[Pancytopenia and aplastic anemia]

MEDICAL GRAND ROUNDS
PARKLAND MEMORIAL HOSPITAL
OCTOBER 9, 1958

CASE 1. [redacted]

This patient expired at age 21 with extreme pancytopenia and an acellular bone marrow (aplastic anemia). Her history in this hospital dated back 7 years. There were 10 separate hospital admissions and close observance in the outpatient clinic. There was an opportunity to observe first hand most of the chronologic sequence of the aplastic state.

First hospital admission ([redacted]-46 to [redacted]-46): At age 14 the patient, a colored female, was admitted with vaginal bleeding which had lasted 11 days. There was profound weakness and she had fainted an occasions. Menstruation began at age 12 and had been regular (28 day cycle, lasting 5 to 6 days, usually 4 pads were used daily). She had had no major illnesses, no operations. A brother was well. Except for pallor the examination was negative. A blood clot in the vagina yielded no tissue. The routine laboratory work indicated RBC 2.1 ml. Hb. 4 gm, WBC 2900, platelets 14,800, reticulocytes 0.5%, evident anisocytosis and poikilocytosis. Sickling was negative; there was no jaundice and the RBC osmotic fragility was normal. She was febrile for 13 days (temp. 101-103°F) during which time she received 8 pints of blood. (There was one chill-fever reaction, temp. 105.5°F). Except for ferrous sulfate and an occasional aspirin no other medication was recorded. She left the hospital markedly improved after 26 days with a Hb of 11.5 gm and WBC of 5100. The bleeding and clotting times were normal.

Second admission ([redacted]-49 to [redacted]-49): The patient was admitted near term, was induced and delivered a normal baby girl. A lump in the breast was biopsied and was found to be benign (adenomatous hyperplasia). There were no complications from the delivery or operation. On admission the Hb was 6.8 gm, WBC 4800. Clotting time and bleeding time were normal. The platelet count was 290,000/cu mm. A bone marrow smear from the sternum yielded a normal differential count (M:E ratio 2.5:1). She was given 3 pints of blood and discharged with normal physical findings for the postpartum state, Hb 9.5 gm, WBC 2850 with 56% mature neutrophilic granulocytes. Medications included codeine, aspirin, penicillin and seconal.

Third admission ([redacted]-50 to [redacted]-50): The patient was admitted with severe menorrhagia, the recent menstrual period had been in progress for 10 days and was attended by profuse flow. The periods prior to this one had been regular but the last 3 periods had been associated with profuse flow. The physical examination was normal including a pelvic examination. The Hb was 3 gm, RBC 1.0 mil, SBC 2600 with 36% mature neutrophilic granulocytes. She developed bilateral retinal hemorrhages and pale areas in the retina considered to be exudates and her vision became impaired. (The vision improved in time; this complication subsided and was not a major feature of the case for 2 years subsequently). There was no jaundice, no azotemia, urinalyses were normal, STS was negative.

Hematologic studies during this admission: Shortly after admission RBC 0.885 mil, Hb 2.5 gm, hematocrit 8%, (MCV 90, MCH 28, MCHC 31), WBC 3000, platelets 310,000/cu mm, reticulocytes 1.8%, sickle cell preparation negative by 3 methods (cover slip 24 hours, vitamin C and CO_2).

A few days after admission: Bleeding time (Duke) 6 min. (N 2-4); bleeding

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time (Ivy) 19 min.(N-4-6); clotting time (Lee-White) 29 min. (N<12); recalcification time 210 secs. (N<130); platelet count 370,000; clot retraction poor in 24 hours; plasma fibrinogen 600 mg%; Rumple-Leede test questionably positive (large purpuric spots). Subsequently the bleeding time remained prolonged while the clotting time returned to normal. The prothrombin time (Quick) was normal. There was no fibrinolysis. A bone marrow preparation from the sternum revealed good cellularity (20% neutrophilic myelocytes, 5% plasma cells and 51% normoblasts) and was read as indicating erythroid hyperplasia, normoblastic type (M:E ratio 1:1).

The patient received 22 pints of blood and had a D & C procedure. No tissue was obtained from the endometrium.

There was no fever throughout the stay. She was discharged improved with a Hb of 11.0 gm, RBC 4.1 mil and WBC of 2400 with 34% mature granulocytes. In the hospital she received penicillin, vitamin K, ferrous gluconate, seconal, aspirin, codeine and chloraquine for giardiasis.

The hematologic service noted the leucopenia without having an explanation for it and suggested a qualitative platelet dysfunction or a capillary dysfunction of the pseudo-hemophilia type as possibilities in the hemorrhagic state.

Fourth admission [redacted]-50 to [redacted]-51): About one month after discharge from the hospital the patient was re-admitted because of vaginal bleeding. In the hospital the metro-menorrhagia continued at a profuse level. Other physical findings except for pallor, were negative. The spleen and liver were not palpable and the lymph nodes were not enlarged.

Laboratory findings: Hb 7 gm and WBC 2500 with 53% mature neutrophilic granulocytes on admission. During the first week the Hb became 2.5 gm, RBC 1.23 mil, WBC 2000 (66% mature granulocytes, no abnormal cells) and platelets were found to be at 30,000/cu mm. Reticulocytes were 2.6%. Urinalyses were normal. The bleeding time was prolonged (9½ mins.) and clot retraction was poor. The Lee-White clotting time and plasma Quick time were normal.

The thrombocytopenia (platelets 15,000 - 30,000) and leucopenia (WBC 1600 - 2000) persisted. Blood transfusion elevated the Hb to 11 gm. Four bone marrow preparations were obtained (ilium, sternum, lumbar spinous process). These preparations were similar. Each was quite cellular and contained adequate numbers of precursors of all formed elements and no abnormal cells. A typical differential count is given:

Myeloblasts	1%	Basophils	3%
Neutrophilic myelocytes	20%	Plasma cells	11%
Juvenile neutrophils	4%	Megakaryocytes	1%
Band "	11%	Polychromatic normoblasts	3%
Segmented "	8%	Orthochromatic "	22%
Small lymphocytes	19%		

Comment on bone marrow preparations: "The bone marrow is quite cellular and has a fairly normal differential count with two exceptions; 1) that from the spinous process and sternum shows increased number of megakaryocytes with poor platelet differentiation and 2) there are increased numbers of mature plasma cells particularly in the sternal preparation".

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The attitude of the hematology service at that time may be summarized in the following note: "We now have 4 recent preparations of bone marrow from multiple sites. The following observations can be made: 1)there is either a normal or increased cellularity; 2) there has been no evidence of leukemia; 3) the differential counts have been of fairly normal proportions with a slight shift to the left of all elements; 4) the recent bone marrow smears show poor platelet differentiation with an apparent increase in cells of the megakaryocytic series. Cells with characteristics commensurate with megakaryoblasts are seen. Frequent degenerated megakaryocytes are seen and on 2 occasions megakaryocytes of so-called polyclast origin have been seen. These findings have developed along with a definite thrombocytopenia. It is considered that the thrombocytopenia and leucopenia and the state of the bone marrow are best explained by two possibilities - "hypersplenism" or "hypersensitivity". In view of the desperate nature of the patient's condition, splenectomy will be recommended provided patient's status permits".

The patient received 13 pints of blood. She remained afebrile. On [redacted]-50 a splenectomy was performed. The spleen weighed 50 grams. Microscopically there was follicular hyperplasia and apparent entrapment of leucocytes and erythrocytes in the red pulp. In general the structure was not significant in appearance.

The metrorrhagia ceased. Immediately postoperatively (for few days) the Hb was 11.5 gm, WBC 2000 and platelet count 150,000. Recovery from the operation was uneventful and the patient was discharged with a Hb of 11 gm, WBC of 2400 and platelet count of 30,000. The bleeding time was 7 to 9 mins. (N 2-4), clotting time 14 mins.

Subsequent course: The patient was followed in the clinic and periodically in the hospital during the following 2 years. There was one bout of metrorrhagia within 3 months of the splenectomy and no other hemorrhagic episode thereafter until the terminal event. The Hb gradually dropped to 5 to 6 gm every few months when she was given 1 to 4 pints of blood. The platelet count remained between 15,000 and 30,000, the WBC between 1200 and 2000 with 20-30% mature granulocytes and no abnormal cells. There was one bout of jaundice associated with an enlarged and tender liver thought due to hepatitis. There were 2 bouts of infection controlled with penicillin. A course of steroid therapy did not change the blood picture. Mostly the patient was afebrile. For these 2 years she was able to care for her daughter, but she did not work. Attempts to obtain an incriminating history of exposure to drugs or chemicals were unsuccessful. The patient used many different cosmetic preparations but it was not possible to consider these as related to her illness.

One month before the final admission and 2 weeks after her last blood transfusion the blood studies yielded the following information: Hb 6.9 gm, (MCHC 30%), platelets 20,000, WBC 2000 (35% mature granulocytes), 1 normoblast/100 WBC, reticulocytes 1%, normal fresh osmotic fragility of RBC, abnormal incubated osmotic fragility of RBC, direct Coombs test negative, mechanical fragility of RBC normal, RBC volume 650 ml (blood volume 2800 ml, patient's weight 41 kg).

Tenth and final admission [redacted]-52 to [redacted]-52): The patient complained of coughing blood. She expired in less than 12 hours following admission with an overwhelming hemorrhagic pneumonitis and respiratory distress. A blood culture yielded B. Subsilis.

CASE 1 (Cont'd)

Postmortem summary: The lungs were heavy and revealed hemorrhagic consolidation (combined weight 1790 gms). Microscopically there was confluent hemorrhagic pneumonitis and pulmonary edema. Within the hemorrhagic foci were large colonies of bacteria and few or no leucocytes. There were hemorrhagic foci throughout the viscera (hemothorax, hemoperitoneum, purpura over abdominal viscera, massive gastrointestinal hemorrhage). There was hemosiderosis. The bone marrow from multiple sites was fatty and hypocellular. Of the cells present plasma cells and reticulum cells were prominent.

Final opinion: Aplastic anemia with terminal bacteremia, hemorrhagic pneumonitis and widespread visceral hemorrhages.

CASE 2. [redacted]

A 6 year old white female was admitted because of severe pancytopenia. The present illness began one month before admission with purpura over the lower extremities.

The patient had received various antibiotics and chemotherapeutic agents periodically during the prior 2 years for upper respiratory infections and bouts of low grade fever. Various known preparations except novobiocin, bacitracin and neomycin had been given the child. Included in the list of medications was chloromycetin.

Three months before admission chicken pox had run its course without complications. The patient was given antibiotics for this. Nine months before admission a bout of pharyngitis was also treated with multiple antibiotic preparations.

One month prior to admission rubeola was diagnosed. As the rash subsided multiple petechiae appeared for a short period. Shortly thereafter she became febrile and was thought to have an urinary tract infection. She was given gantrisin, a drug she had received previously. A hemorrhagic pharyngitis ensued. Leucopenia and thrombocytopenia were detected. She was managed with penicillin, erythromycin, steroids and vitamins. The purpura became more intense.

When admitted here the temperature was 102.6°F, pulse 130, resp. 38. The patient was lethargic. The skin was covered by many small and large hemorrhages.

Laboratory findings: Hb 11.8 gm, (MCV 85, MCH 27, MCHC 32), platelets 16,000/cu mm, WBC 1000 (mature granulocytes 12%), reticulocytes 0.1%. Blood transfusions had been given.

A bone marrow aspiration revealed only plasma cells, reticulum cells and rare normoblasts. The picture was characteristic of the aplastic state.

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The urine had 2+ proteinuria, 10 WBC/hpf, and was loaded with Gram negative rods. The culture yielded E. coli, paracolon intermedium. The blood culture yielded Ps. aeruginosa and paracolon intermedium.

Intravenous penicillin and achromycin were started. Progressive respiratory distress developed. Tarry stools were passed. The patient died 18 hours after admission.

The postmortem examination demonstrated confluent hemorrhagic pneumonitis with many bacterial colonies and few inflammatory cells; hemorrhagic pyelonephritis, extensive visceral hemorrhages and an aplastic bone marrow.

Drug dependent leucoagglutinins were demonstrated with achromycin, penicillin and gantrisin. The results with chlorcmycetin and erythromycin were questionable, streptomycin gave negative results. RBC and platelet agglutinins were not demonstrated.

Opinion: Acute aplastic state suspected as drug induced.

CASE 3 [redacted]

A 50 year old colored female had been treated for thyrotoxicosis with radioactive iodine (I-131). In the clinic she had been followed for 6 years with diastolic hypertension (160/120), vaginal pain and peripheral edema. She had been digitalized. Four years before a WBC was 3400 and Hb 10.3 gm. She was admitted to [redacted] from [redacted]-58 to [redacted]-58 with an acute myocardial infarction and ventricular tachycardia. She was given quinidine from [redacted]-58 to [redacted]-58. On [redacted]-58 pronestyl was started. She was not digitalized but received heparin and danilone. The peripheral blood was as follows: RBC 3.5 mil, Hb 10.4 gm, hemat. 33%, (MCV 95, MCH 30, MCHC 31); WBC 2500 (38% mature neutrophilic granulocytes); reticulocytes 0.2%, platelets 530,000. A sickle cell preparation was negative. She was discharged improved with a ventricular rate of 65.

Three months after discharge this patient was seen in the EOR with gastroenteritis. The WBC was 8200. She was given asparine. The patient was readmitted to the hospital from [redacted]-58 to [redacted]-58 with tachycardia and frank congestive failure. Cedilanid was given on admission and digitoxin was started and given throughout the hospital stay. Pronestyl was given until [redacted]-58 and then quinidine was given and continued. The patient was eventually discharged improved on quinidine and digitoxin.

Hematologic studies: RBC 3.0 mil, Hb 7.8 gm, Hemat. 26.4%, (MCV 88, MCH 26, MCHC 29.6%), platelets 104,000; WBC 2700 (55% mature neutrophilic granulocytes). Two bone marrow preparations were obtained from the sternum. Each appeared hypocellular although the eventual differential count indicated about 30% neutrophilic myelocytes and 44% normoblasts.

The patient was considered to have leucopenia, anemia, hypocellular bone marrow and a tendency to thrombocytopenia. The cause for these disturbances was not forthcoming although a drug sensitivity was suspected.

Additional comment: The patient has a refractory anemia of hypoplastic type with definite leucopenia and a tendency to pancytopenia. This is a very common problem. Is it drug induced? What is the hematologic prognosis? What can be done with respect to the drug possibility? To be sure, this patient's outlook appears more impaired by cardiovascular complications but still the hematologic features could at any moment become of serious import.

CASE 4. [redacted]

This 21 year old colored male [redacted] has had frequent admissions to the hospital for epistaxis associated with severe pancytopenia. On [redacted]-56 he first appeared with a six months history of recurrent nosebleeds. A history of ingestion of 4-Way cold tablets and cough syrup for several years was elicited. Steroids were highly effective in coping with the epistaxis.

The laboratory data are given in the accompanying table (see page 7A).

In [redacted] 1957 there were two chill-fever reactions to blood transfusions. He was given no more transfusions after this time but instead has been on steriod therapy (Meticorten 10-20 mgm. daily).

Physical examination except for epistaxis was negative.

In [redacted] 1958 the Cushing-like state appeared. At the same time hematologic remission became complete.

CASE 5. [redacted]

A 41 year old white male was observed in a local clinic with a neuroma of the foot. A routine WBC was 4500 with 50% mature granulocytes. The Hb was 14.6 gm and there were adequate numbers of platelets in the blood smear.

He was next in a local [redacted] from [redacted]-57 to [redacted]-57 because of pneumonitis. This abated on penicillin therapy. A definite leucopenia was noted (WBC near 2000). Bone marrow aspiration was unsuccessful and a bone marrow biopsy showed an adequate cellularity considered compatible with regeneration following toxic injury of marrow cells. All elements were shifted to the left; there were no abnormal cells present.

In [redacted], 1957 lesions on the dorsum of the left hand on biopsy revealed a suppurative granulomatous inflammation. This lesion responded to x-ray therapy.

From [redacted] to [redacted], 1957 he was followed on an outpatient basis. There was anemia (Hb 9.6 to 12.9 gm), leucopenia but normal platelet counts.

In [redacted], 1957 the Hb was 6.5 gm and the WBC 1150 (6% granulocytes). He was re-admitted to the [redacted] from [redacted]-58 to [redacted]-58. A history of prominent dexedrine intake was obtained. There was mild cervical and axillary lymphadenopathy. The spleen was 7 cm below the costal margin. It was firm. Minimal skin purpura was present. The laboratory data indicated: Hb 8.4 gm; WBC 1350, (3% granulocytes), platelets 54,000; the direct Coombs test was negative; RBC fragility (osmotic and mechanical) was normal and the serum bilirubin was normal.

He was treated with hydrocortisone, INH and penicillin. On [redacted]-58 he left the hospital on his own volition. His local physician placed him on Meticorten.

On [redacted]-58 he was admitted to this hospital extremely ill. There was severe diffuse bronchopneumonia (Ps. aerugenosa cultured from sputum) and bacteremia due to Ps. aeruginosa. Laboratory tests indicated; Hb 9.3 gm, WBC 800, platelets 30,000. Multiple antibiotics were given. He succumbed 2 days after admission. Postmortem examination revealed an acute necrotizing pneumonitis and early but diffuse myelofibrosis. The bone marrow preparations were quite cellular (plasma cells and reticulum cells were present).

DATE	WBC	PLATELETS	MCV	MCH	MCHC	RETICS.	Hb.	BONE MARROW
[redacted]-56	3300	32,000	85	24	28		5.5 gms.	Plasmacytosis, no megakaryocytes, erythroid hyperplasia, mast cell hyperplasia
[redacted]-56	3700	12,000	101	32	32	1.7%	8.4	Relative lymphocytosis and plasmacytosis, hypocellularity of granulocytes, mast cells
[redacted]-57	2700	4,000	113	39	34	1.7%	6.4	Granulocytes virtually absent; no platelets or megakaryocytes seen. 3.0% plasma cells
[redacted]-57	2900	12,000			33		4.0	250 mgm. Imferon followed by 5.0% retics.
[redacted]-57	2050	8,000	143.5	49	35	4.2%	3.2	Hypocellularity. Relative erythroid hyperplasia
[redacted]-58	1800	12,000					4.4	
[redacted]-58	3100	10,000					6.4	
[redacted]-58	5300	36,000					10.3	Relatively normal marrow - some mast cells present
[redacted]-58	6800	112,000					12.8	

CASE 6 [redacted]

A 42 year old white female entered the hospital with an acute febrile illness associated with chills and extreme weakness. Three weeks before a hemorrhoidectomy had been performed and the wound had failed to heal properly. She had frontal and parietal headaches and aching in the paranosal sinus areas. "Antibiotics" had been given without abatement of the febrile state.

The past history indicated that the patient had been somewhat indisposed for 6 to 12 months before the operation. She complained mainly of weakness and easy fatigability. The last menstrual period began 8 days before the operation, lasted 2 days, ceased for 2 days and returned for 5 days. Prior to this there had been no menstrual irregularities. She had sinusitis in the past for which her sinuses had been "drained"; there was a "strep throat" 9 years earlier and during the 8 months prior to admission rather extensive dental repair had been in progress.

The patient admitted the intake of many proprietary preparations obtained at the drug store as well as some medications by her physician, the nature of which was not known.

On examination the temp. was 102.4°F, pulse 110, resp. 28 and BP 100/70. There was tenderness over the frontal and maxillary sinuses. The chest was normal. The spleen was readily palpable 5 cm below the costal margin. The liver was felt 4-5 cm below the costal margin in the MCL. The rectal area was granulating over a circumference about 3 cm. wide.

Laboratory data: Throat, blood and urine cultures were sterile. The Hb was 10.5 gm, (MCV 91, MCH 28, MCHC 31), platelets 84,000 and WBC 1350 (no neutrophilic granulocytes seen, lymphocytes 95%, monocytes 2%, eosinophils 3%).

Bone marrow differential count (sternum):

Myeloblasts	1.5%	Megakaryocytes	0.5% (degenerate
Neutrophilic myelocytes	2.0%	Normoblasts	21.5%
Mature "	0.0%		
Eosinophils	11.5%		
Lymphocytes	59.0%		
Plasma cells	4.5%		

Comment: No leukemic cells were seen, degenerated cells 50/100 viable appearing cells.

Course: For 9 days the course was febrile (temp. 100-104°F). There were night sweats and the patient was frequently irrational and delirious. For sedation chloral hydrate and seconal were given and an occasional aspirin. A pelvic examination under anesthesia was negative. A liver biopsy gave normal results. ACTH was given for 12 days. Achromycin was given until a cellulitis developed. Staphylococci were recovered. This infection was controlled with erythromycin.

Nine days after admission the WBC was 1500 with 15% neutrophilic granulocytes. The WBC gradually rose to 7000 on the 16th day with 14% neutrophilic granulocytes and 9300 on discharge (17th day) with 20% granulocytes. At this time the Hb was 14.4 gm (after 2 pints of blood) and the platelets 140,000/cu mm.

CASE 6 (Cont'd).

A second bone marrow preparation shortly before discharge revealed 1% myeloblasts, 6% neutrophilic myelocytes and 17% mature neutrophilic granulocytes. The preparation was adequately cellular.

Comment: The diagnosis was acute aplastic anemia with agranulocytosis. "The general features suggested a reaction to a drug although a specific agent was not identified".

Additional course: The splenomegaly persisted and the neutropenia recurred and remained fixed (WBC 2500 - 4500). Weakness and fatigability were the main complaints. The bone marrow preparation gave normal results. The neutropenia abated following splenectomy. She has been reasonably well since the operation (now 3 years). A tooth abscess one and a half years ago was attended by leucocytosis.

CASE 7 [redacted]

A 15 year old white female complained of easy fatigability of 6 weeks duration. Ten days before she had a "cold" (sore throat and fever) which subsided after injections of penicillin. There was no other drug intake by history except aspirin. During this episode she was found to be anemic. There was no other historical matter of note except that a maternal aunt had recently been diagnosed as having acute lymphatic leukemia. There had developed some ecchymoses over the skin but the menstrual periods had been regular and not excessive. Three small ulcers had developed in the floor of the mouth next to the teeth. Except for pallor, an occasional bruise and the buccal ulcers the physical examination was negative (liver and spleen not palpable, lymph nodes not enlarged).

Hematologic findings: RBC 1.77 mil, Hb 6.4 gm, hematocrit 19.7%, (MCV111, MCH 36, MCHC 32); WBC 1600 (segs 11%, eos. 1%, mono. 2%, lymphs 81%); platelets 10,000 - 20,000; direct Coombs test negative; mechanical and osmotic fragility normal; hemolytic index 40; serum bilirubin 0.6 mg%; bleeding time 8 mins. clot retraction very poor; clotting time normal; Quick time 12 seconds. Four bone marrow preparations were obtained (2 from sternum, 2 from ilium). These were similar and indicated hypocellularity and similar differential counts as follows:

Myeloblasts	4%	Basophilic normoblasts	4%
Neutrophilic myelocytes	11%	Polychromatic "	23%
Mature neutrophils	7%	Orthochromatic "	22%
Eosinophils	3%		
Lymphocytes	25%		
Plasma cells	1%		

The bone marrow preparations were considered consistent with an aplastic state in the early phases of regeneration. A note of that time summarizes the view then: "This patient has a prominent depression of red cells, white cells and platelets in the blood. The first bone marrow preparation was hypocellular and consistent with an acute aplastic anemia. The next three bone marrow preparations were more cellular and indicated generation of the bone marrow. Neither in the peripheral blood nor in the bone marrow did we find any indication of abnormal cells; in other words, we found no indication of leukemia. We believe that this patient has acute aplastic anemia due to injury of the bone marrow, probably by a toxic agent with which she has come in contact".

CASE 7 (Cont'd)

The patient was given ACTH and placed on Cortisone. She was given 2 pints of blood and discharged to her physician.

The pancytopenia remained severe and there was no symptomatic improvement. Five months later the patient was reconsidered from a hematologic view. At this time the following was detected; RBC 2.1 mil, Hb 7.2 gm, platelet count 15,000 - 30,000, WBC 1900, reticulocytes 1.2%. Bone marrow preparations were obtained from the same four sites as on the former occasion. A typical differential count and the comment are given:

Myeloblasts	7%	Lymphs, small	33%
Promyelocytes	11%	Plasma cells	1%
Myelocytes	10%	Polychromatic normoblasts	7%
Young neutrophils	2%	Orthochromatic "	20%
Band "	4%		
Segmented "	4%		
Eosinophils	1%		

Comment: "Arrest hyperplasia of granulocytic series (28% myeloblasts and myelocytes, 10% mature granulocytes). Erythroid hyperplasia (M:E ratio 2.7:1). Lymphatic infiltration (33% small lymphocytes). The cells from the various bone marrow sites yield similar appearance and ample cellularity. In this and other respects the preparations depart markedly from the former ones obtained in June, 1954. The latter were hypocellular. There is marked variation in the cells; some are small "blasts" with meager cytoplasm, others are large with irregularly lobulated coarse nuclei having prominent nucleoli. The picture is considered to represent a leukemic transformation although an atypical arrest hyperplasia has not been completely excluded. A significant number of promyelocytes and myelocytes contain reddish orange round inclusions not unlike viral inclusions. Opinion: arrest hyperplasia; atypical, probably leukemia".

The subsequent course and features of this case were considered consistent with acute leukemia of the leucopenic type (includes pancytopenia). The patient succumbed 13 months after the first admission to the hospital.

Additional comment: The early features of this case appeared consistent with acute aplastic anemia. The lymphocytes in the bone marrow may have been misjudged although subsequent study did not support this. Later the bone marrow became consistent with acute leukemia.

CASE 8 [redacted]

A 61 year old white male had been in the hospital on 29 occasions from 1951 until his demise in 1955. On each occasion the main complaints were referrable to a severe anemia (Hb about 5 gm). There were always adequate numbers of WBC and platelets. Several bone marrow preparations indicated adequate numbers of precursors for the granulocytes and platelets but very few normoblasts. The spleen and liver became palpable. During his admissions he was given over 150 blood transfusions. These were frequently complicated by chill-fever reactions. During the last year he developed pigmentation of the skin and diabetes mellitus. The diagnosis of exogenous hemochromatosis was considered appropriate.

The laboratory data on his final admission included: Hb 6.1 gm and platelets adequate; WBC 14,000, urine with sp. gravity of 1.020 with a trace of albumin and

CASE 8 (Cont'd)

a 4+ sugar and with 4-5 white cells. Bromsulfalein retention was 25%. Blood glucose 294. Inorganic phosphorus 2.5. Acid phosphatase 0.9, alkaline phosphatase 7.9 BU. Total protein 8.5 with albumin 1.8 and globulin 5.7. Bilirubin was 0.4 and 0.8 total. Cholesterol was 192 with 77 esters. Blood sugars continued to remain elevated in the range of 350 mg. to 280 mg% per day, the urine spill was around 50 gm. per day. The blood serology was negative. Prothrombin time was approximately 50%.

The patient succumbed with a cerebrovascular accident. A postmortem examination was not obtained.

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