

During the course of treatment, a series of differential blood counts were made at stated intervals after *x*-ray exposure, in order to study the immediate effects of the *x*-ray on the blood. The results are tabulated in Table 2.

TABLE 1.—LEUCOCYTE TABLE.

Date.	Whites.	Hbg.	Date.	Whites.	Hbg.	Date.	Whites.	Hbg.
1905.						1906.		
3-16	135000	70	7-15	145150	70	2-12	101860	..
3-18	168000	70	8-26	153750	..	2-13	152783	..
3-19	184000	70	9-9	235000	..	2-14	178250	70
3-22	188000	..	9-20	235000	..	2-15	157870	..
3-26	270000	70	10-17	244400	..	2-16	150240	..
3-27	242000	..	10-22	228300	..	2-18	143875	..
3-28	297000	65	10-31	202000	70	2-19	129840	..
3-29	248000	..	10-31	178000	..	2-20	145150	..
3-30	248800	70	11-27	188440	..	2-21	146420	..
4-1	282000	..	12-8	140155	..	3-14	109500	70
4-2	282000	..	12-9	164230	..	3-15	94120	..
4-3	305000	70	12-11	181000	..	3-21	71300	..
4-5	310000	..	12-14	210000	72	3-22	61120	..
4-6	248000	..	12-14	187000	..	3-23	57320	..
4-7	311000	..	12-16	176000	..	3-27	54750	..
4-9	297000	..	12-17	192000	..	3-28	38195	..
4-12	360000	..	12-19	192255	..	3-29	36925	..
			1906.					
4-15	363100	..	1-1	131000	..	4-4	25464	..
4-16	378000	..	1-10	115860	..	4-5	16552	..
4-17	365500	70	1-12	98400	..	4-6	17061	80
4-18	342500	..	1-15	99125	70	4-9	13243	..
4-19	330500	..	1-26	165266	..	4-10	10443	..
4-20	294200	..	1-29	168170	..	4-11	8405	..
5-1	282000	..	1-30	270460	..	4-12	8150	..
5-15	274000	..	1-31	285230	..	5-16	4680	80
6-6	260000	70	2-2	140055	..	6-1	4800	..
6-26	252000	..	2-7	124000	..	6-10	5220	..
7-7	133900	..	2-10	132415	..			
6-28	163500	..	2-7	101860	71			
7-11	165380	..	2-11	115865	..			

\* Fowler's sol. given 5 gtt. t. i. d., 1 drop increase a day.

† Fowler's solution, gtt 15 t. i. d.

‡ Fowler's solution discontinued.

TABLE 2.—RESULTS OF X-RAY TREATMENT.

Date.	Time.	Time of Exposure.	Leucocytes Total.	Lymphocytes per cent.	Polynuclears per cent.	Eosinophiles per cent.	Basophiles per cent.	Myelocytes per cent.	Degenerates per cent.
3-27	9 a.m.	8.15	244400	2.4	48.2	1.	5.6	39.6	4.2
	11 a.m.	15 min.	282000	2.5	47.5	1.3	6.2	37.8	4.7
	1 p.m.	.....	300000	2.3	48.0	.5	4.0	36.2	9.0
	3 p.m.	.....	296800	2.8	46.0	.3	5.0	37.2	8.7
	8 p.m.	.....	282000	1.5	50.0	.7	6.0	35.8	6.0
3-28	9 a.m.	None.	248000	2.3	50.0	1.4	5.7	35.5	4.7
4-16	9 a.m.	8.3	278000	2.1	56.4	.7	5.0	32.2	3.6
	11 a.m.	30 min.	300000	2.6	54.8	.4	3.5	32.4	6.3
	1 p.m.	.....	302000	2.5	51.2	.3	4.2	34.0	7.8
	3 p.m.	.....	296000	2.6	54.6	.4	4.4	31.0	7.
	8 p.m.	.....	280000	2.8	53.8	.9	4.7	32.0	5.4

In Table 2 it will be seen that the exposure to *x*-rays, at one time 15 minutes and another 30 minutes, was followed by a gradual increase in the number of leucocytes which reached its maximum about 5 hours after the exposure. The number of degenerates increased in one instance from 4.2 per cent. to a maximum of 9 per cent. and in the other from 3.6 per cent. to a maximum of 7.8 per cent. Nearly all degenerates are disintegrating myelocytes, in many cases consisting only of a remaining network of fibrils. The increase in the number of degenerates seems related to the general leucocyte increase after exposure.

## URINARY FINDINGS.

The quantitative estimation of the total phosphates and earthy phosphates was carefully made, in order to determine whether or not the destructive action of the *x*-rays on the white cells and tissues caused an increased elimination of earthy phosphates. As the table below shows, the quantity of earthy phosphates is, if anything,

slightly diminished. This may be due to the fact that the calcium salts are partly deposited in the kidney tissue, and may be the explanation of the calcification found by Warthin<sup>3</sup> in the kidneys of leukemic patients, treated for long periods with *x*-rays.

TABLE 3.—URINARY FINDINGS.

Date.	Amount in U. Cn. 24 hours.	Gms. Total Phosphates.	Gms. Earthy Phosphates.	Albumin.	Casts.
3-19	800	1.60	0.32	Trace.	Few granular.
3-20	750	1.40	0.38	Trace.	Few granular.
3-21	1500	1.25	0.40	Trace.	Few granular.
3-22	1250	1.8	0.29	Trace.	Few granular.
3-24	700	1.18	0.12	Trace.	Few granular.
3-25	1075	1.69	0.10	Trace.	Few granular.
3-27	700	1.78	0.20	Trace.	None.
3-28	1000	2.3	0.40	None.	None.
3-29	925	1.99	0.30	None.	None.
3-30	1175	.90	0.17	None.	None.
3-31	700	1.00	0.16	None.	None.
4-1	870	.70	0.17	None.	None.
4-6	1400	1.4	0.12	None.	None.
4-8	925	.85	0.20	None.	None.
4-10	1200	1.5	0.20	None.	None.
4-14	1050	1.4	0.11	None.	None.
4-18	1250	1.3	0.12	None.	None.

## SUMMARY.

1. The beneficial therapeutic value of *x*-ray treatment in Hodgkin's disease is well demonstrated in the case reported. The decrease in the glandular enlargement was comparatively rapid, but the enlargement will probably recur unless *x*-ray treatment is persisted in.

2. In the case of leukemia, for a long time the *x*-ray treatment did not inhibit the further progress of the disease process, as is indicated by the great increase in the leucocytosis for three months after treatment was begun. After using the *x*-ray treatment systematically for over one year, the leucocyte count finally returned to normal. This was not accompanied by much decrease in the splenic enlargement. The use of arsenic as an adjuvant to *x*-ray treatment seemed of much benefit.

3. The immediate effect of *x*-ray treatment is to increase the number of leucocytes in the general circulation. This increase is accompanied by a large increase in the number of degenerate cells, most of which are disintegrating myelocytes. No toxic symptoms have developed during the long course of treatment. Although the leucocyte count has remained normal for a period of two months, the patient was advised to continue the use of the *x*-rays at intervals to prevent a recurrence of the blood condition.

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## POLYCYTHEMIA.\*

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In 1892 Rendu and Widal reported the discovery of a peculiar condition characterized by the rare combination of chronic cyanosis, enlarged spleen and increased number of the erythrocytes occurring with primary tuberculosis of the spleen. In 1899<sup>1</sup> they reported two similar

3. International Clinics, Vol. V.

\* Read before the St. Louis Medical Science Club.

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1. Rendu and Widal: "Splénomégalie tuberculeuse sans leucémie avec hyperglobulie et cyanose," Bull. Soci. méd. des hôp., III Ser., 1899, p. 528.

cases. In 1904 Turck<sup>2</sup> reported seven cases and reviewed exhaustively thirteen cases reported in the literature up to that time (Vaquez,<sup>3</sup> M. Martin and Lefas,<sup>4</sup> Cominotti,<sup>5</sup> Cabot,<sup>6</sup> 2; McKeen,<sup>7</sup> Saundby and Russell<sup>8</sup> 2, Rosengart,<sup>9</sup> Osler<sup>10</sup> 4). In 1905 Reckzeh<sup>11</sup> reported five cases, presented some experimental results on the production of this condition on animals and reviewed the literature of twenty-nine cases previously reported. This makes in all a total of thirty-four cases so far reported.

#### REPORT OF AUTHORS' CASE.

*Patient.*—Mrs. E. S., aged 40, housewife. Russian Jew.

*History.*—Family history was negative. Until her thirtieth year she had uninterrupted good health. From that time she dates the beginning of a chronic headache, vertigo and a noticeable diffuse redness of the skin. About five years ago she had a Ménière-like attack of vertigo, which was described as a "sudden rush of blood to the head," causing extreme vertigo and excruciating headache. This lasted about one minute and was suddenly succeeded by a syncopal sensation, without unconsciousness, followed by marked general weakness. A feeling of anxiety and premonition of death was marked during the attack. About this time she noticed for the first time a "lump in her side" (below the left costal arch). In 1902, she presented herself at the Jewish Hospital Dispensary, from the records of which we collected the following history and findings up to Dec. 10, 1905. Her complaint at that time was headache, vertigo, pain in the region of the ovaries, poor appetite, general weakness and a progressive loss of weight during the preceding two years.

*Menstrual History:* Three normal births (no puerperal hemorrhages). Menses were normal until two years previous when periods became irregular, being absent for two or three months and followed by a scanty menstrual discharge of from two to four weeks' duration, accompanied by more or less pelvic pain.

*Physical Findings:* Nutrition fair. Color good. Pulse 96. Temperature 99.4. Heart and lungs normal. Abdomen relaxed and tender on pressure. Spleen enlarged. No plasmodia in blood.

*Gynecologic examination (Dr. Ehrenfest):* "Uterus large; surface smooth. Cervix large, with small erosions. Adnexa normal. Curettement tissue, normal histologically." Quinin gr. v., t. i. d.; increased headache and vertigo. In 1903 she had a severe, prolonged hemorrhage following the extraction of a number of teeth. During the same year she was confined to bed for two weeks with severe cramps in the calves of the legs.

March 22, 1904: "Abdominal pain, headache, poor appetite and the usual menstrual disturbances" are recorded.

Dec. 6, 1904: "Spleen still enlarged. Liver in a state of ptosis. Pain in the cardiac region. Some cough and expectoration. Temperature 98.6." The following year she visited the dispensary occasionally still complaining of the above symptoms in more or less severity with no new physical findings.

On Dec. 10, 1905, she complained of the following: Ever constant headache; vertigo; burning and sensory disturbances of the skin; poor appetite; "cramps" in the abdomen; dragging pain in the back and left side; frequent burning micturitions; amenorrhea two months; insomnia; general weakness and debility. The cough and expectoration of previous years had been of short duration.

*Examination.*—This showed a poorly nourished and developed neurotic woman of small stature. There was diffuse dusky-red discoloration of the skin turning to purplish-red in hands and lips, increased by emotional influences. Pulse was 86; temperature 98.4; respiration slow and regular.

*Scalp:* The scalp was tender, more marked on the left side. The ears were a translucent red.

*Face:* There were mild diffuse cyanosis, dilated venules also on cheek and nose, and tenderness and hyperesthesia on the left side about the eye. The conjunctiva was injected. Pupils were equal and reacted to light and accommodation. Movements of the eye-lids and the eyes were normal. Fundus was dark red; the disc was pink, veins were large and dark blue. The lips were purplish red, the gums, dusky red. Tongue was clean, purplish red. Mucous membrane of mouth was dark red. The tonsils were not enlarged.

*Neck:* The veins were not dilated or pulsating, there was no murmur or hum, and no glands were palpable. The thyroid was not enlarged.

*Chest:* Lungs were normal; no emphysema. The apex beat was in the sixth left interspace in the nipple line, it was circumscribed, forcible and compared well with the pulse. The dullness extended to the apex beat on the left, to the lower margin of the third rib above and to the mid-sternal line to the right. Upper sternum was not dull. Sounds were pure, distinct and rhythmic; the second aortic was slightly accentuated. There was no arteriosclerosis. Blood pressure was from 135 to 140.

*Fluoroscopic Examination (Dr. Carman):* "No abnormal shadows over lungs on mediastinum. Heart reaches just beyond the nipple line, sixth interspace to the left and just beyond the midsternal line to the right."

The splenic shadow corresponded to the description below. Abdomen was relaxed, full in upper third, and tender on the left side. No ascites. Liver, superior border reached sixth interspace, the lower border one finger below costal arch in the mammary line; the margin was blunt, no irregularities, tenderness or pulsation.

Gall bladder was negative. The spleen was greatly enlarged, extending to the mid-line of the abdomen to the right and the lower pole reached to the level of the umbilicus; the notch was palpable on the right border just below the costal arch. Surface was smooth; consistency firm, there was tenderness on pressure; the organ was easily movable; there was no peritoneal friction rub. Hemorrhoids were present.

There was tenderness over the sternum and other superficial bones. The legs were not cyanosed; there were no varicose veins. The toes were slightly cyanosed and cold. Other findings were practically normal. There were no abnormal muscle or joint findings, no edema. Glands were not enlarged. Reflexes were present and equal; there were no other sensory abnormalities.

*Urine (single specimens, not catheterized):* Yellow color. sp. gr. 1.007. Albumin, a trace; albumoses negative; blood negative; sugar negative; urobilin negative; casts negative; epithelium and leucocytes present.

*Blood Examination:* Erythrocytes 10,909,000, leucocytes 9,600, hemoglobin above 120.

*Course of Disease.*—From December 10, symptoms did not materially change. Constant headache and vertigo more or less severe, and attacks of pain in the left side of the face, about the eyes and in the upper jaw were constant complaints. Pain in the left hypochondrium and back occurred frequently. Appetite was poor, and there was discomfort and pain in the stomach and sometimes abdominal "cramps." She vomited once, a yellowish substance containing no blood. There were the usual menstrual disturbances previously described. Prolonged scanty menses produced no change in blood findings. The diffuse cyanosis and enlargement of the spleen were sta-

2. Turck: Beiträge zur Kenntniss des Symptomenbildes "Polycythämie mit Milztumor und Zyanose," Wien. klin. Wochschr., 1904, Nos. 6 and 7.

3. Vaquez: "Cyanose accompagnée d'hyperglobulie excessive et persistante." Société de biologie, 7, V, 1902; and "Hyperglobulie et splénomégalie," Bull. Soc. méd. des hôp., 1899, p. 579.

4. Martin and Lefas: "Tuberculose primitive et massive de la rate," Bull. Soc. méd. des hôp., 1899, p. 547.

5. Cominotti: "Hyperglobulie und Splenomégalie," Wien. klin. Wochschr., 1900, No. 39.

6. Cabot: "A Case of Chronic Cyanosis Without Discoverable Cause, Ending in Cerebral Hemorrhage," Boston Med. and Surg. Jour., 1899, vol. cxli, No. 29, and vol. cxlii, No. 11.

7. McKeen: "A Case of Cyanosis Difficult to Explain," Boston Med. and Surg. Jour., 1901, p. 610.

8. Saundby and Russell: "An Unexplained Condition of Chronic Cyanosis, with the Report of a Case," Lancet, 1902, p. 515.

9. Rosengart: "Milztumor und Hyperglobulie," Mitteilung aus den Grenzgeb. d. Med. u. Chir., 1903, vol. ii.

10. Osler: "Chronic Cyanosis with Polycythemia and Enlarged Spleen," Amer. Jour. of Med. Sciences, August, 1903.

11. Reckzeh: "Klinische und experimentelle Beiträge zur Kenntnis des Krankheitsbildes der Polycythämie mit Milztumor und Zyanose," Zeitschr. f. klin. Med., 1905, vol. lvii, Nos. 3 and 4.

tionary. General weakness and debility was marked so that the patient was frequently confined to bed for a few days. Temperature was never above 98.6. Pulse ranged from 80 to 90. Respiration was never increased or irregular.

## BLOOD FINDINGS.

Date.	Source of Blood.	Erythrocytes.	Leucocytes.
Dec. 10, 1905.....	Finger.....	10,000,000	9,600
Dec. 11.....	Finger.....	10,666,000	7,600
Dec. 25.....	Finger.....	10,908,000	6,600
Dec. 30.....	Finger.....	10,004,000	7,400
Jan. 14, 1906.....	Finger.....	9,698,000	8,400
Jan. 25.....	Ear.....	8,037,000	9,400
Feb. 25.....	Toe.....	10,320,000	8,500
Feb. 25.....	Ear.....	10,648,000	8,640
Feb. 25.....	Finger.....	12,584,000	7,800

Average of the three taken at same time, Feb. 25, 1906, 11,150,000 erythrocytes; 8,313 leucocytes.

Macroscopically the blood was deep, dark-red in color and very thick. It flowed sluggishly and spread with difficulty between cover glasses. Coagulation time, four minutes (1 mm. tube).

Hemoglobin:<sup>12</sup> Nine estimations taken at different times and from different parts of the body ranged between 180 and 200 per cent. One estimation from the ear was 150 per cent.

Color index, 1 or slightly above 1. Specific gravity, from 1065 to 1075 (one estimation of 1058 was made, but was considered low on account of technical error). The spectroscope gave bands of oxyhemoglobin.

Fresh Drop: The cells were crowded closely together; equal in size; symmetrically round in form; color dark, going to center of cell. No apparent increase in leucocytes. Polymorphonuclear cells predominated among the whites. Stained specimens invariably gave the following differential count: Lymphocytes, 11 to 14 per cent.; small, 11 per cent.; large, 3 per cent.; leucocytes, 9 to 11 per cent.; transitional, 6 per cent.; mononuclear, 5 per cent.; polymorphonuclear, 75 to 76 per cent.; eosinophiles, 1 to 1.5 per cent.; polychromatophylic erythrocytes, a few. Mast cells were not increased; there were no myelocytes or erythroblasts.

Treatment.—This has been entirely without results. Quinin, gr. V. t. i. d., increased vertigo and headache. Administration of salicylates, iron and tonics for a long time had no favorable effect. Caffein, bromids and sedatives did not decrease the symptoms. Nitroglycerin, 1/100 gr. every hour for two days produced no change in the symptoms. Valerianates, hydrastis, etc., did not alter the condition. Fowler's solution gtt. xxx daily for three weeks caused no change in the clinical symptoms or blood findings. Three x-ray exposures over spleen, of five minutes duration, and two exposures over the face produced no change in the symptoms or blood findings. We wish to take this opportunity of expressing our indebtedness to the authorities of the Jewish Hospital Dispensary for the privilege of reporting this case. Especially to Dr. J. Myer do we feel grateful for the many favors shown in connection with the preparation of this report.

## NOMENCLATURE.

Enough of these cases have been reported to establish this condition as a clinical entity. On account of its obscure nature, however, the terminology has been variable. Some of the titles under which the cases have been reported are the following: "A Case of Marked Cyanosis Difficult to Explain." "Unexplained Condition of Chronic Cyanosis." "A Case of Chronic Cyanosis Without a Discoverable Cause." "Polycythemia and Enlarged Spleen." "Polycythemia, Enlarged Spleen and Chronic Cyanosis." "Polycythemia with Splenomegalie," etc., etc. Some writers have referred to it as "Vaquez disease." Since Osler's splendid article some of our own countrymen have suggested the name of "Osler's dis-

ease." Turck,<sup>13</sup> considering that the condition has the same relation to the erythroblastic myeloid tissue that myelogenous leukemia bears to the leucoblastic marrow suggests the name of "erythemia" or "erythrocythemia." Polycythemia, while it is only one of the cardinal findings and does not include the other constant findings or, as yet, an established pathologic basis, has become by usage a rather popular term for this syndrome.

## ETIOLOGY AND PATHOLOGY.

On account of the variety of pathologic findings no definite etiology has yet been established. There are no constant predisposing causes in the cases so far reported. Heredity and previous diseases bear no relation to this condition. In three cases it followed tuberculosis of the lungs; malaria in one; syphilis in one; organic heart disease (postmortem) in one; primary adenoma of liver was present in one (Turck); malignant tumor of the thymus one case (Reckzeh<sup>11</sup>). The age at which it appears has been previously considered to be between thirty-five and sixty, but Turck's report shows that it occurs at early adult life. Reckzeh reported one case in a child of 10 years old. Weil reported two cases of congenital cyanosis with enlargement of the spleen in the absence of heart lesions, in one of which at autopsy pathologic changes of the thymus and bone marrow (macroscopically) were found. If these cases can be accepted it may be said that it does occur in infancy. As to sex Osler's report gives it as occurring most frequently in the males. But analysis of all the cases shows it to be about equally divided between the sexes.

Singularly enough, in the first three cases reported there was found a primary fibrocaceous tuberculosis of the spleen. Collet and Gallarandin reported a case of tuberculosis of the spleen which showed clinically a deep red skin, progressive emaciation and dark red blood. (No blood examination). Cominotti's<sup>5</sup> case presented at postmortem fibrous splenitis, small nodes of hyperplastic parenchyma cells in liver and caries of spine (no histologic examination). Scharold reports a case of miliary tuberculosis characterized clinically by pigmentation and cyanosis (no blood examination reported). Widai, regarding the pathogenesis, says that it is a functional activity of the marrow probably caused by the decreased function of the spleen due to tuberculosis of that organ. Vaquez says that the blood-forming organs must play a rôle, primarily or secondarily, on account of the pologlobulism. He thinks that the cyanosis is an accidental condition and need not necessarily be present. These findings led the French to conclude that primary tuberculosis of the spleen was the cause of this peculiar syndrome. Since then, however, many cases have come to autopsy in which no tuberculosis of the spleen or other organs has been found.

Turck in his conclusion says: "Naturally I can draw no positive conclusion. I can say that tuberculosis of the spleen, although demonstrated in some cases, will not explain the condition. The symptom complex has been reported with different causes. In some cases a splenic and in some a combination of splenic and liver involvement of a yet unknown character have occurred with the symptom complex. In my opinion, the most probable explanation of this syndrome is a primary hyperplastic affection of the erythroblastic myeloid tissue with histologic changes in the spleen (and liver not yet demon-

12. The blood was diluted with an equal amount of n/8 NaCl solution and the estimation of this dilution by Dare's hemoglobinometer multiplied by two. This method was proved to be accurate by numerous estimations on dilutions of normal blood.

13. Turck: "Splenomegalie Hyperglobulie und Zyanose," Mitt. d. Wien. Gesellsch. f. inn. Med., 1902, Nos. 6 and 7, Wien. klin. Wochschr., 1902, No. 14 and No. 6.

strated.)” He argues in support of this theory that: 1. A number of cases have come to postmortem presenting no tuberculosis of the spleen. 2. No other one pathologic finding of the spleen reported will explain this condition, as the findings of that organ are variable. 3. In three cases the liver was found to be enlarged before the spleen. 4. No other organs than the liver and spleen have been found affected which would explain the condition. 5. The blood findings have shown a hyperplasia of the erythroblastic marrow, with also an accompanying hyperplasia of leucoblastic bone marrow. 6. A hyperplastic condition of the erythroblastic myeloid tissue has been found in some of the cases postmortem. 7. Rosengart found in one case blood cells and changes in the spleen and liver histologically (derived from hyperplastic erythroblastic myeloid tissue). The demonstration of the last two points, he thinks, has substantiated his theory that the changes in those organs (spleen, liver and bone marrow) are analogous to the changes which take place in them with hyperplasia of the leucoblastic myeloid tissue in myelogenous leukemia. Turk’s blood findings, however, do not correspond with the findings of other writers. He found a leucocytosis and evidence of hyperplasia of the leucocytic myeloid tissue (increase of the granular leucocytes; polymorphonuclear, mast cells and myelocytes) and erythroblasts; and it is these elements which Rosengart found histologically in the spleen, that form a basis for Turk’s hypothesis. With the exception of Cabot’s one case, however, these blood findings do not occur in the records of other men.

Reckzeh<sup>12</sup> believes that the stagnation of the blood is the probable cause. He says that it is an established fact that the syndrome has occurred in tuberculosis of the spleen, but it is also a fact that it has occurred in absence of tuberculosis of the spleen. He reports a case of a malignant tumor of the thymus causing compression of the superior vena cava having cyanosis, enlarged spleen and polycythemia. His experiments on animals confirmed his belief that compression producing stagnation of the blood was sufficient to produce the syndrome. He says that diminished tonicity of the veins may result in sufficient stagnation of the blood to produce the condition. Turk<sup>13</sup> claimed that up to the time of his article all writers were certain that the blood findings were not those of stasis. Reckzeh’s case, in which there was a demonstrable cause (malignant tumor of the thymus) producing a stagnation of blood might not be accepted, especially by the American writers, who have rather considered the absence of a mechanical cause as one of the positive findings. Furthermore, this case showed polycythemia only in the upper part of the body which was affected by the venous obstruction; the lower part giving a blood count which would be barely above normal (4,400,000, 6,800,000). The spleen in this case was hyperemic and only slightly enlarged. He had a slight degree of success in only two of his animal experiments. While he produced the clinical symptoms of dyspnea, cyanosis and venous dilatation in both, the polycythemia was only 6,000,000 in one case and 6,200,000 in the other.

Cabot’s<sup>6</sup> one case presented at postmortem, meningeal hemorrhage and passive hyperemia of the organs. Zemlich<sup>14</sup> reports one case in which death took place from cerebral hemorrhage. Saundby and Russell<sup>8</sup> reported one case showing spleen of 1440 gm.; normal consistency, no tuberculosis, old mitral heart lesion; liver large and firm, 1890 gm., brain congested, arachnoid opaque; marrow

of femur normal macroscopically (no histologic examination made). Russell suggests a careful examination of the suprarenal bodies in order to account for the extreme muscular weakness.

Further investigation consisting of careful clinical examination including a comparative analysis of arterial, venous and capillary blood taken from different parts of the body at the same time, estimations of the viscosity of the blood, blood culture and inoculations, etc., and complete histologic examination of bone marrow, spleen, thymus, liver, adrenals and other tissues will no doubt do much to clear up the pathology of this condition. Then the establishment of an anatomic basis will only open the field for more investigation on the etiologic factors producing the pathology.

#### ANALYTIC SUMMARY OF CLINICAL FINDINGS.

An analysis of twenty-five cases shows the clinical findings to be variable. Common to the majority of cases are cyanosis, enlargement of the spleen, headache, vertigo, and the blood findings of polycythemia without a positive mechanical or accepted anatomic cause. Diffused marked cyanosis occurred in twenty-one cases; localized or mild cyanosis occurred in three of the others. Dilated venules were common to practically all clinically, and venous congestion was a common postmortem finding. Enlargement of the spleen occurred in twenty-one cases, accompanied in the majority and preceded in a few by enlargement of the liver. In the majority of cases the splenic enlargement was moderate and in only two was the liver enlargement excessive. Localized pain and tenderness in the region of the spleen and pressure symptoms from that organ were reported in nearly all the cases. Headache of a chronic and constant type was present in twenty. Vertigo was noted in sixteen, and in five of these, paroxysmal attacks simulating Ménière’s disease occurred. Besides these symptoms, general weakness, disability and greater or less sensory disturbances were marked complaints. The blood findings in general showed polycythemia or polyglobulism. This increase of the erythrocytes and other elements of the blood is not confined to any localized area of the body, but is diffuse or generalized. The number of red cells varied from 5,300,000 (Cominotti<sup>9</sup>) to 12,000,000 (Cabot<sup>6</sup>); average 8,500,000 to 10,000,000. These were normal with the exception of a few cases in which erythroblasts and polychromatophilic cells were reported (Turk and Cabot). The leucocytes varied from 4,000 to 31,000. In half the cases they were not increased above normal. The differential count in the majority of cases was practically normal. Turk found in his seven cases an increase of the granular leucocytes (polymorphonuclear 92 per cent. in one case) and a decrease in the lymphocytes. The latter seems to be a constant finding in a greater or less degree. A few myelocytes were found in all of Turk’s cases and in one by Cabot. Blood platelets were found to be increased in number. The hemoglobin percentage was usually markedly increased; the average was from 120 to 180 per cent. Cominotti reported one case in which it varied from 70 to 80 per cent; and Rosengart one case in which it was 200 per cent. Specific gravity was usually increased, varying from 1053 to 1083. Spectroscope examination, when made, showed oxyhemoglobin. Reckzeh found blood serum increased one per cent. in one case.

Among the less common symptoms, the following have been reported: Symptoms of cerebral congestion in a number of cases; edema of the brain, one case; cerebral

14. Zemlich: New York Med. Jour., Oct. 14, 1905.

hemorrhage, one; paraphasia, two; paralysis, two; one of which was hemifacial; neuralgia of face, two; tuberculosis of the lungs, one case; bronchitis, four; emphysema, not marked, two; dyspnea, three; edema of lungs, three. The heart was frequently found enlarged, with a systolic murmur at the apex in a few cases; the second aortic sound was accentuated in some cases and there were changes in the mitral valve in one; the heart was competent in all cases. Arteriosclerosis was present in four cases; the pulse was not increased in frequency or arrhythmic; it was generally of high tension. Blood pressure was usually increased, but was not so high as might be expected, averaging from 135 to 140. Hemorrhages were not especially frequent. Epistaxes occurred in a few cases; constant oozing from gums in one case; hemorrhage (severe) after extraction of teeth, two cases; hemoptysis, one; hematemesis, two; bloody stools,

there was a marked involvement of the liver. Indican occurred in two cases; in one in large amount. The specific gravity was usually low. Casts were present in some of the cases. In many of the cases the urine was normal. Among the symptoms of the special sense organs, the conjunctiva was injected in many cases. Fundus was usually deep red, the veins were generally enlarged, dark purple and sometimes tortuous. Tinnitus was not frequent. Besides cyanosis brown pigmentation of the skin occurred in some cases. Tenderness of the bones was marked in a few cases. Erythromelalgia occurred in the onset in one case. Glands were usually not affected, but were enlarged in one case—probably specific; there was regional involvement from malignant tumor of thymus in one case. The thymus was affected (postmortem) in two cases. Temperature and respiration were normal in the majority of cases.

## REPORTED CASES.

Author.	Number of Erythrocytes.	Size and Form of Erythrocytes.	Normoblasts.	Polychromatophiles.	Number of Leucocytes.	Lymphocytes.	Leucocytes Mononuclear and Transitional. Per cent.	Polymorphonuclear. Per cent.	Eosinophiles. Per cent.	Mast Cells. Per cent.	Myelocytes. Per cent.	Hemoglobin. Per cent.
Turck, 1 . . . . .	9,965,000	Normal . . . . .		Few . . . . .	33,800			90				
" 2 . . . . .	7,500,000	Few microcytes . . .			12,300	6	11	75	Not included.		1	140
" 3 . . . . .	8,220,000	Many microcytes . . .	Few . . . . .		19,000	6	11	85		1.1		112
" 4 . . . . .	10,625,000	Many poikilocytes . .			20,400			80		2.3		180
" 5 . . . . .	8,430,000	Few microcytes . . .			26,700			84	3	1.9		180
" 6 . . . . .	9,670,000	" " " " " " " " " "		Constant . . . . .	16,500			81	Not +	Not +	Few . . .	25 gm†
" 7 . . . . .	8,043,000	" " " " " " " " " "		" " " " " " " " " "	30,000			92	Not +	Not +	" " " "	25 gm†
" 8 . . . . .	9,350,000	" " " " " " " " " "		" " " " " " " " " "	9,200			82	Not +	Not +	" " " "	20 gm†
" 9 . . . . .	7,704,000	" " " " " " " " " "		" " " " " " " " " "	12,100			90			" " " "	19 gm†
" 10 . . . . .	8,024,000	" " " " " " " " " "		" " " " " " " " " "	31,500	4	6.8	87	6.8	1.4	" " " "	125
" 11 . . . . .	9,700,000	" " " " " " " " " "		" " " " " " " " " "	36,300	4	6.8	87		1.4	" " " "	120
" 12 . . . . .	10,426,000	Few poikilocytes . .		" " " " " " " " " "	18,730			73	Few . . .		" " " "	120
Reckzeh, 1 . . . .	6,500,000	Normal . . . . .			25,000			75				100
" 2 . . . . .	12,500,000	" " " " " " " " " "			10,000	2	23	73				120
" 3 . . . . .	10,000,000	" " " " " " " " " "			10,800,000	2	23	75				120
" 4 . . . . .	5,400,000	" " " " " " " " " "			10,200	2	23	75				120
" 5 . . . . .	7,100,000	" " " " " " " " " "			15,000	6	18	80				120
" 6 . . . . .	4,400,000	" " " " " " " " " "			5,200	6	18	80				120
" 7 . . . . .	6,800,000	" " " " " " " " " "			12,000	6	18	80				120
" 8 . . . . .	10,600,000	" " " " " " " " " "			11,000	4	24	75	1			120+
" 9 . . . . .	10,200,000	" " " " " " " " " "			11,000	4	24	75	1.8			125+
Osler, 1 . . . . .	9,952,000	" " " " " " " " " "			4,000			79	.5			120
" 2 . . . . .	7,172,000	" " " " " " " " " "			21,800	14	4	59				125
" 3 . . . . .	10,200,000	" " " " " " " " " "			23,000			59				120
" 4 . . . . .	10,616,000	" " " " " " " " " "			5,100							120
" 5 . . . . .	11,692,000	" " " " " " " " " "			5,100							120
" 6 . . . . .	8,250,000	" " " " " " " " " "			8,300							120
Cabot, 1 . . . . .	9,252,000	" " " " " " " " " "			5,800	15		80	3	.8	Few . . .	110
" 2 . . . . .	12,000,000	" " " " " " " " " "			10,600						Few . . .	120
" 3 . . . . .	10,462,000	" " " " " " " " " "			20,000						Few . . .	150?
Russe and Saundby	19,000,000	Normal . . . . .			Not increased							
McKeen . . . . .	9,380,000	" " " " " " " " " "			9,000	18		74	2			120+
" 2 . . . . .	9,480,000	" " " " " " " " " "										120
Zemlich . . . . .	6,480,000	" " " " " " " " " "			13,200	12	5	85	2.5			120
" 2 . . . . .	9,240,000	" " " " " " " " " "										120+
Cominotti, 1 . . .	5,300,000	Few macrocytes . . .			6,000							120+
" 2 . . . . .	7,500,000	" " " " " " " " " "			3,000							70
" 3 . . . . .	5,500,000	" " " " " " " " " "			7,500	47?	2	40	10			80
Engelbach and Brown . . . . .	8,037,000	Normal . . . . .	None . . . . .	Few . . . . .	6,600	11	9	75	1	Few . . .		60
" 2 . . . . .	12,584,000	" " " " " " " " " "			9,600	14	11	76	1.5			180
" 3 . . . . .		" " " " " " " " " "										200

\* Malignant tumor of thymus gland.

† F. Miescher's

one; genital hemorrhage (not occurring at labor), three; hemorrhages of skin, one. Among the gastrointestinal symptoms appetite was usually poor; stomach symptoms frequent; vomiting occurred in a few cases; constipation was common. Genital symptoms were usually negative, but in three cases seemed to bear some definite relation to the onset of the disease. The condition followed early menopause in only one case, and was associated with irregularity of menses and menorrhagia in three cases besides the one reported in this article. The urinary findings were abnormal in about one-half of the cases; one case followed nephritis. Albumin was present in over half of the cases; in large amount in a few. Albumoses are not reported. Urobilin is reported present in the majority of Turck's cases and in a few others in which

## COURSE OF DISEASE.

The general course of the disease is progressively worse, with remissions of short duration. The most acute case was one of three months (Turck). The average duration was from six to eight years. Vaquez reports a patient living after the presence of symptoms for ten years. In the case reported in this article the patient has had symptoms for eleven years and is still able to do housework except during acute exacerbations.

## DIAGNOSIS.

A positive diagnosis is made on the findings of chronic cyanosis, enlargement of the spleen and polycythemia without an anatomic explanatory cause. The cyanosis may not be generalized as some patients have shown it

only on the mucous membrane. Enlargement of the spleen may be slight and was entirely absent in two otherwise typical cases. On account of the treatment and prognosis an effort to diagnose primary tuberculosis of the spleen should be made. Reckzeh comments on the impossibility of such a diagnosis even after an exploratory incision. He says that primary tuberculosis of the spleen occurs in acute cases, as reported in one case by Scharold, in which death took place in seventeen days. Also that in the chronic form there may be only a gradual enlargement of the spleen without temperature or any other general or local sign upon which to base a diagnosis. He further suggests caution as to exploratory operation on account of the hemorrhagic diathesis. The number of erythrocytes must be increased to at least 8,000,000 per cm. m. (Reckzeh), and this condition of the blood must be diffuse as to body location. (This limitation of the number of red cells and the distribution of the polycythemia would exclude one of Reckzeh's own cases as well as some that have been reported by other men).

**Differential Diagnosis.**—Other conditions causing chronic cyanosis must be excluded. Among these are abnormalities of development of the heart and aorta; patent foramen ovale and ductus arteriorius, stenosis of conus of pulmonary artery, imperfect ventricular septum, and congenital dilatation of aorta; organic heart disease, congenital or acquired; adhesive pericarditis; aneurism; emphysema; and eccentric causes; growths, exudates, etc., causing stasis of venous circulation from pressure. All other enlargements of the spleen are easily differentiated from this condition by the blood findings. Enlargements, displacements and deformities of the liver due to other causes must be differentiated because in some of the cases enlargement of the liver was the first sign discovered. A great many other conditions presenting abnormal increase in the number of erythrocytes must be excluded. An excessive elimination of the fluids from the blood, as severe diarrhea, dysentery, cholera and diabetes may show polycythemia. The use of Levicowater was produced it (Donke and Ewald<sup>6</sup>). Any condition causing impeded circulation may cause polycythemia, as well as cyanosis. Lauselt demonstrated this in organic heart disease. Arsangeli first claimed that it is produced by compression. Compression of bandages of an extremity has produced a slight localized polycythemia. Boston says that in cases of cyanosis there is likely to be an increase in the erythrocytes in the peripheral blood. In a case of anemia with cyanosis of the extremities the finger count was 4,600,000 and that of the ear 1,800,000. (This point must be considered in every blood examination.) Chronic lung disease has given polycythemia as high as 9,000,000 (Toisson, Vaquez, Pelet, Krehl, A. Tusti, Carnuhaci). Lues has also shown this increase in red cells (Verault, Meruer, Egger, Wolf, Koeppe, Jaruntawski, Schroeder). Addison's disease, besides having a pigmentation which may also be present in this disease, may have marked polycythemia (7,700,000, Neuman). Abnormally high red-cell count has been demonstrated in a paralyzed extremity. Obesity may also have this blood finding. Of the intoxications, carbon monoxid, ether anesthesia and phosphorus poisoning (Jaksch, 8,250,000) have shown increased number of red cells. The polycythemia of high altitudes and early infancy is well known. This condition is easily differentiated from other local and general conditions causing headache and vertigo by the

presence of chronic cyanosis and the blood findings. It is also easily separated from other obscure blood diseases by careful blood examination.

#### PROGNOSIS.

The prognosis is absolutely bad as to cure. Nearly all cases have slowly progressed to a fatal termination.

#### TREATMENT.

The treatment has been very unsatisfactory. Quinin and arsenic produced no good results (Reckzeh). Ehrlich recommends a diet containing not more than 6 mg. of iron (Bunge table). Turk got good results in two cases from Fowler's solution—30 gts. daily for a prolonged period. In both cases the red cells were decreased about 2,000,000 and the spleen decreased in size and symptoms subsided in one of them. Nitrites and aconite have been recommended to reduce the blood pressure. Osler observed the disappearance of headache after administration of the nitrites. Cabot says that the use of thyroid extract for three months produced no favorable results. Venesection has afforded a temporary relief, but has caused no marked change in the blood findings. Vaquez and Laubry<sup>15</sup> noted improvement of general symptoms in one case after three x-ray exposures at seven-day intervals, the blood findings remaining unchanged. Reckzeh reported three cases of splenectomy for isolated tuberculosis of the spleen resulting unfavorably and eight cases of isolated tuberculosis of the spleen resulting in a cure. Cominotti reported two splenectomies for this condition, one resulting unfavorably from late infection (52 days after operation). One patient survived the operation, but at the end of a year's time the blood findings showed polycythemia, with no increase of the leucocytes.<sup>16</sup>

**ADDENDUM.**—Since this article went to press another article on Polycythemia, with special relation to the etiology of "Migraine ophthalmique" has been reported by Köster.<sup>17</sup> He adds another case, reviews twenty-eight cases found in the literature, and gives some additional references.<sup>18</sup>

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15. Vaquez and Laubry: "Cyanose avec Splénomégalie et Polyglobulie," *Trib. Méd.*, 1904, No. 33.

16. Other articles on this subject are: Breuer: "Polycythaemie mit Splenomegalie," *Mitt. d. Wien. Gesellsch. f. inn. Med.*, 1903, No. 16. Weintraud: "Polyglobulie und Milztumor," *Zeitschr. f. klin. Med.*, vol. iv, p. 91. Preiss: "Hyperglobulie und Milztumor," *Mitt. aus den Grenzgeb. d. Med. und Chir.*, vol. xiii. Zaudy: *Wien: klin. Wochschr.*, 1902, p. 102. Schmidt, R.: "Erythrozytose (Hyperglobulie) und Milztumor," *Münch. med. Wochschr.*, 1904, p. 1207. Kikuchi: "Fall von Polycythämie," *Prag. med. Wochschr.* Dr. Joseph Sailer reported 2 cases before *Gen. Med. and Phys. and Surg.*, Feb. 13, 1905. Ascoli, M.: *Riforma Medica*, Dec. 21, 1904.

17. *Münch. med. Wochenschr.*, No. 22 and 23, 1906.  
18. Deruschinsky: *Dritter Kongress russischer Chirurgen in Moskau*, 18-21, xii, 1902; Collins: *New York Med. Record*, lxi, 21, 1903; Frommherz: *Münch. med. Wochenschr.*, No. 40, 1903; Zaudy: *Schmidts Jahrb.*, vol. 286, No. 4, 1905.

**Differential Diagnosis of Pneumonia and Pleurisy with Effusion.**—Differentiation is sometimes very difficult, and in such doubtful cases Pavitzky recommends Leube's sign for differentiating a cavity in the lungs from pneumothorax. Auscultation of the lungs in pneumonia reveals bronchial respiration, which is heard directly under the ear of the physician, and if the patient coughs numerous râles are to be heard simultaneously and close to the ear. In pneumothorax and in pleurisy with effusion the râles sound as if they were at a great distance from the ear of the examining physician. This peculiarity of auscultation is a certain sign for differentiating pneumonia from those cases of pleurisy which present the clinical picture of pneumonia, when even an exploratory puncture may not prove decisive. His communication is published in the *Russky Vrach.*, No. 20, 1906.