

the fact that the œdema was the consequence of a severe attack of measles in a previously healthy child and was due to the malnutrition produced by severe diarrhoea which developed as a sequel and which was sufficient to produce the condition after only three weeks' illness.

The treatment is general and symptomatic, but of special drugs digitalis seems the best. The pathology of the condition is not any better known than is that of renal œdema, but I suppose admits of the same explanation—viz., a weakening of the capillary walls so that they permit the transudation of serum into the subcutaneous tissue, but this does not satisfactorily account for the fact that in most cases it is the subcutaneous tissue only that is affected.

The only book in which I have found this condition thought worthy of separate treatment is that of Holt. Henoch refers to a case of the kind and Pilatow describes a case of "anasarque sans albuminurie" in a boy, five years of age. This also followed troublesome diarrhoea and anasarca developed rapidly, but recovery was complete in three weeks. Eustace Smith refers to dropsy without albuminuria, as do the few writers who mention it at all, under the heading of nephritis. I have seen several instances similar to that described and did not realise until I looked up the literature of the subject that so little was written about it.

## ROYAL DEVON AND EXETER HOSPITAL.

### A CASE OF ACUTE LYMPHATIC LEUKÆMIA.

(Under the care of Dr. W. GORDON.)

FOR the notes of the case we are indebted to Dr. R. V. Solly, pathologist to the hospital.

The patient, a female, aged 13 years, an Italian, was seen by Dr. W. Gordon on March 9th, 1906, in consultation with Dr. J. A. W. Pereira of Exeter. She was then complaining of considerable pain in her left side (splenic region) and in the calves of both legs. The pain in the left side began on March 2nd and the pains in the legs three days later. Previously to the 2nd she had been quite well. She had been menstruating since the 5th and most excessively. She looked very anæmic and ill. Her gums were somewhat swollen and had bled a little but there was no ulceration or sign of septic stomatitis. The spleen was enlarged and acutely tender. The calves of the legs were also very tender. There were enlarged and tender glands on both sides of the neck, in both axillæ, and in the groins, some of those in the neck being as large as a small hazel-nut. Her temperature was 102° F. The microscope showed a very remarkable increase of white corpuscles and a stained film showed these to be almost wholly lymphocytes. She was admitted into the Royal Devon and Exeter Hospital on March 10th.

On admission the patient's state was found to be as above. The tongue was dry, rather coated with brownish fur; the gums were pale but were not bleeding. The spleen projected three and a half inches below the ribs and was three and a half inches broad just below the edge of the ribs. It was acutely tender. Liver dulness began at the sixth rib in the mammary line, and measured five and a quarter inches vertically. Its edge was tender. There was also a good deal of tenderness over the ribs in front of the chest and over the calves of the legs. The heart's apex beat was situated in the fifth space, almost a quarter of an inch external to the left mammary line. There was a reduplicated first sound but no bruits were present (position recumbent). No optic neuritis was present.

A blood count by Dr. Solly on March 11th gave the following result: hæmoglobin, 60 per cent.; red corpuscles, 2,912,000 per cubic millimetre; white corpuscles, 796,000 per cubic millimetre; colour index, about 1. Differential count of leucocytes: polymorphonuclear, 1.6 per cent., or 12,736 per cubic millimetre; small lymphocytes, 11 per cent., or 87,560 per cubic millimetre; large lymphocytes, 86 per cent., or 684,560 per cubic millimetre; and large mononuclears, 1.4 per cent., or 11,144 per cubic millimetre (large hyaline). No eosinophiles were seen. There were a very few normoblasts present. No mast cells were seen. The small lymphocytes were like those in normal blood, with very little protoplasm, the nucleus being large and taking the basic stain very deeply. The large lymphocytes were of about the size of a polymorphonuclear as a rule, but some were a little larger and others rather smaller. They consisted of a very large nucleus, taking the basic stain less strongly than the small lymphocytes, and around this nucleus generally a ragged narrow rim of protoplasm, more deeply

basophile than the nucleus, but in others it was impossible to differentiate any protoplasm around the nucleus. The large mononuclears were like those found in normal blood and consisted of a rather faintly staining nucleus, round or kidney shaped, and abundant clear non-granular protoplasm. The stain employed was Leishman's. On March 12th a second blood count was made by another observer who found: red corpuscles, 2,368,000 per cubic millimetre; and white corpuscles, 848,000 per cubic millimetre.

The treatment employed was increasing doses of arsenic and the application of the x rays daily for ten minutes over the spleen. On March 11th slight epistaxis occurred, the menstrual period continuing. On the 13th the spleen was found to be only two and a half inches below the ribs and measured only three inches across, the liver dulness remaining the same. Both kidneys were easily felt, seeming to be somewhat enlarged. There was slight albuminuria. The patient was now free from pain and appeared generally better. The tonsils were noted to be much enlarged. On the 15th she was in a very excitable state, continually whining, although she said she was in no pain. The period still continued and there was bleeding from the gums. From this point she gradually became worse and died comatose on the 16th, the whole duration of her illness only being 14 days.

*Necropsy.*—At the post-mortem examination (which took place 17 hours after death) the body was found to be very anæmic but not emaciated. On opening the thorax the thymus was seen to be persistent. It was about three and a half inches long and one inch broad. On the surface of the heart were petechiæ and the muscle was very pale. The clots in the cavities of the heart were of a greyish-purple colour. The valves were normal. The lungs were pale but crepitant. The spleen weighed 26 ounces; it was rather soft and ecchymosed at its upper part. The liver weighed 3 pounds 2 ounces and was rather pale, fatty, and soft. Both kidneys were very pale. There were many nodules of about the size of a pea, of a pale yellow colour, scattered through the substance of both kidneys. There was no enlargement of the solitary or agminated intestinal glands. The uterus was normal but contained clot. The bronchial and mediastinal lymphatic glands were enlarged, soft, and hæmorrhagic and the glands in the neck and lumbar region were also enlarged. There was a large hæmorrhage situated in the white substance of the right frontal lobe of the brain and a smaller one in the white substance of the left parietal lobe. These hæmorrhages were evidently the immediate cause of death. The bone marrow of the femur was red and hæmorrhagic.

*Histological examination of organs.*—The bone marrow consisted almost entirely of large and small lymphocytes. A few myelocytes were seen, a fair number of normoblasts, and a few giant cells. As regards the kidney a section through the white nodules gave an extraordinary appearance. There was an enormous infiltration of lymphocytes, closely crowded together, and among them were seen remnants of the urinary tubules with the protoplasm of the cells, granular and much swollen. The glomeruli exhibited many lymphocytes in their substance, but it was difficult to say whether these were infiltrations or simply within the vessels. The liver cells were granular and separated from one another by lymphocytes. In parts were seen small accumulations which were evidently infiltrations similar, though of microscopical size, to those in the kidneys. The Malpighian corpuscles of the spleen were difficult to define as the whole pulp was densely infiltrated with lymphocytes. The lymphatic glands were not markedly altered from normal. The thymus and the tonsils both consisted of a network packed with lymphocytes. The lymphocytes in all these organs were mostly rather small and stained deeply and consisted apparently entirely of nucleus with no demonstrable protoplasm, but there were also present larger cells with a small amount of protoplasm round the nucleus, both protoplasm and nucleus taking the basic stain.

*Remarks by Dr. GORDON and Dr. SOLLY.*—The interest of the case depends in the first place on its extremely rapid course, rapid even for this disease, its entire duration, so far as can be reasonably determined, being only 14 days. In the next place a definite though very brief improvement took place under x ray treatment. Byrom Bramwell<sup>1</sup> has reported a case of lymphatic leukaemia treated by the x rays where there was a fall from 300,000 leucocytes per cubic millimetre to 80,000. In spite

<sup>1</sup> Edinburgh Medico-Chirurgical Society, THE LANCET, May 20th 1905, p. 1340.

of this there was no general improvement and a distinct inflammatory reaction took place over the spleen. In spleno-medullary leukaemia, however, great improvement has taken place under this treatment, both as regards the general state of the patient and also the blood and condition. The red cells and the hæmoglobin both increase and the white cells fall both as regards number and percentage of myelocytes. The spleen also shows marked shrinking in size. C. Melland,<sup>2</sup> W. Ironside Bruce,<sup>3</sup> and W. B. Ransom,<sup>4</sup> have all reported cases where this occurred and J. C. G. Ledingham<sup>5</sup> reports the same change but sounds a warning note as regards the danger of x-ray treatment, quoting Halber and Linser, who were able by prolonged application of the x rays to small animals completely to deplete the blood of leucocytes, the lymphoid cells being affected first.

The number of leucocytes, over 800,000, was certainly enormous but cases of acute lymphatic leukaemia have been reported where the number of leucocytes present have been 918,000 (R. C. Larabee<sup>6</sup>), 920,000 (Mitchell Stevens<sup>7</sup>), and 1,300,000 (J. G. Slade<sup>8</sup>). In this case the lymphatic glands, though enlarged, were not markedly changed and the main change had taken place in the kidneys which were studded with lymphoid nodules; in the spleen, where the pulp was hardly distinguishable from the Malpighian corpuscles; and in the bone marrow which consisted mainly of lymphoid tissue. This is interesting in the light of C. Melland's<sup>9</sup> paper contributing to the discussion on the rôle of the lymphocyte at the annual meeting of the British Medical Association in 1904, where he expresses the opinion that the large lymphocytes in the blood of acute lymphatic leukaemia are not true lymphocytes but retrograde myelocytes and a return to a more primitive and less differentiated form of cell and that both spleno-medullary and lymphatic leukaemia are myelogenous. D. G. Hall and F. G. Bushnell,<sup>10</sup> in an account they gave at the Pathological Society of a case of acute lymphocythæmia and a case of myeloid splenic anæmia, stated "that there was evidence that leucocytes and erythrocytes had a common ancestor in lymphoid cells, from which cell there was no doubt both granular and non-granular leucocytes were derived in the foetus. In the polymorphism of leucocytes of myelocythæmia might be seen the confirmation of this common origin of leucocytes, for all transitions existed between myelocytes, large lymphocytes, and polymorphonuclears in this disease." Cases of mixed cell leukaemia pointed in the same direction.

C. Melland in the paper quoted above gives photomicrographs of large lymphocytes, with a definite rim of protoplasm, just like those in our case, and also describes other large lymphocytes where a margin of neutrophile granules can be seen. There can be no doubt that these large lymphocytes which generally but not always predominate in cases of acute leukaemia are not normal constituents of the blood. Their fragility and peculiar morphological characters and staining reactions absolutely separate them from the large mononuclears of normal blood.

A. G. Phear<sup>11</sup> has reported a case of acute leukaemia where there were 19 per cent. of normal corpuscles and 81 per cent. of these large lymphocytes not normally found in the blood (327,000 per cubic millimetre). He also gives a very complete account of the histology of the affected organs (the liver, the spleen, the lymph glands, the tonsils, and the solitary glands of the large intestine) with excellent illustrations where the same large cells were seen. In his case, as in most cases of acute leukaemia, including ours, the thymus was persistent.

In Phear's case and in four cases reported by Rose Bradford and Batty Shaw in 1898<sup>12</sup> there were distinct ulceration of the gums and stomatitis, and Thomas McCrae<sup>13</sup> in reporting five cases of acute leukaemia states that in two of them there was distinct tonsillitis and that in one case streptococci, and in the other streptococci and staphylococci,

were isolated from the blood. These cases are certainly so acute that they have all the appearance of an acute septic infection.

## Medical Societies.

### ROYAL MEDICAL AND CHIRURGICAL SOCIETY.

#### *Mitral Stenosis and Pregnancy.*

A MEETING of this society was held on June 12th, Mr. J. WARRINGTON HAWARD, the President, being in the chair.

Dr. HERBERT S. FRENCH and Mr. H. T. HICKS communicated a paper on Mitral Stenosis and Pregnancy. They considered that the dangers of pregnancy in cases of mitral stenosis have been over-stated and attributed the over-statement to the fact that previous statistics had been based mainly upon cases of mitral stenosis which had come under observation because heart failure had developed during, or soon after, pregnancy. Statistics so obtained tended to leave out of count all those subjects of mitral stenosis who go through pregnancy without developing cardiac symptoms. They had endeavoured to obviate this source of error by analysing the obstetric histories of 300 women over 20 years of age who had mitral stenosis with or without other valvular lesions. The cases had not been selected but were consecutive in the records of Guy's Hospital. As a result of their study of these cases they concluded:—"1. That comparatively few are sterile. 2. That the majority bear children well. 3. That when heart failure develops in relation to pregnancy it is very often not with the first pregnancy but after several. 4. That the treatment should be the same as for non-pregnant cases of mitral stenosis. 5. That it is not just absolutely to negative marriage in all women with mitral stenosis. The dogmatic 'No' of Jellett and of Porak is unjustifiable. It is right that the physician should make clear to the engaged couple or to their near relatives the risk run. He should distinguish between one case and another. The risk should not be minimised but it should not be exaggerated. Whether the woman marry or not, it is likely that she will not reach old age; but if she has survived 20 with good cardiac compensation the likelihood that pregnancy will accelerate the time of heart failure does not seem to be so great as is stated in the most recent text-books."

Sir DYCE DUCKWORTH said that he had been in the habit of declaring that it was unwise for women with mitral stenosis to marry and, although the statistics brought forward by Dr. French and Mr. Hicks tended to show that the risk was not so great as had generally been accepted, he did not feel inclined to alter his practice. He referred to the tendency of rheumatic subjects to propagate their proclivity towards the disease.

Dr. G. E. HERMAN thought that the risk encountered in marriage and pregnancy had been much exaggerated but that there was a distinct liability to cardiac failure during the last two months of pregnancy. Induction of labour was useful in such cases.

Mr. J. T. GARDNER said that he had been in the habit of regarding mitral stenosis in its relation to pregnancy as by no means a serious matter. With regard to the question of sterility statistics had been vitiated by the avoidance of pregnancy on the grounds that it was likely to prove dangerous to life.

Dr. C. C. GIBBES agreed in thinking that the danger of pregnancy to subjects of mitral stenosis had been over-estimated. He had seen the occurrence of pregnancy help in promoting cardiac compensation.

Dr. F. J. POYNTON gave statistics showing the greater frequency of rheumatism and of mitral stenosis in females as compared with males and explained how the mortality amongst the males was greater both during childhood and adult life. He considered that pregnancy rendered a woman subject to virulent forms of endocarditis and to severe attacks of chorea. The same tendency was observed in the inoculation of animals in a pregnant condition.

Dr. W. F. V. BONNEY referred to three cases of malignant endocarditis occurring as the result of puerperal sepsis in which the organism concerned was the ordinary streptococcus pyogenes.

Dr. W. S. A. GRIFFITH was disinclined to underrate the

<sup>2</sup> Brit. Med. Jour., July 1st, 1905.

<sup>3</sup> THE LANCET, Jan. 27th, 1906, p. 211.

<sup>4</sup> Nottingham Medico-Chirurgical Society, THE LANCET, Feb. 17th, 1906.

<sup>5</sup> THE LANCET, Feb. 10th, 1906, p. 366.

<sup>6</sup> Boston Medical and Surgical Journal, THE LANCET, April 1st, 1905, p. 873.

<sup>7</sup> THE LANCET, Jan. 21st, 1905, p. 153.

<sup>8</sup> Clinical Society, THE LANCET, March 4th, 1905, p. 572.

<sup>9</sup> Brit. Med. Jour., September, 1904.

<sup>10</sup> Pathological Society, THE LANCET, Feb. 24th, 1906, p. 518.

<sup>11</sup> Transactions of the Royal Medical and Chirurgical Society, 1901.

<sup>12</sup> Transactions of the Royal Medical and Chirurgical Society, 1893.

<sup>13</sup> Brit. Med. Jour., Feb. 25th, 1905.