On examination of the abdomen I found the right kidney freely movable, it could be pushed well beyond the middle line in front and down into the pelvis, and upwards under the ribs, but when it was once reduced to its normal position it remained there, and could not be readily disturbed unless the patient walked about for some time. Deep inspiration sometimes forced it downwards, and then it would suddenly shoot from the margin of the thorax towards the umbilicus. On palpation the whole organ could easily be caught up in the hand and its form traced. The kidney was unusually firm, a little smaller than normal, and the slightest pressure of the hand caused sickening pain. So long as it was not pushed under the costal margin it could be rolled from side to side freely, and very often suddenly slipped out of the hand in a downward direction. The percussion over the kidney gave a dull, tympanitic sound, and in the loin, whether the kidney was replaced or not, there was a deficiency of resistance compared with the opposite side.

Operation and Result.

On June 18th the ordinary incision was made through the parietes in the lumbar region, but the kidney could not be found in its normal position, and when pressed up to the depth of the wound by the hand it was found that in order to reach the organ the peritoneum required to be opened. On opening the peritoneum a careful examination was made, when the kidney was found to have a distinct mesonephron, and showed the organ was surrounded by peritoneum on all sides. An incision was made through the peritoneal layer covering the kidney, the fibrous capsule was split, and the kidney parenchyma brought in position to the edges of the parietal wound. There was no fatty capsule. Four sutures were inserted into the kidney and the depth of the wound packed with iodoform gauze. The patient made an uninterrupted recovery, gained rapidly in strength, the appetite rapidly increased, and she was dismissed from the Sandford Home on August 10th.

Dr. Petrie, writing to me on October 1st, says "that since the patient returned home she has gradually improved, is sleeping better than she has done for years, and the right kidney seems securely anchored. She is looking altogether healthier and plumper, and is able to take a short walk daily without discomfort."

A CASE OF LEUKANAEMIA

WITH GREAT HYPERPLASIA OF THE SPLEEN AND PREVERTEBRAL HAEMOLYMPH GLANDS AND WITH INCREASE OF CONNECTIVE TISSUE IN THE BONE MARROW.*

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By leukaemia (W. Von Leube¹) I understand a morbid condition in which clinical symptoms found in pernicious anaemia are combined with blood changes and anatomical changes in the organs characteristic of leukaemia or pseudo-leukaemia, whether of the "lymphocytic" or "mixed-cell" type. The present case seems to combine certain features of pernicious anaemia with those of a "mixed-cell" pseudo-leukaemia. I intend first to give an account of the case, including the anatomical-pathological findings, and then to draw what conclusions I can as to its pathological nature.

The patient, P. von E., a German, aged 58 years, was admitted under my care at the German Hospital on December 10th, 1903, suffering from great anaemia, progressive weakness, anorexia, and tinnitus.

History.

The history was that he had enjoyed fairly good health till twelve months ago. In fact he seems to have been able to insure his life about one year before admission. The symptoms of his illness, wax-like pallor and weakness, with anorexia, commenced about that time—that is to say, about the end of 1902; but at first there seems to have been improvement under treatment.

He had never suffered from malaria or been out of Europe. He had lived in England since 1865. He had had attacks of gonorrhoea, and in 1868 had had a chancre, but apparently without any signs of secondary syphilis. He had never had any kind of haemorrhage.

Condition after Admission, in December, 1903.

The patient is somewhat fat, flabby, and very pale. His faint-yellowish wax-like pallor and puffy appearance are such as Addison described in pernicious anaemia. There is no evidence of anything abnormal in the heart or lungs, excepting a soft systolic murmur at the cardiac apex, and a few crepitations at the base of the left lung. The liver and spleen are greatly and uniformly enlarged. The hepatic dullness commences above at the sixth rib in the right nipple line, and in the same line the lower edge can be felt at the umbilical level. The splenic dullness commences above at the eighth rib in the left axillary line, and the organ is so enormously enlarged that its lower edge can be felt in the hypogastrium below the level of the anterior superior iliac spine, and in the front of the abdomen its right margin is felt considerably to the right of the navel. No distinct ascites. Some oedema of lower extremities and loins. Urine, of specific gravity 1016, free from albumen and sugar (see later note). Bowels open regularly. No vomiting. No cough. Pulse about 88 per minute, regular. Radial arteries somewhat thickened.

* Microscopic preparations were shown at the Pathological Society, on May 17th when the paper was accepted as read.

After-history.

In spite of treatment, the patient steadily lost strength. The oedema increased and became very noticeable in the face. At last he hardly had strength to swallow, and died quietly early on January 15th, 1904.

There was slight fever (about 100°F.) during the first days in the hospital, but afterwards the temperature seldom rose above 99°F. The pulse, as recorded on the chart during the last days of life, varied between 76 and 96 per minute.

The urine was of specific gravity 1014 to 1020, pale, acid, and free from albumen and sugar. On only two occasions was a lower specific gravity noted, and on only two occasions was a trace of albumen detected. The amount of urine was at one time below the normal, but during the last period reached about 1,800 c.cm. per diem.

The Blood.—On admission (Dr. Camptche, December 11th, 1903), the red corpuscles numbered 1,800,000, and the white cells 3,000 per cubic millimetre, the haemoglobin was 25 to 30 per cent. of the normal, and there was a good deal of poikilocytosis. The following differential count of the white corpuscles was made by Dr. G. L. Eastes, January 7th, 1904:—Small lymphocytes 49.4 per cent., large lymphocytes 9.6 (total lymphocytes 59.0), polymorphonuclear leucocytes 37.5, eosinophile leucocytes 0.5; myelocytes, 3.0; no eosinophile myelocytes. During the count of 400 white cells, 30 erythroblasts (24 normoblasts, 2 microblasts and 4 megaloblasts) were seen. There was poikilocytosis and polychromatism (neither extreme) and likewise leucopenia. On January 14th (the day before death) a rough blood count was made, the red corpuscles being estimated as about 1,200,000 the white cells as about 12,000 in the cubic millimetre, and the haemoglobin richness as about 25 per cent. of the normal. During the last days of life, therefore, the number of white cells appears to have considerably increased.

Necropsy (January 15th, 1904).

Brain.—Examination not permitted.

Thorax.—The heart showed nothing noteworthy, and weighed 11 oz. (312 grams). There were some pleuritic adhesions over part of the left lung and great hypostatic congestion of the left lower lobe, but otherwise the lungs appeared free from disease. There was a moderate amount of serous fluid in the pericardium and both pleurae.

Abdomen.—There were many small peritoneal petechiae.

The spleen was enormously enlarged, weighed 66 oz. (1,872 grams), and its capsule was slightly thickened. On section the splenic substance appeared normal to naked-eye examination, excepting that it contained one pale nodule below the capsule, of about the size of a large cherry, which subsequent microscopic examination showed to be an infarct.

The liver was uniformly enlarged and weighed 88 oz. (2,496 grams), but to naked-eye examination showed no cirrhosis or other distinct structural changes.

The kidneys were of normal size and weighed together about 10 oz. (256 grams). The cortical substance was not diminished and the capsules stripped fairly well. At one or two spots below the capsules there was slight increase of connective tissue (that is, by subsequent microscopic examination). The right kidney contained a few small cysts. In the left kidney was a minute cystic papillary adenoma, with the remains of a haemorrhage into it.

Nothing abnormal was found by naked-eye examination in the pancreas, suprarenal glands, stomach, or intestines excepting a few small petechiae in the gastric mucosa.

The lymphatic glands generally were not obviously enlarged, but the prevertebral tissue about the bifurcation of the aorta was studded with small red haemolymph nodes. Most of these were small and oval in shape, about 3 mm. by 4 mm., but their sizes varied and some were much bigger (10 mm. by 20 mm. or so), and some alongside of the aorta, owing to their elongated shape, or because they lay close together end to end, might almost be compared to leeches² in appearance.

Bone Marrow.—The left humerus was sawn through longitudinally, and the whole of the fatty marrow of the shaft was found to have undergone transformation into a red substance (red metaplasia) of unusually firm consistence. Owing to the markedly firm texture of this bone marrow no good films were obtained for microscopic examination. (For the examination, however, of microscopic sections see later.)

MICROSCOPIC EXAMINATION.

Sections were stained with eosin and haematoxylin, and haematoxylin alone, and by Ehrlich's triacid stain, Mann's long eosin-methyl-blue method, and by some other blood stains.

The bone marrow (from the shaft of the left humerus) was almost destitute of the normal fat vesicles. It showed a stroma of a kind of loose connective tissue containing blood, myelocytes, non-granular large mononuclear cells³, and abundance of erythroblasts. The erythroblasts, conspicuous by their deeply and almost homogeneously stained nuclei, were not uniformly distributed, but, as usual, occurred here and there in greater numbers, that is, in clusters. They were of various sizes, some large, some small, but mostly of medium size (normoblasts). Many of them possessed more than one nucleus or a partially divided nucleus, and often the nucleus appeared to have been split up into many fragments or droplets. There were likewise a good many giant cells in the bone marrow, and a few coarsely granular eosinophile cells were seen. The fibrous stroma was best seen in a portion of

bone marrow which was paler than the rest, and contained less blood. In this portion (see Fig. 1) the bone marrow had

Fig. 1.—Illustrating the connective-tissue change in a portion of the bone marrow. The nuclei and fragments of nuclei of erythroblasts are represented by deep black dots. $\times 220$.

been practically converted into a kind of loose connective tissue containing conspicuous groups of erythroblasts. I regard this connective tissue change in the bone marrow as one of the most remarkable features in the case.

The Liver.—Microscopic examination revealed a very remarkable condition, which, however, was not equally well-marked in all parts of the organ. The columns of hepatic cells were separated and seemed to be pressed on by groups of cells which on the whole were similar to those described later on as forming peculiar "clumps" in the spleen. The groups of cells which thus separated the columns of hepatic cells, were chiefly composed of myelocytes, non-granular large mononuclear cells and erythroblasts (or the nuclei only of erythroblasts), but scattered about here and there were likewise coarsely granular eosinophile cells, and (in some parts) giant cells. The presence of these giant cells in some sections of the liver (they were not found in the spleen) formed one of the conspicuous features of the case (see Fig. 2). The cell accumulations just described occupied the

Fig. 2.—From a section of the liver, showing erythroblasts (their nuclei and fragments of nuclei are represented by deep black dots), giant cells, and white corpuscles accumulated together in an irregular space between the hepatic cells. $\times 220$.

positions normally occupied by the intra-acinous hepatic capillaries. In some places the cells seemed to be actually within the walls of capillaries, but in other places they seemed to form regular "growths," and that they could not have been in the circulating blood stream at the time of death is proved not only by the examination of the blood shortly before the patient's death, but also by the appearance of the blood as seen in rather larger blood vessels in the microscopic sections. Moreover, no similar accumulations of cells were present in or about the capillaries of the pancreas and liver. It is difficult to imagine how the circulation in the liver could have been carried on during life, seeing that the spaces normally occupied by the hepatic capillaries were stuffed by the cell accumulations of which I have been speaking. This difficulty was especially noted by Mr. S. G. Shattock, whom I have to thank for kindly looking through

the microscopic preparations of the case with me. It must be remembered, however, as I have already stated, that not all parts of the liver were affected to the same extent.

The Spleen.—In regard to the small infarct, I need not add anything to what I stated in the account of the necropsy. The Malpighian corpuscles (and the lymphocytes in them) appeared normal. The splenic pulp, however, was permeated with erythroblasts and mononuclear cells similar to those found between the columns of hepatic cells. Here and there were coarsely granular eosinophile cells. All these kinds of cells were fairly equally distributed throughout the splenic pulp, just like the red blood corpuscles were, excepting at certain spots where they occurred, without admixture of erythrocytes, crowded together in dense circular or elongated clumps. Some of these "clumps" were evidently within splenic capillaries and blood sinuses (see Fig. 3) whilst others appeared to be filling up mere clefts in the splenic stroma.

Fig. 3.—From a portion of the splenic pulp showing erythroblasts (deep black nuclei) and other cells (nuclei only represented) occupying a splenic capillary and sinus. To the left of the capillary is one of the small "clumps" referred to in the text. Red corpuscles are only faintly indicated. $\times 220$.

The sections of the kidneys showed nothing noteworthy beyond what has already been mentioned. The pancreas appeared not to be diseased. The haemolymph glands resembled lymph glands in structure excepting for the presence of blood in the sinuses. Besides lymphocytes and erythrocytes they contained erythroblasts and large mononuclear cells apparently similar to those permeating the splenic pulp; also a few coarsely granular eosinophile cells and a few giant cells.

Sections of the different organs were also stained with methyl-violet for amyloid changes, but with negative result. Microchemical tests failed to show the presence of free iron in sections of the spleen, liver, and kidney.⁴

REMARKS.

The main features of the case may be summed up as follows:—

1. Progressive waxy pallor and asthenia with maintenance of subcutaneous fat.
2. Changes in the red blood corpuscles rather similar to, but not so extreme as, those met with in true pernicious anaemia.
3. Absence of true leukaemic changes in the blood, but presence of slight myelocythaemia and presence of the inverted proportion of lymphocytes to polymorphonuclears which is found in cases of lymphatic pseudoleukaemia (Hodgkin's disease, etc.).
4. No abnormal amount of pigment in the urine.
5. Changes found after death in the haemopoietic tissues similar to those which occur in cases of "mixed-cell" leukaemia or pseudoleukaemia.
6. Abnormally firm consistence and increase of connective tissue in the bone marrow from the shaft of a long bone.
7. Absence of enlargement of the ordinary lymph glands, but great hyperplasia of the spleen (haemal gland) and pre-vertebral haemolymph glands.
8. Absence of any reaction in sections of the spleen, liver, and kidneys for free iron such as is found in pernicious anaemia.

Charcot-Leyden crystals were not noticed in the bone marrow, etc., but were not specially looked for.

In spite of the poikilocytosis the disease in the present case

seems not to have been secondary to any excessive haemolysis, but to have been primary in the bone marrow, and I would regard it as a myelogenic form of splenic anaemia of adults, doubtless allied to what French authors have termed "anémie splénique myéloïde." Therefore the case cannot be adduced as an example of pernicious anaemia being followed by or becoming transformed into leukaemia, though it is probable that similar cases have been erroneously supposed to illustrate such a course of events. It is also highly probable that similar cases, owing to enlargement of spleen and liver, have been clinically regarded (in spite of the poikilocytosis) as examples of Banti's disease.

In the German cases, I believe, enlargement of haemolymph glands was not noted.

It is very tempting to suggest that in the present case both the spleen (haemal gland) and the prevertebral haemolymph glands were actively engaged in supplementing the erythrocyte-forming functions of the diseased bone marrow, but I have no conclusive evidence to support such a supposition. From what has been lately written on the subject⁶ it seems that no really satisfactory evidence has been brought forward to show that in adults erythrocytes are produced in the spleen and haemolymph glands either in health or in disease.

NOTES AND REFERENCES.

¹ W. von. Leube, *Deutsche Klinik*, Berlin, 1902, No. 42; and J. Arneith's haematological account of Leube's case in *Deut. Arch. für klin. Med.*, Leipzig, 1901, vol. lxxix, p. 331; also H. Luce, "Ueber Leukanämie," *Deut. Arch. für klin. Med.*, Leipzig, 1903, vol. lxxvii, p. 215. "Leukanæmia" is obviously a term coined out of "leukaemia" and "anaemia," and will, I believe, be found well suited as a clinical term for the present class of cases. ² This comparison of the appearance of very long prevertebral haemolymph glands to leeches has been borrowed from Dr. H. D. Rolleston. ³ I do not use the term "large mononuclear cell" in the limited special sense often attached to it. ⁴ No Prussian blue reaction was obtained by the "long" method employed by Abbott for pieces of tissue which had been lying in formalin (*Vide Trans. Path. Soc. London*, 1900, vol. li, p. 76). ⁵ *Vide* Vaquez and Aubertin, "Nature de l'Anémie Splénique Myéloïde," *Société de Biologie*, Paris, May 14th, 1904. ⁶ See especially "The Pathology of Pernicious Anaemia with special reference to the changes occurring in the Haemolymph Nodes," by Dr. A. S. Warthin, *American Journ. Med. Sci.*, 1902, vol. cxxiv, p. 674.

NOTE ON THE ANTI-HAEMOLYTIC (HAEMOSOZIC) PROPERTIES OF NORMAL URINE.

BY

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NORMAL aseptic human urine does not, as a rule, dissolve human red blood corpuscles, even when the mixture of urine and red blood corpuscles is kept for many days at the temperature of the room (20° C. to 30° C.). The red blood corpuscles of many pathological urines also sink to the bottom of the vessel and often remain apparently intact, even when no care is taken to secure the asepticity of the urine. In a previous paper we showed the serum of rabbits which had received injection of human urine dissolved human red blood corpuscles in vitro.

We were thus led to inquire whether normal urine contained an antihaemolytic (haemosozic) substance neutralizing the haemolysins present in the sera of animals previously injected with urine.

Experiments showed that a serum markedly haemolytic for sheep's red blood corpuscles is obtained by injecting sheep's urine into rabbits, and that the injection of the urine of the ox produces serum haemolytic for the red corpuscles of the ox. Miss B. Sheldon Amos, working in this laboratory, has found that the injection of small doses of urine produces marked changes in the composition of the blood, and that, occasionally, the injection of so small a quantity as 2 c.cm. of normal urine into a rabbit causes the serum of that animal to become haemolytic.

In connexion with these experiments, it must be remembered that rabbit's serum always dissolves to some extent sheep's red blood corpuscles, and less frequently it haemolyses slightly those of man.

In order to demonstrate the haemosozic property of normal urine, we mixed a given quantity of human red blood corpuscles, previously washed twice in normal salt solution and centrifugalized, with a given quantity of haemolytic serum. In another tube, we added to a similar mixture a certain quantity of freshly passed normal urine. In order to avoid errors

due to greater or lesser dilution, physiological salt solution or normal rabbit's serum was added whenever necessary, so that each tube contained exactly the same quantity of fluid. The following experiment may serve as an example.

EXPERIMENT.—Rabbit (No. 23) received on the first, fifth, and tenth days 3 c.cm. of normal human urine (total 9 c.cm.). The serum was found haemolytic for human corpuscles. The serum of this animal we call Serum 23.

	Serum 23.	Serum normal (rabbit).	Human urine.	Red corpuscles (human).	Result.
Tube I.....	20 drops	o	20 drops	2 drops	+ in 18 hours
" II. ...	20 "	20 drops	o	2 "	++++ "
" III....	10 "	o	30 drops	2 "	∞
" IV....	10 "	30 drops	o	2 "	+++ in 18 hours

(N.B. +++ means complete haemolysis. + means slight haemolysis: that is, red corpuscles remain undissolved at the bottom of the tube, the supernatant serum being slightly tinged with haemoglobin. ++ and +++ are immediate stages. ∞ indicates that no haemolysis has taken place.)

Haemolysis, therefore, was only very slight or totally absent in the tubes to which urine had been added.

Similar experiments made with various samples of haemolytic sera (produced by the injections of urine) always gave the same results.

The haemosozic property of the urine of the same individual varies, for whereas 20 drops of urine passed by one individual at 9 a.m. may prevent the haemolysis of a given quantity of haemolytic serum, the same quantity of urine of the same man passed at 11 a.m. may no longer prevent the haemolysis of the same serum, though all the other conditions of the experiment remain the same.

The red corpuscles remaining in contact for some hours with urine, when removed from the medium, washed and suspended in haemolytic serum are haemolysed just like those which have never been in contact with urine, and the urine in which such corpuscles have been suspended for two or more hours loses none of its haemosozic properties. The red corpuscles, therefore, do not absorb in that time any haemosozic substance present in urine. The haemosozic substance or substances have not been isolated from the urine, but the following properties have been ascertained.

First, the haemosozin is practically destroyed by heating to 120° C. or to 100° C for 30 minutes.

Secondly, the haemosozin is precipitated almost completely by absolute alcohol, but a slight quantity of haemosozic substance is always found in the filtrate. One may argue, either that the haemosozin is slightly soluble in alcohol, or that there are two haemosozins one of which is soluble in alcohol, and the other is not.

Thirdly, the haemosozin is precipitated almost entirely by saturating the urine with ammonium sulphate. The precipitate dialysed until it is entirely free from salts has marked haemosozic properties.

THE DETERIORATION OF VISION DURING SCHOOL LIFE.*

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THERE are nearly a million children attending the Board schools in London and such a large number of these had obvious defects of vision that two years ago the Board decided thoroughly to investigate the condition of the children's eyesight. The children in our schools are divided into three departments:

1. Boys between 8 and 14 years of age.
2. Girls " 8 " 14 "
3. Infants " 4 " 8 of both sexes.

The work was carried out on purely scientific principles. A child was taken to have normal vision who distinguished objects subtending an angle of one minute, this being determined by the ability to recognize letters 9 millimetres square from a distance of six metres. Only children in the boys' and girls' departments were to be included in the test, and it may

* Paper read at the International Congress of School Hygiene at Nuremberg, 1904.