

—that wonderful living fluid which carries life and nourishment to every tissue, giving to the body its power of action and of feeling, and to the brain its power of thought and memory; which is so delicately constituted that by the invasion of a minute organism or the raising of its temperature two or three degrees it may be so profoundly altered that the whole body at once becomes disturbed, action impeded, and thought confused; and which, if it should undergo clotting within the vessels is changed from a source of healthy action to a cause of mortal danger or even of sudden death.

I say how little we really know of the vital chemistry and physiology of the blood. Here is a wide and fertile field for our advancing physiological chemists. I have only tried to make some small contribution to our clinical knowledge and I desire to thank you, Mr. President and the Council of the College, for giving me this opportunity and my audience for the kind patience with which they have listened to these lectures.

A CASE OF SPLENOMEGALIC POLYCYTHÆMIA, WITH REPORT OF POST-MORTEM EXAMINATION.

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THE patient in this case, a farm labourer, 45 years of age, was admitted into the London Hospital on July 26th, 1905, under the care of Dr. F. J. Smith at the request of Mr. A. Leigh Chignell. We are indebted to Dr. Smith for permission to publish the case, as he was away on holiday during most of the time that the patient was under observation. The patient's earlier history is contained in the following account kindly furnished by Mr. Chignell.

The patient first came under my care about seven years ago when I was called to see him as he had been found on the road in a fit, having fallen down while coming home from work. When seen he was in a dazed condition and the symptoms as described to me were "that he twitched all over and his body was thrown into various movements and was believed to be unconscious." There was no return of any of the symptoms and he resumed work in four days. He enjoyed good health until three and a half years ago when he suffered from a large carbuncle on the left side of the chest. Under treatment this healed up satisfactorily. He first noticed a peculiar twitching of the muscles of the face and especially of the mouth at this time and his face became pigmented and covered with acne spots. After six weeks he returned to his work. On Jan. 30th of this year he came to me for ulcerative stomatitis of a severe form affecting the whole mucous membrane of the mouth. He had been feeling uncomfortable after food for some time and the bowels were constipated. Under treatment the stomatitis recovered but the dyspeptic symptoms continued and giddiness and a feeling of faintness complained of. He attempted to return to work but fell down on the way and the symptoms from this time increased and vomiting appeared. He also lost flesh. The vomiting was irregular, occurring sometimes frequently in the course of one day whilst at others it would be absent for several days in succession. In June hæmatemesis occurred several times but the amount of blood brought up was small. The pulse at this time was slow and the heart appeared displaced. The temperature was normal or subnormal throughout. He complained of no pain except in the head, but there was tenderness on pressure over the stomach and spleen. Some enlargement of the spleen was noticed in March but it may have been present earlier. Giddiness was the most distressing symptom and grew worse, facial twitching also appearing. During the last weeks that he was under my care he became very forgetful. He was always a steady man and hard worker.

The family history showed nothing of interest except that the patient's father was alleged to have died from ague at the age of 55 years. On admission the patient was found to be a well-developed man of medium build. His face was covered with acne; the lips and nose were of a deep purple colour; there was no clubbing of fingers or oedema. The teeth were mostly carious and the gums were swollen, spongy, and inclined to bleed. On abdominal examination a large tumour was felt in the left side projecting from beneath the ribs and extending to the middle line and downwards to the umbilicus. The tumour was firm, dull on percussion, not tender, and exhibited a distinct notch. The liver could not be felt but seemed slightly enlarged on percussion. There was no ascites. The apex beat was in the fourth space, one inch outside the mid-clavicular line and of a heaving character. The area of cardiac dulness extended to the third rib above and to the left edge of the sternum.

The heart sounds were clear. The pulse was slow (from 50 to 60 beats a minute) and of good volume. The arterial walls were very much thickened and tortuous. There were no enlarged glands. The lungs were normal. The average amount of urine passed was about from 30 to 35 ounces a day. The specific gravity varied from 1022 to 1030; a faint trace of albumin was present during most of his stay in hospital but no sugar. The knee-jerks were normal; the pupils reacted sluggishly to light. On ophthalmoscopic examination the discs were rather red and the retinal veins were engorged. The temperature during the whole illness was normal or slightly subnormal but rose to 108° F. at death.

Examination of the blood and blood pressure.—On admission blood taken from the lobe of the ear contained 8,000,000 red cells per cubic millimetre and 110 per cent. hæmoglobin (Haldane). The white cells were not estimated. On August 9th the blood pressure (Riva Rocci) was 140 millimetres of mercury. On the 11th blood taken from the ear contained 11,000,000 red cells, 17,160 white cells, and 120 per cent. hæmoglobin. On the 28th three and a half ounces of blood were withdrawn from the arm and citrated. The blood pressure just before the venesection was 130 millimetres and just after 145 millimetres. The viscosity of the citrated blood was estimated by Dr. F. Parkes Weber, who found that by the method which he has previously described¹ the coefficient of viscosity of the blood was 11·8 times the coefficient of viscosity of water. The specific gravity of the citrated blood estimated by the method of weighing was 1·071. On the 30th a drop of blood from the ear contained 22,000 white corpuscles per cubic millimetre. A differential count which Dr. A. E. Boycott was kind enough to make gave the following result:—

Differential Count of White Cells.

| | Per cent. | In c.mm. |
|-----------------------|-----------|----------|
| Lymphocytes | 5·6 | = 1232 |
| Intermediates | 2·4 | = 528 |
| Large hyalines | 4·0 | = 880 |
| Neutrophiles | 82·8 | = 18,216 |
| Eosinophiles | 2·8 | = 616 |
| Mast cells | 2·4 | = 528 |
| | 100·0 | 22,000 |

No abnormal leucocytes. Nothing abnormal in red cells. No nucleated red cells found.

On Sept. 1st a drop of blood from the ear contained 7,500,000 red cells and 130 per cent. of hæmoglobin. On the 16th a drop of blood from the ear contained 20,000 white cells, of which the following was Dr. Boycott's differential count:—

| | Per cent. | In c.mm. | |
|-----------------------|-----------|----------|-----------------------------------------------------------------------------------------------------------------------|
| Lymphocytes | 4·4 | = 880 | |
| Intermediates | 3·2 | = 640 | |
| Large hyalines | 3·2 | = 640 | |
| Neutrophiles | 83·2 | = 16,640 | The high percentage of eosinophiles and mast cells points against the condition being an "inflammatory" leucocytosis. |
| Eosinophiles | 3·6 | = 720 | |
| Mast cells | 2·4 | = 480 | |
| | 100·0 | 20,000 | |

Nothing abnormal about red cells. No nucleated red cells found. No myelocytes found.

Progress of the case.—The patient complained for some time after his admission to hospital of pain in the back of the head and would often hold his head between his hands. There was never any vomiting; his bowels were constipated. Shortly after admission he began to be troubled with failure of eyesight which gradually increased until he became quite blind. The fundi were examined on several occasions but nothing was found beyond slight hyperæmia. The failure of vision was accompanied by a great mental change; he became dull and stupid and unable to understand what was said to him. He was restless at nights and slept badly. This progressed till finally a state of complete somnolence was reached when he lay like a log in bed and was wet and dirty but still able to swallow food when it was put into his mouth. The tumour in the abdomen underwent a marked change during this time and became somewhat tender and gradually receded until finally it could be just felt one

¹ Paper with Mr. J. H. Watson, Transactions of the Clinical Society of London, 1904, vol. xxxvii., p. 131.

finger's breadth below the costal margin. Towards the end the cyanosis of the face and extremities became even more marked and he was quite unable to swallow anything. Death took place with coma and hyperpyrexia on Sept. 21st, about eight weeks after his admission to hospital. The treatment employed consisted in the administration of iodide and citrate of potash. Large saline enemata were administered with a view to dilute the blood and on one occasion he was bled to 16 ounces. None of these measures, however, had any effect upon his condition.

Necropsy.—The post-mortem examination was performed by Dr. Miller with the following result. Rigor mortis was present. The external appearances were as follows: the body was greatly wasted; the face was florid; there was deep congestion of the back. There were no enlarged glands. On opening the abdomen the muscles and cellular tissue of the abdominal wall were found to be deep red. The veins of the mesentery and intestines were greatly injected. Dense adhesions were found enveloping the spleen and between the liver and diaphragm. The liver, spleen, stomach, duodenum, mesentery, pancreas, suprarenals, and kidneys were removed together and dissected after removal. The spleen (which weighed 38½ ounces) formed a tumour projecting considerably below the costal margin. It was densely adherent to the surrounding structures and was large, hard, and of irregular shape. On section it was found to consist partly of purple structureless spleen pulp and partly of many areas resembling infarcts. They were of various sizes and sharply demarcated from the spleen pulp. They were firm and fibrous at the periphery but somewhat softer in the centre. Most of them were yellow but a few were a dull red. There were two small round accessory spleens. The liver weighed three pounds four ounces; its anterior surface was densely adherent to the diaphragm; the capsule was smooth elsewhere. The liver substance was unduly firm and very greasy. It was bronze-red in colour. There were not much congestion and no appearance of nutmeg. As regards the kidneys, the right weighed six ounces and the left seven ounces. The perinephric fat was yellowish-red. The capsules were thin and stripped readily; there were no cysts. The surface was smooth. The colour was a uniform deep purple. The cortex and medulla were natural. The pelvis and vessels were natural. No gross morbid lesion was found. Both suprarenals were large, soft, and difficult to define. The condition was apparently a hyperplasia. No gross morbid lesion was present. They each weighed one and a half ounces. The ureters, bladder, prostate, and testes were natural. The pancreas was firm and dull red in colour; it was not apparently altered in size or shape. As regards the alimentary system, the œsophagus was natural. The stomach was natural in size and shape. There was great injection but no ulceration. The duodenum and the small and large intestines showed great injection but no ulceration. The appendix was healthy. The mesentery showed great injection of veins. There was no enlargement of glands. The abdominal aorta was somewhat stained; otherwise there was no change. The vena cava and iliac veins were natural but very full of black fluid blood. The tongue was natural. The tonsils and the glands of the neck were not enlarged. The thyroid weighed 13 ounces. Its lateral lobes were enlarged, unduly firm, and of a red yellow colour. No trace of the thymus was found. The larynx and trachea were healthy. The diaphragm was at a slightly higher level than normal—the fourth space on the left side and the fourth space on the right side. The heart was pushed up into the fourth space. The pleuræ were very dense. There were adhesions between the diaphragm and the base of the lung on each side; otherwise they were free. The lungs were small and aerated throughout. There were many subpleural ecchymoses. A few small, dry, hard patches of purple substance peripherally situated and wedge-shaped were found, resembling infarcts. No sign of tubercle was present. The pulmonary veins were enormously distended with black fluid blood. The bronchial glands were not enlarged. The pericardium was not thickened; there were no adhesions. There was a slight excess of clear fluid. Some sub-pericardial ecchymoses were seen about the base. The heart weighed 12½ ounces. The right side and the left auricle were full of black fluid blood. The left ventricle was almost empty and firmly contracted. The endothelium was stained. The myocardium was difficult to cut and extremely fibrous in patches, especially in the papillary muscles. The valves and orifices were not altered. The endothelium was natural. The coronaries were not changed. The aorta

was slightly stained. The left femur was sawn in half lengthwise; the upper quarter was red and with cancellous bone; the middle half was deep red and pulpy; and the lower quarter was yellow and with cancellous bone. The marrow of the right fourth rib was deep red and fluid. The skull was opened and the dura mater was found to be intensely injected to the smallest veins. The dura mater was opened and considerable œdema of the pia arachnoid and injection of the meningeal vessels were found. There was no gross change in the vessels at the base. The brain weighed 3 pounds 4 ounces; it was natural in size and shape. The occipital poles were diffuent. Examination after hardening showed that the tips of both occipital lobes, the tip of the left temporo-sphenoidal lobe, and the extreme edges of the lateral lobes of the cerebellum were the seat of dry, almost powdery, yellow softening. The left lenticular nucleus and the right optic thalamus were red and disintegrated. The pituitary body was apparently natural. Microscopical examination of the kidneys, suprarenals, and thyroid showed enormous congestion of all the capillaries and a good deal of fibrous overgrowth in the adventitia of the small arteries. The cardiac muscle showed a high degree of fibrosis, the muscle bundles being imbedded in masses of dense fibrous tissue although the muscle fibres themselves appeared to be normal. The arterioles of the heart wall showed great thickening of the adventitia.

Specimens of the spleen, bone marrow, and liver were submitted to Dr. J. C. G. Ledingham of the Lister Institute who kindly reported upon them as follows:—

Report by Dr. LEDINGHAM.—"Paraffin sections of the spleen and marrow fixed in sublimate were stained with hæmatoxylin-eosin, van Gieson's picro-fuchsin, hæmatoxylin, Unna-Pappenheim's methyl-green-pyronin, and Giemsa's azur-eosin.

Spleen.—A section was made through an infarct-free area. There is no increase in the connective tissue of the spleen trabeculæ nor does the pulp reticulum show any tendency towards fibrosis. In parts, however, the supporting tissue, especially in the vicinity of the large blood-vessels, presents a broadened-out and somewhat hyaline appearance resulting from lymph transudation. The Malpighian nodes are represented by a few small scattered remnants formed of three or four concentric rows of lymphoid cells mingled with clumps of hyaline material. These small nodes are not sharply differentiated from the surrounding pulp and some of them contain, besides hyaline masses, numerous pigment particles and nuclear detritus either lying free or imbedded in the cytoplasm of epithelioid cells which have wandered in from the periphery of the node. The most marked feature of the spleen pulp is the extreme congestion of the venous sinuses, the thin walls of which have in many places given way. A large number of these channels, however, still retain their endothelium intact. The following cell types are met with in the spleen pulp. 1. Small lymphocytes and large non-granular mononuclear cells. These are the most frequent types. 2. Large mononuclear cells with vesicular nuclei and strongly basophile protoplasm (basophile myelocytes) occur here and there in small clumps. 3. Polynuclear neutrophile cells occur in large numbers. Small foci formed entirely of these cells along with nuclear detritus are often observed, suggesting almost some infective process. No organisms of any kind were detected in them (careful search was made for tubercle bacilli). 4. Mononuclear and polynuclear eosinophile cells were present in small numbers. 5. A few megakaryocytes were noted. 6. Epithelioid cells were met with here and there, some of them apparently exercising phagocytic functions. 7. The pulp was carefully searched for the detection of erythroblastic foci and a very few minute clumps of proliferating nucleated red cells were observed. Their nuclei frequently presented karyorrhexis or even actually budding, a feature to be noted in the marrow foci (*vide infra*).

Numerous sections were made through portions of spleen containing the infarct-like areas noted in the protocol. The centre of the caseous mass consisted of amorphous material with a few leucocyte shadows. The periphery was formed of dense connective tissue containing congested blood-vessels and outside these again was another connective-tissue zone containing enormous numbers of extravasated red blood corpuscles. Numerous epithelioid cells containing in their interior blood pigment and red blood corpuscles in various stages of disintegration were also present. No tubercle bacilli were detected in the areas after careful search, but so far as their histology went in the absence of actual

tubercles or bacilli they might very well represent the result of some tuberculous process. In view of the small number and size of erythroblastic foci in the spleen pulp one cannot conclude that the spleen was exercising any important function as a red blood cell forming organ. Nor was there much evidence of active red cell destruction except as already noted in the vicinity of the caseous areas.

Marrow.—The fat cells of the marrow have not entirely disappeared. The most notable feature is the dilatation of the thin-walled blood-vessels with red blood corpuscles. These congested blood-vessels traverse the whole section but there are no hæmorrhages into the substance of the marrow proper. The endothelium of the sinuses remains quite intact. The following cell types were noted. 1. Large mononuclear cells with somewhat vesicular nuclei and basophile protoplasm were most frequent. In morphology these cells correspond to the basophile myelocytes or undifferentiated cells of Dominici. Neutrophile myelocytes and polynuclear cells were present in fairly large numbers, though the granulation was difficult to demonstrate. Transition forms can readily be traced between these basophile cells which may sometimes attain a large size and the giant cells presently to be described. 2. Eosinophile cells, both mononuclear and polynuclear, occur in large numbers and in Giemsa preparations make a remarkably beautiful picture. 3. The giant cells present are of two types. Sometimes as many as ten may be seen in one field of the oil immersion Leitz $\frac{1}{2}$ th, oc. 4. Cells with large-lobed nuclei assuming the most bizarre shapes are most numerous. The protoplasm of these cells is slightly basophile. Many of them appear to be developed directly from the basophile undifferentiated cells already noted and in which mitotic figures are frequent. The second type of giant cell possesses a straggling irregular nucleus which is intensely pyknotic and a cytoplasm which is inclined to be acidophile. These cells frequently contain entire leucocytes in their interior. They are evidently degenerated megakaryocytes. 5. Lymphoid cells are not very numerous. 6. Mast cells occur in small numbers. 7. With the Unna-Pappenheim stain plasma cells are found to be as scarce in the marrow as in the spleen pulp. 8. Here and there one sees erythroblastic foci, generally of small size but sometimes fairly large clumps of developing nucleated red cells are met with. The nuclei stain intensely while the cytoplasm takes on a yellowish stain. Frequently the nucleus is broken up or presents a budding appearance. It is possible that this irregular division is the explanation of the great variations in size and shape of the red cells in blood films *intra vitam*. One could not conclude from a single section that red blood cell formation was actively proceeding, but when one reflects that large tracts of marrow were in a similar condition one must infer that the polycythæmia is to be explained by a general increase of the erythroblastic functions of the marrow. The large number of granular cells in the marrow certainly indicates an increase in the leucoblastic function of that tissue and would explain the polynuclear leucocytosis in the circulating blood that is so marked a feature of most of the recorded cases.

Liver.—The interacinar capillaries are greatly congested with red blood cells, though polynuclear cells are also frequent. The liver lobules and acini are quite intact and the cells apart from very slight fatty infiltration appear healthy. Clumps of bile pigment occur in some of the liver cells and here and there one sees the lumina of the smaller bile channels filled with inspissated bile thrombi. There are no focal necrotic areas and no micro-organisms.

Remarks.—There can be no doubt that clinically this case belongs to the group characterised by chronic cyanosis with polycythæmia and splenomegaly, of which examples have been recorded by Vaquez, Saundby and Russell, Rosengart, Osler, Parkes Weber, and others, and for which Parkes Weber² has suggested the name of "myelogenic polycythæmia." The increased number of red cells (from $7\frac{1}{2}$ to 8 millions per cubic millimetre) and the splenic enlargement together pointed to such a diagnosis. In addition, there was found by Parkes Weber an increase in the viscosity of the blood such as he has described in a previous case of his own, whilst a polynuclear leucocytosis which was present in our case has also been met with in some previously recorded examples of the disease. The cerebral and mental symptoms, too, which were such a marked feature in our patient have also been remarked in such cases before.

We are fortunate in being able to add another to the few

recorded necropsies on cases of this group, and as far as an explanation of some of the most striking clinical symptoms is concerned the result was satisfactory enough. The loss of vision, for instance, and along with it probably the attacks of giddiness and the final stupor, may be held to be explained by the extensive areas of thrombotic softening in the occipital lobes of the brain. It cannot be said, however, that much light is thrown upon the pathogeny of the disease by a study of its morbid anatomy. That the amount of blood-forming tissue in the bone marrow was increased there can be no doubt, which, with the absence of any signs of increased blood destruction in the liver, would point to the polycythæmia being the result of an increased formation of red cells. The enhanced viscosity of the blood which is the consequence of the polycythæmia and the abnormal strain which it throws upon the arterioles may perhaps explain the high degree of vascular fibrosis met with. The fibrotic degeneration of the heart was certainly a most striking feature of the morbid anatomy but was perhaps merely secondary to the thickening of the walls of the coronaries.

As regards the softening in the occipital lobes of the brain and the large pulpy areas in the spleen, there can be no doubt, we think, that they were due to thrombotic necrosis, the consequence of stagnation of blood which the high viscosity of the latter tended to induce. We found no evidence of any primary tuberculosis of the spleen such as has been alleged to occur in some of these cases and are inclined to think that in such descriptions areas of infarction may have been mistaken for tuberculous foci.

In conclusion, we would like to take the opportunity of expressing our indebtedness to those who so kindly helped us in the investigation of the case; to Dr. Parkes Weber especially for much advice and suggestion and for estimating the viscosity of the blood; to Dr. Boycott for his careful reports on the histological features of the blood; and to Dr. Ledingham for his minute investigation of the histology of some of the more important organs.

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SPIROCHÆTA PALLIDA (SPIRONEMA PALLIDUM) IN SYPHILIS.*

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(Concluded from p. 667.)

IN Siegel's papers,^{2 3 4} in addition to the methods of staining and the description of the characters of his cytorhynchus luis, some details of previous discoveries in syphilis are given⁴—e.g., Klebs, Döhle, Stassano, &c.

Fr. Schultze,¹²⁹ Freund,¹³⁰ and Merk¹³¹ contribute papers on the cytorhynchus.

Spirochæta in yaws.—Castellani in Ceylon^{113 114 115} and Wellmann in Central Africa¹¹⁶ about the same time found spirochætæ in films from the cutaneous papules of yaws some of which in form correspond closely to those of syphilis. I have seen one of Castellani's preparations through the kindness of Dr. J. O. Wakelin Barratt. There is no question as to the great similarity to spirochæta pallida. Castellani will not draw any conclusions as to any possible relationship between yaws and syphilis, though in this connexion it is of interest that Mr. Jonathan Hutchinson¹³¹ holds in the face of great opposition that they are closely related, probably identical diseases.

Staining methods.—As I have indicated, Giemsa's method, or various modifications of it, is generally considered the best, but Leishman's modification of Romanowsky's stain also gives good results (Castellani,¹¹⁵ Dudgeon¹²²), while in the hands of Leishman himself it gives *better* results than Giemsa's stain. It must be acknowledged that the new Giemsa's stain, in containing methyl alcohol as a solvent, approximates to Leishman's stain which existed before it. Of Giemsa's new solution 15 cubic centimetres are added to 10 cubic centimetres of distilled water. The films which have been previously fixed in alcohol are stained for an hour at room temperature. The films may be

² THE LANCET, May 13th, 1905, p. 1259.

* The "superior," or raised, figures occurring throughout refer to the bibliography at the end of the article.