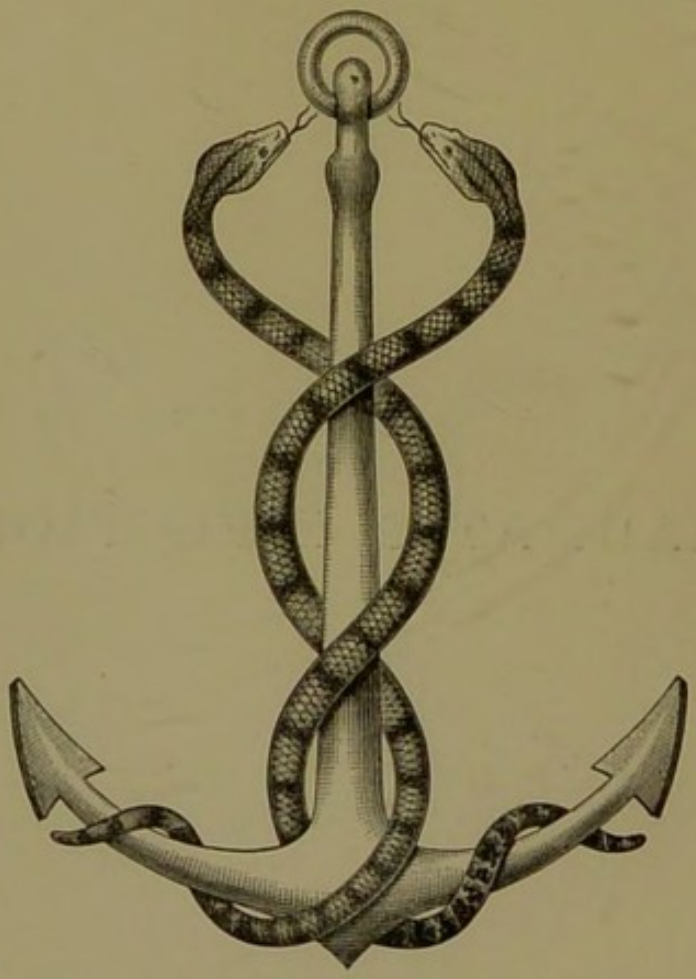
Traumatic infection : Hunterian Lectures delivered at the Royal College of Surgeons of England / by Charles Barrett Lockwood.

TRAUMATIC INFECTION.



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TRAUMATIC INFECTION

HUNTERIAN LECTURES DELIVERED AT THE ROYAL COLLEGE OF SURGEONS OF ENGLAND.

BY

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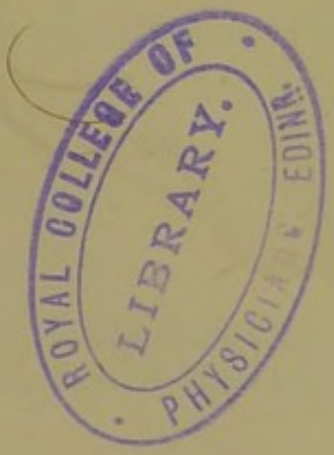

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PREFACE.

THIS book is a reprint of Lectures which have already appeared in the *Lancet*, and which, as Hunterian Professor, I had the honour to deliver in February and March 1895, at the Royal College of Surgeons of England. I venture to reprint them in the hope that they may thereby be more useful to my fellow-workers in this difficult subject. I also wish very heartily to thank those gentlemen who have assisted me with the investigations.

C. B. LOCKWOOD.

19 UPPER BERKELEY STREET,
PORTMAN SQUARE, W., *December* 1895.

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TRAUMATIC INFECTION.

LECTURE I.

SOME LOCAL INFECTIONS.

GENTLEMEN,—For some years, with the help of friends and pupils, to whom I am deeply indebted, I have worked at various kinds of traumatic infection. The results are given in these lectures. It will be obvious, and I am fully conscious, that in many instances the inquiries are incomplete; nevertheless, I venture to hope that light is thrown upon some conditions, and that what has been done may be helpful to my fellow-workers. Throughout these lectures the gaps which ought to have been filled are pointed out, and no attempt has been made to give an appearance of completeness.

Methods of Investigation.

My plan has been to choose cases of traumatic infection of which the clinical history and morbid anatomy were known and work out their morbid histology. Nearly all the cases were under my observation when surgical registrar in St. Bartholomew's Hospital, and of many of them I conducted the *post mortem* examination. This order has not always been strictly adhered to, but, as an extra control, the clinical history and morbid anatomy were often purposely left unascertained until the morbid histology and bacteriology had been investigated. Although it may be rather tedious and prolix, I propose to illustrate each branch of my subject with these cases, giving the clinical history, morbid anatomy, morbid histology, and, as far as possible, the bacteriology of each. I venture to surmise that it must be advantageous to an audience of surgeons to be able to consider all of these together and in continuity. A short commentary follows each case, and in this some of the more recent researches bearing upon it are mentioned. I need not speak about the clinical and anatomical methods. For histological purposes the tissues were obtained as fresh as possible and hardened in alcohol. The sections were stained in various ways. Sometimes good results were

obtained by Gram's method, but nearly all the best were got by using, upon Dr. Klein's advice, a staining solution which was used by Canon to demonstrate the influenza bacillus in blood, and which is called Czenzynke's solution.[1] This is a mixture made by adding together a concentrated watery solution of methyl blue 40 per cent.,[2] eosin solution (in 70 per cent. of alcohol), 20 per cent., and distilled water 40 per cent. The sections of the hardened tissues were soaked in the above solution for not less than seventy-two hours, and often for seven or eight days. The sections were mounted in the usual way. As the bacteria are stained blue and the tissues pink, their presence is easily ascertained; but we have found the pink ground most unsuitable for microphotography. However, Czenzynke's solution has stained bacteria when nearly all of the ordinary methods have failed. Nevertheless, it has one great demerit. Many of the specimens fade and lose their brilliance after a few months, so that it is necessary to draw them at once. Microphotography would be especially useful under these circumstances, but, unfortunately, it cannot be used for the reasons given. I have, therefore, been

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[1] *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, bd. xi., 1892, p. 149.

[2] I am accustomed to add 5 per cent. of carbolic acid to the watery solution. It keeps longer and acts quite as well, if not better.

obliged to make drawings of the most instructive of the sections.[1] These, together with the specimens themselves, are displayed for your inspection. The drawings have been made into lantern-slides by my friend, Mr. Cosens, to whom I am deeply indebted for invaluable assistance. My experience of Czenzynke's method shows that it should be used with caution. The protoplasm of the connective tissue cells often holds particles of the aniline blue, so as to simulate bacteria. However, the irregular shape and size of the particles, the absence of that peculiar translucent hue which dyed bacteria possess, and the presence of a nucleus, is enough to prevent an error. No material was discarded until all kinds of methods had been tried upon it. Many months were often devoted to these endeavours. The ultimate result was often highly satisfactory.

Cadaveric Bacteria a Source of Error.

In work like this there is great danger of mistaking bacteria which have grown in the tissues after death for those which may have existed during life. In hot weather these cadaveric bacteria grow very quickly, and material can seldom be obtained for histological

[1] A $\frac{1}{12}$ in. oil immersion objective by Zeiss, and a No. 3 eye piece were used for this purpose.

examination until some hours after death. However, I trust it will be acknowledged that this source of error has been guarded against throughout these lectures. In doubtful cases the question is discussed in the commentary, and some material has been put aside because the tissue changes and bacteria were probably of *post mortem* origin. An important *rôle* has not been ascribed to bacteria unless they were present in numbers and amidst tissue changes such as could only have occurred during life, and such as might reasonably be ascribed to their presence. The bacteria of putrefaction are distinguished by morphological peculiarities, by the situations in which they grow, and by the absence of pathological changes in their vicinity. But much work remains to be done at the cadaveric bacteria, and even with the greatest caution they remain an abiding source of error.

Classification of Material.

The various cases which have been investigated fall naturally into the following groups:—First, those in which the infection was local; second, those in which the infection had entered the blood, but had not passed any further; third, those in which the infection of the blood had passed into the tissues, producing changes there; and, lastly, some mixed infections. This classi-

fication of the cases is suggested more by convenience than scientific accuracy. Reasons will be given to show that even in the typical local infections there may have been some passage of bacteria through the blood to the kidneys, and perhaps to other organs.

Mycotic Peritonitis.

I propose to begin the local infective diseases with acute inflammations of some of the serous sacs, commencing with septic peritonitis. And, first, a case will be given to show how easily peritonitis may be overlooked, and how bacterial invasion of the peritoneum may be unsuspected. In the following case I believe that an infection of the peritoneum had occurred, although during life no signs of it were recognised, and after death none were apparent to the naked eye.

Case 1.—The case was that of a woman aged sixty-nine years, who had had a multilocular ovarian cyst removed. The peritoneum was drained for forty-eight hours after the operation because blood oozed from some slight adhesions. She did well until the fifth day, but then her temperature, which had hitherto been normal, rose to 101° F., and remained about that height until the tenth day, when she died. During life the abdomen seemed free from inflammation, and the fatal

issue was attributed to bronchitis. At the examination, which I made twenty hours and a-half after death, the wound was almost healed, and I expressly noted that no inflammation, fluid, or lymph could be seen in the peritoneal cavity, but merely slight localised hyperæmias. Around the pedicle of the right ovary, which was secured with silk, I especially noted that there was hardly any inflammation or lymph. All the abdominal viscera were healthy except the kidneys, which were chronically inflamed. The left pleural sac contained three-quarters of a pint of purulent fluid, and the parietal and visceral pleuræ were covered with flakes of lymph. The lower lobe of the left lung was pneumonic and sank in water. The stump of the ovarian pedicle was examined histologically. There was slight hyperæmia, and here and there on the surface small masses of lymph, composed of exudative cells and bacteria. Amongst the latter were long bacilli with rounded ends and usually in pairs, and almost as big as anthrax bacilli; also short ovoid and very thick bacilli, together with vast quantities of smaller bacteria which grew singly, in pairs, and short strings. There may have been micrococci, but so many were slightly elongated that it is possible that all of them were minute oval bacilli (Fig. 1). Many of the smallest bacteria had entered the lymph paths, and had filled both those

near the surface and many of those in the depths of the peritoneum (Fig. 2). Here they surrounded a nuclear cell, which suggested that they had either been carried into the lymph paths by a wandering leucocyte or had surrounded one after their entrance. If these bacteria-laden cells were phagocytes, they must have been

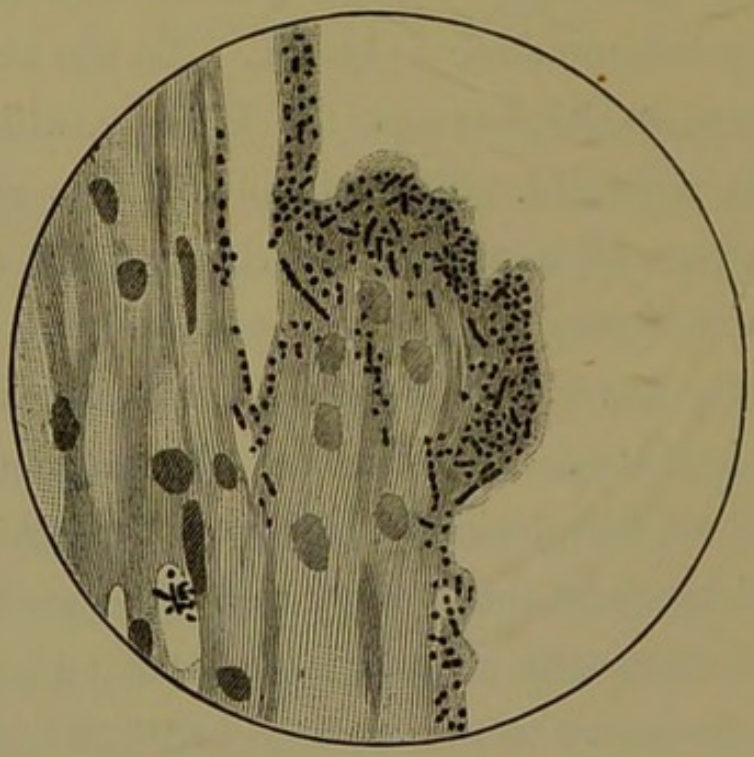

FIG. 1.—Mycotic peritonitis. Lymph upon ovarian pedicle. The bacteria are upon the surface and in the lymph paths.

singularly inefficient. Some would say that the bacteria which were found in this case were mere saprophytes which had travelled from the intestines after death. But if this were so, it seems strange that they should only be found in the lymph and in the lymph

paths leading from it. The uninflamed part of the peritoneum had no bacteria either upon its surface or in its depths. The silk upon the pedicle contained no bacteria, and none could be seen in the lymph in its immediate vicinity. I should suppose that the chemicals in which the silk had been soaked may have

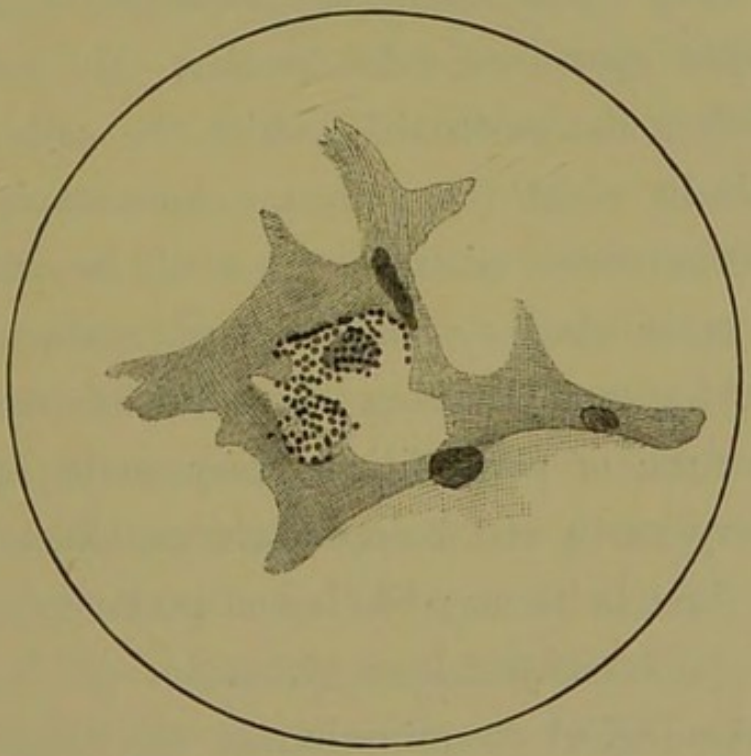

FIG. 2.—Mycotic peritonitis. Bacteria in lymph spaces of ovarian pedicle.

preserved it from infection. If this be so, it would help to explain those cases in which silk is not extruded from wounds which are obviously septic. Until the histological examination, I had no suspicion that such numbers of bacteria would be found in the peritoneum. The question arises as to the share they had in the

fatal ending. They hardly seem to have compassed this by acting locally upon the peritoneum. During life the clinical signs of peritonitis were wanting. However, I have no doubt but that they were the cause of the pleuro-pneumonia, which will presently be described.

Pawlowsky[1] has made an important observation which bears upon such cases as this. He describes a variety of acute peritonitis which he calls mycotic peritonitis, in which there are no macroscopic appearances, but in which microbes can easily be obtained by pressing cover glasses upon the peritoneum and afterwards drying and staining them in the usual way. But this form of peritonitis is very acute, and death occurs very early and before fibrinous effusion or pus has had time to occur; life is not prolonged as in the instance which has just been given.

The histological examination of the lungs showed catarrhal pneumonia and pleuritis, with more corpuscles than fibrin in the exudation. The methods of Gram and Loeffler give negative results. But after we had all failed Mr. Goffi obtained for me beautiful specimens showing that the pleuritic lymph was crowded with bacilli. Many of these were the shape and size of

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[1] *Centralbl. f. Chir.*, Leipzig, 1887, pp. 886 and 887.

tubercle bacilli; some were slightly curved and some might have contained spores. They were distributed indiscriminately in the lymph, but some grew in short leptothrix. The lymph also contained vast numbers of small, short, ovoid bacilli. Both of these varieties may have belonged to the same species, and were the same as some of those seen in the peritoneal lymph. I was uncertain of the presence of these bacilli in the pneumonic lung. It probably contained pneumococci. Pleuritic exudation is not very hard to examine. In three other cases I have found in it streptococci (Fig. 8), pneumococci, and septicæmic bacilli respectively. With pneumonic lung I have been most unsuccessful, and when pneumococci have been seen they have been in such small numbers as to excite doubts as to their being the cause of the pneumonia. Acute inflammations of the lungs are associated with various bacteria. In the 128 cases examined by Weichselbaum[1] the diplococcus pneumoniæ was found in 94; a streptococcus in 21; staphylococcus pyogenes aureus and albus in 5 cases of pneumonia secondary to typhoid fever and osteomyelitis; and a bacillus pneumoniæ, similar to Friedländer's pneumococcus, in 15 cases. In 11 cases of pleuritis a chain coccus was found. In

[1] "Ueber die Aetiologie der acuten Lungen und Rippenfellentzündungen." *Wien. med. Jahrb.*, 1886, p. 483 *et seq.*

conclusion, this case suggests that surgeons ought to be very cautious in assuming the absence of peritoneal infection. Also, that much might be learnt by a more rigorous and scientific examination of fatal cases. Towards the end of these lectures I will instance other cases to show the fallacy of a mere naked eye examination of the tissues.

Diffuse Septic Peritonitis.

During the past year I have been so fortunate as to cure by operation three cases of diffuse septic peritonitis. When we consider the clinical history and morbid anatomy of these cases such a result could hardly be hoped for. I have therefore tried to ascertain what light morbid anatomy and bacteriology threw upon the possibilities of recovery. The material which was used had all been collected long before the successful results occurred.

Case 2.—To illustrate the rapidly fatal form of acute septic peritonitis I will give the case of a boy, aged eight years, who was operated upon for the cure of a right inguinal hernia which he had had since his birth. At the time of operation there was an old septic sinus leading into the inguinal canal. This sinus was the result of a previous attempt to perform the

radical cure. It led towards a ligature which, as afterwards appeared, had been placed upon the stump of a Meckel's diverticulum. It is unnecessary to give the details of the operation, but it will suffice to say that the boy died forty-eight hours after, with the usual signs of diffuse septic peritonitis. The highest temperature recorded was 102° F. At the examination the abdomen was distended, the viscera inflamed and coated with viscid lymph, and the pelvis and flanks nearly filled with purulent fluid. The chief focus of inflammation was around the right internal abdominal ring. No fæcal matter could be found in the abdominal cavity. Twenty inches from the cæcum a Meckel's diverticulum grew from the ileum. It had been divided and encircled by silk ligatures, which still fastened it to the abdominal wall. The sinus, which has been mentioned, ran towards these ligatures and opened into the abdominal cavity. It was evidently the centre of the septic peritonitis. The other end of the diverticulum was attached to the top of the right testicle. The microscope showed that all the peritoneal vessels were distended with blood, in which no bacteria could be found. In some places the blood cells were extravasated amongst the tissues, but otherwise the substance of the peritoneum had undergone hardly any alteration. Its surface, however, was covered with a thin layer of

lymph, which was here and there crowded with swarms of small, short bacilli, growing in pairs and short chains (Fig. 3). The bacilli were confined to the surface lymph except in one place, where a single group lay about a hundredth part of an inch within the substance of the peritoneum (Fig. 3). Elsewhere the

FIG. 3.—Diffuse septic peritonitis. Bacteria in the lymph upon the surface of the peritoneum and just within its substance.

lymph paths contained neither pus cells nor bacteria. The inflammatory lymph consisted of cells with some fibrin. It is not certain, but probable, that these bacteria were intestinal in origin, and very likely the bacillus coli communis. The slightness of their pene-

tration into the peritoneum may be explained by the very feeble mobility which the bacillus coli communis possesses, or by assuming that the swarms in which it grows are ill adapted to penetrate the tissues or to pass along the lymph paths. Therefore, in some kinds of diffuse septic peritonitis the peritoneum itself is not penetrated by the bacteria for many hours and its tissues are almost uninjured. Apparently, so far as the serous membrane itself is concerned, there is nothing to forbid recovery. Indeed, there is a close similarity betwixt the case which has just been described and one of my cases of diffuse septic peritonitis which did recover after laparatomy.[1] In my case the peritonitis was of not less than forty-eight hours' duration, and was caused by a perforation of the ileum, which I found and sutured. At the operation the intestines were emptied of their fæcal and gaseous contents and the peritoneal sac thoroughly washed out and drained. Whilst operating I observed that the mesenteric lymphatic glands were swollen to at least thrice their natural size. I did not then know what evil effects these inflamed glands might exercise. Fortunately, they seemed to depart without disturbance.

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[1] *Med.-Chir. Trans.*, London, vol. xxviii., 1895, p. 1 *et seq.*

The Lymphatic Glands in Diffuse Septic Peritonitis.

Being inquisitive to know the characters of the lymphatic glands in diffuse septic peritonitis, I examined them in another case due to ulceration of the vermiform appendix.

Case 3.—The patient was a boy aged seven years, whose illness began suddenly with a violent pain in the right side of the abdomen. This was soon followed by distention, inflammatory obstruction, and fæcal vomiting. The abdomen was opened on the third day, and an inflamed and perforated vermiform appendix was removed. The peritoneal cavity was washed out and drained, but he died in four hours. I obtained portions of the peritoneum and some of the swollen lymphatic glands within eighteen hours of his death. The appearances of the peritoneum were almost the same as in the previous case (*Case* 2, Fig. 3). The lymph upon the surface of the portions examined was scanty. It was composed of proliferated peritoneal cells, with hardly any fibrin. Amidst the cells were bacilli of various morphological varieties, but mainly short bacilli, singly and in pairs. In some places bacteria with morphological characters of cocci and diplococci were seen, and these coccus forms had begun to penetrate the substance of the peritoneum, although

the bacilli were confined to the surface. The peritoneum itself seemed to have undergone hardly any alteration, except that its endothelium was proliferating. I have lately observed another case of septic peritonitis in which the surface lymph contained bacilli and micrococci, and the depths of the peritoneum micrococci alone. In this last instance the micrococci were in chains, and easy, therefore, to identify. The swollen lymphatic glands were more vascular than healthy ones, and the vessels in their hila and along their trabeculæ were distended with blood. The lymph paths were very wide and had probably been distended with fluids; some of them, especially those of the cortex, were crowded with leucocytes which retained methyl blue. However, no bacteria could be found in any part of these lymphatic glands, and I think it doubtful whether any were present. I am indebted to Mr. Blandford for much patient labour at this material. Thus in rapidly fatal diffuse septic peritonitis neither the peritoneum nor the swollen lymphatic glands are for many hours in an irremediable state.

Operative Peritonitis; Perforative Peritonitis.

If my observation is correct—and I know how easy it is to be mistaken—that the peritoneum was infected

with both bacilli and micrococci, a point of some interest arises. Waterhouse,[1] Walthard,[2] and others speak of "perforative peritonitis" and "operative peritonitis." In the first bacilli are found, in the second micrococci. This generalisation would have been more probable if Beinstock had been right in his assertion that the intestines were only inhabited by bacilli. Escherich has shown, however, by plate cultures that cocci also inhabit the intestines. Culture experiments might easily lead to the inference that the fluid of perforative peritonitis contained nothing but bacilli. On various occasions I have inoculated culture media from the peritoneal fluid in perforative peritonitis. Like others, I have obtained a growth of bacillus coli communis, not because it was the only microbe present, but because the media suited it best. In cover glass preparations of the exudations in perforative peritonitis many more morphological varieties of bacteria can be seen than can be grown either in the presence or absence of oxygen; indeed, culture experiments taken alone abound in fallacies. In a case of diffuse septic peritonitis due to a perforating ulcer of the duodenum I could see in the exudation:—(*a*) minute bacilli, singly

[1] "Prize Essay," Edinburgh. For abstract see *Virchow's Archiv.*, bd. cxix., p. 2.

[2] *Arch. f. exper. Path. u. Pharmakol.*, Leipzig, 1892, p. 275.

and in pairs; (*b*) bacilli about the size and shape of tubercle bacilli; (*c*) short, plump bacilli of some magnitude; (*d*) cocci and streptococci; (*e*) saccharomyces; and (*f*) moulds. Inoculated into broth, this exudation grew short bacilli, in pairs and short chains. Some of the chains might have consisted of streptococci, some of which were seen in the exudation. In the case (*Case* 2) to which I have just referred, we have to consider the possibility of the original infection having been one of micrococci. In this event the bacilli may have emigrated into the lymph which the cocci had produced from the intestines and after the death of the patient. Before saying anything more about perforative peritonitis I propose to contrast a case of streptococcus peritonitis with those which have just been described.

Streptococcus Peritonitis.

Case 4.—A girl, sixteen years of age, was admitted with inflammatory swellings about the right humerus, the lower end of the left radius and ulna, and of the left calf. She also had a distended and tender abdomen, but without sickness or obstruction. She had not been well for three weeks and attributed her illness to a wound of the thumb which she received

whilst at work making lace. The scar of a recently healed wound was seen upon the thumb. The swelling about the right humerus was opened, and some greenish pus escaped. Soon after the operation she began to vomit and speedily died. During her illness her temperature was usually about 101° F. At the

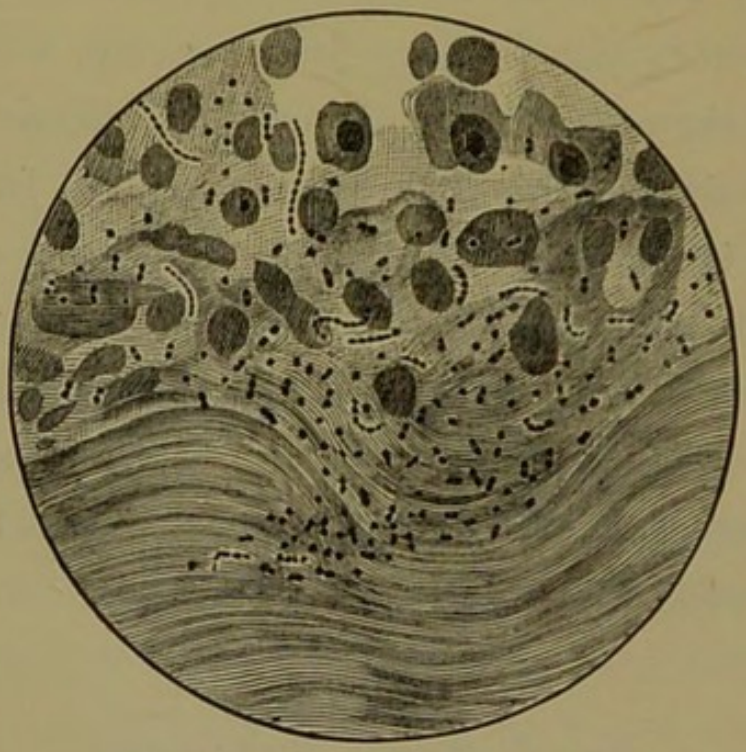

FIG. 4.—Streptococcus peritonitis. Lymph upon the surface of the peritoneum.

examination, which was made in the winter twenty-six hours and a-half after death, the swellings of the arms and legs were noted, and an abscess the size of a hazel nut was found near the root of the tongue, amongst its muscular fibres. The thoracic viscera were normal, except the bases of the lungs, which were

congested. The peritoneum was much inflamed and contained a quantity of pus, some of which filled the pelvis. The vagina, uterus, and Fallopian tubes were healthy; but the left ovary contained an abscess as large as an orange, which had burst, and, Mr. Berry believes, started the diffuse septic peritonitis. The

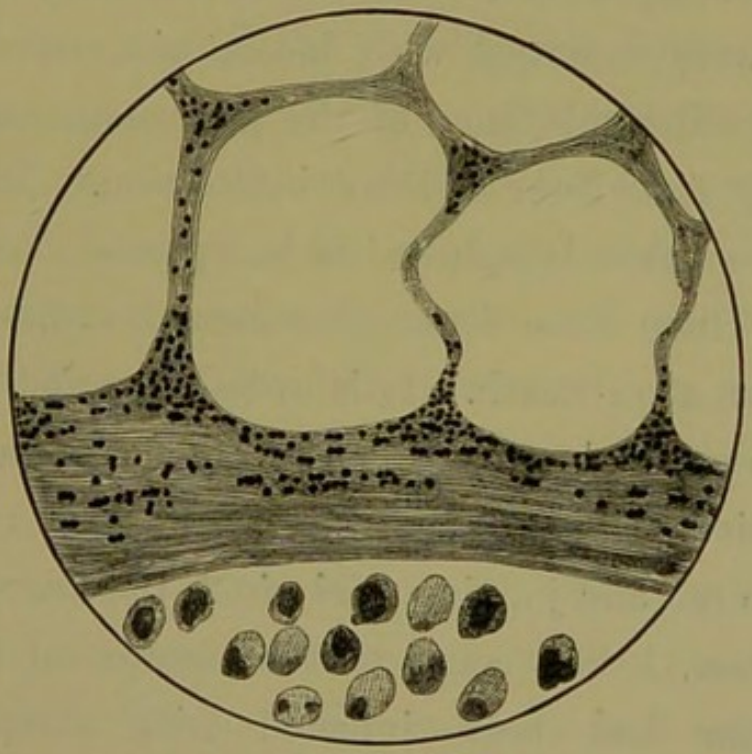

FIG. 5.—Streptococcus peritonitis. Streptococci in the depths of the peritoneum.

spleen was large and soft, and the liver covered with punctiform hæmorrhages. The histological examination showed that the surface of the peritoneum was covered with lymph consisting mainly of corpuscles with very little fibrin (Fig. 4). This lymph contained vast numbers of cocci, singly, in pairs, and in

chains of various lengths. In places these cocci had penetrated far into the substance of the peritoneum and had reached the subperitoneal fat. Here they were thickly crowded in the connective tissue trabeculæ between the fat cells (Fig. 5). Many of the lymph paths were crowded with vast numbers of cocci, diplococci, and streptococci. The blood vessels of the peritoneum were engorged with blood, but contained no bacteria. The substance of the peritoneum was comparatively free from cellular infiltration. Here and there the surface lymph had in it leptothrix of slender bacilli. These were few and scattered, and, I believe, had grown after death. It is to be regretted that the liver, spleen, and other organs were not obtained for examination. Before the history of this case was known to me, and judging solely from the microscopical appearances, I had come to the conclusion that the peritoneum had been infected with streptococcus pyogenes. This is usually found in abscesses and suppurations about the female genital organs, and is also one of the commonest causes of pyæmia. Döderlein and others have shown that vaginal pus usually contains streptococcus pyogenes, often associated with other microbes. Thus the case may have been one in which an abscess of the ovary had existed for some time, and then suddenly burst and caused

diffuse septic peritonitis, followed by pyæmia; or the original point of inoculation may have been the thumb; and the abscess in the ovary, like those of the root of the tongue and of the arm, may have been an ordinary pyæmic abscess. Whichever way the ovarian abscess formed, it seems to have been the source from which the peritoneum became infected. The histological appearances support the view that at first the micrococci grew upon the surface of the peritoneum, afterwards penetrated into its substance and into its lymph paths, and finally caused a general infection. It is unnecessary to point out that in such a condition as this our present surgical remedies would be of no avail. The histological examination of this case is, unfortunately, very incomplete. I was only furnished with some portions of the peritoneum. Further knowledge of these peritoneal infections is urgently needed, but it is doubtful whether culture media will supply what is wanted.

Streptococcus Pleuritis; Streptococci and Bacilli in Wound.

I have now described several cases illustrating the effects of bacteria upon the peritoneum. I next purpose to describe a case to show their effects upon the

pleura, and incidentally their distribution in a large septic wound of the axilla.

Case 5.—A man, aged thirty-nine years, who was strong and well nourished, and with nothing in his appearance to suggest a predisposition to infection, had a large lympho-sarcoma, which filled the right

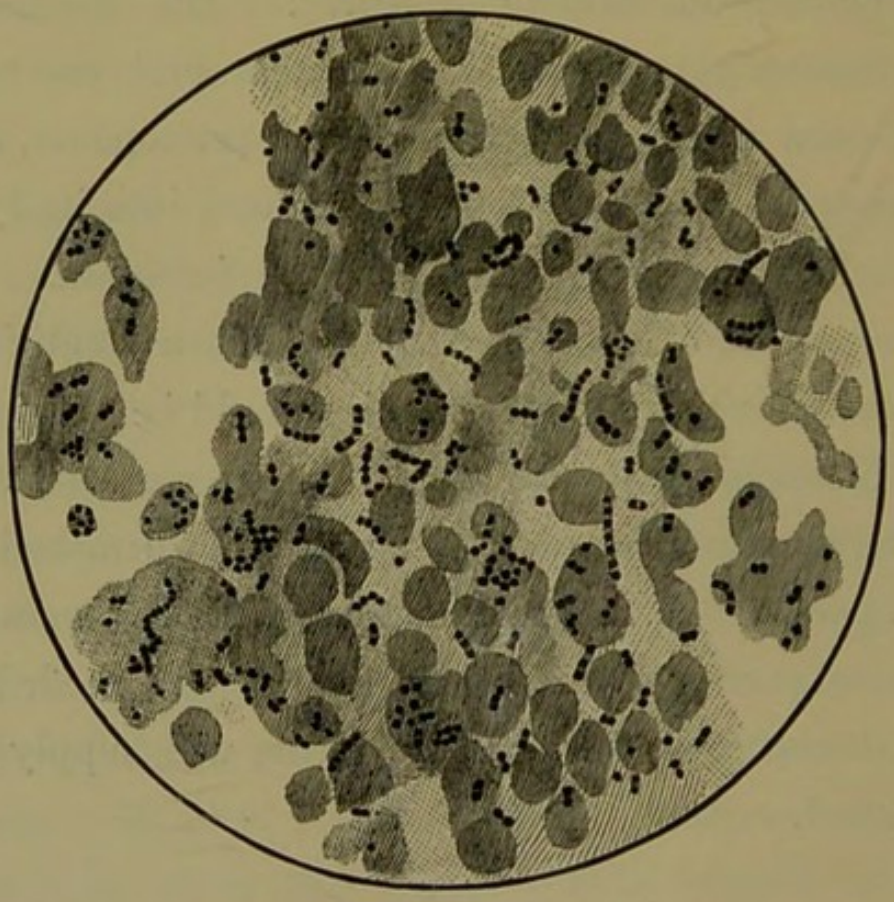

FIG. 6.—Streptococci in lymph of a septic wound in the axilla.

axilla. A severe operation was performed for its removal. At this operation a good deal of blood was lost, but not a very excessive or very dangerous quantity. Whilst attempting to dissect the growth

from the chest wall the surgeon made a small puncture into the pleural cavity, and air was heard to enter and leave the chest. After the operation symptoms of infection soon became manifest. Upon the second day the temperature steadily rose to 102·2° F., with a rapid pulse and respiration, and he seemed much exhausted, but without suffering any pain. A quantity of blood-stained serum ran through the dressing of cyanide of mercury gauze. There was also emphysema of the cellular tissue of the neck and chest. He became gradually worse, and died upon the third day, all the symptoms having gradually become aggravated. The temperature rose during reaction to 104° F., and fell a little before the end, but rose again during the last hours. The examination showed that the tumour had been partially removed, and that there was a small puncture of the pleura in the third intercostal space. The axillary wound contained a few drachms of thin pus, and was covered with a layer of ashen lymph. The whole pleura was covered with a layer of lymph, and contained two or three ounces of blood-stained fluid, as did likewise the pericardium. In other respects the body seemed healthy, and no other signs of sepsis were found. The surface of the wound was covered with granular exudative cells, which had also infiltrated the underlying tissues. The exudation was full of

cocci, diplococci, and streptococci (Fig. 6). Many cocci had passed along the lymph paths and vessels, which had been divided in the incision. Clots in the smaller vessels contained occasional cocci and diplococci, but in the deeper tissues many small vessels were packed with cocci. Amongst these many diplococci and occa-

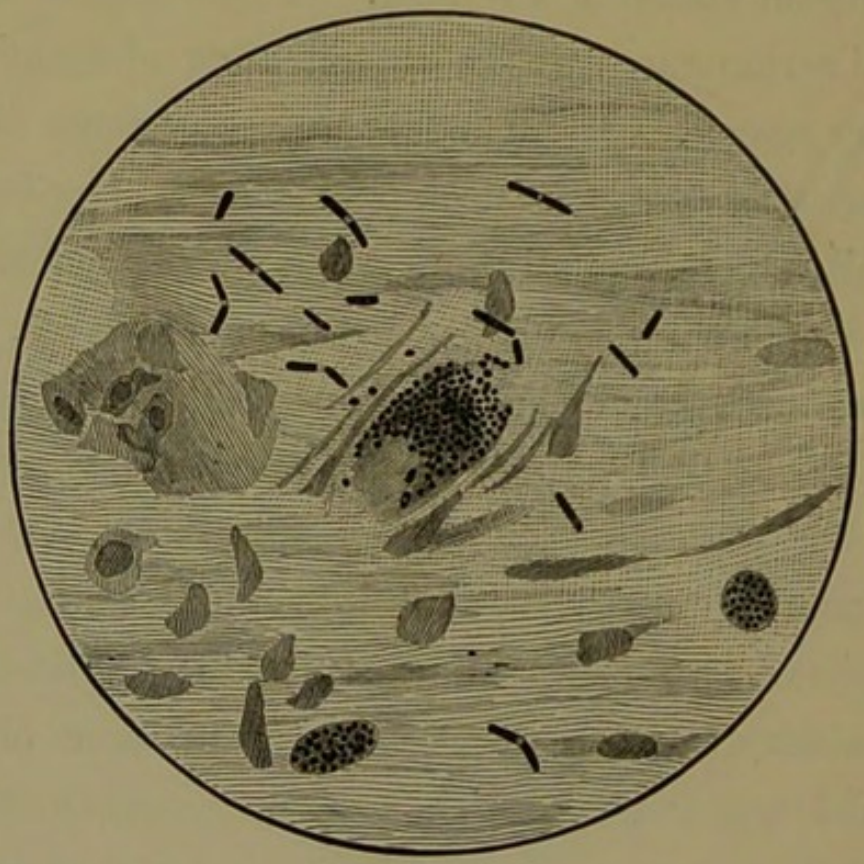

FIG. 7.—Septic wound of the axilla. Cocci in a vessel (? lymphatic). Bacilli in the depths of the tissues.

sional short strings could be made out (Fig. 7). The streptococci in the axillary lymph were scattered indiscriminately, and not collected in dense masses such as were found in the pleuritic exudation which I

am about to describe. For long I thought that cocci were the only bacteria in this wound; but after many attempts bacilli were found in the lymph and in the tissues next to the wound. These were about the size of anthrax bacilli (Fig. 7), but with rounded ends. They possessed no spores, and grew singly and in pairs. They stained by Gram's method, but were seen best by Czenzynke's. The discovery of these bacilli raises several interesting questions. Some might consider that they may have been mere putrefactive bacteria which had grown after death. This may be the truth, but is a pure assumption. Indeed, they are not at all unlike bacillus septicus in their morphological characters, and they also seemed to resemble that anærobic microbe in another particular. The lymph upon the surface of the wound, where presumably oxygen might be present, was almost free from them, although it contained quantities of streptococci (Fig. 6); the tissues, on the other hand, contained many bacilli, so that it looked as if the latter sought a habitat where there was little oxygen. To me the discovery of these bacilli is very interesting. After many examinations I had concluded that the wound was infected with nothing but streptococci. Probably culture experiments would have hardened me in this belief. It is improbable that a strict anærobe,

such as this bacillus seemed to have been, would have grown by the ordinary methods which I and most others have hitherto adopted. It is evidently rash to make positive statements about the bacteria of any wound upon the mere evidence of cultures. The lymph upon the surface of the pleura was from one to two millimetres thick. It was composed of exudative cells and fibrin, mixed with vast quantities of streptococci. The latter, unlike those in the axilla, grew in luxuriant chains entwined in dense and entangled masses buried in the lymph (Fig. 8). Many chains of cocci projected from the surface of the lymph into the pleural sac. The pleura had undergone the usual inflammatory changes, but these were confined to its surface and the lung was almost unaffected. The kidneys, liver, and spleen were examined for bacterial invasion but none was found. The fatal result was, therefore, caused by a local invasion of the axilla and pleura, and clearly the latter was enough to suffice. It is obvious that this infection might have been conveyed to the wound either during the operation or when the dressings became saturated. However, the temperature had begun to rise before the last event. It seems probable that both the wound and the pleura were infected at the same time, either by the instruments or by the atmosphere. The rapidity of the

invasion, the high temperature, and the profound constitutional disturbance are all, I believe, ordinary features of virulent streptococcus invasion. The production of lymph in the wound and upon the serous membrane is also a common consequence of their

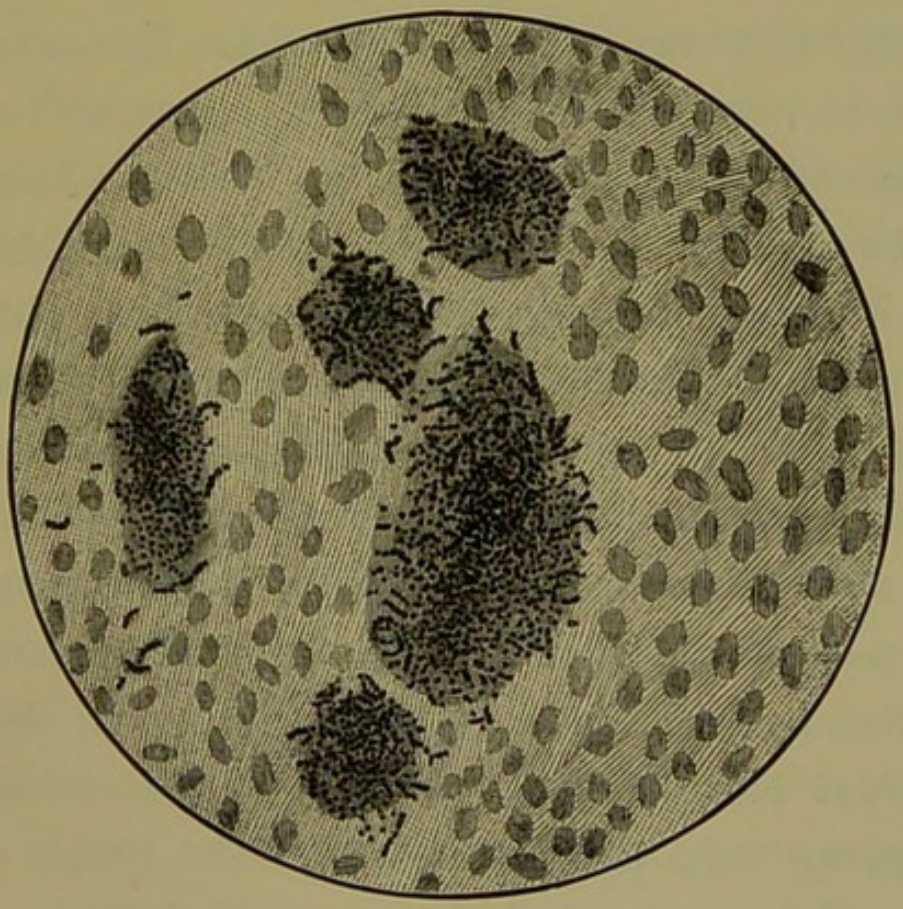

FIG. 8.—Streptococcus pleuritis. Entangled masses of streptococci in lymph upon the surface of the pleura.

activity. In the next lecture I shall describe a similar layer of pleuritic lymph which owed its origin, not to micrococci, but to bacilli. Had bacilli been found in the pleuritic lymph in this case the question would

have been much more complicated. It seems reasonable to suppose that the comparative fewness of the streptococci in the axillary lymph and their luxuriance in that of the pleura is explained by the different conditions under which they grew. Various antiseptics were used for the wound, which was also drained; the pleura had none of these applications. In contrasting these two cases of invasion of the *pleura* and of the *peritoneum* by streptococci, the most striking difference is the small production of lymph in the peritoneum and its thickness in the pleura. Associated with this we have to notice that the streptococci had penetrated deeply into the peritoneum, whilst the pleura was hardly affected at all. Moreover, it is singular that the streptococci are irregularly scattered throughout the peritoneal lymph and in the substance of the peritoneum itself, but in the pleuritic lymph they are collected into entangled masses of considerable size. (Compare Figs. 4 and 5 with 8). The lymph which covered the pleura had the same physical characters as the lymph which I have produced in rabbits by the subcutaneous application of unsterilised croton oil or unsterilised mercury. This septic lymph differs but little physically from that which is caused by sterilised croton oil, sterilised mercury, or pure carbolic acid. Biologically and chemically the difference is great

because bacteria and their products are present in one case and not in the other. The presence of the bacteria has, when critically examined, a slight but important effect upon the physical characters of the lymph; it is more fluid, its edges are ill-marked and shade off gradually into the surrounding inflammation, and, last, it has hardly any tendency to organise. The lymph which is caused by carbolic acid and mercury in the absence of bacteria is firm and consistent, its edges are abrupt and sharply defined, and if the rabbit be killed a week after the application of the chemical, and injected with carmine gelatine, it may be seen with the naked eye that numerous small vessels have begun to penetrate the lymph. The organisation of some kinds of aseptic lymph seems, as far as I can ascertain, to have been overlooked by those who have worked at this subject. It is, nevertheless, a point of some interest and importance. The conditions under which septic lymph organises or disappears are worthy of inquiry. Recently I opened the abdomen of a boy seven years of age, who had diffuse septic peritonitis due to a perforation of the ileum. The abdomen contained pus and lymph, and much of the latter was left behind. The child recovered, but I have often wondered what became of the septic lymph which was left behind. In another case an incision was made over

the cæcum for the purpose of finding the vermiform appendix. This was prevented by recent adhesions, which were so abundant and bled so much that they could not be separated without a great risk of lacerating the bowel. The cæcum was accidentally opened, and six weeks afterwards, when I closed the opening, to my astonishment the adhesions which had been so troublesome had disappeared and the cæcum and neighbouring intestines looked almost normal.

Bacterial Invasion of the Peritoneal Lymph Paths in Septic Peritonitis.

The foregoing observations tend to show that the intestinal bacteria do not, like the streptococcus pyogenes, easily penetrate into the substance of the peritoneum. The following, however, seems to suggest that after time has elapsed even the intestinal bacteria may invade the peritoneal lymph paths. It also illustrates how difficult it is in practice to distinguish betwixt operative peritonitis and perforative peritonitis.

Case 6.—A man, thirty years of age, had suffered for five years with symptoms of gastric tumour or ulcer. These culminated in stricture of the pylorus, with dilatation of the stomach and its attendant troubles. To dilate the pylorus an abdominal section was done

and an incision made in the front wall of the stomach. When the pylorus had been dilated this wound was closed with a row of sutures in the mucous membrane and another in the serous coat. For a few days the operation afforded some relief, and food was taken by the mouth. On the seventh day severe pain occurred in the region of the stomach, and upon the eighth day the patient died of septic peritonitis. This was not accompanied by any rise of temperature; indeed, his temperature was usually sub-normal. I made an examination twenty-two hours after death, and found that the wound in the stomach had given way. The whole peritoneum was inflamed, with a quart of purulent fluid and stomach contents in the flanks and pelvis. There was much lymph around the wound in the stomach and about that in the abdominal wall, with some suppuration along the sutures. The piece of peritoneum which was examined was taken close to the wound in the abdominal wall. The ulcer in the stomach was not malignant[1] and the body was healthy, with the exception of what has been described. Histologically[2] the tissues of the peritoneum had not undergone much alteration. The surface cells

[1] The specimen is in the museum of St. Bartholomew's Hospital (No. 1951 b).

[2] I am indebted to Dr. Addison for much labour at these tissues. Our most successful specimens were stained with alkaline methyl blue.

had proliferated and some inflammatory corpuscles infiltrated its substance, but this infiltration was not very marked. Nor was there much congestion of the blood vessels. Amidst the lymph upon the surface were a great variety of bacteria, cocci, diplococci, and bacilli of various lengths and thicknesses (Fig. 9). Here and

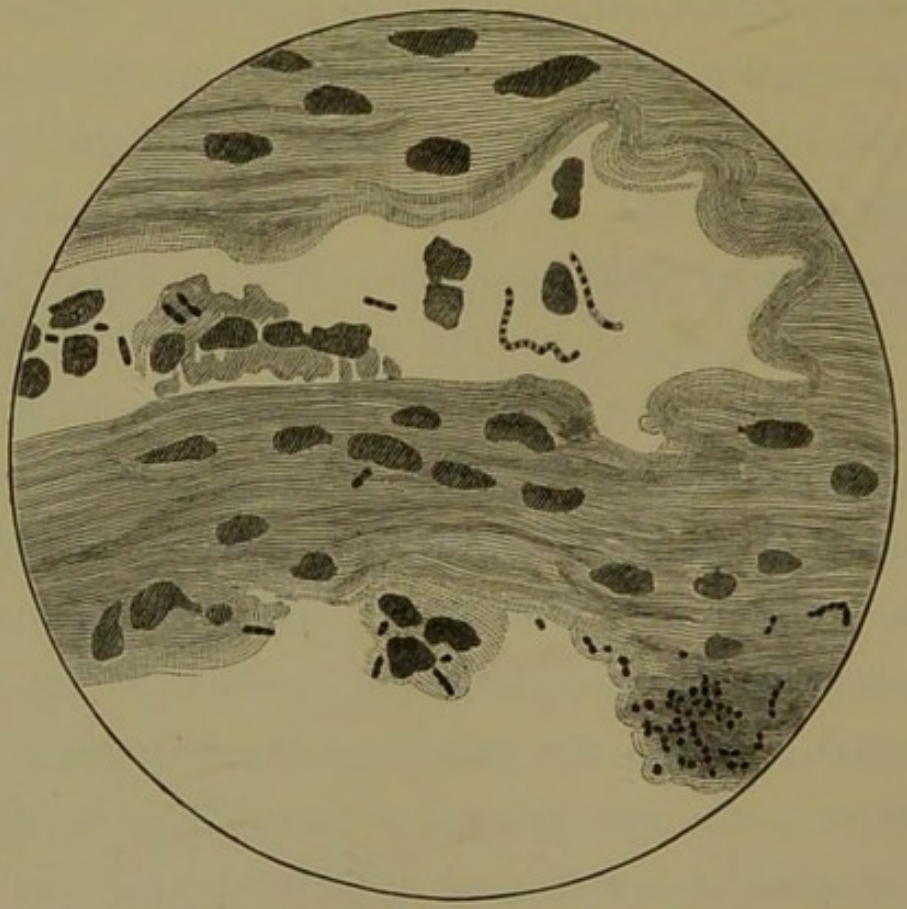

FIG. 9.—Bacterial invasion of the lymph paths in diffuse septic peritonitis.

there the bacteria were collected into groups, and it was difficult to say whether these were swarms of short bacilli or clumps of staphylococci. Similar bacterial forms were seen in the adjacent lymph paths. But in

these spaces chains of bacteria were conspicuous. It is difficult to say whether these chains consisted of cocci or of short bacilli. The lymph paths also contained bacilli of considerable size (Fig. 9). In addition to bacteria they were partially filled with exudation corpuscles, and some material which looked like coagulated albumen, such as is often seen in the renal tubules in certain kinds of acute nephritis. In the depths of the peritoneum, as far as the subperitoneal fat, there were small, dense collections of bodies which had the appearance of cocci and diplococci. These were always arranged round a nucleus and were not contained in any space. I am ignorant of their meaning. Some, I believe, would call them phagocytes laden with bacteria.[1] The liver and kidneys of this case were also examined, but no bacterial invasion was discovered.

The history of the case leaves a doubt as to whence these bacteria originated. It is possible that they came from the outside, for the wound was septic, or from the interior of the stomach. The contents of the stomach possess a luxuriant flora and could well furnish the bacteria which were found; various articles of diet, the saliva, and the pharyngeal and nasal mucous membranes supply it with a vast variety of bacteria.

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[1] These specimens were stained with alkaline methyl blue.

De Bary's[1] work has an important bearing upon this question. He examined the contents of healthy and diseased stomachs. The acid material from healthy stomachs contained hardly any bacteria in comparison with that from cases of cancer of the pylorus, stenosis of the pylorus, or of ulcer of the stomach. Gillespie[2] and Macfadyen[3] found many varieties, including the bacillus coli communis. At the same time they note that healthy gastric juice has fair antiseptic properties; but Macfadyen and others have remarked that in the contents of the intestinal canal more bacteria can be distinguished microscopically than can be recognised in cultures inoculated from those contents. Barbacci has also tried to show that the bacillus coli communis is of less importance in causing perforative peritonitis than other bacteria which are present, but will not grow in cultures. Thus in the case just given either the stomach or the wound could furnish the bacteria seen in the lymph and in the lymph paths. The number of bacilli, however, suggests that they come from the stomach. The absence of any rise of temperature during the peritonitis also suggests that it was not

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[1] "Beitrag zur Kenntniss der niederen Organismen im Mageninhalte." *Arch. f. exper. Path. u. Pharmakol.*, Leipzig, 1886, bd. xx., p. 243.

[2] "Bacteria of the Stomach." *Journ. Path. and Bacteriol.*, Edin. and London, vol. i., p. 284.

[3] *Journ. Anat. and Physiol.*, London, vol. xxi., 1886, p. 237.

caused by the ordinary pyogenic cocci. The presence of strings of bacteria in the lymph paths is consistent with what we already know of these kinds of organisms. In erysipelas, cellulitis, and lymphangitis the streptococci travel along the lymph paths, their passage being facilitated by their shape, which is well adapted for narrow channels; on the other hand, clumps of staphylococci or of bacilli would, it might be supposed, find it difficult to pass along the narrow channels of the tissues. Thus we find that such an organism as staphyloccus aureus is usually associated with acute localised suppurations or inflammatory wound gangrene (Ogston), and streptococcus pyogenes with spreading inflammations such as erysipelas or cellulitis.

Intestinal Bacteria in other Conditions: Hepatic Abscess.

During these investigations I have met with intestinal bacteria in other diseases besides perforative peritonitis, and it may not be out of place to refer to these occurrences. For instance, the following[1] illustrates their presence in abscess of the liver.

Case 7.—A man who had lived six months in India

[1] I am indebted to Mr. Poynder for very clear notes of this case, and to Dr. Norman Moore for permission to use them.

and had had ague and dysentery there, returned to England, and had an attack of hepatitis in August 1887. This seems to have subsided, and to have been followed by a second attack of dysentery and a fresh hepatitis in June 1892. The abscess in his liver probably dates from this time. In February 1893 Dr. Norman Moore diagnosed an abscess of the liver and obtained some pus from it with a sterilised needle and after proper disinfection of the skin. Having been called in to open the abscess, I performed laparotomy. As the liver was not adherent it was stitched to the edges of the wound, and forty-eight hours later the abscess was opened. The patient made a good recovery. Cultures inoculated from the wound before opening the abscess remained sterile; others inoculated from the pus grew the bacillus coli communis in pure culture. The pus was very thick and of a slightly greenish tinge, and occasional short bacilli could be seen in it, but living plasmodia were not looked for. The amœba coli was not sought for in this pus when it was fresh, but none could be seen in stained specimens. My colleague, Dr. Galloway,[1] who has done good work at this subject, showed me the amœba coli in the pus of a hepatic abscess which

[1] *Brit. Med. Journ.*, London, 31st March 1894.

I opened for a patient of Dr. Clifford Beale. I have recently failed to find the amœba coli in an empyema of the gall-bladder. The pus contained streptococcus pyogenes, and possibly other organisms.

The exact relation of the bacillus coli communis to hepatic abscess has been much debated by Kartulis, Councilman, Osler, Manson, Galloway, and others, and will not, I venture to think, be decided by mere clinical or bacteriological evidence. Experimental pathology may, however, be expected to throw light on this question. Zancarol[1] performed a series of experiments by injecting dysenteric evacuations, hepatic pus, and cultures from hepatic pus into the recta of cats. These are, so far as I can tell, the only direct experiments upon this disease. Zancarol claims that any of these may produce dysenteric ulceration of the intestine with accompanying abscess of the liver. He seems doubtful whether the amœba coli causes abscess of the liver in dysentery. He attributes potent effects to streptococci. Although the following experiments performed upon rabbits teach but little, yet they show that the relationship of the intestinal bacteria to abscess of the liver is not so simple as at first glance it seems to be. I

[1] "Pathogénie des Abcès du Foie." *Rev. de chir.*, Paris, 1893, tome, xiii., p. 671 *et seq.*

mention them here because they may be of help to others—at least by telling them what to avoid. Laparotomy was performed upon a healthy rabbit and a loop of intestine drawn out. Two cubic centimetres of a broth culture of bacillus coli communis, grown from the case of liver abscess which has just been described, were injected into the mesenteric vein. The animal died during the night, and slight peritonitis was found. The animal seems to have been poisoned by the culture. Next, the liver of another rabbit was exposed, and one cubic centimetre of a broth culture of the same bacillus was injected into it. At the end of a week the animal, which seemed to be fat and well, was killed. The injection appeared to have produced no result, but the presence of numerous psorospermal foci forbade any positive statements; at all events, no large abscess or destruction of liver substance had occurred. The injection of a solution of rabbits' fæces in water into the mesenteric veins of another rabbit made the animal ill, and when it was killed at the end of a week there were found to be several small abscesses at the periphery of the liver; but here again the result seemed uncertain because so many psorospermal foci were present. These experiments made me think that something more than

intestinal bacteria were required to cause hepatic abscess.

Intestinal Bacteria in other Conditions: Typhoid Abscess.

It is now so well known that the typhoid bacillus can cause abscesses that a case in which that occurred would hardly be worthy of record if it did not also illustrate another point—namely, that bacteria may continue to live in the human body for months or years. This is shown by a case in which I found the typhoid bacillus in an abscess, a year and three months after an attack of typhoid fever. The interval which elapsed between the infection and the discovery of the bacillus in an abscess was, I think, clearly substantiated. The patient was a young woman, aged nineteen years, who came with a subacute abscess over the front of the tibia. It contained ordinary thick, dirty-yellow pus. The cells of this pus were degenerated, and amongst them were some bodies which were taken to be short bacilli. These grew upon gelatine with all the ordinary characters of typhoid bacilli. The gelatine was not liquefied, and the bacilli grew upon its surface in greyish white layers with irregular edges. In the depths it formed fluffy colonies. The growth was slow at summer temperature. The bacilli were about four

times as long as they were broad, with rounded ends and with spores which did not cause any bulging; they grew occasionally in short strings of four or five elements. This patient said she had been liable to abscesses ever since she had been in hospital for typhoid fever. Dr. Goodall has kindly informed me that she went into the fever hospital on 4th April 1892, with typhoid fever, and that whilst there her case was complicated with abscesses in the axilla and neck. The abscess from which I obtained the pus was opened on 17th June, 1893—at least one year and three months after the onset of the disease. It is so unlikely that this patient could have had a fresh infection with typhoid bacilli, that I think we must conclude that those found in the abscess must have lived in her body for at least a year and three months after their introduction. During the greater part of their sojourn they seemed to have caused but little inconvenience to their host. With the exception of the subacute abscess, her health was good. The bacilli seem to have been living for months at the place where they afterwards caused the abscess, and had not been recently deposited there from the blood. The note says that during the months which preceded the abscess its site was occupied by a painful swelling which appeared and disappeared several times.

The typhoid bacillus seems particularly fitted for throwing light upon the question how long bacteria live in the body. Its early effects are so palpable that there is seldom much doubt as to the approximate date of the inoculation. Instances similar to that which I have recorded have been published by Hintze[1] and others, but none of the cases seem to have lasted so long after the fever. In Hintze's case the bacillus was found in an abscess of the chest wall two months after the fever; Werth found them in an ovarian cyst eight months after; Orloff found them in an abscess over the tibia six and a half months after; and others have found them at shorter times. It seems reasonable to suppose that other bacteria may lurk unnoticed long after their introduction. I ought to add that staphylococcus pyogenes aureus and the bacillus coli communis have been found in the abscesses which follow typhoid fever.

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[1] *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1893, bd. xiv., p. 445 *et seq.*: "Ueber die Lebensdauer und die Eiter-erregende Wirkung des Typhus Bacillus im Menschlichen Körper." I am indebted to Dr. Turney for having called my attention to a case of Sultan's in which the bacillus of typhoid was found in an abscess six years after the original infection. *Deutsche med. Wchnschr.*, Leipzig, August 23rd, 1894, p. 675.

LECTURE II.

SOME INFECTIONS OF THE BLOOD; SEPTICÆMIAS.

Definitions.

Gentlemen,—In its strictest acceptation the term "septicæmia" should, I think, apply to conditions in which bacteria flourish in the blood without passing through the walls of the vessels into the tissues. At the same time, the bacteria may be present, and even multiplying, at the original seat of inoculation. Koch's [1] mouse septicæmia is a disease of this type. In it the bacillus multiplies at the point of inoculation, and invades the blood, but is not given up by the blood to the tissues. Whilst the animal is alive, and after it is dead, the bacilli are found in its blood, and also in various blood vessels throughout the body. Hitherto it has been difficult to demonstrate the occurrence of pure septicæmia of this type in man.

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[1] "Traumatic Infective Diseases." *New Sydenham Soc.*, 1880, p. 33 *et seq.*; also Baumgarten, *loc. cit.*, p. 496.

Septicæmia and Sarcosepsis.

There ought, theoretically, to be a converse condition to septicæmia—one in which the bacteria flourish in the tissues, but refuse to enter the blood. Malignant œdema, or, as English surgeons more often call it, diffuse spreading traumatic gangrene, seems to be such a disease. It is well known that in it the bacillus septicus spreads along the lymph paths and shuns the blood. This peculiarity is perhaps explained by the profound aversion which the bacillus has for oxygen. After death the bacillus septicus may spread into the blood, which has then presumably lost its oxygen. Thus we may have a true sepsis of the blood or septicæmia, and a true sepsis of the tissues or sarcosepsis. Most often, however, these two are combined.

The study of the human septicæmias is surrounded by many difficulties. Everyone has seen in histological sections of organs the blood coagulated in the larger vessels, and when this work was begun I thought it might be possible to see bacteria in this coagulated blood in cases of septicæmia. However, I have been most unsuccessful in finding bacteria in the blood of these so-called natural injections, and it seems clear that as yet nothing can be hoped for from this source. This absence of bacteria from the blood of the larger

arteries and veins of men and animals who have died from septicæmia is rather mysterious, but even in such a marked septicæmia as anthrax the bacilli are not at all easily seen in the blood of the larger vessels.[1] Perhaps streptococci ought to be excepted from this assertion. Cornil and Babes[2] found streptococci in these natural injections, and I shall allude to a case of streptococcus poisoning in which cocci and diplococci were seen in the blood and also in the smaller hepatic veins. I have, however, more than once found bacilli in the blood clot in vessels not far from septic wounds in cases of septicæmia (*vide* Fig. 13). Here, however, the mycosis may have been local and not general.

It is by no means easy to demonstrate any kind of bacterial invasion of the blood in human beings. To begin with, it is not always right or expedient to obtain specimens of blood during life, or to obtain them from favourable sources. I myself have always failed to see anything definite in blood obtained by puncturing the fingers of septicæmic patients. Culture experiments with blood obtained in like manner may also be fallacious, because, to mention only one objection, of the impossibility of always disinfecting the skin. There

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[1] *See* also Flügge, "Micro-organisms in Disease." Translated by Watson Cheyne. *New Sydenham Soc.*, 1890, p. 238.

[2] "Les Bactéries," vol. i., Fig. 206, p. 536.

still remain, however, the tissues and organs for examination, and they afford, I hope to show, signs as unmistakable as in mouse septicæmia or anthrax.

Great difficulties have been experienced in discovering any bacteria whatever in septicæmic tissues. Experimental pathologists are quite familiar with the occurrence of bacterial emboli in the capillaries of animals after the intravenous injection of pyogenic cocci or of other bacteria. Also, since the investigations of Recklinghausen, Klebs, Hueter, and of many others, bacterial emboli have been repeatedly described and figured in the organs of men and animals who died from pyæmia,[1] and I could adduce many examples of my own; but hitherto the occurrence of similar emboli in septicæmia hominis has hardly been recognised, although the need of objective evidence of the kind has been severely felt. Indeed, in its absence there can be no doubt whatever that many cases of septicæmia have been thought to have been toxæmias, septic intoxications, or sapræmias. The importance of being able to determine the true cause of death in septicæmia and toxæmia by the examination of the tissues hardly requires to

[1] Fraenkel und Pfeiffer, "Atlas der Bakterienkunde," Parts XII. and XIII., Fig. 126 *et seq.* Also Koch, "Etiology of the Traumatic Infective Diseases," 1879. Bowlby, "Surgical Pathology," 1887, p. 60, Fig. 5. Ziegler's "Pathological Anatomy," Part II., 1886, p. 55, Fig. 212, &c.

be mentioned. Writing in 1890, Baumgarten[1] said that, although bacteria have been found during life by Ogston and Rosenbach in the blood of those suffering from septicæmia, nevertheless direct evidence of their presence in the internal organs was wanting. He himself made the attempt to demonstrate their presence, but failed to do so. Cohnheim,[2] who has done so much to elucidate embolism, says nothing concerning bacterial emboli in the capillaries in septicæmia hominis. Von Eiselsberg[3] and many others have both before and after death demonstrated bacteria in the blood in a variety of septic conditions by using culture media. This method, however, is not always possible, and is apt to be fallacious. Von Eiselsberg and the authorities whom he quotes do not seem to have seen bacteria in the blood vessels or capillaries after death. In one of our most recent and best works upon pathology[4] the author, speaking of septicæmia, says: "We are peculiarly ignorant of what the organisms are which grow

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[1] "Lehrbuch der Pathologischen Mykologie," p. 362. Braunschweig, 1890.

[2] "Vorlesungen über Allgemeine Pathologie." Berlin, 1877.

[3] "Beiträge zur Lehre von den Mikro-organismen im Blute," &c. *Wien. med. Wchnschr.*, 1886, p. 133. Also, "Nachweis von Eiterkokken im Blute als Diagnostische Hilfsmittel." *Wien. klin. Wchnschr.*, 1890, No. 38, p. 731.

[4] Hamilton, "Text-book of Pathology," vol. ii., Part II., p. 1019. London, 1894.

in the blood of man as a result of putrefaction." But in pathological literature are to be found brief references to the occurrence of bacterial emboli in the capillaries of those who have died from septicæmia. Klein[1] says that in several cases of human septicæmia he found large numbers of minute bacilli in the blood vessels of the lymphatic glands, and he figures such a vessel distended with bacilli. Cornil and Babes[2] say that Ziemacki examined a large number of those who had died from septicæmia, and always found zooglœa of micrococci in the organs. These micrococci or zooglœa were always the same, and were more numerous in acute than in chronic septicæmia. The micrococci were never found in non-infectious maladies. Klebs[3] has also described and depicted proliferation of micrococci in the pulmonary capillaries in puerperal septicæmia, following septic thrombosis of the internal spermatic vein. Leber and Wagenmann[4] have described

[1] "Micro-organisms and Disease," third edition, 1886, p. 120, Fig. 55.

[2] "Les Bactéries," Paris, 1890, p. 464. Ziemacki's original work is entitled "Beiträge zur Kenntniss der Micro-organismen bei Septicæmia." I regret I have been unable to obtain it. A reference is given in the *Ztschr. f. Hyg.*, Leipzig, 1883, Part II.

[3] "Die Allgemeine Pathologie," Part I., pp. 300 and 301, Fig. 50. Jena, 1887.

[4] "Infantile Necrose der Bindehaut mit letalem Ausgang durch allgemeine multiple Streptocokken-Invasion des Gefässsystems." Von Graefe, *Arch. f. Ophth.*, Leipzig, 1888, bd. xxxiv., p. 250 *et seq.* These authors give references to similar observations in children who died from congenital syphilis and other diseases.

an invasion of the vascular system by streptococci, but their attention is chiefly devoted to a local invasion at the point of inoculation, and they say little concerning the internal organs. I propose to refer to their observations when describing emboli in the capillaries of the liver in streptococcæmia. Cornil and Babes in their work on Bacteria depict the capillaries of the lung of an infant, the minutest vessels of which were filled with bacilli which resembled those of rabbit septicæmia. These authors also describe and depict bacteria and cocci in the capillaries of the skin of a child which died from septicæmia. Doubtless other references are to be found, but enough has been said to show that little is known concerning the occurrence of capillary bacterial emboli in septicæmia hominis.

Bacillary Septicæmia with Sarcosepsis.

I long thought the following was a case of septicæmia such as came within my definition of that disease; but after many searches bacteria were at length discovered in the pneumonic exudation. Whether these were merely cadaveric, or whether they were pathogenic, I do not know. So little, however, seems to be known about septic pneumonias that it is better to describe what was found rather than to

assume something which may be false. I shall, however, presently describe cases of septicæmia in which there seems to have been a true infection of the blood, such as occurs in mouse septicæmia. The case I am about to describe has a melancholy interest for me, as it is the only one of its kind I have ever had.

Case 8.—A woman, aged sixty-two years, had a rapidly growing and ulcerated carcinoma of the breast, with involvement of the axillary lymphatic glands. Although the tumour had only grown for four months it was of large size, and the skin over it was cancerous in an area five inches long and three broad. In the centre of this area, in the region of the nipple, the skin had ulcerated and the cancer was fungating. After consultation with my colleagues I removed the whole of this extensive disease, together with the axillary glands. The wound was brought together with difficulty, a drainage-tube was placed in the axilla, and many pints of sublimate lotion (1 in 2000) were used for irrigating the wound and the axilla. The skin was dusted with iodoform and a dressing applied. After the operation the patient was very restless and delirious and unable to understand what was said. These symptoms began with reaction and became progressively worse. After a while the restlessness and

delirium were followed by apathy and stupor, and she died on the seventh day. Her temperature was highest on the last day, when it rose to 102·4° F.; the day before it had been 101°, and it was the same the third day; but with these exceptions it remained somewhere near 99°. The wound was painful from the beginning. About forty hours after the operation a little fluid soaked through the dressings, so they were changed. There was some redness of the skin, but the incision looked well. The drainage-tube was blocked with greyish blood clot which had a peculiar odour, but not that of putrefaction. No bacteriological examination was made at this time, because the symptoms were thought to be due to iodoform; but the general and local conditions speedily became worse. The wound emitted a fetid odour and was covered with ashen lymph without pus. Therefore, the whole wound was opened and swabbed with tincture of iodine and fomented. The fetor abated, and the wound afterwards underwent no alteration. General infection had, however, obviously supervened from an early stage. The macroscopic appearances were, as usual in septicæmia, far from characteristic, and taken alone would have left the nature of the disease in doubt. There was a large and fetid wound due to the removal eight days previously of a large ulcerated carcinoma of the breast, together with second-

arily infected axillary glands. The liver, spleen, and kidneys were normal, and no abscess or thrombus could be found anywhere. Both lungs were engorged with blood.[1] Secondary nodules of carcinoma were met with in the liver, kidneys, and lungs. Portions of these three organs were histologically examined by various methods of staining, together with blood from the heart and fluid from the wound. The microscopic examination of the tissues yielded the following results :— Pathologists have always laid great stress upon the condition of the spleen in septicæmia hominis, but its tissues were normal and no bacteria were seen, although several methods of staining were employed. The same applies to the liver. In the lungs, however, numbers of the capillaries were filled with small, non-spore-bearing bacilli with rounded ends, and usually in pairs (Fig. 10). At first glance the capillaries looked as if they were filled with micrococci, but in many of the emboli separate short bacilli could be discriminated, and occasionally chains of three or four. The bacilli were lodged in the smallest capillaries, oftenest in those which had a diameter equal to one coloured corpuscle, but seldom in those which had a diameter equal to two. Many of the smallest

[1] From the notes of Mr. Berry, surgical registrar in St. Bartholomew's Hospital.

capillaries of the air vesicles were filled with bacteria, but the vasa vasorum of the smaller pulmonary vessels were clearly their favourite seat. They stained rather more purple by Czenzynke's method than some other bacteria which I am about to describe. The lungs themselves were engorged with blood, and many of the

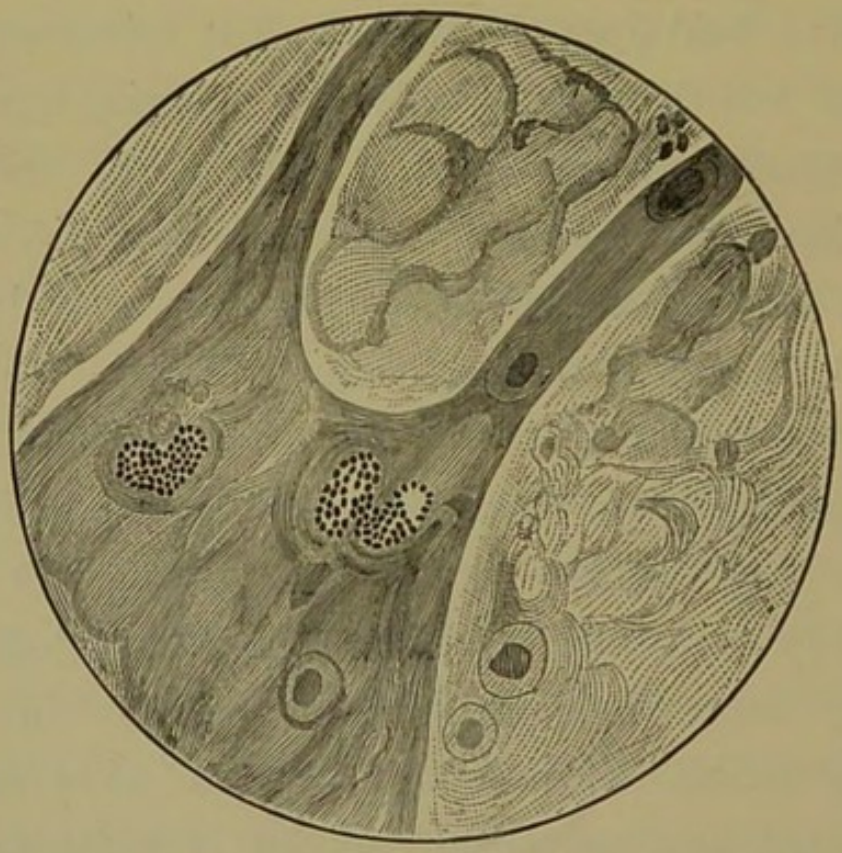

FIG. 10.—Bacillary septicæmia. Short bacilli in the capillaries of the lung.

air vesicles were full of exudation, with large nucleated and granular cells in its midst (Fig. 11). A number of different kinds of bacteria were growing in this exudation. The most numerous were small, almost round

bacteria, which grew in dense swarms, or in pairs, or chains of three or four elements. They were the same as the bacilli in the capillaries; where they grew in swarms within the tissues of the lung their resemblance was exact. The pairs had no capsules. Here and there the bacilli lay within the exudation cells. Like

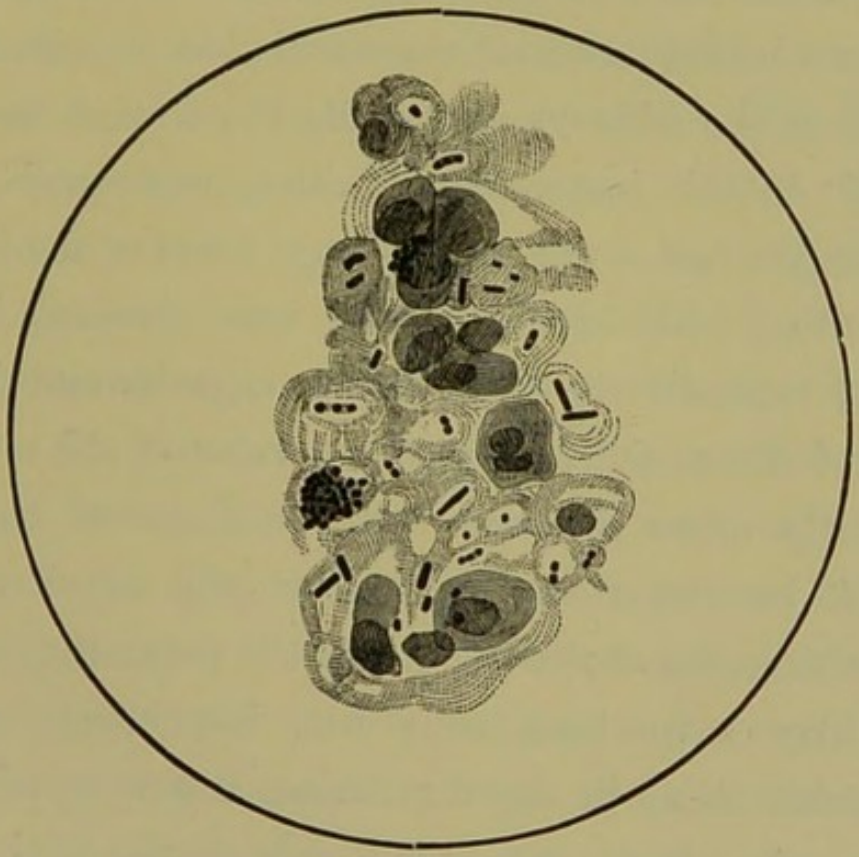

FIG. 11.—Bacillary septicæmia. Exudation into air vesicles in pneumonia complicating septicæmia.

those in the capillaries, they did not stain by Gram's method, but did by Czenzynke's. Along with these small bacilli were others which were long and rather slender, and not unlike tubercle bacilli. I thought, as

intermediate grades were present, that they might be the mature stage of the small bacilli. In the exudation were also numbers of big, thick bacilli of variable length. These stained by both Gram's and Czenzynke's methods. The more healthy parts of the lung contained none of these bacteria, except the small kind, which filled some of their capillaries. When pyogenic cocci are introduced into the circulation of animals the vessels of the kidneys are usually the seat of bacterial emboli; in this instance of bacillary septicæmia, however, only a few of the smallest capillaries of the kidney were filled with bacilli. These were situated in the cortex, immediately beneath the capsule, and in the walls of the straight arteries and veins of the medulla. Presently other instances will be given of bacterial emboli in the vasa vasorum of the renal vessels. Doubtless some of the bacteria in the pulmonary exudation may have been cadaveric, but others closely resembled those in the capillaries, and were probably pathogenic. It is not at all easy to think that the bacteria in the capillaries did not get into them during life. I have no hesitation in believing that they were carried there by the blood stream, and that they are evidence of the septicæmia from which the woman was thought to have died. I have examined the organs of those who died from burns, fractures, cellulitis, bron-

chitis, pneumonia, pleurisy, and other diseases by the same methods, and have never met with similar appearances in the capillaries. Nor have I been able to find them in kidneys or lungs which were beginning to putrefy. Moreover, the presence of bacteria in the capillaries is consistent with the clinical history and with the bacteriological investigation of the wound, heart's blood, and tissues. Bacteria with the same morphological characters as those in the capillaries of the lung were found in the fluids of the wound and in the blood of the auricle. In both, however, they were mixed with other kinds of bacteria, so that a satisfactory investigation was difficult and uncertain. The sanious and fetid fluid from the axilla contained cocci, diplococci, and staphylococci, and staphylococcus pyogenes aureus was separated from it by plate cultures. It also contained quantities of small, oval, sporeless bacilli similar to those in the capillaries of the lungs and kidneys. These also grew in short chains and occasionally looked not unlike diplococci, their ends staining more than the centre. An attempt was made to identify some of the bacteria in the wound. The earlier cultures had the same odour as the fluids of the wound and grew bacteria with similar morphological characters. Mice, rabbits, and pigeons died two or three days after inoculation with cultures from the

axillary fluid. Their blood contained small oval bacilli, usually in pairs. This bacillus grew rapidly at 20° C. or 35° C. upon the surface and in the depths of culture media. The growth upon the surface was smooth and white, with abrupt, irregular edges. That in the depths consisted of small delicate white dots. Gelatine was not liquefied. The agar-agar acquired a greenish opalescent tinge. No gas was produced, and odour was absent from the older cultures. Mice died about forty-eight hours after inoculation. This bacillus was also separated from the juice of the spleen and liver. Some of the foregoing characters are like those of a bacterium which Pasteur found in fowl cholera, Gamaleia in septicæmia of birds, and Koch in rabbit septicæmia. The opalescence of agar-agar is, however, a peculiar feature. It has been observed by Babes in cultures of his proteus septicus. The wound contained other kinds of bacilli. Some were straight with rounded ends, and about the size of tubercle bacilli; others, with sharp, indistinct ends, grew in long chains; others were short and plump; whilst others were large and grew in pairs, and looked like kidneys lying with their hilums towards one another. The bacilli with sharp ends I have seen in the pus of acute septic meningitis caused by otitis media. I cannot say to what extent these various forms represent distinct species of bacilli. Malvoz, in his admirable

monograph,[1] claims that the colon bacillus is extremely polymorphic. In the same culture he has seen ovoid forms, almost like cocci, a small bacillus with rounded ends, and, last, a long filamentous bacillus. By adding naphthol, alcohol, bichromate of potash, or boric acid to the media in which it is growing the bacillus pyocyaneus assumes the form of bacillus, of long bacillus, of leptothrix, of spirillum, or of spirochæta.[2] From the pus of a case of septico-pyæmia occurring after parturition Karlinski[3] obtained a pleomorphic bacterium closely allied to the proteus varieties of Hauser. It assumed coccus, bacillus, or spirillum characters according to the ways in which it was grown, and was pathogenic for white mice. No details are given of any other examination of the pus, blood, or tissues of the person from whom Karlinski obtained the bacterium.

It is quite a usual circumstance to have several kinds of bacteria in the wound and for only one kind to invade the body. For instance, in the profoundly septic wound of a patient who died after internal urethrotomy I found bacilli and cocci of various kinds. But the pus of a pyæmic abscess only contained streptococci. The

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[1] "Le Bacterium Coli Commune comme Agent Habituel des Péritonitis d'Origine Intestinale." *Arch. de méd. expér. d'anat. path.*, Paris, 1891, p. 596.

[2] Macé, "Traité Pratique de Bactériologie," Paris, 1891, p. 512.

[3] *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1889, bd. v., p. 193.

bacilli did not seem to have passed beyond the wound. The blood of the auricle in this case of septicæmia also contained numbers of the small oval bacilli, usually in pairs, and many large straight, round-ended bacilli. The latter were, I think, cadaveric. Nevertheless, when some of this blood was inoculated into a rabbit, it died from peritonitis, and similar bacilli were found directly after its death in the lymph.

Although so many bacterial forms were present in this case, yet the septicæmia seems to have been caused by the small oval bacillus. My reasons for thinking so are as follows:—(1) a small oval bacillus was found in the capillaries of the lungs and kidneys; (2) the same bacillus was found in the blood of the heart; (3) the same bacillus was found in vast numbers in the fluid of the wound; and (4) it was highly pathogenic for animals. Babes[1] concluded from his systematic work that there were several kinds of septicæmia. In one kind all the organs contained a special non-saprogenous bacterium of a highly pathogenic type; in another the bacilli were less pathogenic and saprogenous; and, lastly, there was septicæmia produced by pus bacteria of exceptional virulence. Babes also adds that most septicæmias are caused by several associated species of bacteria.

[1] Cornil et Babes, "Les Bactéries," p. 466. Paris, 1890.

I endeavoured to find out whence the bacillus had come which had caused this septicæmia. All the usual precautions of aseptic surgery had been used in the operation. Just before the incision, the skin of the breast and the ulcerated surface were finally washed with a solution of sublimate, 1 in 1000 parts of water, although it had previously been washed and soaked in the same solution; but on reflection it seemed highly improbable that this was an efficient disinfection, and, therefore, the fatal infection may have come from the ulcer.

About this time I had under my care another patient who had a cancerous ulcer of the breast. The discharges from this had the same odour as those of the previous case. Cultures inoculated from the ulcer had the same odour, and killed white mice in forty-eight hours. Their blood contained small ovoid bacilli, usually in pairs. Some were not easily distinguished from diplococci. A small ovoid bacillus was separated from the cultures which killed the mice. It was the same as that grown from the wound and organs of the case of septicæmia which I have just described. The greenish opalescent tinge which the growing bacilli imparted to agar-agar was very striking.

Hitherto, so far as I can tell, no bacillus with pathogenic properties has been found in cancer juice or

cancerous ulceration. Scheurlen's[1] so-called "cancer bacillus" was the bacillus epidermidis,[2] and had no resemblance to the small ovoid bacillus which produced an opalescent substance; nor can I find any reference to a pathogenic bacillus[3] in the writings of others.

From what has been said, it is clear that the secretion of cancerous ulcers would repay study by a competent bacteriologist. It is not sufficiently recognised that these cancerous ulcers are such a dangerous source of infection. Quite apart from operations, they frequently give rise to sapræmia, septicæmia, or pyæmia. That precautions ought to be taken to avoid infection from cancerous ulcers during operations is obvious. It is less clear what those precautions should be. When last I had to operate upon an ulcerating scirrhus, the whole surface of the ulcer was swabbed with pure carbolic acid. This succeeded, and the wound healed by first intention under a single dressing. However, recently one of my colleagues who knew of my experience and experiments had a death from septicæmia after the removal of an ulcerating carcinoma, although pure carbolic acid had been used and every other precaution taken. This case will be described next. Upon

[1] *Deutsche med. Wchnschr.*, Leipzig, 1888, p. 1033.

[2] Kanthack, *Brit. Med. Journ.*, London, 2nd Aug. 1891, p. 476.

[3] *See* also Baumgarten, "Lehrbuch der Pathologischen Mykologie" p. 729.

another occasion of the same kind I should begin by destroying all the ulcer with an actual cautery.

Bacterial Invasion of the Heart in Septicæmia.

Case 9.—Another case of septicæmia similar to the last occurred in the same ward a year and five months later. There is the closest similarity in the clinical history, morbid anatomy, and morbid histology of the two cases, and therefore I will mention it next. The patient was a woman, fifty-five years of age, who came into the hospital because of a scirrhous cancer of the right breast. The tumour had grown for more than a year, and had involved the axillary glands. In its centre the growth had ulcerated over an area as large as a half-crown, and some very foul discharge was secreted by the raw and fungating surface. The operator was acquainted with the history of the previous case, and therefore extra care was taken to disinfect the ulcer and the surrounding skin. The latter was, as usual, washed with soap and water, its sebaceous matter removed with ether, and then it was disinfected with a solution of biniodide of mercury, 1 part in 500 parts of water. Also carbolic gauze soaked in a solution of biniodide of mercury was kept applied to it for many hours. Just before the operation the surface of the

ulcer was brushed over with pure carbolic acid, and covered with a layer of alembroth gauze fastened on with collodion. At the operation the breast, pectoral fascia, and the axillary lymphatic glands were removed. The wound, which was very large, was closed with flaps of skin, drained, and dressed in the usual way. Nothing can be said with certainty about this patient's mental state, because she had delusions before the operation; but she became violent directly after the operation and was never afterwards rational. She remained weak, restless, and sleepless, and after some hours of delirium was semi-comatose and collapsed, and died on 10th October, the sixth day after the operation. During the last forty-eight hours it is expressly said that her pulse was extremely feeble, and was only maintained by the continual administration of brandy and of other cardiac stimulants. From having been 80 in the minute the pulse rose to 130 towards the end. The respiration hardly altered, but kept from 24 to 30 per minute. Her temperature was not much raised at first. On the fifth day it reached 102·6° F.; and on the sixth and last it rose to 103° and then to 106·6°, when she died. As a rule it ranged about 100° F. Albumen was found in the urine, but blood corpuscles and bacteria were not sought for. The wound during

this illness became red and inflamed, but the edges did not come apart. Blood-stained fluid escaped by the drainage tube, but this contained no pus, nor had it the odour of putrefaction. It seemed to me to possess a peculiar faint odour. When the flaps were open to avoid retention of discharges a large raw surface was exposed, from which blood-stained serum exuded. This exudation contained vast numbers of small ovoid bacilli. Their average length was about 1 μ, and their average breadth about 0·75 μ; but some were nearly twice as long. These bacilli multiplied by fission, and were usually in pairs. Occasionally chains of four occurred. Although there were differences in the morphology of these bacteria, nevertheless I am inclined to think they all belonged to one species.

The naked-eye examination did not give much information. The axillary vein was not thrombosed, but some of the veins of the neck were full of gas. The heart was flabby and dilated, and weighed twelve ounces; it was not otherwise diseased. The lungs were œdematous and congested at their bases. The kidneys were greatly congested and studded with small hæmorrhages. The spleen weighed five ounces, and was not diseased. Histologically, the lungs had undergone very slight alteration. Their smaller vessels were distended with blood, and many acini were filled with catarrhal

cells; but the evidences of bacterial invasion were either absent or not clear enough to be spoken of with certainty. I think it is probable that the small, slightly oblong bacteria had lodged in some of the minuter capillaries of the smaller pulmonary vessels and bronchioles. In the kidneys the vascular engorgement was very marked, and most of the vessels were packed with blood corpuscles, and, as usual, no bacteria could be seen amongst them. A great deal more hæmorrhage was found with the microscope than was apparent to the naked eye. Some of the extravasation was recent, some was older—perhaps a week old—and beginning to undergo the usual alterations. The renal epithelium was cloudy and desquamated in places. Some of the tubules were filled with albuminous exudation. These morbid conditions were accompanied by hardly any bacterial invasion. Occasional bacterial emboli were found in the minute vessels near the capsule and in the vasa vasorum of larger vessels near the hilum. These emboli were widely scattered and most difficult to find. They were composed of small bacteria which were very slightly oblong. The same kind were found in much greater profusion in the heart (Fig. 12). To the eye the heart was merely flabby and dilated, and histologically its structure was not much altered. The muscular striations were quite clear. Some of the

smaller vessels were dilated and full of blood, with here and there small inter-muscular hæmorrhages. But the evidences of septicæmia were unequivocal. Many capillaries and small vessels were filled with bacteria. These were small and almost round, being about 1 μ long and 0·75 μ wide. They grew in swarms,

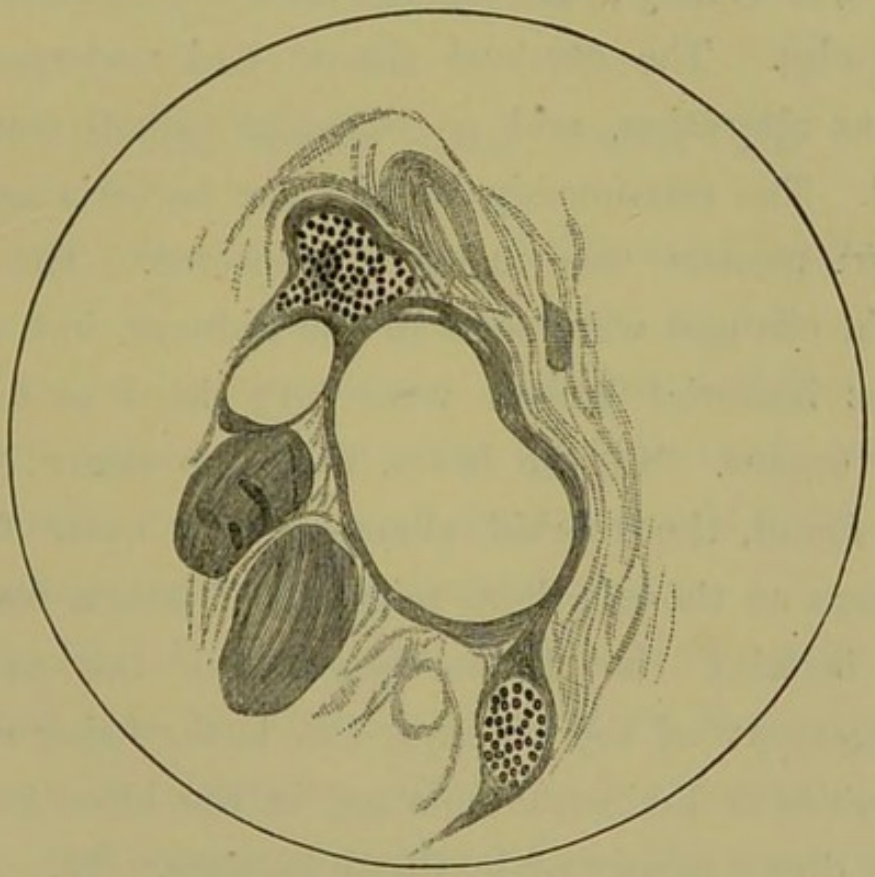

FIG. 12.—Bacillary septicæmia. Vessels of the heart filled with short bacilli.

in pairs, and in short chains. In some places they seemed to have begun to emigrate into the inter-muscular spaces. These small oblong bacteria have the closest morphological resemblance to the bacilli in the

vasa vasorum of the vessels of the last case, and I think that they belong to the same species. It is to be regretted that no histological examination was made of the heart in that instance. The cells of the liver had undergone fatty infiltration, but no bacteria could be found in that organ. The vessels of the brain were dilated, and many of the smaller ones stuffed with blood corpuscles. The cerebral tissues had undergone no obvious alteration, and no bacterial emboli could be found. The relationship betwixt the bacteria and the morbid process was rather unexpected. The chief morbid changes were seen in the kidneys, but nevertheless bacterial emboli were very hard to find in these organs. In the heart, where so many emboli were found, the morbid changes were quite trivial. It seems as though there might have been a relationship betwixt the hæmorrhages and the vascular engorgement of the kidneys, the latter being due to ptomaines or toxines circulating in the blood and not to the direct agency of localised bacteria. This is also the only case in which the brain was searched for bacterial invasion. Although the result was negative, it is merely an isolated and imperfect observation. I should expect that bacteria would lodge in the brain in some cases of septicæmia, just as they do in the heart, kidneys, liver, lungs, or other organs. The histological

examination throws a certain amount of light upon a point in the clinical history. Towards the end of the disease it may be remembered that the pulse beat rapidly and the heart's failure was so marked that cardiac stimulants were given for its relief. The accumulation of bacteria in the cardiac vessels may help to explain these cardiac symptoms.

Bacilli in the Blood during Life.

I have reason to think that small short bacilli, such as were found in the foregoing cases, may be seen in the blood of living patients. Mr. Maxwell has given me preparations of blood which certainly contain bacilli with similar morphological characters, and which were made under the following cicumstances :—

Case 10.—A man, aged twenty-three years, was admitted into the medical wards of St. Bartholomew's Hospital in November 1894, with ulcerative endocarditis and septicæmia. The endocarditis was probably an acute attack which had supervened upon an old disease. Twice before the patient had had rheumatic fever, and once before an attack of chorea. The acute endocarditis was accompanied with aphasia, paralysis of the right side, and double optic neuritis. Although the signs of septicæmia were not of the acutest kind,

nevertheless they were very clear. The temperature was raised, and usually ranged betwixt 100° and 103° F. A hæmorrhagic rash appeared upon the buttock. Delirium was almost constant at night, and towards the end he became restless and unconscious. The urine contained a trace of albumen, but was not examined for bacteria. The duration of the septicæmia may have been a little over a month. When the disease was at its height Mr. Maxwell obtained blood from the finger which contained small short bacilli singly, in pairs, and in small swarms. Their size was variable, some being as big as staphylococcus aureus and others thrice the size. They all, however, belonged to the same species, and the large elements were simply those which were in the act of division. The specimen which contained such an abundance of bacteria was obtained after the skin had merely been washed with soap and water; but four days later some blood was obtained after the skin had been scrubbed with soap and water, rubbed with ether, and disinfected with a 5 per cent. carbolic lotion. The blood still contained the same bacteria, but in much fewer numbers. Attempts to grow these bacteria upon culture media ended in failure.

Experimentalists are quite familiar with the disappearance of bacteria from the blood after massive doses have been injected. Saprophytes disappear

most quickly, and in a few hours none survive; but even pathogenic bacteria soon diminish in numbers, and may entirely vanish.[1] Thus, there is nothing surprising in the occurrence of many bacteria upon one day and their diminution upon another. Dr. Kanthack, our pathologist, has of late had no difficulty in finding staphylococcus aureus and streptococcus pyogenes in the blood during life in pyæmia and ulcerative endocarditis. In cases of so-called septicæmia none were found, and these all recovered.

Septicæmia with Bacterial Invasion of the Heart, Pericardium, and Pleura.

Case 11.—One of the cases of septicæmia (*Case* 8) which has been described died on 19th May 1893. It was preceded by another in the same ward which died rather less than a month before, on 26th April 1893. The two cases resemble one another in some particulars, but differ widely in others. They will be contrasted after I have given the details of this, which was the first to occur. The patient was sixty-five years old and had been a widow for two years.

[1] Numerous references are given by Thomas in Neubauer and Vogel's "Harnanalyse;" also by Wyssokowitsch in the *Ztschr. f. Hyg.*, Leipzig, 1886.

In August 1890, a small carcinoma was removed from the right breast, together with some enlarged axillary glands. This operation was followed by no recurrence *in loco*, but in April 1893, the left breast was amputated for the same disease, and the axillary lymphatic glands,

FIG. 13.—Bacillary septicæmia. Bacilli in blood clot in the anterior jugular vein. In some parts of this clot the bacilli grew in leptothrix.

being enlarged, were removed. The day after the operation the woman was quite comfortable, without pain, and with a normal temperature. Upon the third day her temperature had risen to 102·2° F., and on the

fourth she was very ill with a temperature of 102·3°, an inflamed throat, and some redness of the wound, unaccompanied with discharge or suppuration. Upon the fifth day, although she felt better, there was some fulness in the axilla, with tenderness about the shoulder. The mind was quite clear except at night, when she was slightly delirious. The urine was acid, with a specific gravity of 1022, and a cloud of albumen when heated. Upon the seventh day she died with failure of the heart's action; her pulse, which had been at the rate of 118 to 120 per minute, fell to 112 and then to 60. The respiration, too, was rapid, having risen from 27 to 42 during the course of her illness. The temperature, which had averaged 102° F., fell to 99·8° on the day she died. There was never any coma, and the mind was clear throughout.

The examination was made twenty-five hours after death. The operation wound was said to have appeared healthy. The brain and organs were normal, with the exception of those in the thorax. The surface of the pericardium was covered with a thin layer of recent lymph, and contained about an ounce of purulent fluid. The lungs were slightly congested and the pleuræ universally adherent by a thick layer of recent yellow lymph. There was very little fluid in the pleural cavities. Recent thrombi were

found in the anterior jugular and in some of the neighbouring veins. As a rule, bacteria are hard to find in blood clots, but in this instance the firmer and most fibrinous part of the clot from the anterior jugular vein contained numerous groups of short bacilli with rounded ends, and often in twos (Fig. 13). In some parts of the clot they grew in leptothrix of some length. This is not seen in the part of the clot which has been drawn. It is shown, however, in Fig. 16. The bacilli were in vast numbers amongst the fibrin, but in places where the blood corpuscles predominated none were seen.

The present seems to be a favourable opportunity for showing a microphotograph which Mr. Cosens has made of a clot from the femoral vein of another woman who died from septicæmia after an operation for necrosis of the femur. The bacteria in the clot are short bacilli, the same morphologically as those which I have just described. The patient died forty-eight hours after the operation with coma and high temperature.

But to return to the case under consideration, the lymph which covered the visceral layer of the pleura was in places a quarter of an inch thick. Mixed with its cells and fibrin were bacilli of more than one morphological variety. By far the most

abundant were small oval bacilli 1·5 μ to 2 μ long and 0·75 μ wide, which occurred chiefly in pairs in short chains of from four to eight or ten elements (Fig. 14), and in small irregular groups. Here and there, especially near the free edge of the lymph, were a few short and thick round-ended bacilli in pairs.

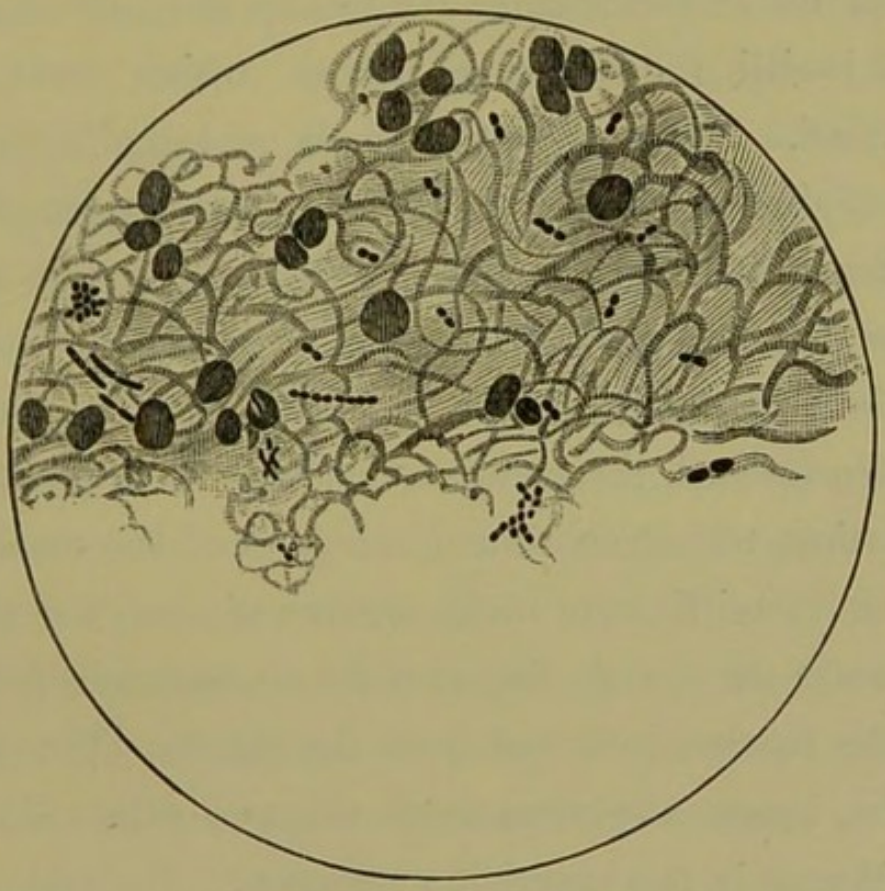

FIG. 14.—Bacillary septicæmia. Pleuritic lymph containing a variety of bacilli.

It seems probable that this was a bacillus which occurs in dead tissues, and is called by Sternberg the "bacillus cadaveris."[1] I cannot speak so con-

[1] "Manual of Bacteriology," p. 4.

fidently about another bacillus which also was present in considerable numbers. It was about the size of the anthrax bacillus, but with oval ends; it grew in pairs, or in short chains with ill-marked intervals between the elements. The pleura was acutely inflamed with engorgement of its vessels and proliferation of its endothelium. Its tissues were interspersed with bacilli the same as those which have been described. Here, again, the small oval bacilli in pairs and chains were by far the most numerous. These filled many of the smallest blood vessels and lymph spaces, but were absent from the blood which distended the larger arterioles and venules. Most of the air vesicles beneath the pleura were filled with pneumonic exudation, which contained numbers of the small oval bacilli. Bacilli were most numerous near the pleura, but both they and the exudation diminished in the vesicles further removed from the pleura. The tissues of the lungs also contained the two other kinds of bacilli seen in the pleuritic exudation. The pneumonia was the same as that in Fig. 11. No bacterial emboli were found in the capillaries of the pleura. The description of the pleural lymph applies to that which covered the pericardium. It likewise contained numbers of bacilli with similar morphological characters. Slight histological differences were also observed. For

instance, the pericardial lymph was thinner and more villous and the subjacent endothelium detached in places as if by vesication. Thus the pericardial and pleural lymph probably contained three kinds of bacilli. The two largest are common in cadavers and may have been saprophytes. The small oval bacillus may also have been of the same nature, but the examination of the tissues of the heart, and, I might add, of the other organs, suggests that it played a much more important part, and was the cause of the septicæmia. Many of the capillaries and smaller blood vessels of the heart were filled with these small oval bacilli (Fig. 15). In many places the dilated inter-muscular lymph spaces were also full of them, and where they were not crowded together the usual chains of from six to ten elements were seen (Fig. 16). Here and there the bacterial emboli filled minute blood vessels beneath the endothelial covering of the heart. Some of the muscle fibres also contained the bacteria in their substance, but not enough to distend their sarcolemma as in a case of pyæmic myocarditis described by Cornil and Babes.[1] The kidneys, too, had not escaped Their epithelium was slightly cloudy, and had desquamated in some of the larger collecting tubules

[1] "Les Bactéries," third edition, vol. i., p. 540 (Fig. 211).

Some of the smaller tubules contained albuminous casts. The bacterial invasion of the kidneys seemed to have been but slight. With much trouble it was ascertained that some of the smaller capillaries and vasa vasorum of the blood vessels and connective

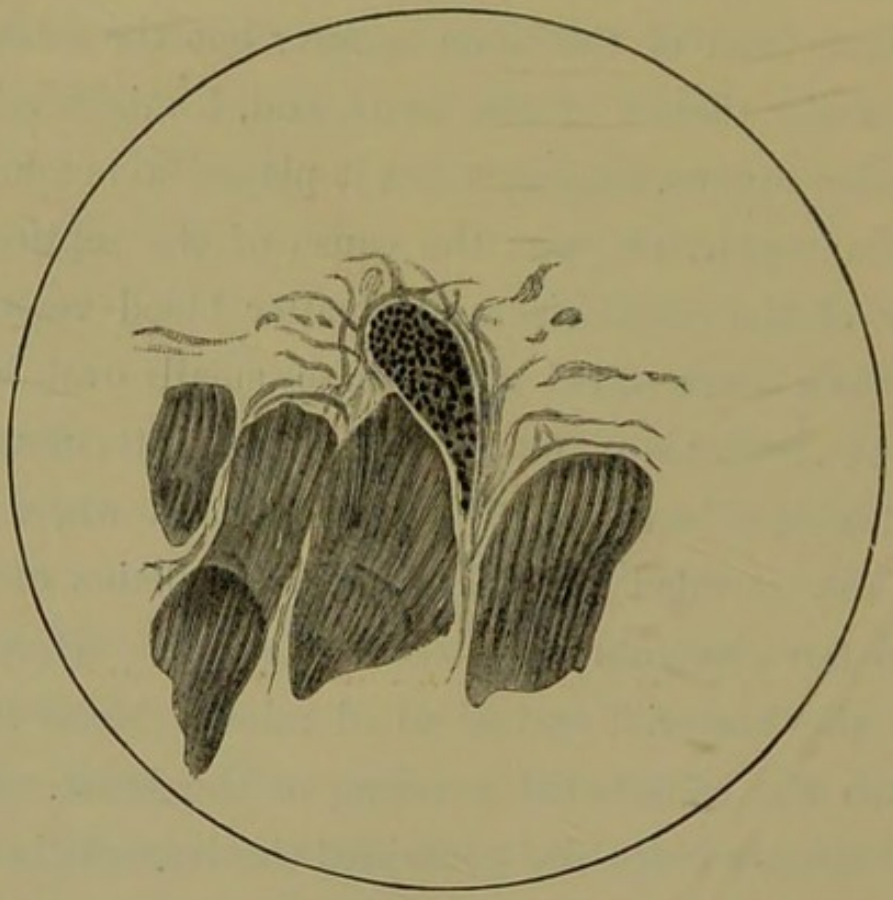

Fig. 15.—Bacillary septicæmia. Short bacilli in the blood vessels of the heart.

tissue of the medulla contained bacterial emboli. It is to be noticed that the histological examination throws light upon two features in the clinical history. Apart from the pericarditis the bacterial invasion of

the muscular substance of the heart is, I think, sufficient to account for the failure in the action of that organ, which seems to have been the immediate cause of death. Next, the bacterial emboli in the kidneys must have had a relationship to the presence of albumen

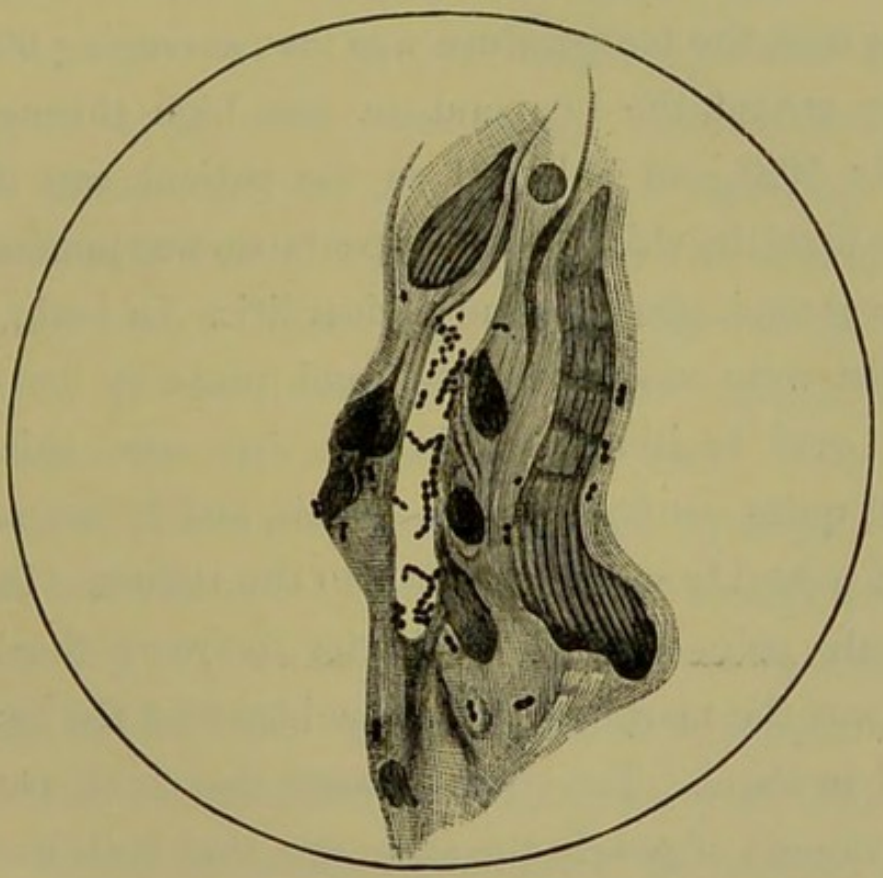

FIG. 16.—Bacillary septicæmia. Short bacilli in the inter-muscular and sub-pericardial lymph spaces of the heart.

in the urine. The association of pleuritis and sub-pleural pneumonia with rapid respiration hardly requires comment.

If we contrast this case of septicæmia with another

(*Case* 8) which occurred in the same ward, the following differences in their clinical symptoms, morbid anatomy, and morbid histology are to be noted:—In the first, the mental condition was characterised by apathy, stupor, and coma; in the second, the mind was clear throughout, with only slight delirium at night. In the first, the temperature was low, averaging 99° F.; in the second, the temperature was high throughout, usually 102°, and only fell as the patient was dying. In the first, the chief morbid appearance was pneumonia, in the second, pleuritis and pericarditis. In both, these diseases were associated with, and probably due to, a small oval bacillus; but in the first case this was almost quite confined to the vessels, and in the second it had passed from the vessels into the tissues. Indeed, the only point of close similarity between these two cases was the morphological resemblance of the bacteria found in them. The circumstances that both patients were women of nearly the same age, that both had had the same disease, and that both had had the same operation done in the same ward and almost at the same time, suggested that they had both incurred the same kind of infection; however, the differences which have been pointed out do not, in my opinion, permit such a simple hypothesis.

Case 12.—The following seems also to have been

a septicæmia in which sarcosepsis was beginning.[1] It differed, however, in important particulars from the preceding. A man, aged seventy-four, had had varicose veins for forty years; these were followed by ulcers, which became septic, and caused cellulitis of the leg and thigh. Free incisions were made into the suppurating areas, but his general condition became serious, and such as is often seen in the septicæmias, from which disease he was thought to be suffering. His mind became dull and apathetic, he was drowsy, and had to be roused to take his food, and he was delirious at night. His thigh was amputated through the upper third, and the operation was well borne. He died, however, twelve hours afterwards from syncope. During his last illness his temperature was usually betwixt 99° and 100° F. It once reached 101° soon after the cellulitis set in. His urine contained no albumen, and had an acid reaction and a specific gravity of 1022.

Mr. Shuter made an examination twenty-six hours after death; the weather was cool at the time. The brain, spleen, and kidneys were normal. The liver was cirrhosed, with stones in the gall bladder. The lungs had scars and calcareous nodules at their apices, and were congested at the base. The heart was thick, soft,

[1] I am indebted to Mr Groves for much assistance in the investigation of this case.

and with fatty walls; the tricuspid valve was ulcerated; the mitral valves were thickened and covered with vegetations; one cusp was almost non-existent. The great vessels were atheromatous. The ulceration was recent, but the other valvular changes were of long standing. Thus there was in the heart enough to explain the fatal syncope. But most of the disease was not of recent origin, and therefore we have to try to find out what precipitated the sudden failure of the heart's action. The main histological evidence of septicæmia was in the heart. The muscular substance had in places undergone slight fatty degeneration, but looked equal to its duties. There was a good deal of fatty infiltration. The venules and intra-muscular capillaries were greatly dilated. Some of the capillaries were full of blood, but the veins contained none. The heart had evidently been engorged with blood. Some of the smaller venules had clearly been plugged with bacilli (Fig. 17). Vast numbers of bacilli still adhered to their interiors, although it looked as if the bulk of them had been dislodged when the section was cut. These bacilli had slightly rounded ends. They sometimes occurred in twos, but not in strings. They were almost 1 μ wide, and their length was twice, thrice, or four times their width. They were as long as, but thicker than, anthrax bacilli. They had evidently

multiplied by fission, but some of the larger bacilli had two or more clear spaces in their substance, which suggested the development of spores. In size and appearance these bacilli were exceedingly like the common and harmless hay bacillus (bacillus subtilis). Although grouped in the interior of the venules, some

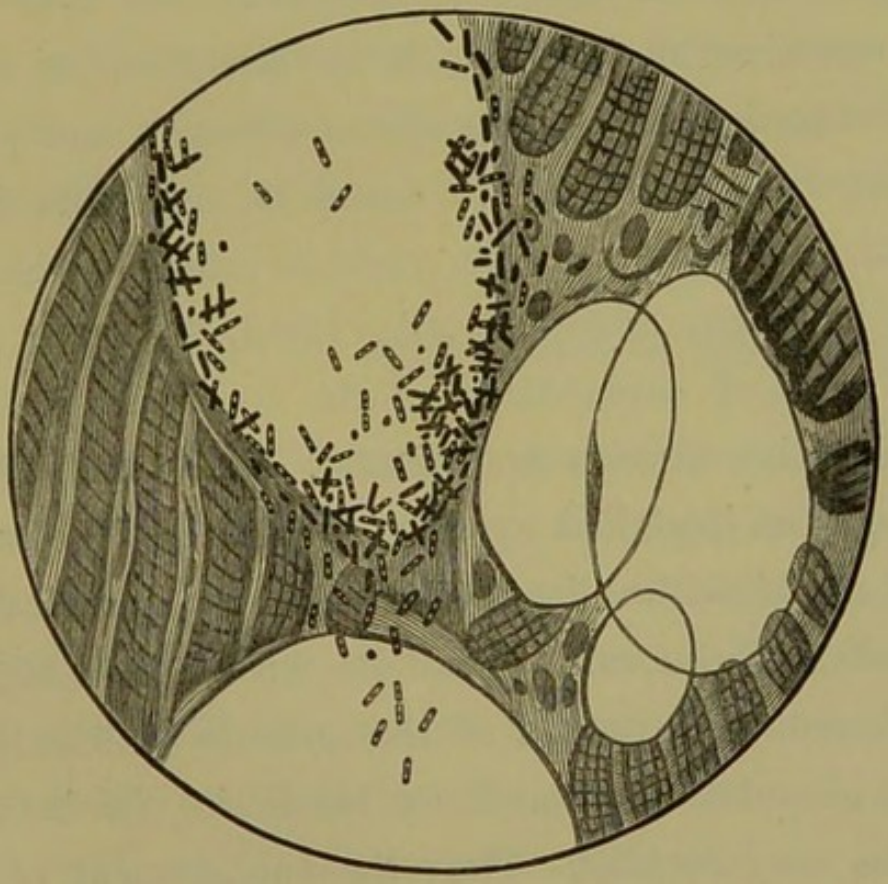

FIG. 17.—Bacillary septicæmia. Large bacilli in blood vessels of the heart.

of the bacilli had penetrated the walls of the vessels and entered amongst the fat and muscular fibres. In places they had clearly been dragged amongst the muscular fibres and fat by the process of section cut-

ting; but elsewhere some of the fat was infiltrated with vast numbers. The lungs were slightly hyperæmic, with catarrhal proliferation of their epithelium. Some of the vessels contained blood clots, but no bacilli could be seen in these, or, indeed, in any other part of the lungs. The kidneys had merely undergone senile changes; they contained no bacteria. The liver likewise contained no bacteria; it was cirrhotic, but not in an advanced degree. The spleen was soft and pulpy, but no bacteria could be found in either its blood vessels or tissues. If I am right in inferring that the heart had been engorged with blood, we would have some kind of explanation of the localisation of the bacilli in its venules and tissues. Karl Huber[1] has shown, by an ingenious experiment, that bacilli circulating in the blood localise themselves in hyperæmic areas. He inflamed the ears of rabbits with croton oil, and then inoculated the tail of the animals with anthrax. The accumulation of anthrax bacilli in the inflamed ear was very decided. Thus the engorgement of this patient's heart may have determined the localisation of bacilli in the vessels. Beyond this it would be rash to go. If we suppose that the disease of the heart constituted a *locus minoris resistentiæ*, at which the bacteria

[1] "Experimentelle Untersuchungen über Localisation von Krankheitsstoffen," *Virchow's Archiv.*, 1886, bd. cvi., p. 142.

congregated, it must not be forgotten that no bacteria were found in the liver, which was cirrhotic, and, I ought to add, congested in places. Judging from their drawing, Cornil and Babes[1] seem to have met with a bacillary invasion similar to this in the case of a child twelve years old who died from a subacute septicæmia following cutaneous ulcerations. The bacilli were found in the vessels of the kidneys, lungs, pleura, and in those of the skin. They were accompanied by a coccus infection, probably streptococcus pyogenes.

The Distribution of Bacteria in Septicæmia.

The unequal distribution of the bacteria is a feature of these cases of septicæmia. They seemed to have congregated in a single organ, such as the heart, lungs, or kidneys, in preference to the others. Whether this is an accidental or constant feature my cases are too few to decide; nevertheless, the possibility of its occurrence ought to be taken into consideration. Clearly the absence of bacteria from the body cannot be inferred from their absence from one or more of the organs. This congregation of bacteria in particular organs has struck other observers. Cornil and Babes[2]

[1] "Les Bactéries," vol. i., p. 476 *et seq.* (Fig. 187).
[2] *Ibid.*, vol. i., p. 545.

refer to it particularly under the heading of "primary bacterial nephritis." It is probable that when bacteria are circulating in the blood, conditions, of which we as yet know little, determine their arrest in particular regions.

The Varieties of Septicæmia: Streptococcus Septicæmia.

That septicæmia is not always a bacillary invasion of the blood, as might be inferred from the foregoing, was, I think, clearly shown by the following case of septicæmia following erysipelas:—

Case 13.—A stout woman, aged fifty-five years, was admitted into the isolation ward with cutaneous erysipelas of the right arm. There were the usual redness, swelling, and bullæ, with enlargement of the axillary lymphatic glands. The general symptoms were severe, with rigors, nausea, and a temperature of 104° F. The erysipelas spread from the arm to the back, shoulder, chest, and abdomen. It was still spreading on the seventh day, and upon the eighth she became restless and collapsed, with a feeble pulse. She died exhausted on the evening of the ninth day. Before the end, the bases of her lungs, especially the left, became pneumonic, and her death was attributed to this complication and to septicæmia.

The examination disclosed nothing beyond what has been stated. There was much œdema of the cellular tissue of the arm, axilla, and chest, with swelling of the lymphatic glands. The left lung was congested, but not solid; the right lung was also congested. The kidneys were much congested and swollen. The serum of the

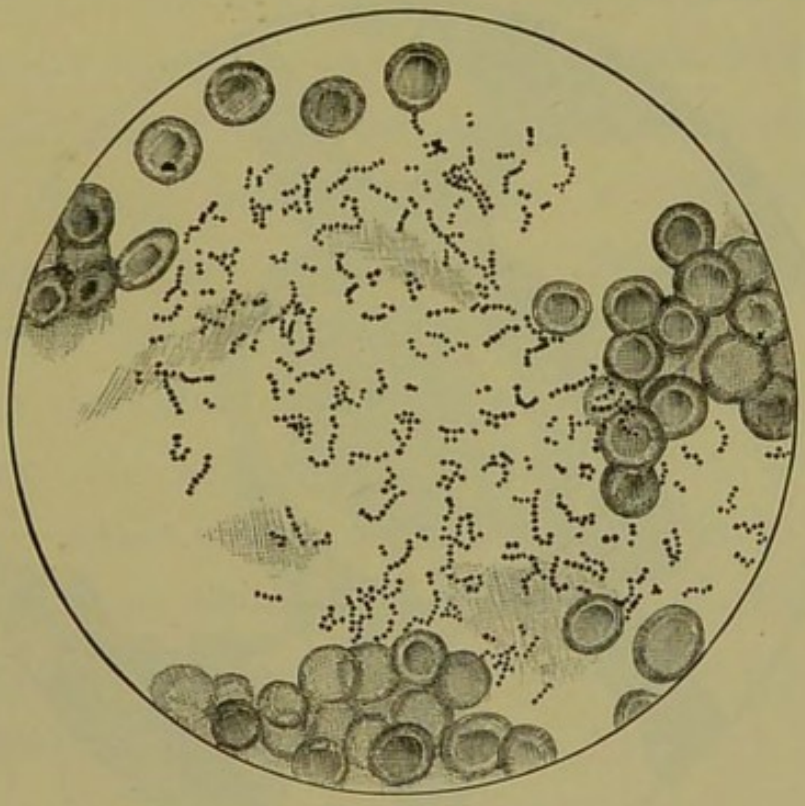

FIG. 18.—Streptococcus septicæmia. Streptococci in the blood of the right auricle. From a micro-photograph by Mr. Cosens. *See* also Article upon Erysipelas by Lecturer in "System of Surgery," edited by Treves, vol. i., p. 161, London 1895.

inflamed cellular tissue contained cocci, singly, in pairs and short chains. These were seen in cover glass preparations. Sections of the inflamed tissues were

crowded with cells, and the cocci could not be seen with certainty. As the disease was of some days' standing, this was not unexpected. The blood of the right auricle contained vast numbers of streptococci in short chains and entangled into masses (Fig. 18). Here and there the blood contained rather long, straight, or

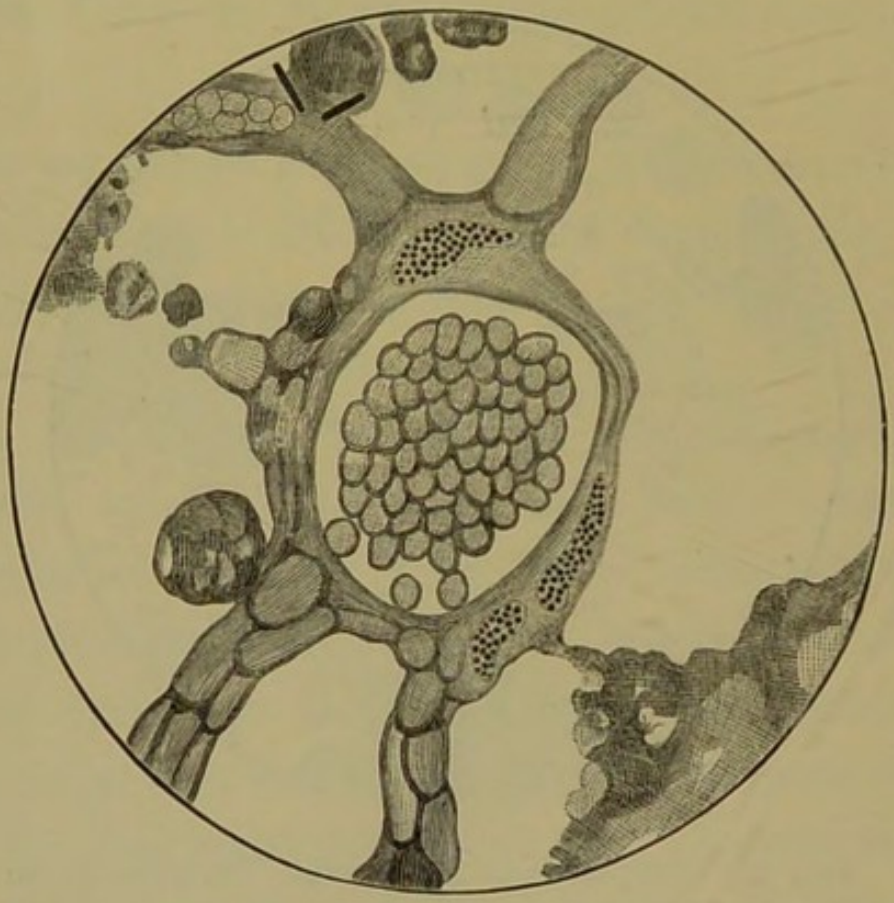

Fig. 19.—Streptococcus septicæmia. Micrococci in capillaries of the lungs. Two cadaveric bacilli are shown in the upper part of the Figure. The blood contained others of the same kind.

slightly curved bacilli, which were probably cadaveric. The lungs were enormously engorged with blood, and the air cells full of catarrhal exudation. Numbers of

the smaller capillaries were plugged with micrococci. The emboli occurred in the capillaries of the walls of the air cells, and also in those in the walls of the pulmonary vessels and bronchi (Fig. 19). No chains could be discerned in these emboli, but none can be seen, as a rule, in similar emboli produced artificially by injecting streptococci into the circulation of rabbits. The kidneys were likewise engorged with blood, and the epithelium of their tubules was in an advanced state of cloudy swelling. Some of the smallest capillaries near the cortex and in the walls of the renal vessels were plugged with micrococci, as in the lungs; in the kidneys, however, the emboli were not so numerous. No bacteria were found in the liver, and the other organs were not examined. It is to be regretted that no examination was made of the heart. The clinical history seemed to show that that organ had not escaped the infection.

LECTURE III.

VARIOUS INFECTIVE CONDITIONS.

GENTLEMEN,—In this third lecture I propose to describe cases of traumatic infection which do not clearly fall under the preceding headings. But first I will describe a case of pyæmia which presented some instructive features, especially that the naked-eye appearances of infected organs cannot in the least be trusted to indicate the absence of infection.

STREPTOCOCCUS PYÆMIA: BACTERIAL EMBOLI IN ORGANS APPARENTLY NORMAL.

Pyæmia is one of the best examples of septicæmia with subsequent sarcosepsis. I only propose to mention one example of pyæmia which was of the streptococcus variety, because it shows how easily the infective diseases may be overlooked if reliance be given to naked-eye evidence, and that bacterial emboli may be found in organs otherwise normal.

Case 14.—An infant, a year and ten months old, was burned upon the arm. The burn was of the second and third degree, and not extensive. It suppurated, and the infant became ill, with a temperature of 102° F. An abscess formed in the subcutaneous tissue of the chest and a rash overspread the body. After the appearance of this rash the infant was isolated, scarlet fever being suspected. Death ensued without any complications such as nephritis, meningitis, or pneumonia. At the examination, the burn, which involved about half the arm, looked quite healthy. The parotid region was swollen, but did not contain pus. The lymphatic glands beneath the angle of the jaw were filled with softening caseous material. There was a subcutaneous abscess as big as the palm of the hand upon the side of the chest and filled with thick pus. All the abdominal and thoracic viscera were individually examined and pronounced to be normal as were also the serous and mucous coats of the intestines. The examination was made by my colleague, Mr. James Berry, whose name is a guarantee for the thoroughness and correctness of it. He concludes his report by saying that "the death was apparently due to the suppuration of the neck and chest: perhaps to some meningeal trouble, as the head was not allowed to be examined." I cannot tell whether this surmise

is correct, but the histological examination of some parts of the body gave the following results:—The abscess wall was composed of fibrino-purulent material mixed with incredible quantities of streptococci in chains, both long and short, especially the last (Fig. 20). To the naked eye the kidneys and liver looked, as Mr.

FIG. 20.—Streptococcus pyæmia. Streptococci in the walls of a subcutaneous abscess. *See* also Article on Pyæmia by Lecturer in "System of Surgery," edited by Treves, vol. i., p. 180, London 1895.

Berry said, quite normal, but the parenchyma of each was beginning to exhibit the early stages of cloudy swelling. Also in the liver a great many of the

small vessels and capillaries of the portal canals, and also the vasa vasorum of the portal veins and of the bile ducts, were plugged with micrococci (Fig. 21). These cocci were so crowded together that chains could not be recognised, but this is not uncommon in streptococcus poisoning. Some blood which had remained in

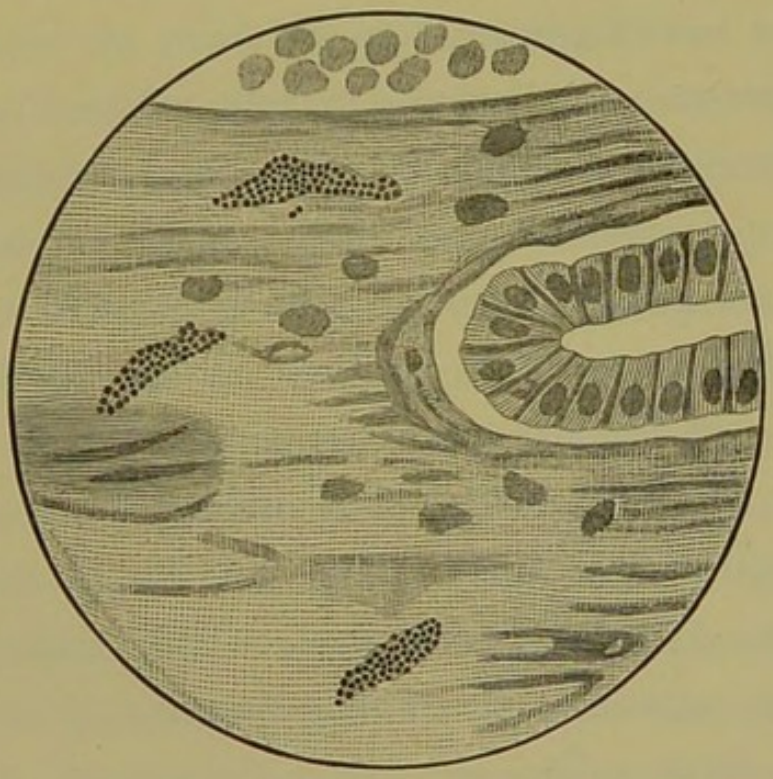

FIG. 21.—Streptococcus pyæmia. Micrococci in the capillaries of a portal canal. In this case the liver and other organs were considered normal to the eye.

the hepatic veins contained occasional diplococci and short chains of cocci. In the cortex of the kidneys similar plugs of micrococci were found in the capillaries of the glomeruli and tubules, and especially in the vasa

vasorum of the renal vessels; but these emboli were much harder to find in the kidneys than in the liver, being less numerous. As regards the cocci in the liver, it seems very evident that they had been carried there by the hepatic artery. It is probable that after a while they would have emigrated from the capillaries into the bile ducts; indeed, the process seemed in places to have begun. Here we have an explanation of the presence of bacteria in bile without a macroscopic focus, such as an abscess, having been discovered. Hitherto bacteria found under such circumstances have been supposed to have been excreted with the bile. Had these plugs gone on to the formation of abscesses, it is clear that the result would be very different from that produced by infection carried along the portal veins, but I am not aware that such differences have been described. It is interesting to note that although the kidneys contained capillaries plugged with micrococci yet albuminuria had not occurred, although it was frequently sought for. Lastly, the presence of the cocci in the vasa vasorum seems to me a fact of some moment. They had not begun to produce changes in the vessel walls, and it would be most interesting to speculate as to the ultimate result had the child survived. This case belongs to a class, the seriousness of which is not always properly

appreciated. Infants are most susceptible to both local and general infection, but the latter is often overlooked. I have no doubt, whatever, but that more searching and systematic examination of the tissues by more exact methods will vastly increase the *rôle* played by septicæmia in surgery.[1] The mortality after burns is a reproach to surgery. It could often be avoided by the skilful use of antiseptics.

Case 15.—To control the investigation of this case of streptococcus pyæmia, that of a child who died with an extensive burn of the chest and abdomen may be mentioned. When the histological investigation of the lungs, liver, spleen, and kidneys was made by Dr. Blackwell and myself we were ignorant of the clinical details or of the results of the post-mortem examination, which was performed by Mr. Berry twenty-eight hours after death. We could find no bacteria in any of the tissues or organs, and came to the conclusion that death had been due to acute bronchitis. We afterwards learnt that this was correct, and that the burns were supposed to have been caused by the application of poultices intended for the relief of the bronchitis.

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[1] Dr. A. S. Blackwell and myself were quite unable to demonstrate the conditions in the liver and kidneys by Gram's method. We succeeded by long immersions in the eosin and methyl blue solutions, from four to six days being requisite. I am much indebted to Dr. Blackwell for his trouble.

The foregoing case of streptococcus pyæmia might have been mistaken for one of scarlet fever in which streptococcus poisoning had occurred had it not been for the abscess upon the chest wall. Cornil and Babes[1] give a figure of the kidney after scarlet fever with a streptococcus embolus in one of the capillaries. Their specimen was apparently the same as that which I have described, except that there was also amyloid disease. The same authors give other figures of streptococci in the renal vessels in scarlet fever.[2] They seem a common complication. Cultures showed that they were the streptococcus pyogenes. Leber and Wagenmann[3] have described a case of streptococcus poisoning in an infant, but seem to have given their attention to the local lesions and not to have examined some of the organs because they looked normal. However, streptococci were found by them in the skin, eye orbit, kidneys, and suprarenals.

Streptococcæmia.

Streptococcæmia is, I believe, not rare in infants and young children. As a rule, they recover from it after

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[1] "Les Bactéries," vol. ii., p. 269 (Fig. 303).

[2] *Ibid.*, Figs. 305 and 306.

[3] "Infantile Necrose der Bindehaut mit letalem Ausgang durch allgemeine multiple Streptocokken-Invasion des Gefässsystems." *Arch. f. Ophth.*, Leipzig, 1888, bd. xxxiv., p. 250.

having sustained severe damage to one or other of their organs. Lately I had under my care in St. Bartholomew's Hospital a case exceedingly like the one which has just been narrated.

Case 16.—The patient was a delicate female child, aged two and a half years. She was admitted with an ulcer about an inch long and half an inch wide at the left margin of the anus. It involved the cutaneous and a little of the mucous surface. At first it spread, but afterwards healed with simple local remedies. When admitted the child also had a loud systolic murmur, which still exists. Her liver, too, was enlarged almost to the umbilicus. Her legs were œdematous, with albumen in the urine. The temperature was usually subnormal, the thermometer as a rule registering 98° F. The co-existence of a point of inoculation, an endocardial bruit, acute nephritis, and swollen liver seemed to me to point so clearly to bacterial invasion that Mr. Furnivall, at my request, examined the blood and the urine. Nothing could be seen in the blood, nor could anything be grown from it upon the usual media. Fresh specimens of the urine, collected with proper precautions, contained cocci in short chains. I attached no importance to the absence of temperature in this case. As a sign of bacterial invasion the temperature is unreliable. It is quite usual to see no elevation of temperature even in

such profound invasions as diffuse septic peritonitis. It is unreasonable to think that all bacterial poisons must be pyrogenous. The temperature, however, rose to 103° F. during the seventh week of her stay in hospital. A skin eruption, which was supposed to be measles, appeared at the same time. At this stage no streptococci could be found in the urine. The cause of the ulcer was never found out. Although a year has passed it has not been followed by any signs of syphilis. This is interesting because the mother had a syphilitic ulcer upon her face, but in the gummous stage, and not, therefore, capable of infecting another with syphilis. That the ulcer of the mother was infected with other bacteria is certain. In a similar case I found staphylococci, streptococci, and bacilli.

Streptococci are easy to see in fluids, and appear in the urine soon after infection. The following is a common example of this:—

Case 17.—A healthy youth, aged fifteen years, crushed his hand and arm in a printing machine on 12th November 1892. Amputation was performed through the arm, and on the 13th his temperature was 101° F.; on the 14th it was 102°, and the urine contained a cloud of albumen. On the 24th he had pronounced pyæmia, with pus containing streptococci in the right hip, knee, and ankle. At the same time his urine contained

numerous streptococci (Fig. 22). No examination was permitted in this case, but in another of acute suppurative periostitis of the tibia following an injury the urine contained a similar cloud of albumen, and after death the kidneys were found acutely inflamed and studded with small abscesses and infarcts. The pus

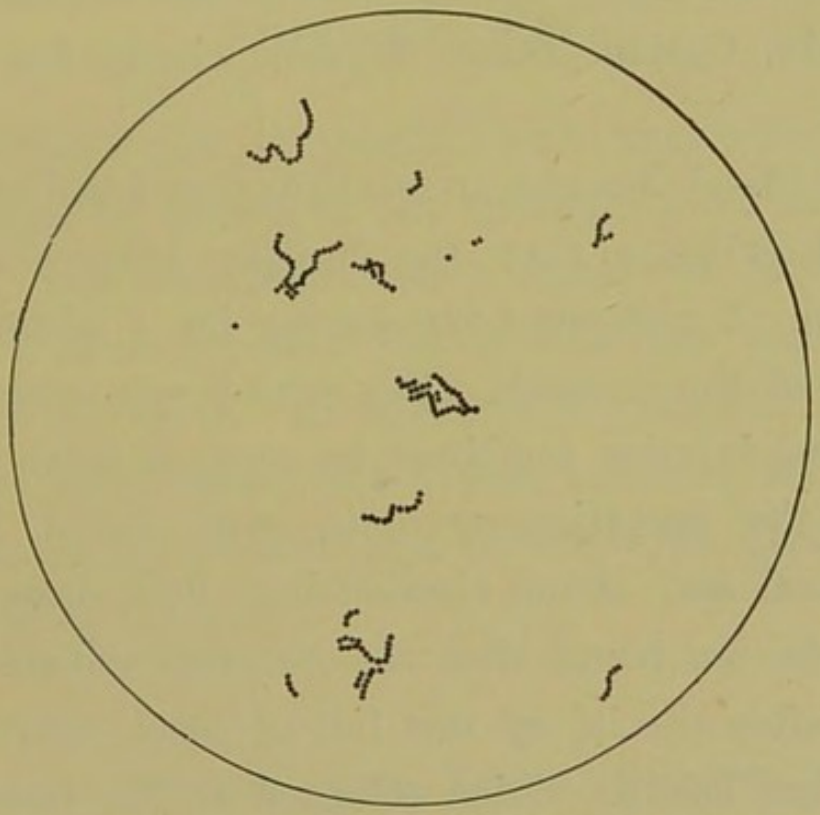

FIG. 22.—Streptococcus pyæmia. Streptococci in pyæmic urine. From a microphotograph by Mr. Cosens.

of the abscesses contained staphylococci similar to some found in the pus from the necrosed tibia.

I do not propose to discuss the conditions under which bacteria escape by the kidneys. This interesting question has been ably treated by Dr. Sherrington in

his recent article, and by others. Sherrington's work[1] leads him to the conclusion that "the evidence is against believing that when this transit of bacteria across the secreting membrane occurs the membrane is still normal in condition, although at the same time it need not be ruptured or pervious to red corpuscles." In the main Sherrington's observations confirm those of Klebs, Ogston, Fodor, Wyssokowitsch, and many others.

Case 18.—I thought at one time that I had obtained clinical evidence that the healthy kidneys excrete bacteria. I performed laparotomy for a pistol-bullet wound of the stomach. The wound was inaccessible, and other injuries combined to cause a fatal ending. After the operation a drain was placed in the peritoneal sac. Some blood-stained fluid drawn from this tube ten hours after the operation and sixty-four hours after the injury was full of cocci, streptococci, and short bacilli. Urine collected at the same time contained similar morphological varieties. The kidneys were histologically normal, with the exception of a slight interstitial nephritis which, I afterwards learnt, was of old standing. This case illustrates the

[1] "The Escape of Bacteria with the Secretions." *Journ. Path. and Bacteriol.*, Edin. and London, vol. i., p. 276. This valuable paper gives a full bibliography.

difficulty of obtaining clinical evidence of the elimination of bacteria by healthy kidneys. Also, assuming the correctness of my observations, it shows that it may be wrong to consider, as I have done, that diffuse septic peritonitis is a purely local infection.

Mixed Infections.

I propose now to proceed with some complicated conditions of infection. In some of these the local disease was associated with a variety of bacteria, of which it seems possible that at least two species had invaded the body. In others it is probable that the original local disease was a pure infection which was supplanted by another of a severer type, capable too of invading the body.

Angina Ludovici with Bacillary Septicæmia.

Case 19.[1]—In this case a bacillary septicæmia closely resembling that which I described in the last Lecture (*Case* 9, p. 63), was unexpectedly met with in that grave disease described by Ludwig and called after him "cynanche or angina Ludovici." In narrating

[1] I am indebted to Dr. C. Addison for much hard work at this case.

this case I propose, after giving the clinical history and morbid anatomy, to describe the septicæmia, and then discuss the cellulitis of the neck and its other complications. It will then be seen that the angina Ludovici is probably a mixed infection of the most complicated kind. Indeed, the examination of this and other cases leads me to think that several pathological conditions are included in the term "angina Ludovici." The case is also an example of the difficulty of the problems which confront inquirers into the infective processes of man. The patient was a man, aged twenty-eight years. He was a heavy drinker. The cellulitis of the neck began without apparant cause and spread rapidly. On the fifth day the usual incisions were made and a little pus escaped. The patient became violent and was thought to be suffering from delirium tremens. On the sixth day œdema of the glottis caused so much dyspnœa that tracheotomy was performed. He became apathetic, drowsy, and unconscious, and died early on the eighth day. The actual cause of death was supposed to have been pneumonia. His highest temperature was 103° F., recorded on the seventh day. His urine contained a trace of albumen. Throughout his illness a purulent discharge ran from the floor of the mouth, and there was the usual horrible fœtor. The drowsiness, apathy, and unconsciousness which supervened

in this case remind me very strongly of the clinical condition of the woman who died from septicæmia after amputation of the breast for ulcerated scirrhus (*Case* 9, p. 63), and soon it will be shown that the same kind of bacillary infection existed in both cases. The delirium also may have been due to the septicæmia, and not, as was supposed, to alcohol. After death I found amongst the swollen and septic tissues of the neck engorged lymphatic glands and a clot in the left internal jugular vein. Both lungs were pneumonic and the kidneys swollen and engorged. The floor of the mouth was sloughing and ulcerated, and infiltrated with fetid pus. The heart and great vessels were normal, but gas escaped as I divided the pulmonary veins. The peritoneal cavity also contained some gas and blood-stained fluid. The spleen was enlarged and friable. The histological evidence of the septicæmia was in the kidneys. These organs were, as I have said, engorged with blood, some of which had remained in the veins and capillaries, forming a natural injection. Here and there this blood contained a large bacillus which will be described presently. But in addition the vasa vasorum of some of the larger vessels of the medulla were packed with bacteria (Fig. 23), which I judged to be small, short bacilli. The appearances of these were the same as those of the cases of septicæmia

which have been already described, and closely resembled the appearances seen in septicæmia artificially induced in animals. Similar bacterial emboli were not found in the capillaries of the lungs, liver, spleen, or neck. The heart and other organs were not examined.

I cannot ascertain that others have alluded to the presence of bacteria in the vasa vasorum. If a frequent occurrence, it would be of importance, and may have a relation to ulcerative arteritis. What part the septicæmia played in causing the patient's death cannot be told, because the case was complicated by other bacteria the presence of which cannot be ignored. In the walls of the renal vessels and in the intertubular tissues there were vast numbers of large bacilli, which, in size, shape, and appearance, exactly resembled Baumgarten's[1] representation of the bacillus septicus, or Fraenkel and Pfeiffer's microphotographs.[2] They grew separately or in long strings (Fig. 23); their ends were slightly rounded, with a width of one millimetre and a variable length, but always many times the width; they contained no spores, but multiplied by fission; they evidently shunned the blood stream, and grew in the

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[1] *Loc cit.*, p. 469 (Fig. 49).

[2] "Mikrophotographischer Atlas der Bakterienkunde," Part 5 (Figs. 45 to 49).

interstices of the tissues running parallel to the muscle cells or connective tissue bundles. A similar absence of bacilli from the blood is observed when animals are killed with the bacillus septicus, and is accounted for by its strictly anærobic properties. But as decomposition ensues they appear, as Flügge says, in the decomposing

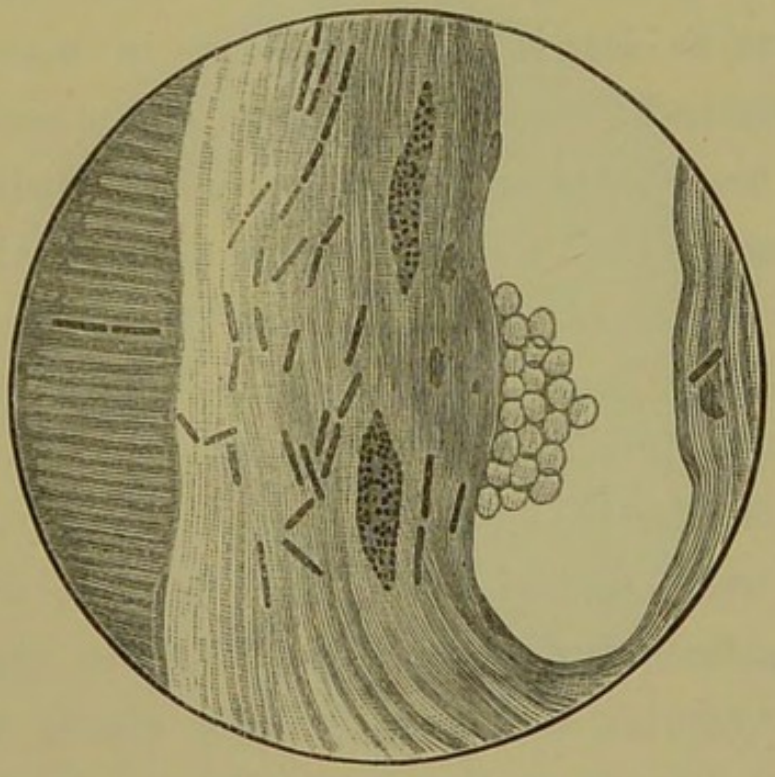

FIG. 23.—Angina Ludovici. Kidney with large bacilli in the walls of the vessels near the hilum ; also with small bacteria in the capillaries.

and oxygen-free blood.[1] In this way their occasional presence in the blood in this case would be explained.

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[1] Flügge, "Micro-organisms with Special Reference to the Etiology of the Infective Diseases," p. 246. Translated by W. Watson Cheyne, *New Sydenham Soc.*, 1890.

The secreting substance of the kidney had not suffered in any considerable degree, but the inter-lobular connective tissue was swollen, with here and there small inflammatory exudations, amidst the cells of which were occasional cocci, diplococci, and streptococci.

Before discussing the meaning of these large bacilli, I propose to describe their presence in other organs. The lungs had the usual histological characters of acute septic broncho-pneumonia (Fig. 24). Their vessels were engorged with blood, forming a natural injection. This blood contained a few large bacilli, the same as those in the tissues of the kidneys. But the walls of the smaller pulmonary veins, like the renal veins, contained considerable numbers. The solidified pneumonic tissues were packed with vast numbers, and they were particularly abundant beneath the pleura and in non-vascular areas. They were clearly the predominant feature in the lung disease. In the lungs the bacilli grew in leptothrix less often than in the kidneys. The pneumonic tissues also contained occasional encapsuled diplococci the same as those described by Fraenkel and others.[1] Their presence was unexpected, and gives rise to speculation as to their

[1] With $\frac{1}{12}$ in. oil immersion (Zeiss) and No. 8 eye-piece these bacteria looked elongated and perhaps lancet-shaped.

meaning in this and other cases. As Netter, Biondi, Vignal, Fraenkel, and others have shown, encapsuled cocci are found in saliva,[1] and may thus, it may be supposed, pass into the air passages and lungs. The purulent tissues of the floor of the mouth were packed with cocci, diplococci, streptococci, and bacilli of

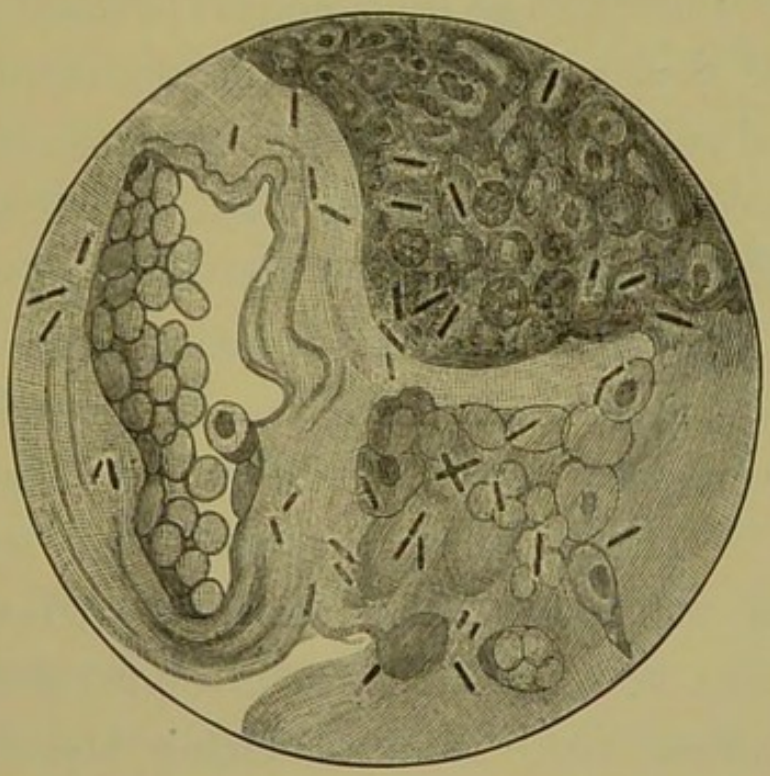

FIG. 24.—Angini Ludovici. Septic pneumonia in angina Ludovici.

various kinds. Amongst the cocci the presence of staphylococcus aureus and streptococcus pyogenes was proved by cultures. The bacilli included the ordinary ones of putrefaction, and, in addition, the sections of

[1] E. Macé, "Traité Pratique de Bactériologie," second edition, p. 280, *et seq.* Paris, 1891.

the deeper œdematous muscles and cellular tissues of the floor of the mouth and of the neck contained many large non-spore-bearing bacilli, the same as those in the kidneys and lungs. These bacilli were most difficult to demonstrate; but Dr. Addison and myself succeeded by soaking the sections for many days in Czenzynke's solution. Thus this case lends support to Baumgarten's[1] statement that acute phlegmon of the submaxillary cellular tissue was an invasion of streptococcus or of staphylococcus pyogenes, sometimes of both together, and to Eisenberg's observation that he found streptococci in the saliva in a case of phlegmonous angina. As Widal and Besançon have recently shown, streptococci are present in the mouth in both health and disease. I do not think, however, that the large bacilli in the floor of the mouth, neck, lungs, and kidneys can be ignored. I was prompted to look for bacilli because some kinds of angina Ludovici have such a close resemblance to acute spreading traumatic gangrene or malignant œdema, a disease which is acknowledged to be of bacillary origin, being caused by the bacillus septicus.

It may not be out of place for me to remark that the bacillus septicus is of the greatest interest to surgeons,

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[1] "Lehrbuch der Pathologischen Mykologie, p. 883. Braunschweig, 1890.

and may, as I have already said, occur oftener than is thought. It was discovered by Pasteur and investigated by Koch, and is also called the "bacillus œdematis maligni." The disease which it causes is also called "gaseous or acute spreading traumatic gangrene." The bacillus septicus is an inhabitant of earth, mud, and decomposing substances of all kinds; hence it may be found in the human body without it having caused the fatal disease. In size and appearance the bacillus septicus closely resembles the bacillus of anthrax. Its ends, however, are slightly round, and its spores, which are not formed whilst the bacillus is in the tissues, are large enough to bulge the bacillus; it is also mobile and is a strict anærobe; it usually produces a quantity of fetid gas. The clinical effects of the bacillus septicus might almost be inferred from its behaviour in the laboratory. The rapidity of its growth and motion is exemplified by the swift spread of the disease, its abhorrence of oxygen by its passage along the lymph paths, its gas-producing powers by the emphysematous crackling, and, lastly, the noxiousness of its ptomaines by the poisoned condition of the patient. But although the production of a fetid gas is one of the properties of the bacillus septicus, yet Sternberg[1] says that pure cultures

[1] "Manual of Bacteriology," p. 491.

often cause inflammatory œdema without emphysema. Very little seems to be known about the behaviour of the bacillus in the human organs. Obviously, any gas which it produced in the lungs would escape and leave no trace, and, probably, the same applies to the kidneys. But in the case which I have just described the escape of gas from the pulmonary veins and its presence in the peritoneal sac are to be noted as evidence of the presence after death of a gas-producing bacillus. Presently, I will describe another case of angina Ludovici in which the emphysematous crackling of the skin and subcutaneous tissues was observed during life, and in which there was also a bacillus in the lymph paths and in the inflammatory exudation (*Case* 21, p. 118). It has lately been claimed that other bacteria besides the bacillus septicus cause acute inflammatory œdema and emphysema of the cellular tissues. Eugen Fraenkel [1] has described such an one and called it "bacillus phlegmones emphysematosæ." It closely resembles the bacillus septicus in all its characters, but is motionless. It was found in four cases of "gas phlegmon." Bunge [2]

[1] *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1893, bd. xiv., p. 622. (Abstract.)

[2] "Zur Aetiologie der Gasphlegmone." *München. med. Wchnschr.*, 1894, No. 46, p. 918. Also *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1894, bd. xvi., p. 831.

in a case of emphysematous cellulitis (gas phlegmon), found the bacillus coli communis and staphylococci, streptococci and proteus together. Rosenbach also observed the coincidence of pyogenic cocci and bacillus septicus.[1] Gärtner[2] has recently described a gas-producing bacillus, which Klein[3] considers identical with the bacillus coli communis. I shall soon describe a case of angina Ludovici in which there was emphysema, and in which a bacillus was seen in the skin and cellular tissues. This bacillus had not quite the morphological characters of the bacillus septicus. We must also take into consideration a bacillus which Klein[4] met with in the tissues of guinea-pigs inoculated with garden earth. It grew in rods of different lengths and was mobile. Moreover, it was an aërobe, and did not liquefy gelatine. In many points Klein's account of his bacillus reminds one of the colon bacillus, which is, of course, a common inhabitant of earth which has been manured. The possibility of these being cadaveric bacilli which had emigrated from the intestines has also to be considered.

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[1] "Micro-Organisms in Human Traumatic Diseases." *New Sydenham Soc.*, 1886, p. 430.

[2] *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1894, bd. xv., p. 1.

[3] *Loc. cit.*, p. 276.

[4] "Ein neuer Bacillus des malignen Oedems." *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1891, bd. x., p. 186.

Although I have examined a great many diseases by the same methods, similar bacilli have not been met with, except in the case of axillary wound with pleuritis (Fig. 7, p. 26), and in a case to be described forthwith. Moreover, in the case of which I am speaking, the bacilli were always most abundant where there was most disease. In a case of pneumonia due to the laceration of the lung by broken ribs the ordinary picture of a fibrinous pneumonia was unaccompanied with bacilli such as were found in angina of Ludwig and the case of fracture of the jaw which I am about to describe. Indeed, in the traumatic pleuro-pneumonia I could not with confidence assert the presence of any bacteria, although it is probable that a few scattered encapsuled cocci were present. All kinds of methods were used to stain the sections. Great labour was expended in examining the lungs of a patient who died from pneumonia after excision of the tongue. The pneumonic exudation was fibrinous, and contained encapsuled bacteria, often in pairs, but no big bacilli. If these bacilli in the kidneys and lungs of this case of angina of Ludwig had been cadaveric, it means, of course, that they had grown after death. Therefore, I should have expected to have found them elsewhere than in the diseased tissues and organs. But none were found in the spleen or liver, although those

are organs which are especially exposed to infection from the bowels. But, throughout these investigations, I have greatly felt the want of more definite knowledge of the cadaveric bacteria, especially their morphological varieties and staining properties. Sternberg[1] gives a brief reference to the subject, and a photograph of cadaveric bacilli. No resemblance can be traced betwixt these and the bacillus found in the tissues of this case of angina. Jenson and Sand[2] also say that many large bacilli are found in animals which have died from asphyxia and lain for twelve or twenty-four hours. They differ from the bacillus septicus, however, in form, microchemical peculiarities, and inoculation effects. It would be no detraction from the importance of these bacilli to acknowledge that they were saprophytes causing putrid decomposition. That, most probably, is their function. But every one knows that putrid decomposition of the tissues and fluids of the body occurs during life in angina Ludovici, and is part of the disease. Even if we assumed that these large bacilli were the chief cause of death, yet the bacteria which swarmed in the floor of the mouth may have played an important

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[1] "Bacteriology," p. 583 *et seq.* (Fig. 197).

[2] "Ueber malignes Oedem beim Pferde." *Deutsche Ztschr. f. Thier-med.*, Leipzig, 1887, bd. xiii., p. 1. Quoted in *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, bd. i., p. 265 *et seq.*

rôle. For the life of strict anærobes like the bacillus septicus and its congeners, oxygen must be either absent or abstracted. Now, many of the saprophytic and pyogenic bacteria, such as those in the foul tissues of the floor of the mouth, consume oxygen with avidity, and prepare and maintain an environment in which the anærobes can live and flourish. Nothing was found at the necroscopy or before to show whence these various bacteria came. It is to be doubted whether normal saliva could produce such effects, although it is well known that it often contains pathogenic bacteria. The important part which the saliva plays in rabies has led to many investigations of its properties by Pasteur and others. Injected into rabbits it causes a rapidly fatal septicæmia, with encapsuled cocci in the blood of various organs[1]; but I cannot ascertain that the bacillus septicus has ever been met with in sputum septicæmia. Biondi[2] injected the saliva of diseased and healthy individuals into the tissues or blood vessels of rabbits, guinea-pigs, and dogs. From these were isolated bacillus salivarius septicus, coccus salivarius septicus, micrococcus tetragonus, streptococcus septopyæmicus, and staphylococcus salivarius pyogenes, but nothing com-

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[1] Macé, "Traité Pratique de Bactériologie," p. 280 *et seq.* Paris, 1891.

[2] "Die pathogenen Micro-organismen des Speichels." *Ztschr. f. Hyg.*, Leipzig, 1887, bd. ii., p. 194.

parable to the bacillus which abounded in this case of angina Ludovici; but the bacillus septicus is so widespread that there is no difficulty in understanding that it might easily have been introduced with some article of diet.

The foregoing suggests that in future cases of angina Ludovici a determined attempt should be made to disinfect the floor of the mouth and tissues of the neck before septicæmia or general tissue infection has supervened. Solutions of peroxide of hydrogen would probably be the safest disinfectant.

Conveyance of Infection by Contiguity; Septic Pneumonia.

Case 20.—A bacillus morphologically the same as that met with in the tissues of angina Ludovici was seen in the walls of a putrid abscess of the lung, which was found under the following circumstances:—A young man, who had been intemperate for two years, was admitted into St. Bartholomew's Hospital after a brawl suffering from wounds about the head and face, a compound fracture of the lower jaw, and concussion of the brain. The day after admission his urine contained a cloud of albumen. He was very restless, and had a temperature of 102° F. He was unconscious, but shouted at intervals. His right arm seemed rather

weaker than the left, but this went away, and he became conscious, and seemed to be progressing towards recovery. The eleventh day after the injury his temperature rose gradually to 101·8° F., and he again became unconscious with fresh symptoms of hemiplegia. During the ensuing week there was no abatement of these symptoms, and as his temperature still ranged between 100° and 102° F. he was supposed to have pyæmia, and a cerebral abscess was suspected. His brain was exposed after the skull had been trephined, but nothing was found. Death ensued the day after the operation, and twenty-four days after his injury. At the necroscopy the brain was normal. There was suppuration around the fractured jaw with about two drachms of fetid pus. The internal organs were congested, but otherwise normal, except the right lung, which was pneumonic, with a putrid abscess in the upper lobe. It was surmised that this abscess was pyæmic. The histological examination did not bear out the supposition that pyæmia had anything to do with his death. The liver and kidneys had suffered from his intemperance. In the liver there was an excess of fibrous tissue and in the kidneys commencing interstitial nephritis. The only change which might have indicated sepsis was slight cloudy swelling of the renal epithelium. No bacteria could be found in either the liver, kidneys,

or spleen. The lungs, however, afforded abundant evidences of bacterial invasion. They were engorged with blood which had extravasated into some of the air cells, but the latter were mainly filled with pneumonic exudation. In some parts this exudation contained swarms of a small, short, round-ended bacillus (Fig. 25)

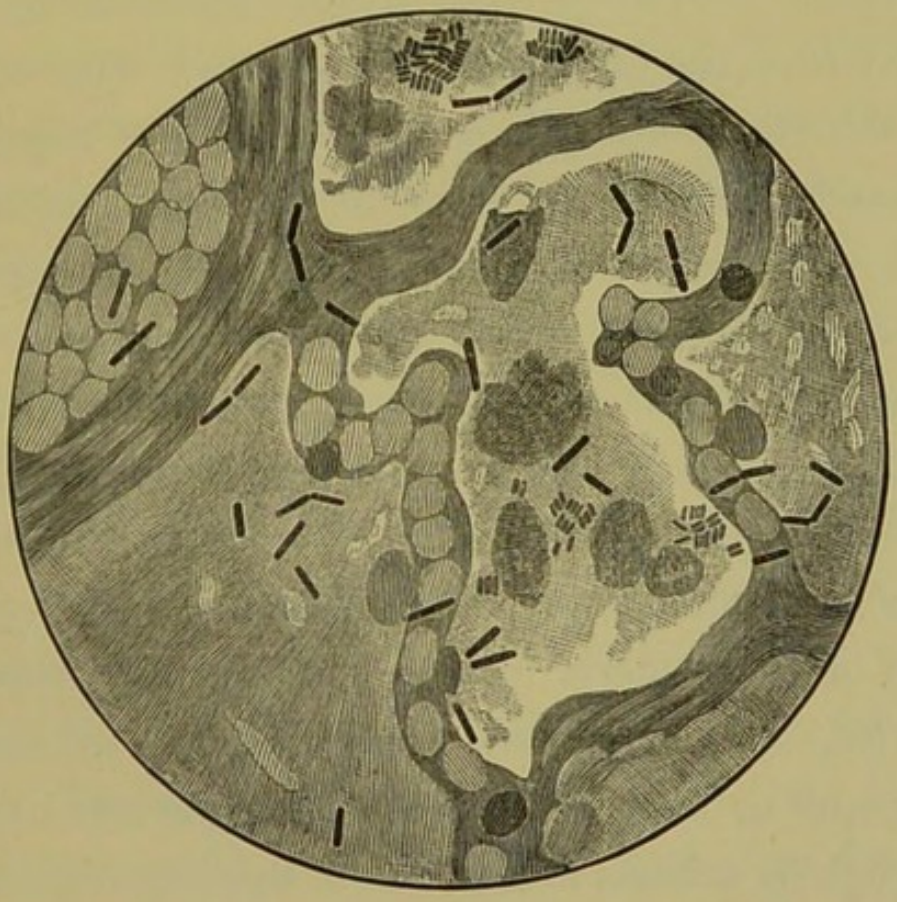

FIG. 25.—Septic pneumonia following a compound fracture of the lower jaw.

similar to the proteus vulgaris of Hauser; but the most striking objects were very large bacilli scattered in numbers both in the tissues of the lung and in the pneumonic exudations. These bacilli had slightly

rounded ends and were 1 μ thick and from 3 to 6 μ long. They contained no spores and multiplied by fission, being often seen in twos or in short chains. The bacilli were abundant where there was most connective tissue, as, for instance, in the adventitia of the pulmonary vessels, thus suggesting that they were anærobes. Doubtless these bacilli originated by contiguity from the fetid abscess of the jaw. The walls of the obliterated air cells contained many of them, also the exudation; but the blood in the vessels contained none, or occasional isolated examples. The lungs contained no bacterial emboli, nor could bacteria be seen in the clots in the vessels. By an unfortunate omission I obtained none of the brain for examination. It may be remembered that the clinical symptoms were like those of cerebral compression, although none existed. None of the bacteria in this lung possessed capsules, but the specimens had been hardened in alcohol. They bore no likeness to Friedländer's pneumo-bacillus, although in animals it seems as if that organism might grow to some size and length.[1]

The Local Infection in Angina Ludovici.

Case 21.—The local tissue changes and some of the characters of the infective process in angina Ludovici

[1] *See* Günther's "Bakteriologie," Plate xii. (Fig. 67).

were seen in a case which Dr. E. Valentine Gibson[1] described. I am indebted to him and Dr. Cameron for some of the inflamed cellular tissue of the neck. Unfortunately, specimens of the other organs could not be obtained. The case was that of a man, aged forty-nine years, who had been a heavy drinker, was attacked with cellulitis of the neck, and died comatose in less than fifty-two hours. Twenty-four hours before he died a sudden dyspnœa nearly ended his life, but he was saved by tracheotomy and incisions, and afterwards there was no obstruction to the entrance of air. Nevertheless, his dyspnœa increased and he became cyanosed before he died. The cellulitis spread from the neck to the chest, and, as it afterwards appeared, to the mediastinal cellular tissue. The swollen tissues were full of gas and began to crepitate. The temperature was in no way remarkable, and was usually about 98° F., but rose to 101° the evening before he died. The urine contained no albumen. At the examination, which was made four hours after death, an ulcer was found upon the side of the neck, and it is probable that this is the point of inoculation. The inflamed cellular tissue was full of fluid, had a gelatinous appearance, and minute bubbles of gas made it glisten.

[1] "A Rapidly Fatal Case of Angina Ludovici," *Lancet*, London, 3rd June 1893.

The mediastinal cellular tissues were also inflamed, but the thoracic and abdominal viscera had nothing noteworthy the matter with them, nor was there any disease of the salivary glands. No bacteria were found in the fluids squeezed from the tissues, and Dr. Cameron reported that he could find "no specific pathogenic micro-organisms in the tissues." By using Czenzynke's method and by staining the sections for many days we found the cellular interspaces and lymph paths crammed with cocci, diplococci, and streptococci in long and short chains (Fig. 26). In places the micrococci lay in dense masses. The tissues were œdematous and their connective tissue bundles swollen. Here and there nests of pus cells had collected, and amongst them were numbers of bacilli. Some of these were about the size of the bacillus anthracis, but with rounded ends. They contained no spores, and were straight or slightly curved. Others were of the same thickness, but shorter. These probably belonged to the same species as the long ones. Finally, the pus had small bacteria in it, of which some were undoubtedly micrococci, but others looked like very small oval bacilli, such as were found in the capillaries of the last case of angina Ludovici.

The discovery of streptococci in this case is quite in accordance with that which others have observed.

They probably belonged to one of the species of streptococcus pyogenes. The presence of the large, round-ended bacilli is of great interest when we recall the fact that during life and after death gas was found in the tissues. This might suggest that the bacillus septicus was present. This would not only explain

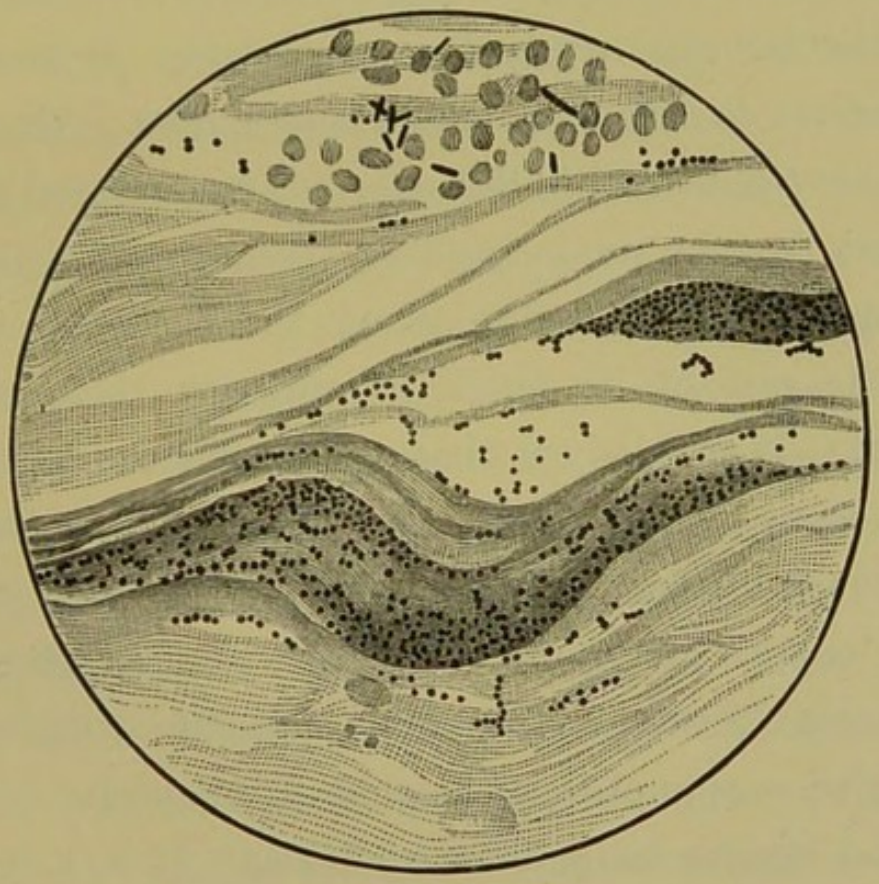

FIG. 26.—Angina Ludovici. Streptococci and bacilli in the cellular tissues.

the emphysema, but also the speed with which the patient died. The size and shape of the bacilli do not, however, agree with the assumption that they were the bacillus septicus. They were only half the usual size

of that bacterium, their ends were more rounded, and they did not grow in strings. They were much more like some form of bacillus coli communis. As I have already said, both this and other bacilli can cause emphysema and inflammation of cellular tissues. The co-existence of the streptococcus pyogenes with the bacilli affords food for reflection. In cutaneous erysipelas and cellulo-cutaneous erysipelas streptococci growing by themselves do not often cause a fatal ending. Nevertheless, the streptococci in this case may have played an important part by producing that absence of oxygen, and perhaps supply of toxins, which the bacillus septicus and the rest of its family require for their proper growth. It is obvious that the conditions would be much more favourable for the growth of the bacillus septicus or similar anærobes if the tissues were packed with oxygen-loving bacteria, like the streptococcus pyogenes. Further, we might speculate whether an excessive consumption of alcohol may not also help to produce similar favourable conditions. It is, I believe, supposed that alcohol uses up oxygen, which would otherwise go to the tissues.

Consecutive Infection; the Pathology of Hectic Fever.

When septic infection occurs during the course of other diseases, its effects, being confused with those of the original disease, are often overlooked or wrongly attributed to other causes. Thus in the course of tuberculous affections, such as chronic tuberculous arthritis or tuberculous caries, a newly-formed sinus or an ill-advised incision is often the starting-point of a new infective process, which is most destructive to the tissues previously deteriorated by the tuberculous inflammation. Locally, the effects of the new septic infection are often attributed to the original disease, and after it has become generalised, the septicæmia is not usually, I believe, recognised as such. The symptoms which accompany it are designated "hectic fever," a phrase unrepresented by any definite morbid anatomy. When septic infection is implanted upon an already established morbid process, I propose to call it "consecutive infection." The following is an instance of it both in its local and in its general manifestations.

Case 22.—A young man had suffered for many months with tuberculous arthritis of the knee. A peri-articular abscess formed and was opened. It extended deeply towards the joint, but was not known

to communicate with it. This opening ultimately healed, but the knee became stiff and bent. The joint was straightened without apparent ill-effects, but soon after the patient was re-admitted, and it was clear that a septic arthritis had been engrafted upon the chronic tuberculous arthritis. The usual local and general symptoms existed together with others, which pointed to breaking down tuberculous disease of the lungs. There was also an unusual feature in the case. His urine had hitherto been normal, but now a very large quantity, of low specific gravity and containing albumen, was passed. The patient died, it was supposed, of hectic fever and exhaustion, with amyloid disease. Afterwards I found an incision on the inner side of the knee, by which a finger could be passed into the joint. The synovial membrane was tuberculous and thickened, and there was complete erosion of the articular cartilages, with caries and necrosis of the tibia, especially near the outer condyle. The lungs were tuberculous and breaking down, with engorgement of the lower lobes. There was also tuberculous ulceration of the cæcum and right colon. The spleen, liver, and kidneys were enlarged and amyloid, and in addition the kidneys had the naked-eye appearances of parenchymatous nephritis; indeed, they were afterwards used at the morbid histology class to demonstrate that not in-

frequent combination of parenchymatous nephritis and amyloid infiltration.[1] But an investigation by Gram's method of staining threw fresh light upon the morbid condition; interspersed throughout the cortex of the kidney were numerous bacilli, singly and in chains, also cocci and diplococci, and capillaries blocked with micrococci. So far as the cocci are concerned, these appearances were the same as those which are experimentally produced by the injection of cultures into the veins of rabbits. By the eosin and methyl-blue method of staining, the capillaries, blocked with micrococci, were conspicuous objects, mainly situated beneath the capsule of the kidney (Fig. 27). Although not quite sure, I thought the emboli were probably composed of streptococci. The bacilli were sparsely scattered, and were apparently *post-mortem* in origin.

The foregoing was, as I have said, considered a typical instance of hectic fever, but whatever hectic fever may be, there is no doubt but that the youth had septicæmia. Long before this, in 1889, I endeavoured to solve this question of hectic fever being in reality a symptom of septicæmia by inoculating gelatin, agar-agar, and serum from the blood of patients with hectic fever. The blood was taken in the usual way from

[1] Ziegler, "Text-Book of Pathological Anatomy," translated by D. Macalister, Part II., p. 59. 1886.

the finger and with the usual precautions. The result was negative in the case of a man aged twenty-two years with tuberculous disease of the hip of four years' duration and with abscesses; also in that of a youth aged nineteen years, who had had morbus coxæ since the age of six. In spite of this failure, I think that this line of investigation ought to be followed up and extended. Indeed this has recently been done, for the occurrence of a mixed infection in tubercle of the lungs has been signalised by Jakowski.[1] He investigated the blood during the hectic stage by cover-glass preparations and cultures. Two out of nine cases gave negative results. In two staphylococcus aureus was found, in two streptococcus pyogenes, in two staphylococcus aureus and albus together, and in one streptococcus pyogenes and staphylococcus aureus. The same point has been written upon by Petruschky,[2] who remarks upon the frequent co-existence of streptococci and tubercle bacilli in sputum and pulmonary tuberculous abscesses. He attributes secondary infection to these streptococci, and advocates early diagnosis

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[1] "Beitrag zur Frage über die sogenannten Mischinfectionen der Phthisiker. Untersuchungen des Blutes der Phthisiker in der hektischen Periode." *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1893, bd. xix., p. 762.

[2] "Tuberculose und Septikämie." *Deutsche med. Wchnschr.*, No. 14, 1893. Ref. *Centralbl. f. Bakteriol. u. Parasitenk.*, Jena, 1893, bd. xiv., p. 216.

and early treatment of the primary tuberculous disease. Although it is well known that tuberculous processes are often complicated by the presence of other kinds of bacteria, hardly anything has been written about their

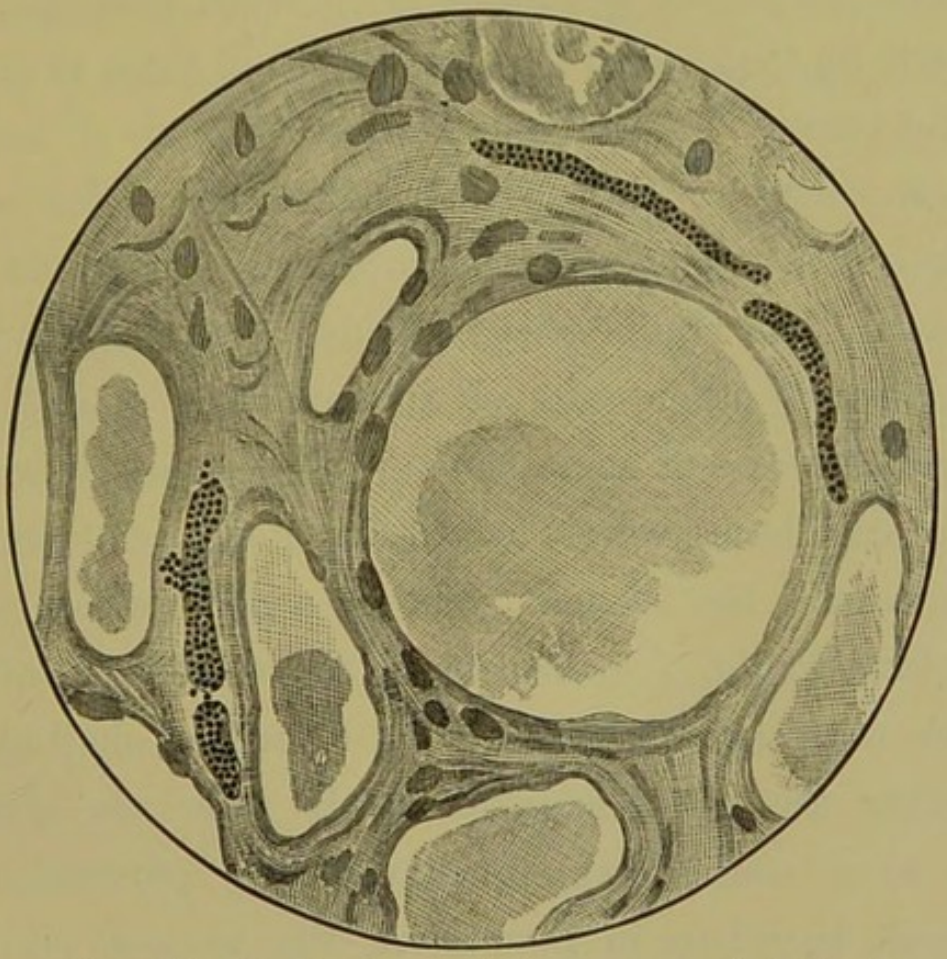

FIG. 27.—Hectic fever. Micrococcus emboli in the capillaries of the kidneys. The kidneys were also in a state of parenchymatous inflammation with amyloid disease.

presence in the circulation. Watson Cheyne[1] has mentioned a case in which he found micrococci in

[1] "Report on the Relations of Micro-organisms to Tuberculosis." *Practitioner*, London, April 1883, p. 302.

the vessels of tuberculous patients. He did not at that time lay much stress upon them, but said, "though quite independent of the disease, [they] probably hastened the death of the patient, or they may have been present simply as the result of lowered vitality, . . . though in that case I have never found them as plugs in the vessels." Cornil and Babes in a case of tuberculous caries of the spine found vessels filled with streptococci.[1] The same microbe was also found by them in the pulmonary glands, peritoneum, and meninges of other cases of tuberculosis. Koch[2] has described a case of acute general tuberculosis in which many capillaries were blocked for a short distance by micrococci. He thought that a mixed infection of this kind would, if looked for, be found tolerably often. Much work remains to be done before we shall know whether the phenomena of hectic fever are always due to a consecutive infection. The ptomaines of tubercle bacilli are in themselves able to cause marked rises of temperature, as was seen during the attempt to treat tuberculous diseases with Koch's tuberculin. Although the foregoing mainly refers to consecutive infection in tuberculous disease, there is, I think, no

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[1] "Les Bactéries," third edition, vol. ii., p. 455.

[2] "Etiology of Tuberculosis;" translated by Stanley Boyd. *New Sydenham Soc.*, 1886, p. 105.

doubt but that it may occur after any form of infective disease which produces the necessary conditions. Amongst these it is probable that typhoid fever ought to be included. That disease sometimes seems to terminate by the superaddition of a septicæmia, the blood becoming infected through the intestinal ulcers.

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