covered with tubercular-like granulations. Practically entire condyle removed and wound closed.

Dec. 10. Plaster cast applied.

Dec. 12. Discharged.

Dec. 31. Knee in good position. Split plaster and begin weight-bearing.

Feb. 17, 1907. Complains of discomfort over outer surface of knee. X-ray shows exostosis of tibia and femur. Re-entered hospital.

Feb. 18. Operation. Knee-joint opened over outer side. Cartilage and synovial membranes thickened and congested. When knee was flexed, condyles were exposed and presented a marked hypertrophic condition. Both ridges removed. Bone and cartilage soft. Wound closed.

Feb. 28. Discharged.

March 3. Patient wearing plaster cast. Slight swelling over outer surface of knee and some pain in right ankle-joint.

June 12, 1907. Considerable thickening about condyles.

CASE 65. M. M., male, eighteen, single. Operation, Jan. 21, 1907.

Linear incision over outer surface of knee. Synovial membrane found injected and thickened. A portion of this was removed. Also one fringe 5 cm. by $1\frac{1}{2}$ cm. and sent for pathological examination. Bone apparently normal according to x-ray and actual finding.

Jan. 26. Persistent pain in knee-joint.

Feb. 11. Septic stitch delayed healing of wound.

Feb. 13. No improvement in motion of joint. Pain very acute with attempted flexion.

Feb. 18. Under chloroform leg forcibly flexed to a right angle with hardly any resistance.

Feb. 21. Forcible flexion accompanied by extreme pain.

Feb. 25. Can flex almost to a right angle. Extension limited to within 10° of straight. Delayed pathological report. Tubercular synovitis.

Feb. 27. Leg put in plaster of Paris bandages. Tonic treatment to improve general condition. Discharged home.

Readmitted Oct. 2, 1907. Patient has been wearing plaster of Paris cast since February. Knee swollen and very painful without cast.

Oct. 23. Excision performed. Bone somewhat osteoporotic.

Nov. 12. Convalescence uneventful. Discharged home.

Dec. 6, 1909. No symptoms for past two years. Excellent result.

CASE 66. J. H. M., male, eighteen, single. Operation, Dec. 30, 1908.

Quadriceps pouch of right knee adherent but not markedly infiltrated. Numerous eroded areas were found over internal condyle of femur and corresponding upper surface of the tibia, with only a few small islands of cartilage remaining. Many of the erosions were deep. There was a distinct fibrous envelope isolating this region from the rest of the joint. When incised about 2 oz. of sero-sanguinolent fluid escaped. The outer trochanter of the femur and opposite surface of the tibia practically normal and very little extension of synovial disease in this direction. One crucial ligament was considerably disintegrated. On the posterior surface of the internal condyle a soft area of bone was found. This was curetted out to depth of $\frac{3}{4}$ inch. The semifluid substance expressed resembled pus, but may have been fat.

Jan. 13, 1909. Discharged home wearing cast.

Feb. 15. Wound entirely healed. Knee is in position of slight hyperextension. New cast applied.

March 29. Knee in good condition.

Dec. 1. Patient still wearing cast. Has had some pain when cast was split, but condition now is improved. To leave off cast gradually. Massage to thigh and calf.

CASE 67. J. St. J., male, seventeen, single. Operation, January, 1909.

No joint cartilage remaining. Considerable healed tubercular tissue removed. Wick put in either angle of wound and leg put up in plaster of Paris. There was considerable ooze from the wound for twelve hours following operation.

Feb. 8. Wick removed.

Feb. 15. Wound septic about inner angle when wick was removed.

Feb. 24. Septic infection readily yielded to treatment. Cast changed.

Feb. 26. Window cut over small granulating area. Slight discharge.

March 8. Discharged home. Leg in 15° permanent flexion.

Jan. 1, 1910. No exacerbation of disease and fair result as to position.

CASE 68. V. R., male, thirty-seven, married. Operation, April 14, 1909.

Left knee-joint excised. Greater part of joint cavity contained healed tubercular tissue. One small focus in head of tibia; otherwise the bone not deeply involved.

April 16. Considerable ooze from joint for twelve hours following operation. No pain or other symptoms to note.

April 28. Renew cast.

May 3. Discharged.

Nov. 12, 1909. Still wearing cast. No subjective symptoms. Excellent result.

CASE 69. U. B.

Both articular surfaces diseased, and there was considerable involvement of the soft parts. Two small foci found in femoral head. In tibial head was a focus which apparently penetrated bone to soft parts.

Dec. 23. No post-operative symptoms. Patient discharged wearing plaster cast.

(To be continued.)

Clinical Department.

THE EXTREME BLOOD PICTURE IN A CASE OF PERNICIOUS ANEMIA.

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THE following case is deemed worthy of report on account of the remarkable degree of oligocythemia presenting, the red blood cell count, dropping to 100,000 per cubic millimeter two hours before death, being the lowest count yet reported. The hemoglobin at that time as nearly as could be calculated was 9% (Sahli).

In the literature on the subject of pernicious anemia, Cabot mentions two cases in which the count fell below 200,000, citing the celebrated case of Quinke, 1877, of 143,000, and referring to two other cases. Hills, 1898, reports 155,280; Naegeli, 1908, 138,000, reports the lowest up to that time. This indeed is noteworthy when one considers that in the extensive and voluminous amount that has been written on this subject, a count of 1,000,000 is frequent; so low as 500,000, uncommon; below that number, rare, and when it is called to our attention that a count of less

than 200,000 is reported in but four cases, it becomes of exceeding interest to learn if possible what might cause or bring about such extreme poverty of the blood. If unexplainable upon the basis of the facts in the case, it is of speculative interest, to say the least.

Before introducing the case it might be well to make in brief a few remarks in regard to the pathogenesis of the condition. The researches of Bunting, who produced experimentally in animals a gradually long-standing hemolysis by the injection of small doses of ricin, proved that a typical megaloblastic metamorphosis of the bone marrow can thus be produced, a metamorphosis identical with that seen in pernicious anemia. With larger doses of this or other hemolytic agents we get, as after experimental exsanguination, a red marrow, whose color is due not to megaloblasts, but to normoblasts and normal red cells. Bunting suggests the interesting hypothesis that in pernicious anemia we are dealing with a hemolytic process produced by a poison which exerts its action over a considerable time; that in an attempt to repair the damage done by this poison, the peripheral layers of the germinal erythrocytic centers are first "peeled off" as in ordinary secondary anemia. Then, as the new formed erythrocytes are rapidly discharged into the blood with the continuation of the hemolytic process and the prolonged stimulation and acceleration of the blood-forming activities, the germ centers where the large immature red corpuscles lie become enlarged, over-active and finally crowd out all the other tissues of the marrow, so that immature red cells, often nucleated and of the large type characteristic of the erythrocytic centers, are discharged into the blood in an unsuccessful attempt to make up for the losses due to hemolysis.

Cabot further says that if, as in cases of anemia due to the fish tapeworm, we can remove the source of blood destruction, the marrow returns to its normal condition, functions in the normal way and the patient recovers. If, on the other hand, as in cryptogenetic anemia, the hemolytic agent cannot be found or removed, the marrow grows more and more bankrupt.

William Hunter holds that the hemolysis which is now generally considered responsible for the disease is of gastro-intestinal origin, citing as evidence an increase in amount of iron pigment normally deposited in the liver and, to a lesser extent, in the spleen. It has been shown, however, that when hemolytic agents are introduced through the blood stream itself, these iron deposits occur in the same way as in pernicious anemia of the ordinary type. It seems more likely, as is generally assumed, that the unknown poison of pernicious anemia stimulates and pathologically exaggerates the normal phagocytic and hemolytic activities of the spleen, lymph glands and marrow. The pigment in the phagocytic cells and stroma of these tissues fails to give the iron reaction. It is in the liver and kidneys that it is changed to hemosiderin, but the primary destructive agencies are in all probability in the hemopoietic organs themselves.

History of case. — Patient, R. G., male, forty years of age, nativity Ireland, has been in this country twenty-two years; is married.

Admitted to Cook County Hospital Feb. 8, 1910, on the service of Drs. Loeb and Mix.

Present complaint. — General weakness, some cough and vomiting. The onset was insidious and indefinite and is dated as beginning about one year ago with soft chancre, following which patient began to lose weight, noticing pallor and progressive weakness and shortness of breath, and "night sweats" were frequent. Several attacks of vomiting during that time; these attacks were unaccompanied by pain, bear no relation to eating. No hematemesis or blood in stool. Coughing has been persistent for the past five months, no hemoptysis, expectorates considerable greenish-yellow sputum.

Previous diseases. — Had muscular rheumatism one year ago, gonorrhoea eighteen years ago, for the past ten years has had urethral stricture, some difficulty in urination and has frequently had urethra dilated. Had a chancre fifteen years ago followed shortly by secondary eruptions. Has since had children who were strong and show no hereditary taint.

Habits. — Has been a "hard drinker" for years. Present occupation a motor-man, formerly a butcher.

Family. — Parents died of old age; two brothers and three sisters living. Wife is living and well. Has living children. There is no history of similar disease in the family.

Physical examination. — General: Shows a poorly nourished, pale, somewhat lemon-tinted, white male about forty years of age, of uncertain gait, good mentality, complaining of general weakness and some numbness of the extremities.

Regional. — Head and neck: Pupils unequal, left smaller than the right, react very sluggishly to both light and accommodation. Tongue is pale and flabby, as is mucous lining of mouth in general. Teeth are poor (pyorrhea alveolaris). Cervical glands are not enlarged.

Chest: Prominence of right clavicle. Lungs: Some râles and impaired resonance over upper right lobe; also roughened breathing in the same region. Heart shows normal area of dullness, no irregularity, a hemic murmur at the base; second sounds are unaccentuated. Abdomen: Spleen and kidneys are not palpable. Liver extends one finger's breadth below the costal margin and is not irregular or tender. No ascites or palpable tumor masses. Inguinal glands palpable but not enlarged. Rectal examination is negative. Genitalia and lower extremities are negative.

Nervous system: Left patellar reflex absent, right reduced. Babinski positive on both sides. No girdle sensation, no acute gastric or shooting pains and no bladder trouble except as could be accounted for by stricture of urethra. Muscles and joint sense gone. Rhomberg positive and gait is noticeably of stamping quality. Numbness and tingling sensation are complained of in the lower extremities.

Functional irritability and some inability to fix attention are present; insomnia has been bothersome at times. Memory is good.

Subsequent history. — The course of the disease from then until the end, thirty-two days after entering hospital, is with but a slight suggestion of remission, progressively downward, and of chief interest are the blood findings. Other points less noteworthy are merely to be mentioned in passing.

Feb. 10, two days after admission, blood examination shows: Hemoglobin, 36% (Sahli); red blood corpuscles, 1,566,000; white blood corpuscles, 4,800; color index, 1, plus.

Feb. 25, hemoglobin, 19% (Sahli); red blood corpuscles, 680,000, showing a drop of over a half million in fifteen days; white blood corpuscles, 4,000; color index, 1, plus.

Differential white cell count (100 cells) show polymorphonuclear neutrophils, 61%; lymphocytes (large and small), 32%; transitional, 2%; neutrophilic myelocytes, 3%; eosinophiles, 1%; basophiles, 1%.

During the differential count eight nucleated red cells were seen, four of which were normoblasts, and an equal number of megaloblasts were present. Marked chromatophilia and a tendency toward macrocytosis is noted. Poikilocytosis is not marked; no blood platelets found.

March 5, hemoglobin, 14% (Sahli); red blood corpuscles, 750,000; white blood corpuscles, 4,200; color index, $\frac{1}{2}$, slightly less than 1, showing if anything a slight degree of improvement in the blood condition over that noted a week previous. In a stained smear at this time one megaloblast only appeared in the field in one of three slides. Both poikilocytosis and polychromatophilia are marked. No normoblasts are found.

March 10, hemoglobin, 12% (Sahli); red blood corpuscles, 780,000; white blood corpuscles, 2,200; color index, $\frac{1}{2}$ approximately, is still less than 1. Here is noted only a small increase in the red cells. The white cells are notably diminished in number and the hemoglobin also on the decrease. Eight to twelve megaloblasts were found on a single slide and four to six normoblasts.

March 12, two hours before death, the final count shows the most interesting changes above mentioned, namely, (1) Hemoglobin, 9%. It is found that Tallquist and the Dare instruments do not register; however, using two volumes of blood where one is called for, with Sahli hemoglobinometer then registering 18%, dividing by 2 for correction, the above result obtains. The instrument is six months old and the acid hematin control has probably not deteriorated. It is possible that the hemoglobin content here is less than 9%, for it must be borne in mind that from deterioration, improper standardization and the age of the individual arise sources of error which must be taken into account before absolute calculation can be made. Webster reports an error of 25% arising from faulty standardization of Sahli's solution. However, a discrepancy in favor of a higher color count is tenable on the same grounds, though inapplicable here, I think. Naegeli mentions as the lower limits in extreme cases, 12, 10, 8, and even 7% hemoglobin.

(2) Red blood corpuscle, 100,000 per cmm. A free drop from the lobe of the ear was obtained with some difficulty owing to the remarkable degree of oligocythemia existing, necessitating a liberal stab. A second drop was taken, a new stab being made in order to obviate possibility of error and for a check and control. Hayem's solution, fresh and recently filtered and in the dilution of 1:100 being used, Thoma-Zeiss counting chamber counting 200 squares, in each case recounting each a second time to avoid possible inaccuracy. An even distribution was noted and microcytes were included in the counting. (Emerson has noted an error of 200,000 arising from overlooking this form of cell.)

(3) White blood Corpuscle, 2,400, an inconsiderable increase over that of the forty-eight hours preceding.

Differential white count of 100 cells at this time shows

	Per cent.
Polymorphonuclear leucocytes,	50
Lymphocytes:	
Small,	28
Large,	11

	Per cent.
Transitional,	1
Neutrophilic myelocytes,	4
Eosinophiles,	0
Basophiles,	0

During the count ten normoblasts, twelve megaloblasts and five intermediates, including the latter with the megaloblasts, give a Von Noorden blood crisis, of megaloblastic type, of 170 per 1,000 leucocytes, — the arbitrary lower limit being taken as 50 per mille. It is here seen that myelocytes were thrown out into the blood at this time. In a crisis of this sort eosinophiles should rise; in looking over the slide none are found; a jump in the red count is usually concomitant or follows shortly. Such was not evident in the present case and serves to illustrate the variability within certain limits of the blood picture of pernicious anemia relative to this point. Emerson, reporting 89 cases, in 20 finds an increase in the number of red cells counted within forty-eight hours preagonal, occurring quite uniformly, making note of interest in the fact that the higher the count with the first symptoms, the higher it is at death. How, then, in the face of such evidence, is such extreme paucity of red cells to be explained, unless we assume that the hemolytic agent causing this destruction was especially and intensely toxic at this period of beginning dissolution or, on the other hand, that vasomotor paresis is paramount in producing a relative local anemia or ischemia, considerations which at best must be purely hypothetical?

Skelton-Barlow stain used throughout.

(4) Color index, 4.5. This is exceedingly high, though hyperchromemia, as we know, is one of the characteristics of the disease. The volume index in this case unfortunately was not taken, but through the kindness of Dr. Capps, who measured 100 cells, we found an average diameter of 8.1 microns (7.5 microns normal), which leaves some discrepancy as to the high color proportional to the size of the individual cell. Capps has shown and upholds the theory that the color index is never increased without corresponding or greater rise in volume index; that it is not due to an increased affinity of cell protoplasm for hemoglobin. And furthermore, this fact proven, it is quite unnecessary to assume a supersaturation of the cell with hemoglobin. Another source of error is suggested by Emerson, who says, "The high color index of pernicious anemia has perhaps with reason been attributed to the fact that microcytes are overlooked." As previously stated, such I think is not the case here. Here applies also what was mentioned under hemoglobin estimation above with regard to source of error relative to defective instrument and so forth.

(5) The drop is pale, watery appearance, showing fluidity especially, and the halo about the drop so often described and rarely found in other diseases according to Cabot. Absence of rouleau formation is noted, as is also delayed coagulation time.

Coma supervened before death, six hours.

Diagnosis. — An autopsy was refused. It is, therefore, impossible to determine anything definite as to actually existing pathology underlying; however, the clinical picture is such that the diagnosis of pernicious anemia seems justifiable on those grounds alone, fulfilling many if not all the requirements suggested by Billings, namely, "when we find a marked oligocythemia, with the presence of many poikilocytes, microcytes and macrocytes, with polychromatophilia, and a

relatively high percentage of hemoglobin with normal or higher than normal color index, it affords a type of blood which is found in no other anemic state. If to this we add the presence of nucleated red cells, and especially of megaloblastic type of red cells and a few myelocytes, which together indicate degeneration of bone marrow, the diagnosis is reasonably certain without post-mortem examination.

As to type, it is of cryptogenetic origin, the idiopathic form called Addison's anemia by Hunter, in that it conforms fittingly to the negative findings, which were emphasized by Addison so early as 1855, namely, cases where there had been no previous loss of blood (in this case slight and occasional epistaxis is noted), no exhaust-diar-rhea, no chlorosis, no purpura, no renal, no splenic, no miasmatic, glandular, strumous or malignant disease.

Ophthalmoscopic examination showed slight hemorrhage into left retina. Urine showed small amount of albumin and an occasional cast, no edema of the extremities or puffy eyelids. Repeated stomach, sputum, and examination of the stools showed neither malignancy, tubercle bacilli or animal parasites. Diminished acidity of stomach contents was noted. No evidence of hemorrhoids or other cause of secondary anemia except slight nose bleed.

The diagnosis of tabes dorsalis is hardly tenable, and, if entertained, must be so on the assumption of a superimposition. Clinical evidence of dorsal column involvement is insistent, sphincter disturbance is absent, as is also a history of crises of any sort, and, in the presence of additional lateral cord involvement, as evidenced by a double Babinski, speaks for a combined cord degeneration due in all probability to the common hemolytic agent which is responsible for the most damaging and terminally destructive changes in the blood.

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Medical Progress.

PROGRESS IN THE THEORY AND PRACTICE OF MEDICINE. GASTRIC AND DUODENAL ULCER.

BY FRANCIS W. PALFREY, M.D., BOSTON.

[Concluded from No. 16, p. 619.]

DIAGNOSIS.

In diagnosis also the influence of surgical evidence has been of great importance. The writings of surgeons, notably those of Moynihan, of Mayo and his associates, of Deaver, of Codman, of Hall, and of a number of reporters from German clinics, presenting large series of cases where the diagnoses were tested by operative findings, have given a far firmer basis for clinical diagnosis than ever before existed. In the light of these findings many discussions have appeared of the significance and diagnostic value of symptoms, of signs and of clinical laboratory tests. As compared with similar discussions in recently previous years there is a notable tendency to lay greater stress upon clinical history and symptoms and to place less reliance upon the findings of the laboratory in the diagnosis of gastric and of duodenal ulcer. Particularly is this true in the case of articles upon duodenal ulcer which from its recent recognition as a common disorder has received the attention due to a new disease. Its symptomatology, in the practice of those who have had the most intimate experience with it, is described by Moynihan¹ as so definite that the history is in itself sufficient for practical diagnosis, rendering other diagnostic evidence superfluous. While this statement must be regarded as an exaggeration, it is undoubtedly true that clinicians at large do not sufficiently appreciate the significance of histories such as are given by the class of patients in whom duodenal ulcers are being demonstrated. A digest of a few of the more important discussions of the symptomatology of duodenal ulcer may, therefore, be profitable in attaching a new significance to a clinical picture which has frequently in the past been denied adequate attention.

Mayo² enumerates the symptoms of gastric and duodenal ulcer in common as follows: (1) Acidity—the regurgitation of acid food and of acid-burning contents from the stomach not containing food; this acid regurgitation from the fasting stomach he regards as almost pathognomonic of ulcer. (2) Pain—seldom absent; described as burning or deep boring in character, temporarily eased by food, but as the patient clearly recognizes, later aggravated in consequence of food taken. (3) Hemorrhage—not a frequent symptom, even occult blood in the stools being rare in comparison to its constant presence in cancer. The presence of blood in the stomach contents or stools must always be suspected of coming from other sources. Single large hemorrhages are more often due to other causes (e. g., cirrhosis) than to ulcer. (4) Vomiting—not frequent on account of the care exercised in eating. (5) Gas—a nearly constant symptom. The