CHART II.

Nov. 11, three days after entrance, the eyes were examined and showed the presence of fresh retinal hemorrhages. Labor now began and she delivered herself on Nov. 12. Forty-eight hours after delivery the blood pressure had dropped from 223 to 180, and marked improvement had taken place in the patient's condition. From Nov. 18 to 23 there was a febrile condition without obvious cause, yet during this the blood pressure continued to fall. A complete recovery was not made in this case. The lowest point reached in the blood pressure was 150 on the 23d of November. At this time she was allowed to sit up in bed and gradually to get up and about. Coincident with this the blood pressure rose again to 170 and remained about that point up to the time of discharge from the hospital. The urine was never free from albumin, the eyesight remained considerably blurred.

Three months later she reported at my office, feeling fairly well. Vision had improved somewhat, but was not yet good. She tired easily, was up two and three times at night to micturate. The urine was pale, of 1,012 specific gravity, and contained a good trace of albumin. The blood pressure was 175. The heart was very slightly hypertrophied, the aortic second was sharply accentuated and ringing.

CONCLUSIONS.

1. The blood pressure in eclampsia is high, and of diagnostic and prognostic importance.
2. In spite of improvement in subjective symp-

toms and increase in the quantity of urine, the blood pressure may remain high.

3. In which case the prognosis is grave, and labor ought to be induced.

4. The continuance of high blood pressure during the puerperium warrants a grave prognosis as to complete recovery.

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TWO CASES OF ATYPICAL LEUKEMIA.

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I. ACUTE fatal anemia with terminal blood-picture of lymphatic leukemia.

C. C., female, twenty-five, married, Italian, housewife, entered the Massachusetts General Hospital on the service of Dr. E. G. Cutler, June 1, 1907. Family history and previous history negative. Habits and hygiene good. Eight weeks before entrance she began to have pain in back, legs, shoulders and head, not involving joints, at times requiring morphia for its relief.

Two weeks before entrance she began to be pale and yellowish, weak, and short of breath on exertion. For ten days she had been in bed; had lost from 15 to 20 lb. in weight. She had several times seen small red and black spots appear suddenly on neck and arms, later disappearing. One week before entrance her throat began to be sore.

Physical examination showed that she was well developed and nourished, but her skin and mucous membranes were pale. Pupils were equal, reacted normally. Left tonsil was reddened, swollen and covered with whitish exudate. Heart's apex impulse in fifth space, four inches to left of mid-sternal line; left border of dullness corresponded; no enlargement to right. Sounds of good quality; no murmur heard. Pulse of rather low tension. Lungs normal. Abdomen normal. Liver and spleen easily felt; liver dullness from sixth rib to costal margin. Slight edema of ankles present. No glandular enlargement. Urine high-colored, acid, 1,017-1,024, without albumin, sugar or bile. Urea, 2.99-2.02%. Sediment showed only squamous epithelial cells. Stool gave negative reaction for blood by guaiac test; no ova or parasites found. Temperature ranged from 99° to 97.4° F.; pulse from 88 to 110; respiration from 18 to 26. Cul-

fatty acid crystals, red and white blood corpuscles. Temperature fell gradually from 103.4° at entrance to 98.4°; pulse ranged from 110 to 140; respiration from 30 to 50. For blood examinations see table.

Patient vomited frequently and her bowels moved from one to four times daily; vomitus once was bloody. She failed steadily and died July 14 after two hours of wild delirium. Autopsy not obtained.

Five examinations of the blood were made; the last one, dated July 14, was completed about half an hour before death. The percentages given in this examination are based upon a differential count of 1,000 white cells, the others upon differentials of 200. The large lymphocytes were mostly of medium size; they were several times observed to be phagocytic for erythrocytes. (See Table of Blood Counts.)

The absence of an autopsy makes the case incomplete and renders any absolute diagnosis impossible, but such evidence as is at hand makes the diagnosis of acute lymphatic leukemia most probable. The striking features are: (1) The acute course, under four months; (2) the extreme and progressive anemia; (3) the overwhelming

TABLE OF BLOOD COUNTS.

	Hb.	Per cent.	Erythrocytes.	Leucocytes.	Per cent in count of 200.						Seen in Count		Platelets.	Stippling.	Polychromatophil.	Poikilocytosis.	Macrocytosis.	Microcytosis.
					Poly. Neut.	Lymph. Large.	Small.	Poly. Eos.	Mast cells.	Myelocytes.	Blasts							
											Nor.	Meg.						
June 1.....	55	2,136,000	3,300	53	45	0	1	1	7	1	diminished	slight	moderate	moderate	little	much		
„ 10....	55	2,044,000	4,400	52	48	0	0	0	1	5	rare	none	marked	„	„	„		
„ 14....	45	2,580,000	6,000	37.5	59.5	1	0	2	2	2	very rare	slight	„	„	„	„		
July 12.....	15	1,072,000	14,700	6.5	92.5	1	0	+	6	2	very rare	marked	„	„	„	„		
					92.9								„	„	„	„		
„ 14....	15	816,000	91,500	6.1	84	8.9	0.1	0	0.9	6	9	* „	„	„	„	„		

*In count of 1000 whites.

tures from the throat were free from diphtheria bacilli, and the exudate disappeared a few days after entrance.

Patient felt very much better after coming to the hospital and was discharged at her own request, June 14, "much relieved," but without any notable change in physical signs.

She re-entered the ward on the service of Dr. H. F. Vickery, July 11, 1907, with a story of progressive weakness ever since discharge. She complained bitterly of pain in the long bones. She had had a normal menstrual flow two weeks after leaving the hospital.

The following changes were observed in physical signs. The skin had become lemon yellow and the mucous membranes exceedingly pale. There were small ecchymoses on neck, front of chest, right shoulder and abdomen. Heart's apex impulse in fifth space five inches to left of mid-sternal line; loud systolic murmur heard all over precordia; pulmonic second sound markedly accentuated. Liver edge questionably felt. Spleen felt two inches below costal margin, hard and tender. Motions of spine limited, apparently by pain and spasm. Moderate tenderness over long bones. Urine pale, acid, 1,010, with a very slight trace of albumin, without albumose, sugar or bile. Urea 1.39%. Sediment showed an occasional red or white blood corpuscle; no casts seen. Stools bloody, with masses of clay-colored feces. Guaiac test for blood strongly positive. Microscopic examination showed fat and

increase, both relative and absolute, in the number of large lymphocytes; (4) the practical absence of platelets in the later examinations; (5) the absence of glandular enlargement. Several similar cases of acute anemia with terminal lymphemia have been reported (Litten, Luce, Körmőczy and others); in some of them the marrow has been examined and has shown lymphoid instead of erythroblastic "hyperplasia" or "degeneration." A case of myelocytic leukemia was reported in 1907 by Hunter in which the blood picture changed in three weeks from pernicious anemia to leukemia, the leucocyte count having risen in that time from 6,000 to 290,000. In 1907, also, a case was reported by Sluka which presented in life the blood of pernicious anemia but showed at autopsy the bone-marrow of large cell lymphatic leukemia. It has been suggested by Dr. J. H. Wright that in the case here reported the disease was wholly a hyperplasia of large lymphocytes or pre-lymphocytic cells in the marrow, manifesting itself at first only by a reduction in the number of circulating erythrocytes and platelets and the attendant clinical symptoms and signs of anemia, but revealing its

existence just before death through the escape or discharge into the blood-stream of some of the essential factors, the lymphocytes. Without microscopic examination of the marrow such a theory "is very largely conjecture." As for the absence of glandular enlargement, so many cases of lymphatic leukemia without glandular enlargement have recently been reported that this case is in very slight degree noteworthy in that respect.

The classification and nomenclature of the so-called primary blood diseases is the subject of lively discussion. It is not yet determined whether there is a disease "leukanemia" with the red cells of pernicious anemia and the white cells of leukemia, or whether fatal anemia with very late lymphemia or entirely without lymphemia but with lymphoid bone marrow shall be called "pseudo-leukemia." In view of the established usage of the latter term in respect to Hodgkin's disease it seems more reasonable to us to call it "aleukemic leukemia." For further discussion of this subject reference may be made to the writings of Pappenheim, H. Hirschfeld, and others published especially in *Folia Hæmatologica*.

II. Acute fatal anemia with hematoma of knee, extreme terminal leucocytosis and hyperplasia of megakaryocytes.

F. M., male, eighteen, single, American, chair-maker, entered the Massachusetts General Hospital on the service of Dr. C. A. Porter July 18, 1907. Family history and previous history negative. Five months previous to entrance he noticed a hard tender swelling just above right knee, extending slowly until it involved the whole knee and thigh; not very painful until four weeks before entrance, when it became exceedingly painful and tender. He gave up work at once and went to bed on account of the pain; since then his appetite had failed, he had grown pale and he had lost much weight and strength.

Physical examination showed that he was frail, emaciated, and very pale. Reflexes normal. Tongue clean. Throat and lungs normal. Heart enlarged slightly to right, not to left. Systolic murmur heard at apex, not transmitted. Pulmonic second sound accentuated. Abdomen normal except for edema and ecchymoses in right flank. Liver and spleen not felt. No glandular enlargement found. Right thigh and knee swollen, hot and tender, but not red. Fluid present in and about joint. Pale yellow ecchymoses in skin over thigh. No edema nor purpura except as above noted. Urine normal in color, acid, 1,023, without albumin or sugar. White count 55,000. Temperature 101.8°, pulse 112, respiration 24.

The patient was admitted from the accident room to the ward with a probable septic knee. On the following day the knee-joint was aspirated by Dr. Jones, who withdrew 5viii of dark, bloody fluid. Stained smears showed red blood cells, polynuclear leucocytes and fibrin; no micro-organisms. The thigh was then opened above the knee and several ounces of similar fluid were obtained from a cavity extending down to bare bone. The bony surface showed no evidence of sepsis or neoplasm. Cultures from both specimens of fluid remained sterile after seventy-two hours of incubation.

The patient failed gradually after operation, vomiting frequently and oozing serum into the dressing. His temperature varied from 98.4° to 102.6° F., his pulse from 112 to 138, and his respiration from 22 to 31. He was seen in consultation July 22 by Dr. J. J. Minot

and July 24 by Dr. H. F. Vickery, who concurred in the diagnosis of acute primary anemia. He died quietly July 25. No autopsy was obtained, but Dr. Oscar Richardson was permitted to remove sufficient bone marrow from the exposed end of the femur to make smears; it was unfortunately too soft to be removed through the wound in condition to be hardened and sectioned. The following examinations were made of the blood:

July 19. Hb. 55%. Whites 63,800. Polynuclear neutrophils 91%, large lymphocytes 8%, small lymphocytes 1%, in a count of 100 white cells. The red cells showed some variation in size and shape, with marked polychromatophilia and stippling, and one megaloblast and one normoblast were seen while counting.

July 20. Whites 106,000.

July 22. Whites 78,400. Reds 1,520,000.

July 24. Hb. 15%. Reds 1,080,000. Whites 222,000. Polynuclear neutrophils 91.46%, large lymphocytes 3.07%, small lymphocytes 2.78%, polynuclear eosinophiles 0.29%, neutrophile myelocytes 2.4%, mast cells absent, in a count of 1,000 white cells. Platelets 1,188,000. The red cells showed considerable variation in size and shape, with a tendency to microcytosis; stippling and polychromatophilia were marked. Seventy-nine megaloblasts and 74 normoblasts were seen in the count of 1,000 whites, or about 34,000 per cubic millimeter. Many of them showed mitotic figures. Some idea of their frequency may be obtained from the fact that as many as eleven were seen in one field of a thin smear with oil-immersion objective and high-power eyepiece.

The bone marrow was soft, semi-fluid, the color of raspberry jelly. The smears showed an apparently normal number of erythroblasts and myelocytes, mostly of small size, and very few polynuclear neutrophils. The giant cells, on the contrary, were markedly and strikingly more numerous than in smears of normal bone marrow; they also were of small average size. It is interesting to note relation between the number of giant-cells in the marrow and the number of platelets in the blood. According to the conclusions of Wright, the blood platelets are detached fragments of the cytoplasm of megakaryocytes (giant cells of bone marrow). If the imperfect examination of bone marrow in smears is a fair index of the general condition of the marrow, the co-existence of increased platelets in the blood and giant cells in the marrow is in harmony with the conclusions of Wright.

No case exactly similar to this has been found in the accessible literature. Large hematomata requiring operation are not very rare in severe anemias and leukemias. Milward reports a case in which there were swellings about the knees supposed to be scorbutic; the case afterward proved to be lymphatic leukemia. Barié and Salmon also report a case of enormous hematoma of the shoulder in a case of acute leukemia. The case reported here was at first supposed to be sepsis; this was disproved by microscopic examination of and by cultures from the fluid removed from the swelling; it was then considered to be perhaps a tumor of bone which had undergone degeneration, but neither the appearance of the bone in the neighborhood nor the microscopic examination of the marrow supports this theory. In the absence of a complete autopsy we are again reduced to conjecture, but the cellular elements of the marrow, taken with the blood picture, point

to the marrow as the most probable primary seat of disease.

It has been suggested that there was a general hyperplasia of the bone-marrow cells, and that the terminal drain, perhaps of the operation and subsequent oozing, drew out the erythroblasts, platelets and polynuclears into the blood-stream but left the giant cells *in situ* because of some mechanical obstruction. It is undoubtedly true that rapid changes took place in the blood just before death and that a very large increase occurred in the number of circulating polynuclears and erythroblasts, but there is no evidence in the smears of marrow of increased formation of those cells, while there is to be seen a great excess of giant cells. In fact, the giant cells may be considered to have interfered with erythrocyte and perhaps with polynuclear leucocyte generation in some such way as the lymphocytes do in acute lymphatic leukemia. In other words, this case may be considered to be a "leukemia" of the megakaryocytes. It is to be said, however, that this is only one way of explaining a somewhat obscure and, in the absence of autopsy, an incomplete clinical and histological picture. Just where the case is to be placed in any system of classifying diseases of the bone marrow is a matter for discussion. If the term "aleukemic leukemia" is admissible, if "leukemia" is taken to mean merely a primary hyperplasia of one or more of the cellular elements of marrow without regard to leucocythemia, why is not "pernicious anemia" a "leukemia"? "That way madness lies." It is likely that in future a system of nomenclature to include all the myelogenous diseases may be adopted, with divisions allotted to erythroblastic, leucoblastic and platelet-forming cells.

In conclusion the writer wishes to acknowledge his indebtedness to Drs. Cutler, Vickery, Porter and Jones for permission to report the cases, and to Dr. J. H. Wright for kindly and enlightening aid in their study.

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ON THE TOXIN OF ECLAMPSIA.

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I. EARLIER RESEARCHES ON ECLAMPSIA.

PUERPERAL eclampsia has been for many years the subject of careful clinical and pathological study. The literature on eclampsia is very extensive and goes back to the early forties. But in spite of this fact very little real progress has

been made in determining the cause of the disease. It is to-day considered a decided pathological entity associated with lesions so characteristic that after death, at least, there can be no doubt about the diagnosis. As to the diagnosis during life, it is a very different matter; personally I have no doubt that many cases of uremia and epilepsy are diagnosticated as eclampsia, and when the patients recover there is no means of knowing that the diagnosis was not correct.

Based on the presence of albumin in the urine, the theory of Frerichs, who pronounced eclampsia a condition secondary to uremia, was for many years the accepted teaching. Frerichs attributed the symptoms to a poisoning of the blood through the retention of urea and the conversion of the latter into ammonium carbonate. We know to-day, however, that cases of eclampsia without albuminuria or signs of kidney disease occur not infrequently. Rosenstein attributed the convulsions to anemia of the brain; others (Cohnheim, Spiegelberg, Schroeder) sought the cause of eclampsia in a spasm of the arteries in the kidneys and brain, produced reflexly by the pregnant uterus. Halbertsma assumed that the convulsions were due to disease of the kidneys secondary to pressure upon the ureters. But many cases of eclampsia have come to notice where each and all of these conditions were absent.

Ludwig and Savor revived a modification of Frerichs' original uremia theory by their assumption that eclampsia was an auto-intoxication due to the retention of poisonous products of metabolism which the kidneys were functionally unable to eliminate from the system. These authors chose carbamic acid and ammonium carbamate as the *materia peccans* in place of the ammonium carbonate of Frerichs. Vollhard succeeded in completely disproving this theory. Numerous theories, some of which have sought to account for eclampsia as due to anomalies of structure and function of the blood vessels and nerve centers (von Herff, Kundrat, etc.), and others which sought the cause in a bacterial invasion or bacteriotoxic poisoning of the system (Albert, H. Mueller, Levinowitch, Stroganoff) have shared the fate of the earlier theories.

Of course, physico-chemical methods of investigation have also had their day. The freezing point of the blood and urine of normal and eclamptic pregnancies was studied by many authors (Koranyi, Kroenig, Fueth, Szili, Dienst, J. Veit, Schroeder, Caspar and Richter). They found that in three fourths of all cases of pregnancy the urine shows an insufficient molecular concentration and consequent insufficient diuresis, which reaches its lowest level at childbirth. Immediately after childbirth the molecular concentration of the urine begins to rise rapidly. The molecular concentration of eclamptic urines was found by most authors to be practically that found in normal cases; Schroeder alone found values in eclampsia which are far below those given as the lowest for the molecular concentration of the urine in normal pregnancies. It is a remarkable fact that with such decidedly insuffi-