared to be more indurated than usual This was explained by the fact that many of these were infiltrated with dark-red blood which caused the bases and edges to appear to be thickened, somewhat masking the typical appearances. The ulcers in the neighbourhood of the ileo-cæcal valve were large and sinuous. About 30 ulcers all told were present in the intestines. The mucous membrane of the rectum was apparently normal ; the rectum was filled with clotted, dark greenish, altered blood. The pancreas weighed 130 grammes. On section it was found to be of pale colour and well lobulated. A few minute hæmorrhages were present upon the surface. The lymphatic glands in the neighbourhood were large and succulent. The liver weighed 1225 grammes. Its serous surface was smooth ; on section it was markedly pale with cloudy swelling. No fæcal necroses were seen. No hæmorrhages were present. The gall-bladder was filled with dark-coloured bile. The wall, where the organ was attached to the liver, was infiltrated with blood. The left kidney weighed 140 grammes. Its capsule peeled off with ease. Many small pin-point hæmorrhages of a dark reddish-brown colour were noticed on the cortex. The surface was congested. On section the organ was very much congested, the glomeruli showing as reddish points. Numerous hæmorrhages were seen in the Bowman's capsules and along the course of the interlobular and straight vessels. The cortex measured 18 millimetres in thickness. The kidney was fairly firm and was of

a dark greyish-brown colour. The right kidney weighed 120 grammes; in all respects it was similar to the left. The mucous membrane of the bladder was pale and showed above a few submucous hæmorrhages. The bladder was filled with clotted blood and there was a very large submucous extravasation of blood in the lower two-thirds of the organ posteriorly, from which the oozing apparently had taken place. The uterus was small; the external os contained blood-stained mucus. The vagina contained no blood. The ovaries were small; the left contained a few clear cysts of small size; there were no hæmorrhages. The Fallopian tubes were normal.

Microscopical examination. — Stained with Ehrlich's hæmatoxylin the fibres of the heart muscle were somewhat thin and wavy. The staining of the nuclei was faint and the transverse striation was indistinct. The longitudinal fibrillation was well marked. Beyond some cloudiness there was no special change. In sections stained by the carbol-thionin and Gram-Weigert methods no bacteria were seen. Hæmatoxylin preparations of the lung showed small irregular hæmorrhagic patches here and there throughout the tissue These were somewhat poorly defined at the margins, passing off gradually into the more healthy condition. The alveolar walls throughout were on the whole rather thin and those within the infarcted areas were much compressed. The walls everywhere stained fairly well. The interstitial tissue showed slight anthracosis. Small areas of collapse were noted in many portions. There was distinct catarrh of the lining endothelium of the alveolar processes, many of the alveoli being filled with, in addition to a few red cells, large mononuclear cells containing granules of pigment and débris. The débris in part consisted of broken-down erythrocytes. No emboli were seen.

Portions of the tissue were stained with osmic acid (Fleming's solution) and Sudan III. for fat. The osmic preparations were the less satisfactory since it was hard to distinguish fatty particles from pigment granules. The Sudan preparations, however, showed very well in places moderate fatty degeneration of the endothelium covering the alveolar walls. Sudan III. possesses the property of staining fat-droplets a golden yellow or carmine colour, according to the size of the droplet. In some places the alveolar walls were distinctly picked out by the stain, showing as a

pinkish network. With a high power this was seen to be due to minute particles of fatty matter dotted throughout the endothelial plates. Certain of the desquamated moncnuclear cells within the alveoli were loaded with fatty matter. Many others, and some also of the lining cells of the walls, contained pigment of a brownish colour, which was not fat but was apparently derived from the broken-down red cells. By the Gram-Weigert stain no bacteria were noted. By carbol-thionin certain of the bronchi were seen to be plugged with exudate, the lining columnar epithelium being desquamated and in part degenerated. The exudate consisted in large part of oval or spindle-shaped mononuclear cells together with crowds of bacteria consisting of coccus forms and medium-sized bacilli having rounded ends. These bacilli varied much in length, some being very short, some were slightly curved, and others were bulbous at the ends. Most showed bipolar staining. Similar bacilli were present in great numbers in the collapsed areas. One small bronchiole was found to contain blood, an infarct having presumably burst into it.

Spleen: the staining agent used was hæmatoxylin. It was not congested and was without any special abnormality except some hyperplasia of the so-called epitheloid plates. The tissue was not œdematous and there was no perisplenitis. By the Gram-Weigert and carbol-thionin methods no bacteria were seen. Liver: the staining agent used was hæmatoxylin. The tissue stained fairly well and the nuclei were distinct. The cells were swollen and cloudy. No particular fatty change was observed and there were no hæmorrhages. Everywhere could be seen in the intercellular spaces within the lobules little scattered groups of two or three polynuclear cells. In the portal sheaths, by the carbol-thionin method, a small amount of acute interstitial infiltration could be made out chiefly along the course of the portal vein. These aggregations were not at all striking, however. In one or two sections also a few small lymphomatous masses could be observed consisting of small round mononuclear cells, with a few larger mononuclear hyaline cells resembling macrophages. No true focal necroses were noted. No bacteria were observed. By the Gram-Weigert method no bacteria were noted. Pancreas: hæmatoxylin was the staining agent used. Except that the tissue stained rather faintly there was nothing specially worthy of note. Kidney: hæmatoxylin was the staining agent used. Numerous areas of hæmorrhage were present both in the cortical

portions and in the medulla. This hæmorrhage was marked in the interstitial substance in various places but was very strikingly shown in those parts where the blood had forced its way into the kidney-tubules, many of which were greatly distended with blood. In the cortical portion the hæmorrhages appeared to be most marked in the neighbourhood of the interlobular vessels running vertically forwards to the cortex. In one section a Bowman's capsule contained much blood and the glomerulus was distinctly compressed. The tubules, mainly the tubuli contorti, which contained the blood, were over-distended and the lining secretory cells were greatly flattened. In the medullary portion the straight and collecting tubules contained blood. Everywhere the extravasation was of recent appearance. Small, more wedge-shaped, masses were common just beneath the capsule. The glomerular tufts were not congested but the lining endothelial cells of the Bowman's capsules were swollen and occasionally desquamated. In a few capsules small masses of albumin could be made out. In the remaining parts the lining cells of the secreting tubules were swollen and granular-looking and the staining was defective. In the medulla and in one specimen surrounding a glomerulus and capsule near the cortex there was fairly extensive round celled infiltration consisting of inflammatory leucocytes. The surrounding congestion was not great, however. The endothelium of the affected capsule was notably catarrhal. One of these infiltrated areas was large enough to suggest an abscess. A few small areas of round-celled infiltration were seen in some sections consisting of mononuclear elements and no doubt to be regarded as the so-called "lymphomata" of Wagner. The osmic acid and Sudan III. preparations showed practically the same features. There was a moderate degree of fatty degeneration affecting in some instances the basement membranes of the Bowman's capsules and very generally the secreting cells of the contorted tubules and the descending loops. Those tubules which contained blood showed this in a very extreme degree. The capillaries of the tufts were, as a rule, free, though certain of them showed slight fatty change. The sections stained by carbol-thionin showed that in the small inflammatory areas there were to be seen short, fine bacilli with rounded ends and with well-marked bipolar staining. By the Gram-Weigert method no bacteria were observed. The small intestine showed by the hæmatoxylin method marked

catarrh of the mucosa, with some mucoid and cellular exudate upon the surface. The lining epithelium was swollen and the cells were active. The mucosa showed a moderate round-celled infiltration. On the submucosa the lymphoid follicles were swollen and proliferated, the epithelioid plates being specially numerous. The acute inflammatory infiltration extended through the muscular wall, round cells in considerable numbers being found between the various layers of muscle. The serosa was free. Small hæmorrhages were present in the submucosa and muscularis. The carbol-thionin method showed a few short bacilli with rounded ends and of moderate size imbedded in the mucus on the surface. None were seen in the deeper layers. By the Gram-Weigert method no bacteria were seen. The blood-vessels were examined very carefully in the lung, liver, and kidney with the view of ascertaining if any clots were present. The most that could be said was that in these different organs the blood in both arteries and veins showed a tendency to break down, the red cells being apparently converted into a fine granular material of pale brownish colour in which a few leucocytes were imbedded. Besides these there were certain large clear mononucleated cells which appeared to be swollen and desquamated endothelial cells. These endothelial cells of the small vessels and capillaries were everywhere more prominent than usual, a condition which has been described by F. B. Mallory[7] as a constant feature in typhoid fever, but found also in diphtheria and some other infectious fevers. Nowhere were definite fibrinous clots of emboli observed. The condition of alteration of the blood is one that we would lay no particular stress upon, for it is one which we have often seen in other cases, particularly in specimens which have been kept for some time in methylated spirit. Nowhere were bacterial emboli, acute arteritis, or phlebitis discovered. The arterioles and the larger vessels showed no histological peculiarities.

Bacteriological examination.—Unfortunately, through an oversight, cultures were not taken from the spleen or mesenteric glands. Agar cultures were made from the heart-blood, peritoneal cavity, and the kidneys. Small round pearly-white growths were developed in the peritoneal fluid. These were elevated and discrete; they proved to be cocci

[7] A Histological Study of Typhoid Fever: Journal of Experimental Medicine, 1898, p. 6111.

staining by Gram's method. They grew readily on all media, liquefied gelatin, coagulated milk, and produced acid. They were regarded as the staphylococcus pyogenes albus. From the heart-blood two varieties were isolated: the first was a thick, elevated, soft, moist growth of a whitish colour and the second was a thinner, more pearly growth, in the shape of more star-like colonies. These were isolated. The first variety were cocci, positive to Gram's method, giving all the cultural peculiarities of the staphylococcus pyogenes albus, and were identical with those found in the peritoneal fluid. The pure growth of the second variety showed a variety of forms, short fine bacilli with bipolar staining, pairs of oval short bacteria, cocci or single short ovoids. Some bacilli present were thicker than the others and somewhat swollen at the ends, apparently involution forms; when of full size the bacilli had rounded ends and were about four times as long as broad. No spores were seen. All were non-motile. These turned litmus milk red and coagulated it, although it took some time to do this. The coagulum was at first in the form of small flakes. It did not liquefy gelatin and did not produce gas in glucose broth. Inoculated into rabbits it proved to be non-pathogenic. Three forms were isolated from the kidney. The first conformed in morphology and cultural peculiarities to the staphylococcus albus. The second presented a variety of forms, short ovoids or cocci, bacillary forms about three times as long as broad with bipolar staining. They were non-motile and without spores; they did not liquefy gelatin and did not produce gas. Litmus milk was unchanged. They were non-pathogenic for rabbits. The third variety was a rather small delicate bacillus producing a greenish fluorescence. The chloroform test did not show any true pigment production. The bacillus was motile; it liquefied gelatin; it did not produce gas or acid and did not coagulate milk. Its reaction to the Gram method was uncertain. A rabbit inoculated through the auricular vein died six weeks later from purulent peritonitis. The original germ was not recovered, however, and the lesions found did not suggest the presence of the bacillus pyocyaneus. The rabbit probably died from some intercurrent infection, the bacillus coli being found in the various organs. The bacillus was finally regarded as the bacillus fluorescens liquefaciens.

The anatomical diagnosis was typhoid fever; typhoidal ulceration of the small, but principally of the large, intes-

tine; general hæmorrhagic diathesis; mixed infection; multiple hæmorrhages from the mouth and nose, the bowels and into the skin, lungs, heart, spleen, kidney, intestines, bladder, gall-bladder, and connective tissues; small spleen; cloudy organs; acute diffuse nephritis; fatty degeneration of the capillaries of the lungs and kidneys; healed old duodenal ulcer; and right old pleural adhesions.

A careful scrutiny of this case shows that it was enteric fever, atypical in the particulars that the intestinal lesions were most marked in the large bowel, that the spleen was small, that there was a general hæmorrhagic diathesis, and that there was a mixed infection with the staphylococcus albus.

We do not think that the fact that the bacillus typhi was not found in the cultures invalidates the conclusion that the case was one of enteric fever, for the intestinal ulcers were characteristic for the age of the condition and the Widal reaction was positive, both facts together being practically conclusive. Owing to an oversight cultures were not taken from the spleen and mesenteric glands, and even if the bacillus typhi had originally been present in the kidney in such a situation it would be apt to be attenuated and would be the more easily overgrown by other forms of germ life. Further, it is notoriously difficult to obtain the bacillus typhi from the blood, so that a negative result in these particulars would have no special importance. Throughout the various organs there were the marked swelling and proliferation of the endothelial cells to which Mallory has directed attention. Altogether the facts above-mentioned, together with the histological appearances of the various tissues, are to our minds conclusive.

With regard to the cause of the extensive hæmorrhages we must conclude that one main factor was the fatty degeneration of the basement membranes of the capillaries and the various endothelial cells which was so noticeable in the case of the lungs and kidneys. It is, of course, possible to say that these changes in the kidneys were due to the acute diffuse nephritis which was undoubtedly present, but it is to be pointed out that the same condition was observed in the lungs where a true inflammation of the parenchyma certainly did not exist. The fact that in the alveoli of the lung in parts where there was no infarction the endothelial cells were desquamated in large numbers and very fatty goes to show very strongly that the condition was a primary one. No doubt, however, as the specimens of kidney clearly show, the fatty degeneration of the cells was most marked

when there were extravasation of blood and pressure upon the cells, so that it is probable a vicious cycle existed as well. The slight alteration found in the blood within certain vessels, if not, indeed, an artefact, was certainly not sufficient to cause any blocking of the lumina. No thrombi, no emboli, bacterial or otherwise, were found nor was there arteritis or phlebitis. Further, there was at no time marked dilatation or insufficiency of the heart as in another of our Montreal cases.

As will be seen shortly, the development of hæmorrhagic manifestations in infectious and other diseases has been, upon histological and experimental grounds, attributed to a variety of factors. Many have sought for the cause in some local disturbance of the blood current, such as would be produced by acute arteritis and phlebitis, thrombosis, or bacterial emboli. In our case we have been unable to discover any conditions of this nature and can only conclude that in so far as any local cause was operative it is to be found in the fatty degeneration of the various endothelia and basement membranes. In what way this fatty degeneration leads to the condition of blood extravasation we do not feel able to say. There would certainly be weakening of the capillary walls, but our studies do not settle whether the hæmorrhages were per rhexin or per diapedesin. Great numbers of sections were examined, but in none could we find actual rupture of the capillaries.

With regard to the ultimate cause of the fatty degeneration, since we are able to exclude any inherited defect, such as hæmophilia or hypoplasia of the vascular system, and can further exclude any pre-existing state of malnutrition, scurvy, rheumatism, alcoholism, and cachexia, we can only refer it, not to any local action of bacteria, but to a condition of systemic intoxication and septicæmia. What particular germs were concerned in this it is difficult to say. The pathological investigation shows clearly that we were dealing with a case of mixed, or at least secondary, infection with the staphylococcus albus, and the history excludes the possibility of primary typhoidal purpura. No doubt all the micro-organisms present played a part in bringing about the degenerative changes, so that we are safe in referring these to the intensity and to the quality of the intoxication, which practically means to qualitative changes in the blood.

With regard to the frequency of the general hæmorrhagic diathesis in typhoid fever, all are agreed that it is very rare, although a petechial eruption, which is probably merely a mild type of the complication, is not so infrequently met

with. Below we have tabulated all the large series of enteric fever cases which we have been able to find recorded.

Authors.	Clinic	Total cases of typhoid fever.	General hæmorrhagic diathesis.	Purpuric eruptions.	Hæmaturia alone.
Ouskow[8]	—	6,513	4	—	—
Berg[9]	Leipsic.	1,626	6	0	53
Liebermeister[10]	Basle.	1,900	3	9	—
Weil[11]	Leipsic.	105	1	—	—
J. C. Wilson[12] ...	German Hospital, Philadelphia.	147	0	0	37
Bosanquet[13] ...	Charing Cross.	215	0	2	—
J. M. Anders[14]	Med. Chir. Hospital, Philadelphia.	266	0	2	—
Osler[15]	Johns Hopkins Hospital, Baltimore.	685	1	—	—
Authors	Royal Victoria Hospital, Montreal.	543	3	2	—
Totals	—	12,000	18	?	?

Of course, fairly numerous cases are met with in the literature in addition to the above, but they could not be included in the table since they did not form part of any extended series of observations. Examples, for instance,

[8] Archives des Sciences Biologiques, St. Petersburg, ii., No. 1, 1893.

[9] Deutsches Archiv, Band liv., S. 161, 1895.

[10] Ziemssen, Handbuch, 1876. Band ii., S. 198; ref. in Curschmann. Der Unterleibstyphus, 1898, Wien, S. 297.

[11] Ibid. (ref.).

[12] Typhoid Fever Report, Philadelphia Medical Journal, Feb. 25th, 1899.

[13] Notes on 215 Cases of Typhoid Fever, Brit. Med. Jour., July 8th, 1899.

[14] Philadelphia Medical Journal, Feb. 25th, 1899, p. 416.

[15] Johns Hopkins Hospital Reports, Studies in Typhoid Fever, vol. viii., 1900.

have been recorded by Trousseau,[16] Barlow,[17] Gerhardt,[18] Wagner,[19] Hawkins,[20] Hughes and Lévy,[21] Adami,[22] Nicholls,[23] Gilman Thompson,[24] and Hamburger.[25] It is possible that some of the cases are not examples of the condition under discussion, as many either occurred before the day of the Widal test or were not controlled by post-mortem examination. The following remarks are based upon a careful study of the recorded cases, any doubtful ones being neglected.

Etiology of the hæmorrhagic tendency.—Comparatively little is known as yet as to the causative factors in the condition. The few authors who have dealt with the subject confine themselves to general statements, nor do the various opinions expressed altogether coincide. A study of the cases recorded, however, goes to show that some of the etiological factors, so-called, have really little weight. A pre-existing scorbutic, hæmophilic, or rheumatic taint does not seem to have been noted. Alcoholism, on which Fereol and Roger[26] and Curschmann[27] laid stress, cannot be of much importance. It was not present in any of Wagner's or our cases, though present in Gilman Thompson's and two of Curschmann's cases.

Others, like Gerhardt[28] and Griesinger,[29] regard defective nutrition due to scurvy, overcrowding, and scanty food as powerful contributory causes. The state of the previous nutrition, however, which on *a priori* grounds would seem to be an important consideration, does not appear to be a factor in all cases. Most of the cases recorded were in a previously healthy condition and some were of unusually good physique.

[16] Clinique Médicale, tome i., 1865.
[17] THE LANCET, April 26th, 1884, p. 745.
[18] Zeitschrift für Klinische Medicin, Band x., S. 201.
[19] Deutsches Archiv für Klinische Medicin, Band xxxvii. ; ibid., Band xxxii., S. 298.
[20] Transactions of the Clinical Society, vol. xxvi., 1892, pp. 50, 51.
[21] Archives de Médecine et de Pharmacie Militaires, August, 1892.
[22] Montreal Medical Journal, 1894, p. 691.
[23] Loc. cit.
[24] Unusual Complications of Enteric Fever, Medical and Surgery Reports of the Presbyterian Hospital, New York, 1898.
[25] Johns Hopkins Reports: Studies in Typhoid Fever, vol. viii., 1900.
[26] Ref. in Brouardel et Thoinot, La Fièvre Typhoïde, 1895.
[27] Der Unterleibstyphus, Nothnagel's Specielle Pathologie und Therapie, Band iii., No. 1, 1898.
[28] Loc. cit.
[29] Virchow's Handbuch der Infektionskrankheiten, Band ii., S. 217.

One of Wagner's cases was scrofulous in childhood and one of the Royal Victoria Hospital patients was puny as a child. A case under the care of Gerhardt had gone through an attack of measles three weeks before and the patient in Adami's case had had pneumonia and empyema. How far these factors were concerned in the subsequent development of the hæmorrhagic tendency is very problematical.

In this connexion the views of Gerhardt are of some interest. He thinks that the hæmorrhagic tendency has been more frequently observed since the introduction of the cold-bath treatment, and thinks further that a too rigid restriction of the patient to an animal diet is an important cause as tending to induce a scorbutic condition.

Leudet[30] in an epidemic which occurred at Rouen in 1869–70 lays stress upon a certain "epidemic influence," whatever that may mean.

Wagner has recorded a curious instance where a family idiosyncrasy seemed to play a part. Of five children in one family suffering at the same time from typhoid fever three developed a more or less pronounced hæmorrhagic tendency. That this was not due to poverty and malnutrition was shown by the fact that one of the sisters so affected was not living at home and was well nourished.

Wagner, Gerhardt, and Curschmann agree that the condition is commonest in childhood and early adult life. Of the cases recorded one patient was eight years and another was 16 years old. The vast majority were considerably under 25 years of age; the oldest was 32 years of age. The age average was 21·4 years. With regard to sex there seems to be an equal liability of males and females to the complication.

The type of the original typhoidal disease seems to be of some importance. The vast majority of cases are found in those suffering from typhoid fever of a severe form. The patients are much prostrated, the temperature is high, the heart's action is weak and rapid, and there may be coma or delirium. The mouth is usually very foul and the excretions may have an ammoniacal odour. In certain rare cases, as Curschmann points out, the hæmorrhagic diathesis may be one form of the "foudroyante" typhoid fever. One of our Montreal cases was, on the contrary, comparatively mild.

The character of the onset of the original typhoidal attack does not give any clue to the development of the hæmorrhagic complication. More than half the cases

[30] Clinique Médicale de l'Hôtel Dieu de Rouen, 1874.

occurred in the ordinary gastro-intestinal type of the disease. In certain cases severe pains in the legs, rhachialgia, and cutaneous paræsthesiæ have been noted.

Pathology.

With the exception of the changes due to the special complication the necropsies show that the anatomical lesions differ very little from the ordinary typhoid. The anæmia is usually marked, as would be expected. Of 11 necropsies of which we have notes the typhoid ulcers were in two cases mainly confined to the large intestine, the ileum showing only very moderate involvement of the Peyer's patches. In Trousseau's case, where death occurred on the eleventh day, the Peyer's patches were softened but not ulcerated. In one of Wagner's, where death occurred on the thirty-ninth day, the ulcers showed signs of healing. In our own case the only feature of note about the ulcers was the extensive hæmorrhages into their bases and margins, giving them a much more red and swollen appearance than usual.

The spleen is, as a rule, found enlarged. The hæmorrhagic patches in the skin may be infected and break down, forming gangrenous ulcers.

Coming to the hæmorrhagic manifestations there is considerable diversity in their character and distribution. Hæmorrhage into a muscle, perhaps one of the slightest forms of the complication, is not very uncommon even in ordinary typhoid fever, but may be part of the general hæmorrhagic tendency. It is supposed to be due to a vitreous degeneration (von Zenker) of the muscle. The hæmorrhages may be minute, petechial, ecchymotic, or may form tremendous extravasations into all the loose tissues. Petechiæ may be present on the skin and all the mucous and serous surfaces. Parenchymatous hæmorrhages occur in the various organs. In fact, no organ or tissue of the body is necessarily exempt. Nor are the external manifestations of the condition a true index to the extent of the internal lesions, for, as Hamburger[31] points out, the most extensive involvement of the internal parts may be present when but little suspected.

The recorded necropsies show that the skin, subcutaneous tissues, and the various mucous membranes are by far the most frequently involved; next to them the lungs, spleen, and urinary organs. Infarcts have been found in the lungs, spleen, and kidneys, and thrombi in the renal and femoral

[31] Loc. cit.

veins, the chambers of the heart, the pulmonary artery, and the cerebral arteries. Curschmann says that embolism of arteries is very rare, but when found is usually in the kidneys and spleen. In certain cases the clotting of the blood has been undoubtedly ante-mortem.

With regard to the ultimate cause of the hæmorrhagic tendency but little is known ; no cases have up to the present been studied with sufficient detail finally to settle the question, but, as already hinted, various theories have been propounded. Curschmann says : "We are uncertain what is the exact nature and mode of origin of hæmorrhagic typhoid, whether it is to be looked for in a certain peculiarity or activity of the typhoid germ or in some complication or state of the body."

The older writers supposed that there was some special change in the blood, a *dissolutio sanguinis;* but while this view has been ridiculed in certain quarters very little better has been proposed for it. Trousseau noted that the blood in "putrid hæmorrhagic fever," as in yellow fever, was of a dark colour and was deficient in coagulating power. This theory is interesting in connexion with Osler's case where the coagulation time of the blood was 10 minutes, sinking to four minutes during convalescence. No doubt this change in the blood is due to the character of the bacterial toxins present, for we know that in diseases like croupous pneumonia and acute rheumatism the coagulating power of the blood is increased. This seems to depend in part upon the number of the leucocytes present in the blood, for they are very abundant in pneumonia and rheumatism. Leucopenia, on the contrary, is the rule in ordinary uncomplicated typhoid fever. We would expect *a priori* that in typhoid fever during the acme the coagulating power of the blood would be diminished. The thrombosis of the crural vein which not infrequently is met with in typhoid fever is never seen during the height of the disease but invariably in the stage of profound asthenia and anæmia, when arterial relaxation and weak driving power of the heart are the rule. An interesting confirmation of this view is seen in a recent case of hæmorrhagic typhoid fever recorded by T. V. Openchowski[32] where the bleeding from the mucous membranes was very obstinate, not yielding to the usual remedies. Suddenly the blood began to clot and the hæmorrhage ceased. The next day signs of croupous pneumonia became manifest. On the contrary, in a case examined by

[32] Klinische Therapeutische Wochenschrift, Jan. 2nd, 1898.

Curschmann, no special external or histological peculiarity of the blood was observed. Further, neither hæmoglobinuria nor hæmoglobinæmia have been noted in these cases.

Any vitiated state of the blood must necessarily react upon the vessels and, arguing from what has been found in symptomatic purpura of other types, would afford a probable clue to the mystery.

Uskow[33] demonstrated swelling of the lining epithelia of the vessels in the gums and periosteum in cases of scurvy, and von Kögerer[34] has observed thrombosis of the vessels in the neighbourhood of the subcutaneous hæmorrhages in both scurvy and morbus maculosus Werlhofii.

Letzerich[35] in a case of purpura isolated a bacillus which when injected into rabbits produced widening of the capillaries with hæmorrhagic injection of the gums. Bacilli were present in the capillaries. The hæmorrhages were said to be due to hyaline plugs which were present at the bifurcation of the vessels. It should be remarked, however, that the presence of thrombi in the various vessels must be interpreted with caution. It is very possible that these thrombi are due to the weak circulation and the relaxed and degenerated condition of the vessels which are present at the time of impending death. They are to be regarded as associated conditions rather than the true cause of the hæmorrhagic tendency.

In one case of purpura occurring in the course of acute endocarditis which we examined recently the subcutaneous tissues were found to contain large numbers of a rather slender bacillus in pure culture and both arteries and veins showed considerable acute inflammation of their walls with some surrounding leucocytic inflammation.

In sepsis and variola hæmorrhagica bacterial emboli have been found in the capillaries and give rise occasionally to ring-like hæmorrhages, particularly about the hair follicles.

According to Litten[36] these are not present in hæmorrhagic typhoid fever and this observation is confirmed by von Recklinghausen[37] and Meyer and by our own studies. It is probable that a variety of factors enter into the causa-

[33] Centralblatt für die Medicinischen Wissenschaften, S. 498, 1878.

[34] Zur Enstehung der Hauthämorrhagien, Zeitschrift für Klinische Medicin, Band x., S. 234, 1886.

[35] Ueber Purpura Hæmorrhagica, Leipsic, 1889 (Vogel).

[36] Die Hämorrhagischen Diathesen, Nothnagel's Specielle Pathologie und Therapie, Band viii., Thiel iii., 1898.

[37] Handbuch der allgemeinen Pathologie der Kreislauf und der Ernährung, S. 87, 1883.

tion, a deficiency in the fibrinogen of the blood, together with relaxation and fatty degeneration of the vessel-walls. No doubt a feeble circulation may be an important element as in our first Montreal case, where the heart was much dilated and its action very rapid, together with cyanosis and coldness of the extremities. These conditions would certainly promote clotting of the blood and since old decolourised thrombi have been found post mortem the possibility of such an occurrence during life cannot be denied.

Numerous attempts have been made to connect purpura hæmorrhagica with bacterial activity. Klebs, Ceci, Jones, Tizzoni, Petrone, Babes and Letzerich, Hanot and Luzet, Widal and Therèse found streptococci; Lebreton and Litten found staphylococci in their cases. Hamilton and Yates[38] in a well-marked case isolated the staphylococcus aureus, the bacillus aerogenes capsulatus, and an unknown bacillus. Kenneth Cameron[39] has also noted a hæmorrhagic tendency in general infection in children with the bacillus pyocyaneus. It seems to us that this attempt to connect the hæmorrhage with the action of those micro-organisms found post mortem is open to fallacy.

Patients who are bleeding into the skin and mucous membranes are in the best of all conditions for bacterial invasion, and, in fact, we see this in those cases which develop abscesses or gangrene in various parts, as they often do. These cases no doubt die, not merely from the exhaustion of anæmia, but from septicæmia. When germs are found in the various organs post mortem under such conditions it is impossible to deny that they may be a result rather than the cause of the hæmorrhagic condition. Still, we know that in some cases bacterial emboli have been found in the vessels strongly suggesting a causal relationship, and to a certain extent the condition can be reproduced in experimental animals. Further, the absence of hæmophilia or other blood dyscrasia points strongly to the action of a bacterial cause. While, then, the bacterial origin of the hæmorrhagic condition is extremely probable the final proof is still wanting.

[38] Montreal Medical Journal, August, 1897.
[39] Ibid., March, 1896.

Onset and Character of Symptoms.

Analysis of the cases recorded shows that the hæmorrhagic tendency may occur at any time during the course of the primary attack. During the first week the condition is rare. In two cases recorded by Roger the hæmorrhage began on the third and fourth days and in one by Ferreol on the fifth. Such are undoubtedly cases of primary typhoidal purpura and strictly comparable to purpura variolosa and scarlatinosa. Griesinger remarks: "In all forms of typhoid, exactly as in small-pox, cases occur where very early, in the first week or later, abundant petechiæ and suggillations into the skin, sometimes into the muscles, set in; intractable nose-bleeding, ecchymoses, and bloody extravasations into the serous sacs, infarct of the lungs, bloody urine, intestinal hæmorrhages, meningeal and brain apoplexy, hæmorrhage into the connective tissue of the iliac fossa and formation of tumours." Cases are slightly more frequent in the second week and most common in the third week. The condition may occur during a relapse, as in Osler's case, or later in a protracted course, as in one of ours where it developed on the fortieth day.

The fact that most cases occur during the third week when the sloughs are separating from the ulcers is an argument in favour of the view that some at least of the cases are due to secondary infection. The recorded cases fall naturally into three groups: (1) primary typhoidal purpura; (2) purpura due to secondary bacterial invasion; and (3) cachectic purpura, occurring later in the disease or during convalescence. It is questionable, however, whether the third class is to be properly separated from the infective category.

The onset of the symptoms varies considerably. Sometimes, though rarely, epistaxis, melæna, or hæmaturia is the first symptom; generally, however, the first signs are in the buccal mucous membrane or in the skin. The hæmorrhages are generally multiple in distribution, petechiæ, bleeding from the mucosæ, hæmaturia, and epistaxis frequently going together. Hæmoptysis is met with and is due to oozing from the bronchi or to infarction.

The skin lesions consist of petechiæ or ecchymoses, the latter being sometimes of large size. If rose spots are present the eruption may take place into or between them. The petechiæ do not disappear on pressure. Sometimes hæmorrhagic pustules are present. Small bluish, elevated subcutaneous nodules are occasionally met with. In some

cases a sort of diffuse subcuticular purplish mottling has been observed. The skin hæmorrhages have been known to occur into a bed-sore or on the application of cold. Gangrene may supervene and œdema.

No special symptoms seem to usher in the hæmorrhagic condition. Neither chills, sweating, nor a septic temperature seem to have been noted. Marked distension of the abdomen is not uncommon and diarrhœa is fairly frequent at the onset. The effect on the temperature is usually very slight, though in severe cases a gradual fall to subnormal has been noted, as in other cases of hæmorrhage. Profound anæmia usually develops. The hæmorrhage is not sudden, but rather a gentle oozing from all the surfaces of the body, and is apt to be precipitated by any slight injury.

Prognosis.

The condition is generally very grave. About two-thirds of the cases recorded ended fatally. The previous history of the patient has some weight. As a rule the earlier the condition sets in and the more extensive it is the more serious is the prognosis.

Treatment.

Treatment is purely symptomatic. Gerhardt, in accordance with his views as to the etiology, discontinues the cold-bath treatment and substitutes a daily warm bath at a temperature of from 33° to 34° C. He includes potato, spinach, and vegetable juices in the diet. To control the hæmorrhage many plans have been tried. On the assumption that the cause is a secondary infection small doses of calomel or other mercurial have been given. One of our Montreal cases recovered under this treatment, as did one which was left alone. Turpentine and ergot were used by Gilman Thompson in his case which recovered.

Attempts have been made to increase the coagulability of the blood by means of calcium chloride as suggested by Wright.[10] In severe cases 15 grains should be given twice daily. This treatment has to be carefully controlled by repeated blood examinations, as if it is too vigorously pressed it may have the contrary effect to that intended. The same writer also advocates inhalation of carbonic

[10] Brit. Med. Jour., Dec. 19th, 1891; vol. ii., 1893, p. 223; and vol. i., p. 237, and vol. ii., 1894, p. 57.