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A REPORT OF CASES OF ANÆMIA, WITH OBSERVATIONS UPON THEIR SYMPTOMS AND MORPHOLOGY OF THE BLOOD.

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I DESIRE to report the following cases, which occurred during the past winter in my service at the Pennsylvania Hospital:

Severe Secondary Anæmia Due to Repeated Metrorrhagia. Lizzie R., aged thirty years, white, married, housewife, born in Russia. Father died from unknown cause; mother died in confinement; has one sister in good health; lost one brother in childhood.

Past History. Has been a healthy woman. Has one child, aged seven years. Ten weeks after the birth of this child an infected right ovary was removed. Menstruation since this operation has been regular. After the operation she never recovered her former color. The present illness began two weeks ago, with constant but rather scanty bleeding from the vagina. She has had slight nose-bleed, with pain in the abdomen, headache, dizziness, ringing in the ears, and slight cough. She states that she has become very pale during this time. Bowels are constipated.

Admitted to the Pennsylvania Hospital March 5, 1902 (hospital No. 4014).

Physical Examination. She is a well-nourished woman. Face seems puffy; pupils equally dilated. Face and skin pallid, not lemon-tinted; mucous membranes and nails practically colorless. The radial pulse quick, of fair volume, and very compressible. Tongue pale, moist, with rather thick, yellowish coat; no venous phenomena. The lungs are normal. Visible cardiac impulse in the fourth interspace, 10 cm. from mid-sternum. On auscultation, a soft, blowing, systolic murmur, best heard in the third interspace, and also present at the pulmonary cartilage. Abdomen round, globular; nowhere tender. Liver and spleen normal in size. Vaginal examination: Neither ovary is felt; the cervix is rather soft, the uterus slightly increased in size. A small amount of dark brown vaginal discharge is present. The urine: Specific gravity 1014; acid; contains neither albumin nor sugar, and no casts. The blood showed: Erythrocytes, 910,000; leucocytes, 5300; hæmoglobin, 17 per cent. The differential count showed: Polynuclears, 80 per cent.; small lymphocytes, 13.6 per cent.; transitionals and mononuclears, 2 per cent.; eosinophiles, 4 per cent.; unidentified cells, 4 per cent. The unidentified cells are polynuclears without granules, and pale staining nuclei. The corpuscles are unusually small; show no polychromatophilia; no megaloblasts found. Three normoblasts were found during the examination of several slides. The patient had a temperature on admission of 100.2° F., which rose to 102° F. the following day. During the next seven days it gradually fell to normal.

She was put upon peptomangan, $\frac{1}{2}$ ounce four times a day, with Fowler's solution, 3 drops, and adrenal extract, 1 grain, three times a day. She was given a fluid diet and 4 ounces of gelatin, twice a day. Her improvement in a week's time was remarkable, the blood count rapidly rising—erythrocytes, 2,630,000; leucocytes, 4600; hæmoglobin, 35 per cent. During this stage the differential count showed a slight diminution in the polynuclear leucocytes, with an increase in the small lymphocytes. One week later the erythrocytes had risen to 3,392,000; leucocytes, 3800; hæmoglobin, 62 per cent. Since her admission to the hospital there has been no evidence whatever of uterine hemorrhage or bleeding from any other source. She complains mainly of headache, thirst, and vague abdominal pains. Discharged at her own request on the 22d of March.

This case shows the rapid and severe anæmia induced by repeated small hemorrhages. The woman, who was rather a plump specimen, appeared as white as alabaster. Blood examination did not show the leucocytosis which is common after losses of large amounts of blood.

During convalescence the number of lymphocytes and normoblasts was not disproportionate, as some observers have noted; nor was there marked change in the size or form of the red cells.

Severe Secondary Anæmia, Cause not Ascertained, followed by Relapse and Death. Adolph K., aged fifty-four years, white, married, born in Germany. Family history not important.

Previous History. Healthy man; no severe sickness in life, no venereal disease; used beer very moderately. Present illness began several months ago with increasing pallor and weakness, shortness of breath, and swelling of the feet. This pallor was preceded by a diarrhoea of several weeks' duration. He was admitted to the hospital on October 24th (hospital No. 2132).

Physical Examination. He is a large-boned, fairly well-nourished man. Rather waxy appearance on face and skin, not lemon-colored. Sclera pearly; mucous membranes and nails very pallid; no pigmentation of skin. Comparatively few teeth remain in either jaw; gums shrunken, not ulcerated. Lungs normal. Heart normal except hæmic murmur at apex. The abdomen negative, with the liver and spleen normal in size. Slight œdema present on the dorsum of the feet and over the tibia. Blood: Hæmoglobin, 25 per cent.; erythrocytes, 2,380,000; leucocytes, 6500; differential count 250: polynuclears, 76 per cent.; small lymphocytes, 16.8 per cent.; transitional and large mononuclears, 5.4 per cent.; eosinophiles, 8 per cent. The urine was normal in color; negative on chemical and microscopic examination. Examination of the stools revealed no intestinal parasites or eggs. Examination of a test-meal showed: Hydrochloric acid, 2 per cent.; total acidity, 40 per cent.; no lactic acid; pepsin present.

He remained in the hospital fifty-eight days, with a rather rapidly increasing red count. Thus by October 29th the erythrocytes were 3,987,000, the leucocytes 8650, with hæmoglobin 43 per cent. At this time there was a decided increase in the small lymphocytes, which reached 22 per cent., while the polynuclears dropped to 64 per cent. This blood state was not constant, for before his discharge the mononuclears again dropped to 11.6 per cent., the polynuclears rising to 76 per cent. He was permitted to return to his home on November 20th, with an erythrocyte count of 4,443,750, and a hæmoglobin percentage of only 50.

The improvement in this case was extremely rapid. He gained in color and in strength under the use of Bland's pills. His blood showed but moderate poikilocytosis, with no macrocytes, while microcytes and elongated forms were fairly numerous. No nucleated reds were found, nor was there adequate cause ever discovered for the intense anæmia. The diarrhoea which was present two months before admission may have been its basis, though there was no evidence of blood in his stools at any time during his stay in the hospital.

I learn as I write these notes that he was admitted within a few days to the wards of my colleague, Dr. Lewis, having had a relapse, which began about February. His blood count upon readmission was: Hæmoglobin, 17 per cent.; erythrocytes, 2,140,000; leucocytes, 8600. He was extremely weak. In a few days the hæmoglobin had dropped to 13 per cent., with erythrocytes to 1,836,000. The eyes, examined by Dr. Harlan, show fields very pale, bloodvessels pale, almost invisible,

but no hemorrhages. The patient was permitted to leave the hospital because of extreme homesickness, and I learn he died twenty-four hours later. The differential count in this case at this time showed a slight polynuclear excess—80 per cent.; no nucleated reds were found.

It is possible that this case may exemplify a severe type of secondary anæmia which rapidly became pernicious.

Secondary Anæmia Due to Cancer of the Stomach. Margaret H., white, aged fifty-six years, domestic; mother of two children; no obtainable family history. Was at work one week before admission. Three weeks before admission is said to have had trouble with her stomach for several days, compelling her to stop work. Admitted to the hospital February 1, 1902 (hospital No. 3603).

Physical Examination. A small, rather stocky woman, somewhat irrational. Very few teeth in either jaw; no ulceration of gums. Face and body rather lemon-yellow in color; the mucous membranes and nails colorless. Pulse small, rapid, compressible. One or two small, bluish discolorations upon the arm; no evidence of hemorrhage elsewhere either in the mucous membranes or the skin. Lungs normal. Heart: systolic apical murmur. Abdomen soft; no mass palpable; wines somewhat on palpation in the epigastric region. No enlarged superficial lymphatic glands. Urine light yellow; contains no albumin or sugar. Blood: Hæmoglobin, 20 per cent.; erythrocytes, 1,000,000; leucocytes, 18,000. Differential count: Decided polynuclear excess, 90 per cent.; moderate poikilocytosis present; numerous nucleated reds; 125 seen in counting 50,000 leucocytes, mostly normoblasts.

In twenty-four hours the patient was decidedly worse; semiconscious; had vomited material, which, unfortunately, was not seen by the resident. Pulse imperceptible, though the heart continued to beat for twenty-four hours longer. Died February 4th. Autopsy showed a small colloid cancer, about 8 cm. in diameter, infiltrating the posterior wall of the stomach near the lesser curvature. There was slight involvement of the lymphatic glands behind the stomach and the head of the pancreas.

This case shows how numerous nucleated red cells may become in the peripheral blood in secondary anæmia. Had this woman been conscious, and had an examination of the gastric contents been feasible, the diagnosis of carcinoma would have been made with some certainty. In pernicious anæmia a terminal leucocytosis is common. The fact, however, that the majority of nucleated cells were normoblasts is an important factor in the diagnosis between the secondary anæmia due to cancer and pernicious anæmia. The cancer here was small and quite recent, and was probably not entirely responsible for the very severe grade of anæmia present in this case; in fact, these cases at times show the typical blood picture of pernicious anæmia.

Chlorosis, with Frequent Relapse and Obstinate Cardiac Symptoms. Maggie M., aged nineteen years, white, single, born in Ireland. Family history good, though one sister is said to be anæmic.

Past History. Menstruated at sixteen years; came to the United States when seventeen. Since arrival here has menstruated but four times. One year ago spent nine weeks in the University Hospital, with illness similar to present one; discharged much improved. Present illness: Sick for six months with headache, pain in both ovarian regions, weakness and shortness of breath on exertion. She has become very pale, and complains of pain in the eyes, left side of the face, in the abdomen, and left arm. Is very nervous, with poor appetite; has a decided fondness for candy and tea. Admitted to the hospital February 9th (hospital No. 3669).

Physical Examination. Rather huxom but pallid Irish girl. Mucous membranes pale; tongue coated; pulse regular, rather full and bounding. Lungs normal. Heart overacts, with loud, booming first sound and systolic murmur at the base. Increase in size of the left side. Liver and spleen normal in size. Abdomen soft and flat; no gastroptosis. Vaginal examination reveals an unusually small, infantile uterus. Pelvis negative. Urine light yellow, acid; specific gravity, 1027; no albumin, no sugar; calcium oxalate. Blood: Hæmoglobin, 33 per cent.; erythrocytes, 2,947,000; leucocytes, 7000; differential count: polynuclears, 71.5 per cent.; small lymphocytes, 18.5 per cent.; large mononuclears and transitionals, 7 per cent.; eosinophiles, 2 per cent.; mastzellen, 1 per cent. Blood cells are small and pale, with large central, non-staining portion. Moderate poikilocytosis; no polychromatophilia. Under forced diet, with large doses of Bland's pills, combined with Fowler's solution and phosphate of soda as a purge, her blood condition improved slowly. On March 7th, hæmoglobin, 52 per cent.; erythrocytes, 4,279,000. On May 9th, hæmoglobin, 60 per cent.; erythrocytes 4,388,000. During all this time, however, the girl's heart would overact upon the slightest provocation. She complained constantly of smothering sensations about the heart, with palpitation. The use of purges to deplete the volume of blood; of local applications, such as the ice-bag over the heart; the use of bromides internally, seemed to be of no avail whatever, and she left the hospital with a greatly improved blood condition, although still complaining of vague pains and suffering with palpitation of the heart from the slightest cause.

This case presents a combination of causes, one of which seems alone able to produce chlorosis. Thus the disease is seen most frequently in girls about the menstrual developmental period; nostalgia is a frequent aid in its production. Dietetic errors—the abuse of tea, toast, and candy as habitual diet—are frequently met with. Its exact pathological basis is, however, difficult to find. Virchow's postulate—a hypoplasia of the heart, bloodvessels, and generative organs—will not hold, for many such conditions are found and no chlorosis exists. Hoffmann's and Sir Andrew Clark's view that absorption of toxins from the intestinal canal is the exciting cause does not cover all cases. It probably is to be found in the functional derangement in the hæmoglobin manufacturing process of the bone-marrow.

Lloyd Jones also believes that the total volume of plasma is much

increased in chlorosis. This will answer for the symptoms present in the above case—the palpitating, dilated heart, with throbbing vessels.

Acute Progressive Pernicious Anæmia; Death; Autopsy. Maggie J., aged thirty-two years, white, married, housewife by occupation; born in Philadelphia. Family history: Father died with asthma and mother of uterine hemorrhage; three brothers died in infancy, from unknown causes.

Past History. Measles in childhood; blindness of the right eye (phthisical eye). When fifteen years of age was severely burned over the back and chest and portion of the abdomen; was eight months in recovering. Has had seven children, five of whom are living, in good health. She states that before each child was born the skin became yellowish in color, and "the jaundice" disappeared after childbirth. Present illness began three months ago, a short time prior to the birth of her last child, which was born early in February, 1902. She complained of heartburn, with vomiting and constant eructation of gas, and a burning sensation in the mouth. Two weeks after the birth of her child (February 22d) she had a large hemorrhage from the bowels, which was repeated upon the subsequent day, though accompanied with less blood. For some weeks before admission she complained of sore gums. Her skin has been yellow for four months, and she states that "the jaundice" has been much deeper before admission than at the present time.

Admitted to the hospital March 18, 1902 (hospital No. 4181).

Physical Examination. She is a medium-sized, fairly well-nourished woman. Face and body are lemon-yellow color. Conjunctivæ distinctly yellowish. The tongue is moist, pallid, with smooth and glazed surface; breath is fetid. There are about six front teeth in the upper jaw, while the few remaining teeth are decayed. The lower jaw contains about seven front teeth; all the molars are missing. The gums on both the upper and lower maxilla are inflamed and suppurating; there are no hemorrhages of the mucous membranes. Chest: The lungs are clear both in front and behind. Heart of normal size, though with soft, hæmic systolic murmur at apex, and a similar but louder murmur at the pulmonary and aortic cartilages. The abdomen is round and very flaccid. There is a slight dark brownish pigmentation over the margins of a large scar, which extends from the middle of the back around to the front of the abdomen. No mass is felt in the abdomen; no glandular enlargement.

She remained in the hospital a little over four weeks. During the first two weeks there was considerable diarrhœa. On two occasions the stools contained a dark, gelatinous blood clot. Her temperature has been maintained between 100° and 101° F. The pulse soft, very compressible, averages 120. No evidence of dyspœa. Rather sleepy mental condition, with disinclination to any exertion. Complains constantly of burning in her mouth and throat. No pains over joints or bones. Cultures taken from the mouth showed large numbers of streptococci pyogenes. On March 30th the stomach contents showed no free hydrochloric acid, no lactic acid; total acidity of 14; combined hydrochloric acid 8, or 0.0288 per cent. The knee-jerks present on both sides increased; no ankle clonus. During the last two weeks of her life the patient developed a diffuse œdema of the back. The face

became puffy and the limbs oedematous. She complained of a constant ringing, of sounds, or music in her ears, and finally became totally deaf. There were no special cardiac or vascular symptoms. Left eye-ground, examined by Dr. Harlan, showed a high degree of astigmatic hypermetropia; disks white; whole fundus pale; venous blood scarcely darker than arterial; extensive retinal hemorrhage, striated and non-striated.

No parasite or eggs were discovered in her stools. Urine (April 13th): 1260 c.c. in twenty-four hours; specific gravity, 1009; reddish-yellow in color. Urea: 1.4 per cent. or 17.6 drachms in twenty-four hours; later examinations of urine showed lesser quantities of urea. No pathological urobilin was present; a large amount of indican was, however, found. Two quantitative estimates for indican gave 84 and 94 milligrammes for the twenty-four-hour specimen.

Blood: The day of admission the blood count was as follows: Hæmoglobin, 16 per cent.; erythrocytes, 744,000; leucocytes, 3700. A differential count showed: Polynuclears, 78.2 per cent.; small lymphocytes, 19.2 per cent.; large mononuclears and transitional cells, 1.2 per cent.; eosinophiles, 1.4 per cent. There was moderate poikilocytosis, with slight polychromasia. There were some megalocytes present; considerable endoglobular degeneration; two megaloblasts and two normoblasts were found. The red cells became fewer in number as time went on, notwithstanding food and medicine and the hypodermic administration of arsenic.

The erythrocytes slowly fell until, during the first week of April, the erythrocyte count was 268,000, with leucocytes 5900 and hæmoglobin 3 per cent. The coagulation time of the blood was six minutes; its specific gravity 1022. Blood cultures: All flasks remained sterile after five days. During the last week of life the woman seemed drowsy and complained but little. Skin dry; hair dry and lustreless; the ear held up to the light was bloodless, and resembled yellow parchment. Nails were bloodless. The condition of the gums was improved, and there was but slight odor to the breath. It was evident that she had lost flesh.

The last blood count was made two days before death. Erythrocytes, 393,000; hæmoglobin, 3 per cent. There was no terminal leucocytosis. The autopsy showed widespread fatty degeneration of the organs, especially the heart and liver. There were in the ileum, several feet above the ileocecal valve, two scars, entirely healed, with slight pigmentation about them. They seemed to be Peyer's patches. There was no involvement of other parts. Spleen and liver of normal size. Bone-marrow dark red, not fatty.

Microscopic Examination. Large numbers of megalocytes and of nucleated erythrocytes, the majority of them megaloblasts; in many the nuclei are undergoing fragmentation. There are comparatively few leucocytes present. The polynuclear leucocytes are almost entirely absent, the majority of the leucocytes being myelocytes and lymphocytes; very few eosinophiles are present.

This case must, I think, be considered from both the clinical and pathological standpoint as one of pernicious anæmia—one of the cases, however, in which pregnancy seems to have been the exciting cause. The symptoms, however, coincide well with that group of cases to which

Hunter has recently called attention, namely, those with pyorrhœa and ulcerative giagivitis, with glazing of the tongue and gastro-intestinal symptoms. That the woman absorbed toxins from her intestinal canal is evident. She had great increase in her indican output, while there was no special evidence, excepting her hæmatogeneous jaundice, in her urine or elsewhere, of great blood destruction. At first the blood examination showed but few megaloblasts and changes in size and shape. In the last two weeks of her life, however, nucleated cells became more abundant, chiefly megaloblasts, though the differential count at no time showed a disproportion of lymphocytes. Of five or six cases of pernicious anæmia seen during the last year, but one case presented this increase in lymphocytes, which is supposed to be characteristic of this disease. In this case I would call attention to the continuous high hæmoglobin index, 1.78 to 2 per cent. The rapid termination of this woman's life did not permit of the extensive changes in the morphology of the blood which are frequently observed in cases of much greater duration. The absence of polynuclear leucocytes in the bone-marrow and their apparent increase in the circulating blood is probably accounted for by the supposition that in such an acute process there is still some bone-marrow remaining unaffected which could manufacture polynuclear leucocytes. (I hope to report this case in greater detail in the future.)

Acute Lymphatic Leukæmia, with Death and Autopsy. Philip O. K., aged sixty-five years, white, married, painter by occupation. Family history of no interest.

Past History. No serious illness in life except numerous attacks of pain and swelling in the joints, called rheumatism. His wife and three or four grown-up healthy children living. Present illness began four days before admission, with headache, general body pains, high fever, and diarrhœa.

Admitted to the hospital November 14, 1901 (hospital No. 2672).

Physical Examination. Medium-sized, spare man, with dry, glazed tongue; teeth bad, majority lost; pyorrhœa. Chalky deposit in the ears, knuckles, elbows, and knees. Spleen much enlarged; rasping, systolic murmur at apex. Urine contains albumin; acid; specific gravity, 1.012; on microscopic examination, hyaline, light and dark granular casts. Two days after admission constantly complained of hyperæsthesia of the entire body. No enlargement of the lymphatic glands. All parts of the skin subjected to pressure have become much reddened, with here and there minute punctate hemorrhages. Fever, which was high on admission, slightly reduced. Five days after admission right-sided pneumonia developed, with death in thirty-six hours.

The blood, examined day after admission: Erythrocytes, 2,731,250; leucocytes, 155,500; hæmoglobin, 60 per cent. On November 19th the leucocytes were 154,000; on the 20th, 205,780; and on the 21st, 283,000. Cultures from the circulating blood (November 21st) showed the presence of the micrococcus lanceolatus. Differential count on November 16th showed: Small mononuclears, 85.8 per cent.; polynuclears, 12 per cent.; large mononuclears, 1.6 per cent.; eosinophiles, 0.4 per

cent.; myelocytes, 0.2 per cent. Bacteriological examination of the gums showed isolated colonies of staphylococci. Examination of the stain films showed little change in the red cells; no poikilocytosis; nucleated cells not found. The small lymphocytes are present in great disproportion. The autopsy showed comparatively little enlargement of any lymphatic glands; the spleen not enlarged; interstitial nephritis, with fatty degeneration of the heart and lobar pneumonia. The examination of the bone-marrow showed the presence of large numbers of lymphocytes, with diminution in the number of polynuclear cells.

This case shows symptoms divergent from the chronic lymphatic leukaemias, and resembles rather an acute infection in its onset. The duration of this man's illness was about eleven days. From the symptoms in recent cases one is struck with the constancy of the presence of an ulcerative process in the gums and dry mouth (xerostoma) in most of the cases; in others, hemorrhages or conditions akin to those seen in scurvy. The most of the cases recently reported have been studied abroad, and perhaps the majority of them were in infants and children.

In the acute cases the differential blood examination is apt to show more large mononuclear leucocytes than were present in this case. His other symptoms, however, are I think typical.

A CASE OF BANTI'S DISEASE, WITH DIFFUSE PRODUCTIVE NEPHRITIS.

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It is the purpose of this paper to discuss a peculiar and interesting pathological condition, exemplified in a case of advanced productive inflammation of the liver, spleen, and kidneys.

At the outset we are confronted by the difficulty of assigning it to its proper position with complete certainty. There are four pathological conditions closely resembling each other, to three of which this case presents considerable similarity.

1. The condition which is known to the Italian authors as "Banti's cirrhosis" or "Banti's disease."

2. Cirrhosis of the liver, with secondary enlargement of the spleen. In a number of such cases there is also an anæmia of a secondary character.

3. Splenic anæmia, in which we have a marked enlargement of the spleen and a pronounced secondary anæmia.

4. Primary splenomegaly of Bovaird (*epitheliome primitive*, Gaucher).

These conditions will be described with more detail in another portion of this paper.