Messrs, Burroughs and Wellcome inform me that the two lots of serum which we used were from different sources, but that both were prepared by aid of six different strains of streptococci from human subjects.

CASE OF FATAL ANAEMIA PRESENTING SOME UNUSUAL BLOOD CHANGES.

BY

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G. E. C., male, aged 43, an insurance agent, was admitted to the Hospital for Diseases of the Chest, Victoria Park, under the care of Dr. Heron, on November 27th, 1900, complaining of weakness and shortness of breath.

History.—The symptoms had started insidiously during the hot weather of August, 1900, when he complained of fatigue and also of occasional giddiness when out walking, causing him to fall once. There was headache and shortness of breath, the latter specially marked on exertion. From the middle of October till the middle of November he had been able to do a little work, although his weakness and fatigue were gradually increasing, and he noticed that his hands and feet were slightly swollen. There had been a little cough for the last two months. Throughout the course of the illness he had at no time complained of vomiting, diarrhoea, melaena, haematuria or epistaxis. There was no history of any former illnesses. His father died of "fever," his mother of typhoid fever, the remainder of his family being healthy.

State on Examination.—The patient was found to be a well-nourished man, very pale, there being a slight suggestion of lemon colour about the nose, his mucous membranes also being extremely pale. He was obviously ill, lay flat in bed, being neither cyanosed nor in pain. There was some oedema of both feet and of the left leg, and slight puffiness about the eyes. There were no haemorrhages anywhere, and the gums, beyond being anaemic, were normal. The temperature was 99°. He had some cough, worse at night, but no expectoration. The lungs showed no abnormal physical signs. There was a short systolic murmur, heard at all the cardiac areas following the first sound, and not conducted into the axilla. Pulse 94. The tongue was furred, the appetite fairly good, the bowels regular. The abdomen was slightly distended, the liver and spleen not palpable. The urine was acid, specific gravity 1014, and contained neither albumen nor sugar.

Progress.—Patient's condition became steadily worse. On December 11th he was delirious, passing his urine and his faeces under him. He resented movement; took liquid nourishment well. There was percussion dullness over the right lung posteriorly, with some increase of vocal resonance. The knee-jerks were brisk. On December 12th, by ophthalmoscopic examination, haemorrhages were seen upon the fundus of the left eye. For the first week after admission the temperature was raised, varying between 99° and 102.2°, with frequent remissions of 1° or 2°. For the last four days of life it assumed the intermittent type, varying between 99° and 103.4°. Patient died on December 12th.

Blood Examination.—On December 8th the blood was distinctly pale in colour. On examination of a film stained with the triacid stain there was seen to be marked poikilocytosis, many of the corpuscles being larger than normal, but some much smaller. The colouring matter appeared not to be diminished. Many nucleated corpuscles were seen, by far the greater number of which were normoblasts, with, however, a few of the unnamed variety, and also one or two cells which were probably megalo-blasts. There appeared to be less tendency than normally to form rouleaux. The white corpuscles were obviously markedly increased in number, and consisted almost wholly of lymphocytes, these showing all varieties of size, from that of small lymphocytes up to that of large mono-nuclear cells (large lymphocytes), so that it would have been impossible to separately classify these two varieties. The lymphocytes, moreover, were more faintly stained than normally. There were very few polymorphonuclear neutrophils, and in all the films examined only one or two myelocytes were seen. On December 11th the poikilocytosis was seen to be more marked; one microblast was seen, and many normo-blasts, the appearances otherwise being similar to those on December 8th. The red and white counts were made from liquid films, the differential counts from films stained by the triacid stain.

Date.	Red Cells.	Haemo- globin.	White Cells.	Differential Counts of White Cells		
				Lymph- ocytes.	Poly- morpho- nuclear Neutro- philes.	Myelo- cytes.
Dec. 1st ...	Per cm. 900,000	20%	Per cm. Increased	—	—	—
Dec. 8th...	480,000	12%	34,000	99.27%	0.55%	0.18%
Dec. 11th...	400,000	12%	45,000	99.06%	0.36%	0.37%
Dec. 12th...	300,000	—	38,000	99.62%	0.37%	None

Thus it will be seen that on December 8th the ratio of red to white cells was 14 to 1; on December 11th was $\frac{8}{3}$ to 1; and on December 12th was just under 8 to 1.

Necropsy.—The visceral pericardium showed many petechiae. The right pleural cavity contained 3 xv of clear fluid, and the lower part of the pleura showed signs of recent inflammation; the upper part was thickened, and there were some fibrous adhesions. The left pleural cavity contained 3 x of clear fluid, but the pleura was not inflamed. At the apex of the upper lobe of the right lung there was a small calcified tuberculous mass, and there was some fibrosis throughout this lobe; both the middle and upper lobes showed pneumonic consolidation. The left lung showed a small caseous and calcareous mass with some surrounding fibrosis near the apex of the upper lobe, and there was a similar mass in the lower lobe, with a small area of pneumonic consolidation at the base. The heart was large and fatty, the endocardium of the left ventricle showing "tabby cat" striation. The liver was not enlarged, but was fatty, microscopically showing advanced fatty degeneration with many lymphocytes between the liver cells. On treating a section with ferro-cyanide of potassium, no trace of iron could be detected. The spleen weighed 12 oz., and was large and firm. The kidneys were fatty. There was an old tuberculous ulcer on the caecal side of the ileo-caecal valve. One mesenteric gland and one of the thoracic glands were enlarged to a slight degree, but on microscopical examination showed no changes. There was nothing else abnormal in the glandular system. The bone marrow showed no departure from the normal. The muscles were dark red. The thymus gland was not enlarged.

From a film stained with eosin and methylene blue $\times 500$.

The case presents some very interesting features. The blood picture as regards the red blood corpuscles is practically that of pernicious anaemia, the diminution in the number of red cells being unusually great even for this disease, being less than one-tenth of the normal number, there being marked poikilocytosis and numerous nucleated cells, the colouring matter, moreover, being diminished only in proportion to the diminution in number of the red blood corpuscles. On the other hand, the white corpuscles exhibited typically the condition found in lymphatic leukaemia, their number being about four or five times the normal, and consisting of over 99 per cent. of lymphocytes, instead of the normal number of about 30, the neutrophils being diminished to about $\frac{1}{3}$ per cent., the normal number being about 70 per cent., and this although the patient was suffering from lobar pneumonia.

The extreme degree of the anaemia, together with the large number of nucleated red corpuscles, would seem to show that the process was an acute one, but the absence of any haemorrhages on the skin or sponginess of the gums, would apparently forbid the case being classified with those described as acute leukaemia. Westphal describes a case in which the blood picture was that of pernicious anaemia, the red cells being diminished to 816,000 per centimetre, and in which there was a leucocytosis amounting to 24,000; the greater number of these consisting of lymphocytes. This case, however, showed many haemorrhages on the skin and mucous membranes, and ran its course to a fatal

issue in about six weeks. Cabot² mentions two cases of lymphatic leukaemia, one with 912,000 red cells and 23,000 white cells (97 per cent. lymphocytes), the other with 700,000 red cells and 600,000 white cells (99.8 per cent. lymphocytes) per cm.

The absence of any notable enlargement of the lymphatic glands is interesting, although there are undoubted cases of lymphatic leukaemia recorded in which a similar condition prevailed.

We are indebted to Dr. Heron, under whose care the patient was, for permission to publish this case.

REFERENCES.

- ¹ Westphal, *Munch. med. Woch.*, 1890, p. 4. ² *A Guide to the Clinical Examination of the Blood*, by R. C. Cabot, M.D., p. 171.

SPONTANEOUS GANGRENE OF BOTH LOWER LIMBS IN A MAN AGED 36.*

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THE following case is of interest as presenting not only unusual features in itself, but also from the diagnostic point of view, as it baffled the most careful efforts of all who came in contact with it in its earlier stages:

History.—A man, aged 36, first came under my care in November, 1899, and was then suffering from what appeared to be an influenza attack, with a slight pleurisy at the left base; he was not very ill, but had a persistent temperature of half a degree above normal, which took nearly six weeks to subside. At that time I examined him as systematically and as carefully as I could, and could find nothing to account for this persistent temperature except the slight pleuritic friction above referred to. In the spring of 1900 he had another similar illness, which did not last so long. In June of 1900 I examined him on behalf of a sickness and accident insurance company, and found the heart and lungs normal, chest expansion unusually good, and chest very well developed; urine normal, liver dullness normal, nervous system normal excepting for the presence of a fine tremor of the tongue and of the hands, the voice was also somewhat tremulous. The pulse was normal as to frequency, but small and compressible; radial arteries normal; temperature normal. I was unable to elicit anything unfavourable in his personal or family history. (I may here mention, however, that I attended his wife in confinement in October, 1899, and that a few ham-coloured maculae appeared upon her face and arms during the puerperium. The baby had "snuffles" for a few weeks. There was no history of any miscarriages, and there has been no further evidence of specific trouble in either.)

As regards the husband's personal habits, I was informed by himself that he had always been temperate as regards alcoholic beverages, and his partner in business also informed me that he had never known him indulge in alcoholic excess of any kind. He was an inveterate smoker. I had, therefore, considering all that, no hesitation in passing him for insurance, but, considering the tremors already referred to, I recommended that he be accepted at an increased premium. He was passed for life insurance by another medical man about the same time and as a first-class risk. From that time till the beginning of the present year he remained in his usual health and attended regularly to his business.

State on Examination.—On January 17th, 1901, I was called to see him at his home, and found him suffering from severe pain—which had been present for about a week before—over the ball of the little toe of the left foot; the pain was very much increased by touching the part, and it extended along the sole of the foot towards the heel. It also extended for a few inches up the posterior aspect of the leg, but was not very severe in that region. The pain was worst at night. Sensation to slight touches was diminished over the little toe. There was no marked tenderness on deep pressure of or on squeezing the muscles of the calf. The knee-jerks and other reflexes were normal. The tongue was slightly coated with a light yellowish fur. The appetite was poor; the pulse varied from 80 to 100, and the temperature was 99° F.

Diagnosis and Treatment.—My diagnosis, failing anything better and in absence of the usual signs of neuritis, was rheumatism, affecting the ligamentous structures of the sole of the foot. I accordingly put him on antirheumatic diet and drug treatment, cutting off alcohol in every form and also tobacco. (It was at this time that I first became aware that the patient had for several years been in the habit of taking several "pick-me-ups" of brandy or whisky every day, and that he was in the habit of having a glass of brandy in his coffee before going to business every morning. It was then obvious that this was the probable explanation of the tremors of hands and tongue.)

Progress.—During the first two or three weeks he improved somewhat under this treatment; the pain was not so severe, but he was still unable to walk. As he was anxious to return to business, I advised that he should go to a watering place and put himself under a medical man there with a view, if the latter thought it advisable, to having local hot-air baths. He therefore went to one on February 12th, placed himself under a medical man there, and was recommended to have the limb subjected to the local hot-air treatment. He was also put on a generous daily supply of alcohol. Notwithstanding this he gradually got worse, the hot-air applications caused excruciating pains in the leg, he lost flesh gener-

ally, and became extremely weak, and the calf muscles of the affected leg wasted considerably. I next saw him on April 24th, when he was seen by a consulting physician who diagnosed neuritis, with which diagnosis I concurred, although even yet the knee-jerks were normal or only very slightly diminished, but at the time no other diagnosis seemed possible. The patient again returned to the watering place, changed his medical man there for another, and the latter asked me to see the case with him on May 11th, the patient still getting rapidly worse. We went again carefully over his case and agreed that it was one of neuritis, although a slight bluish tinge and slight coldness of the foot made us take the question of Raynaud's disease into consideration. Opinions and treatment alike, however, the patient gradually got worse, and about a week later the coldness and blueness of the foot had become more marked, and definite gangrene set in. On May 22nd he was brought home, and on arrival I could detect no pulse lower than in the common femoral at the groin. I accordingly called Mr. Horrocks in, and he amputated the limb about 7 inches above the knee, on the following day.

Operation.—The method used was short anterior and posterior flaps of skin, with circular section of the muscles. The main vessels were thrombosed above the seat of amputation, and there was practically no haemorrhage. The anaesthetic used was ether. There was a very moderate amount of shock following the operation, and the pulse, which before the operation had been 106 and the temperature 102.4°, fell respectively to 84 and 98° the same evening.

Subsequent Progress.—Two days later the temperature had fallen to 97.4° and the pulse to 73. The following day—that is, the third day after the operation—the patient began to complain of severe pain in the calf of the right leg, and of numbness and tingling pain in the right foot. On inspection the foot was found to be somewhat pale and cold, and pulsation could not be detected in the posterior tibial artery at the ankle, and was somewhat doubtful in the popliteal space. By the fifth day the pulse had again reached 110, but the temperature did not rise over 99°, and gangrene of the right foot was evident. I then advised amputation of the right leg, and made arrangements for Mr. Horrocks to operate the same day, five days after the first operation.

Second Operation.—The operation was done in the same way as the former one, only an inch lower down, that is, 6 inches above the knee, and ether was again the anaesthetic. The same condition of the vessels was found as in the left leg. The shock was much greater than on the former occasion, the temperature dropping that evening to 97°, and the pulse being 131.

After-Progress.—The following day the temperature began to go up, and on the second day after operation reached 102.2°, and it became evident that sepsis had occurred. I therefore took out some stitches and irrigated the wound, and by the fifth day the wound had become fairly clean and healthy in appearance. From that time on recovery was uneventful: the temperature never rose above 99.4°. To prevent a tendency to gaping of the wound, where it had been necessary to remove the stitches, I applied extension to the stump. The left stump healed in about three weeks after amputation and the right in about four weeks. Five weeks after the first operation the patient was able to sit up, the tongue had become clean, it had almost lost its tremor, and the appetite was better than it had been for several months; the pulse, however, still kept between 90 and 100. Insomnia was a prominent feature throughout, and I had to use hypodermic injections of morphine pretty freely. On July 31st he went to the seaside, and came back in the middle of September looking and feeling better than he had done for six or seven years; his appetite was excellent, and he had gained 2 stone in weight. Since his return he has resumed his business; at present a pair of artificial legs are being made for him.

On examining the amputated limbs I found thrombi filling all the arteries from the popliteal downwards, and on dissecting the right leg I found that the gastrocnemius was of normal appearance, but on reflecting that muscle and examining the soleus underneath I found that the latter had lost the usual red colour of healthy muscle, and had assumed a colour resembling yellow ochre. This I take to be an indication that the thrombotic process had started below and spread upwards, thus cutting off the blood from the soleus (which in its lower part is supplied by a branch of the posterior tibial artery), before the supply was cut off from the gastrocnemius, which is supplied by one of the crural branches of the popliteal higher up. On making a considerable number of sections of the arteries of this limb I failed to find any cause for the thrombosis, but on examining sections of the posterior tibial and popliteal arteries of the left leg I found well-marked calcareous degeneration of the middle coat of the artery, and here and there patches of atheromatous thickening of the intima. When placed in acid and examined under the microscope the sections give an effervescence of CO₂, thus verifying the diagnosis of calcareous degeneration.

As to the precise cause of atheroma everything is not definitely known; probably it is but part of that general fibrosis which, sooner or later, causes each one of us to "shuffle off this mortal coil"; and probably gout, rheumatism, syphilis, and alcoholism are simply accidental factors which accelerate its onset. Heredity in many cases is an important factor, as is evidenced by its appearance occasionally in children who are too young to have suffered from any self-contracted vice. Young found it in an infant, Wilson in a young child, and Andral found it in the aorta of a child 8 years old.¹ It may be taken as an axiom in medicine that "a man

* Read before the Bradford and District Medico-Chirurgical Society.