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CHRONIC CYANOSIS, WITH POLYCYTHÆMIA AND ENLARGED SPLEEN: A NEW CLINICAL ENTITY.

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The group of cases here reported, with those collected from the literature, are worthy of careful study, as we have here in all probability "a definite clinical entity and one which is new to medical science," to use the words of Saundby and Russell in describing their case. The condition is characterized by chronic cyanosis, polycythæmia, and moderate enlargement of the spleen. The chief symptoms have been weakness, prostration, constipation, headache, and vertigo. A further analysis will be reserved until after the consideration of the cases:

Case I. *Cyanosis for years, of unknown origin; albuminuria; rapid pulse; polycythæmia; high vascular tension.*—Dr. K., aged forty-four years, consulted me October 28, 1901, complaining of a rapid pulse and diffuse cyanosis. He has been a very healthy man, active and vigorous, of good habits; has had no serious illnesses. He has been uneasy about himself, as he had detected a trace of albumin in the urine. For several years his wife has noticed that he has had a very congested appearance, and the eyes would often be deeply suffused. I have seen him at intervals for the past five years and have known him to be a very blue-faced man. He has been of a constipated habit. His eyes are somewhat prominent, but his wife says this is natural to him. He has constantly a feeling of fulness in the head, sometimes a sensation of vertigo, and for these symptoms he consulted me.

He was a well-built, well-nourished man; the face much suffused; the ears looked a little blue; the conjunctivæ were injected, and the lips distinctly cyanotic. The tongue also looked cyanotic. The general surface of the skin looked suffused and the anæmia left after pressure of the hand on the skin was very marked and very slowly

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obliterated. The feet and hands were quite cyanosed. The radials and temporals were moderately sclerotic. Pulse 120, regular. Apex beat in fifth, just inside the nipple line; sounds clear; aortic second a little accentuated. There was no enlargement of the thyroid. No enlargement of the liver; moderate enlargement of the spleen, the edge of which was palpable. The chest was well formed, not barrel-shaped; the cervical muscles not prominent. Expansion of the chest good. No sign of emphysema. Expiration not prolonged. Once or twice he called on cold days to show the extreme cyanosis, and twice he came in with cough, which troubled him chiefly at night.

Several careful analyses of the urine were made by Dr. Futcher. The specific gravity ranged from 1012 to 1017; albumin was constantly present, as a rule only a trace; no sugar. On centrifugalizing there were a few hyaline and finely granular casts.

I was very much puzzled as to the nature of this case, and thought that he had some chronic degeneration of the kidneys, with slight arterio-sclerosis, but I did not think it could be advanced, as there was no marked hypertrophy of the heart, and the aortic second was not specially ringing. I could not account for the cyanosis.

Blood. The examinations were made by Dr. Futcher. Drop from ear almost black in color; flows sluggishly. A striking feature is the slowness with which the drop spreads under the cover. With the usual-sized drop the field is found almost filled with red cells; they look natural. Another striking feature is the relative scarcity of leucocytes. Red blood corpuscles, 9,952,000; leucocytes, 4000; hæmoglobin, 120 per cent. (Fleischl). No measurements of the red cells were made. Several counts were made, as it was thought that there might have been a mistake.

Two observations of the blood pressure, taken on the right arm when he had been in the sitting posture for about ten minutes, gave maximum pressure, 203 mm. Hg.; minimum pressure, 175 mm. Hg. Five minutes later the maximum pressure, 200 mm. Hg.; minimum pressure, 172 mm. Hg.

I saw this patient repeatedly during 1902. There was very little change in the condition. The cyanosis was always marked. He was able to attend to his practice. There was no shortness of breath; the heart's action became slower. I once counted it at 72, but he said that it was often at 120 per minute. The last examination of the urine, November 14th, showed only a trace of albumin and a few hyaline casts. The spleen never became much enlarged, but it was always easily palpable. He went to California and has since been under the observation of Dr. McBride.

Case II. *Recurring attacks of nausea and vomiting; remarkable cyanosis, of some years' duration; pain in side; polycythæmia; albuminuria.*—M. C. (General Hospital Nos. 31202, 34970, 38753, 40820, 42041), aged thirty-five years, a Russian Jew; tailor by occupation; admitted for the first time on July 11, 1900, complaining of constipation.

The family history was unimportant.

Personal History. The patient has always been well. Since coming to this country, six years ago, he has been pressing in a tailor-shop, and has had to work standing. He denies gonorrhœa and syphilis. He uses alcohol moderately. Ever since coming to the United States the patient has been troubled with constipation, the bowels never moving

more frequently than every second day. This is worse in the summer. Three years ago, during the summer, the bowels on one occasion were constipated for fourteen days. There is no pain during these attacks. For a long time he has been dark in color; he does not know for how long, but his friends have noticed it.

The patient's bowels moved eight days before admission after taking licorice powder. He had been constipated for four days previous to that. Seven days ago the patient began to vomit after each meal. He has vomited daily since. Castor oil, Epsom salts, and licorice powder have been ineffectual. There have been no other symptoms save that of drowsiness. The patient has voided very little urine during these eight days.

On examination the patient was a well-nourished man, with marked cyanosis of the face, hands, and mucous membrane; the tongue was heavily coated.

The physical examination proved entirely negative, except for the cyanosis already noted. The temperature reached 102° shortly after admission, and fell to normal by midnight and remained so. On this day the blood count was: red blood corpuscles, 7,172,000; leucocytes, 21,800; hæmoglobin, 120 per cent.; no malarial parasites found; Widal reaction negative.

On July 16th the blood count was: red blood corpuscles, 6,520,000; leucocytes, 14,400; hæmoglobin, 102 per cent. The patient is feeling very much better and the bowels are moving regularly.

The patient was admitted for the second time on May 27, 1901, complaining of vomiting, which came on five days before admission. The patient admitted excessive indulgence in soda-water on the day of the illness. He states that he has vomited "every moment" since the onset, and that there has been some blood in the vomitus, which is very foul-smelling. The bowels have been constipated since the onset. He has eaten nothing for several days. There is no abdominal pain.

May 29th. Dr. Futcher noted that the cyanosis was still very marked, especially in the buccal mucosa, and that there was a marked pyorrhœa alveolaris. Slight tenderness in the right iliac fossa. The spleen and liver were not enlarged.

27th. The blood count gave red blood corpuscles, 8,900,000; leucocytes, 23,000; hæmoglobin, 125 per cent.

28th. Vomiting continues unabated. Calomel, cerium oxalate, and lavage have been ineffectual in stopping it. Analysis of the vomitus: total acidity, 85; free HCl, 37; no lactic acid.

29th. Red blood corpuscles, 10,200,000; hæmoglobin, 112 per cent.

30th. Lips very livid; the general surface of the skin, including face, trunk, and extremities suffused. The imprint of the hand disappears very slowly, and the nails are a little cyanosed.

June 1st. Patient's bowels were finally moved by a high enema. The blood count was as follows: Red blood corpuscles, 7,576,000; leucocytes, 30,000; hæmoglobin, 115 per cent.; specific gravity (chloroform and benzol method), 1068.

4th. The patient was discharged feeling greatly improved, the bowels having commenced to move somewhat more freely.

The patient was admitted for the third time on April 29, 1902, complaining of an attack of vomiting, hiccoughing, and constipation, which began seven weeks previously. He had vomited bile several times.

The attacks of vomiting have lasted for ten or twelve days at a time and recurred repeatedly. The blood count on admission was as follows: Red blood corpuscles, 7,144,000; leucocytes, 8,600; hæmoglobin, 110 per cent.

On April 30th Dr. McCrea noted that the area of stomach tympany was slightly increased; cyanosis still present; considerable pigmentation of the skin. Differential count of the leucocytes: Polymorphonuclear, 79.4 per cent.; small mononuclear, 14 per cent.; large mononuclear, 2.4 per cent.; eosinophiles, 1.8 per cent.; transitionals, 2 per cent. A test-meal showed free HCl present; no lactic acid. On two successive days after a long fast the stomach-contents were removed and revealed a fair amount of free HCl. The blood count on May 12th was little changed.

On May 22d the patient was discharged improved, the bowels moving regularly.

The urine had a specific gravity of 1010 to 1020, with a trace of albumin and a few casts, usually hyaline, but on one admission granular.

The fourth admission was on November 7, 1902, the patient stating that he was awakened at 4 A.M., three days before admission, with a pain in the left side, followed by vomiting, which has been continuous since. No blood in the vomitus. Constipation for five days. The patient has not eaten anything since the onset and has taken very little water. There has been some hiccoughing. Blood count: Red blood corpuscles, 7,316,000; leucocytes, 12,300; hæmoglobin, 112 per cent. The cyanosis is still very marked. There is some dyspnœa, vomiting, and hiccoughing. A differential count of the leucocytes shows a slight increase in the polymorphonuclears and a diminution in the small mononuclears since the previous record. The specific gravity of the blood is 1083.

November 12th. Red blood corpuscles, 8,300,000.

15th. Red blood corpuscles, 6,700.000. Coagulation time, one and a half minutes. Specific gravity, 1072.

19th. The vomiting persisted until two days ago and the vomitus showed at all times free HCl; no lactic acid; slight starch digestion. The constipation was also very obstinate until yesterday. Discharged improved.

Patient admitted for the fifth time on January 28, 1903, and for the sixth time March 11th. On both of these occasions the chief symptoms were pain in the left side and the obstinate constipation. He says that the pain brings on the vomiting. The vomitus is at first frothy and white, later greenish in color. The pain is deep below the tenth and eleventh ribs on the left side, and extends toward the posterior axillary fold. On his last admission the cyanosis was extreme, the face was almost black, and the expression very anxious. There was no albumin in the urine, but on March 30th there were a few granular casts. The blood pressure was 125; the specific gravity of the blood 1081. The bowels were freely moved, and this always gives him relief. On the last admission there was very little vomiting, yet the cyanosis was never more marked.

May 25th. Patient has been keeping very well and is at work. He complains of pain in the left side, under the ribs, and says that as he walks he keeps his hand over the sore spot. The cyanosis is marked,

quite as much as at any time in the hospital. The impression of the hand on the skin of the trunk remains a long time. The spleen is not palpable; the vertical flatness is about four inches in extent. He thinks that the skin has become darker.

CASE III. (Dr. Lowman.) *Chronic cyanosis; enlarged spleen; polycythæmia; headache; increased tension; albuminuria.*—While making a visit at the Lakeside Hospital, Cleveland, with Dr. Lowman, my attention was directed to a patient who was unusually cyanosed and who had an enlarged spleen. On further examination the case was found to belong to the group under consideration. I am indebted to Dr. Darby, Dr. Lowman's first assistant, for the notes of the case.

Female, aged forty-four years, married, of English descent, admitted to the ophthalmological division of the hospital for double pterygium, failing vision, and headache; for the latter she was transferred to the medical service. The condition of the fundi was negative, with the exception of tortuosity of the vessels.

The family history was negative.

She had had the usual infectious diseases. She had been a very healthy woman of good habits. There was no history of syphilis. She had not had winter cough or attacks of asthma. She has two children living and well. For many years, she does not know how long, she has been blue. She has had no cough, no special shortness of breath on exertion. For four years she has had headaches, which have become more intense during the past four months. They begin over the left eye and extend backward and down the neck.

On examination the patient is well nourished; the skin is dark in color, and there is a general cyanosis, particularly marked on the face, arms, and upper part of the trunk; the feet and toes are blue. Everywhere the impression made with the finger disappears slowly. The conjunctivæ are suffused. The eyes are not specially prominent. There is well-marked pterygium. Looking more closely at the face there are some distended venules about the nose and cheeks. The lips are quite cyanosed, and the tongue and buccal mucous membranes have a dusky blue color. The radials are moderately sclerotic; the vessels seem full and the tension high. The apex beat of the heart cannot be felt; there is no visible shock; no enlargement upward or to the right. The sounds are clear; the second pulmonic is accentuated. The chest is not barrel-shaped. Percussion note is clear everywhere, and there are no bronchitic râles; no prolongation of expiration.

The abdomen looks normal. On palpation the spleen is enlarged, extending 7.5 cm. below the costal margin; the anterior margin and the notch are easily felt. The upper limit of flatness is on the eighth rib. The liver is not enlarged.

Blood. April 13, 1903, red blood corpuscles, 11,616,000; leucocytes, 5100. Differential count: Polynuclears, 59 per cent.; lymphocytes, 32 per cent.; large mononuclears, 8 per cent.; eosinophiles, 0.5 per cent. Hæmoglobin, 120 per cent. Specific gravity, 1067. A subsequent examination made on May 8th gave the red blood corpuscles 10,692,000.

Urine. No excess of the daily amount; clear in color; specific gravity ranged from 1010 to 1016; reaction acid; a trace of albumin and a moderate number of hyaline and granular casts.

At my suggestion the patient was put upon sodium nitrite, and Dr.

Darby writes, under date of May 8th, that the headaches have entirely disappeared.

CASE IV. (Dr. Stockton.) *Chronic cyanosis; general weakness; headache, and general pains, with attacks of weakness and shortness of breath; pigmentation of skin; death; autopsy.*—When speaking of the condition with Dr. Lyon, of Buffalo, he mentioned a remarkable case of chronic cyanosis in the Buffalo Hospital under the care of Dr. Stockton, and on his return he found that there was polycythæmia. To the former I am indebted for the following notes, and to the latter for permission to use them:

J. T., a Turkish Jew, aged forty-six years, married, a shoemaker, had been admitted to various Buffalo hospitals (General, Erie County, German, etc.) for several years on different occasions, and died in the German Hospital, Friday, May 1, 1903.

His chief complaint was general weakness, chronic headache; pain in the feet and legs, made worse by walking; general diffuse pains in the abdomen, pains also over the region of the heart, moderate chronic constipation, a slight cough, and occasional attacks of shortness of breath.

For about twenty years he has had a slight cough, off and on, worse in the winter and at night. Headache has troubled him for the same period (twenty years), and indefinite pain in the chest has been felt more or less during the past twenty years. His general strength had been of exceptional vigor until about six years ago, when it began to fail. About four years ago he began to grow much darker and bluer in his skin—cyanosed. Then he began also to have pains in different parts of his body, pain and a prickling sensation in the legs and feet, pain in the right chest and right shoulder; pain in the abdomen, not localized, but diffuse and general; headache continuing. The pain in different parts of the body was not constant, but shifted from time to time. However, the headache and the pain in the legs and abdomen were present with tolerable constancy and have continued so up to his death. The pain was described as dull and aching. In addition to the pains, he had marked weakness during the last six years of life.

Constipation was never a marked feature of the case, though the bowels were generally sluggish. The appetite was poor and capricious. He had nausea occasionally, but never vomited.

During the past four years he had been going from hospital to hospital, spending a few months at a time in each, until he felt better, then returning to his home and trying to work, but soon being required to return to a hospital because of his weakness, headache, body pains, and sometimes shortness of breath. In the hospital he would remain in bed most of the time, or sit quietly in a chair, occasionally walking slowly around the ward or going to the dining-room for his meals.

Cyanosis. The most striking feature of the case during the past four years has been a high-grade, extreme, general cyanosis, making the patient an object of general interest and curiosity in the various hospitals where he sojourned. His entire skin was dusky and bluish and his mucous membranes livid, resembling the appearance of a "blue baby" with congenital heart disease; in fact, he was jocularly called the "blue baby." This cyanosis was constant, though at times after rest in bed it improved somewhat, and again at other times was much intensified.

Pigmentation. The skin was generally dark and showed fine punctiform mottling or pigmentation, suggesting capillary extravasation as a cause, though no definite history of subcutaneous hemorrhages could be obtained. The naturally pigmented parts of the body were much more deeply pigmented than normal. The mucous membranes showed no appreciable areas of pigmentation.

Dyspnœa. During the last three years of life he had occasional attacks of increased weakness, cyanosis, and dyspnœa, his body becoming cold, so that his wife had often thought him dying. In the hospital, however, dyspnœa was seldom marked, though the respirations were generally moderately increased.

Physical Examination. A short, stocky, well-built, and well-muscled man. Cyanosis as already noted. Pigmentation as already noted.

Heart. The heart sounds were always clear and without murmur at any time, but were generally rather weak, except the second pulmonic sound, which was somewhat accentuated. The heart's area by deep percussion was slightly enlarged to the left and right. In the sixth interspace, about one and a half inches to the left of the nipple line, could be seen an area of pulsation, the chest wall dimpling inward with each systole—*i. e.*, systolic retraction. This sign required a careful inspection to be seen.

Vessels. The arteries were soft and compressible. The veins were everywhere full and visible. There was slight throbbing of the vessels of the neck, above the clavicles, thought to be arterial.

Thorax. The lungs were everywhere hyperresonant on percussion, and the area of resonance extended downward at the bases behind somewhat, and in front on the right side the area of liver dulness did not begin until the seventh space was reached in the parasternal line. The area of resonance above the clavicles was not appreciably increased. On auscultation the breath sounds were soft and expiration was not prolonged. Occasional wheezes and sibilant râles could be heard over both lungs on different occasions during the last few months of life. (Dr. Thayer, who saw this case with Dr. Lyon, tells me that the state of the chest did not suggest to him emphysema.)

Liver. Flatness began in seventh space in parasternal line and extended vertically downward to about two inches below costal margin, where the edge could be felt.

Spleen. Never palpable, and its area on percussion was less than normal (perhaps explained by the emphysema of the lungs).

Abdomen normal.

Glands normal.

Legs. Occasionally very trifling œdema was observed over the ankles, more distinct on the left side. No œdema elsewhere was ever observed.

Eye Examination, February, 1903. Both disks hyperæmic. Retina surrounding disks thickened. Vessels, particularly veins, engorged and tortuous.

Urine. An occasional trace of albumin; otherwise negative.

X-ray Examination of Thorax. Nothing abnormal except slightly enlarged heart.

Blood. The blood from the ear or finger-tip was on many occasions during the last few months of life examined and found extremely dark in color, and so thick that it would adhere to one side of thin filter

paper without penetrating it. The depth of color and darkness of the blood was far beyond the range of estimation for hæmoglobin by the color scales of the various hæmoglobinometers. The red corpuscles were never counted until the day of death, when they were counted at 8,250,000. Differential leucocyte count normal. Leucocytes were generally about 8300, never showing a hyperleucocytosis.

Pulse. The pulse was generally about normal, occasionally after exertion rising temporarily as high as 120 to the minute.

Temperature always normal.

Respirations. The general respiratory rate was from 22 to 25 per minute, once reaching 50 after severe exertion, with symptoms of collapse. On the afternoon of death the respirations were 38 per minute.

Death occurred on May 1, 1903, at 7 P.M., at the German Hospital in Buffalo, after three days' residence in the hospital. The patient died, without any special symptoms or discoverable complications, in collapse and after a few hours of drowsiness deepening into semiconsciousness.

The full report of the autopsy is not yet available, but Dr. Lyon writes that the heart was about normal; the lungs showed moderate emphysema, with cyanosis and œdema; the spleen was moderately enlarged. Nothing definite was found to account for the condition.

Cases from the Literature.

CASE V. (Vaquez, *Bulletin Médical*, Paris, 1892, vi., 849.)—Male, aged forty years. For ten years extremities cyanosed; veins distended. Then palpitations, dyspepsia, bronchial catarrh. Three years ago vertigo (Ménière type); buzzing and whistling in ears; staggering and eddying of objects; vomiting; no unconsciousness. Gums swollen, bleeding on irritation.

On examination, chronic cyanosis; no œdema. Heart: No definite auscultatory phenomenon. Blood: Red blood corpuscles, 8,900,000; leucocytes, normal.

Second admission: Paroxysmal vertigo. Attack of pain in lumbar region, ended by discharge of red blood corpuscles in urine, lasting four to six days. Liver enlarged, 20 cm. in right mammary line. Spleen 24 cm. in extent. Urine, three litres daily; same amount of fluid as ingested. Blood: Finger, 8,450,000; elbow, 8,200,000, once 9,130,000; specific gravity, 1080; hæmoglobin, 165 per cent.; hyperalkalinity of blood.

Pathology. Probable hyperactivity of hæmatopoietic organs, for of two cases of congenital cyanosis, one, with red blood corpuscles, 7,000,000, had a large spleen; the other, with 4,500,000, had no palpable spleen.

CASE VI. (Cabot, *Boston Medical and Surgical Journal*, December 7, 1899.)—Female, aged forty-six years, widow, masseuse. Six years before admission she had sudden loss of consciousness, with settling of blood on one side of face and thick speech, which lasted several days. Four years later, after a period of hard work, she began to have periods of collapse, mental and muscular; face became purple, eyes injected; she was once thought to be drunk; vasomotor phenomena often present. Sciatica two weeks before admission; ecchymoses on thigh.

On examination, cyanosis of the face and tongue. Heart: No murmurs. Urine: Trace of albumin; a few hyaline casts. Blood: Red blood corpuscles, 10,460,000; leucocytes, 20,000; hæmoglobin, 150 per cent. Heart apparently normal; pulse 90. No note on the spleen.

Course. Rested well in summer, but still cyanotic. Thyroid treatment had no effect. Later on, after tooth extraction, bleeding lasted half a day; made her better. Soon afterward she had attacks in which her legs began to move spontaneously, the feet moving around each other. A second attack on the train in two weeks. Soon weakness of left arm and leg, headache, vomiting. She died comatose.

Autopsy. Hemorrhage, middle meningeal; passive congestion of all the viscera.

CASE VII. (Cabot, *Boston Medical and Surgical Journal*, March 15, 1900.)—Female, aged forty-nine years, spinster. Complaint, vertigo, weakness, bad taste, constipation. Blue line noted. Given potassium iodide and cascara.

One year later, trace of albumin and hyaline casts in the urine. Lead detected in the blood. Blood: Hæmoglobin, 120 per cent.

Father died of "consumption of blood."

Otitis media at eighteen years; several attacks of rheumatism. Menopause at forty-six years. Since then vertigo, palpitation, and headache; dizzy most of time. No tinnitus or nausea or eye symptoms. Cyanosis of lips for six months. Constipation. Four months ago three teeth drawn; then stomatitis set in. Itching at night. Polyuria.

On examination, cyanosis of face and mouth, hands and feet. Heart: Slight systolic murmur at pulmonary area. Spleen enlarged up and down. Hæmoglobin, 120 per cent. In one week vertigo and cyanosis diminished. Hæmoglobin, however, remained at 120 per cent. Four years later, red blood corpuscles, 12,000,000; spongy, bleeding gums; vertigo and staggering; skin bronzed. Lost twenty pounds in six years. Spleen a hand's breadth below ribs. Red blood corpuscles, 9,252,000; leucocytes, 10,600; hæmoglobin, 110 per cent. After venesection, red blood corpuscles, 10,032,000; normoblasts, 5. Later spleen reached to navel; red blood corpuscles, 11,352,000. Examination of gastric contents: No free HCl.

CASE VIII. (McKeen, *Boston Medical and Surgical Journal*, 1901, cxliv., 610.)—Male, aged fifty-three years, German, packer in iron foundry.

Family history unimportant.

Personal History. Dyspnœa twenty years ago, eight days; recurred at intervals of six months to two years. Alcohol, beer, and whiskey used moderately.

Present Illness. One and a half years ago cyanosis of face and hands following an attack of dyspnœa. The cyanosis has persisted since, with exacerbations. Works right along; exertion causes no dyspnœa or cyanosis. Every second or third day blurring of vision, sweating, vertigo, staggering; no headache or tinnitus. When blue the hands are cold and numb. For two years frequent attacks of diarrhœa, sometimes with prolapsus recti.

On examination, no dyspnœa; respirations 18 to the minute. Cyanosis of face, hands, and feet. Fingers clubbed. Erythema on

shoulders and chest. Eyes congested. Tongue cyanotic. Gums swollen and bleeding. Many of the teeth loose. Arteries slightly thick. Heart, no murmurs. Lungs hyperresonant. Spleen one inch below rib, descending to two and a half inches on deep inspiration. X-ray showed emphysema. Urine: A trace of albumin, granular casts, red blood corpuscles, and leucocytes. Blood: Red blood corpuscles, 9,380,000 to 9,840,000; leucocytes, 9000; hæmoglobin, 120 per cent.

Case IX. (Saundby and Russell, *Lancet*, 1902, i., 515.)—Male, aged forty-three years, an electroplater. First visit on April 13, 1891, complaining of pains in body, especially abdomen; headache for three or four months. Spleen enlarged. Urine: Specific gravity, 1010; a trace of albumin; no casts.

Second visit on January 29, 1898, complaining of cyanosis.

Family History. Mother died of phthisis.

Personal History. Syphilis at nineteen years, gastric fever at twenty-four years, later jaundice.

Present Illness. Eight months ago pains, gnawing, in abdomen, worse in morning; no vomiting; constipation. For six weeks loss of flesh and weakness.

On examination, dull, speech thick, memory and attention poor. Cyanosis of face. Fingers clubbed. Teeth bad. Bronzing of legs. Spleen extends to middle line and navel; hard, slightly tender. Heart: No murmurs. Red blood corpuscles, 9,000,000; hæmoglobin, 120 per cent. Once a few hyaline casts. He grew drowsy, jaundiced, and cyanotic. Later, red blood corpuscles, 7,360,000.

Autopsy. Hypertrophy of left ventricle. Spleen, 1440 grammes; consistency normal. Brain congested. Suprarenal small, dark, soft. Thymus not noted.

Weil (*La Semaine Médicale*, June 29, 1901) has a brief note on two cases of hyperglobulism, with cyanosis, lasting from birth, in two children, one aged two years, the other four years. The blood count is not given. In one the spleen was enlarged, in the other normal. No heart disease.

Analysis of the Cases.

Six of the patients were males and three females. All were in the middle period of life, the youngest thirty-five years and the oldest fifty-three years. There was nothing in the occupation or in the station of life of any moment. The features may be considered in detail.

Cyanosis. Naturally this attracts most attention and has been the feature which has led to further investigation. As is usual in all forms of cyanosis, it is most marked about the face and hands, but in Dr. Lowman's case and in both of my patients the skin of the entire body was of a dusky blue. When first seen the suffusion of the conjunctivæ and the prominence of the eyes, as in Case I., may add to the startling appearance of the patient. The cyanosis is more intense in cold weather, and is aggravated by any existing bronchial catarrh. On bright, clear days, with but little moisture in the air, it may lessen

greatly, as in Case I. The period over which the cyanosis has been noticed varies from ten years (Case V.) to three or four years (Case I.). While constant, as a rule, it may vary greatly in intensity. In Case II. the patient usually came in very deeply cyanosed, the condition aggravated, no doubt, by the vomiting and the loss of liquids, but after a few days, when the bowels were moved, the color became less intense; but I saw this patient only the other day, some six weeks after his last attack of nausea and vomiting, and he was intensely cyanosed. There is no respiratory distress with the cyanosis. While the skin looks full and tense and the face and hands bloated, yet marked dilatation of the larger superficial veins is not noted. On close examination of the skin, many fine, dilated venules are seen.

Blood. The viscidity is greatly increased. All observers have remarked not only upon the unusually dark, but upon the thick and sticky character of the blood drop. An extraordinary polycythæmia is a special feature of the affection. The maximum blood count was 12,000,000 per c.mm. in Cabot's second case. In eight of the cases the count was above 9,000,000 per c.mm., and in the ninth (Case IV.) it was 8,250,000 per c.mm. There have been no measurements of the red blood corpuscles. The statement is made that in the polycythæmia of congenital heart disease the red blood corpuscles are smaller than in that of high altitudes. The percentage of hæmoglobin has been high, ranging to (in Case V.) 165. Usually the range has been from 120 to 150. In Case IV. it is stated to have been above the scale. The specific gravity of the blood in Case V. was 1080, and in Case II. it ranged from 1067 to 1083. In eight of the cases the leucocyte count ranged from 4000 in Case I. to 20,000 in Case VI. As a rule, in a majority of the cases it has been below 10,000 per c.mm. In Case II. on one admission the count reached 30,000 per c.mm.

Spleen. In seven of the nine cases the spleen was enlarged. In four of these the enlargement may be termed great, reaching nearly to the navel. In Case VI. there was no note. In Case II. it was not enlarged.

The liver was enlarged in Case V.

Urine. In seven of the cases a trace of albumin was noticed, with hyaline, sometimes granular, casts. In Cases V. and VII. there was no note on the urine. The specific gravity was usually low.

Pigmentation of the Skin. As might be expected from the prolonged existence of the cyanosis, the skin was noted to be pigmented in several of the cases (II., III., IV., VII., IX.).

Symptoms. The symptoms have been very varied. Most of the patients have complained of headache, weakness, and prostration. Headache was a prominent symptom in four cases, vertigo in four, constipation in four, pains in back and abdomen in three cases.

Attacks of nausea and vomiting were a special feature in Case II., and are mentioned as present in Case V. Cough and shortness of breath were each present in one case. Fever was not noticed in any of the cases. The pulse was noticed to be of high tension and the vessels sclerotic. There was no œdema of the skin. The torpor, mental and physical; the sensation of fulness in the head, with headache, vertigo, and in some cases nausea and vomiting, remind us of the symptoms to which mountain climbers and aeronauts are subject. Three of the cases were fatal. In Case IV. the patient died in collapse after a few hours of drowsiness. In Case VI. the patient died comatose, with cerebral hemorrhage. In Case IX. the patient became drowsy and died in coma. The autopsy in Case IV. showed the heart to be about normal, moderate emphysema of the lungs, with cyanosis and œdema and moderately enlarged spleen. In Case VI. there was passive congestion of all the viscera and hemorrhage from the middle meningeal artery. In Case IX. there was hypertrophy of the left ventricle, with congestion of the brain.

REMARKS. *Chronic cyanosis*, a common enough feature in clinical work, is met with:

1. In organic disease of the heart, particularly in congenital malformation, in chronic myocardial and tricuspid lesions in children and adults, and in cases of adherent pericardium.

2. In certain diseases of the lungs, particularly emphysema, and in long-standing pulmonary tuberculosis of the fibroid type. Practically there are only two conditions in which patients walk into the hospital or into our consulting-rooms with extreme cyanosis, congenital heart disease, and emphysema.

3. In the methæmoglobinæmia of chronic poisoning with coal-tar products, as antipyrin and acetanilid, etc. In this condition, too, the patient may startle one by the markedly cyanotic appearance.[1]

There are a good many people whose normal condition is one of great fulness of the bloodvessels of the skin, so that in cold weather there may be marked cyanosis of the ears and of the face. We all know the stout, hearty, full-blooded man with rubicund face—the type which has been well described by Clifford Allbutt in his *Lane Lectures*—a common one among draymen and in men of that class, who live much in the open air and who drink freely. In them cyanosis, though not necessarily present, may be very marked in the face and hands when the temperature is low. As a rule, the peripheral circulation is

[1] I am sorry I have not got a blood count in a case of this sort. As a rule, there is anæmia; in a remarkable case which I saw with Dr. T. R. Brown, the hæmoglobin was only 50 per cent. Unfortunately no count was made of the red blood corpuscles. In the case of a physician with extreme cyanosis from long-continued use of antipyrin, a blood count was made, and I remember that the red corpuscles were not above normal, but I have not the actual figures.

active and the normal condition is a vivid hyperæmia of the skin associated with dilatation of numerous small venules.

Cyanosis, local or general, indicates one fact—diminished oxygenation of the blood corpuscles. In the deepest cyanosis of the ear or of the finger-tip the blood count may not be above 5,000,000 per c.mm. Only recently Dr. Futcher examined for me the blood of a red-faced, short-breathed Englishman, whose skin seemed fairly bursting with blood and whose fingers and ears were quite cyanosed. The red blood corpuscles were only just above 5,000,000 per c.mm. In the local cyanosis of Raynaud's disease the blood count may be very little above the normal. I have a patient at present in the wards in whom the blood count from the cyanosed foot ranges from 4,500,000 to 6,500,000; the count from the ears about 5,500,000 (Dr. Briggs). A few weeks ago, in Dr. Brayton Ball's wards of the New York Hospital, I saw an interesting case of coma (which turned out to be due to a fracture of the skull) with the most intense localized cyanosis in the fingers of one hand, active, vivid red hyperæmia of the fingers of the other hand, and normal-looking blood distribution in the ears. The count, very kindly made for me by Dr. N. B. Foster, was practically normal and the same in all three situations. Contrariwise, the anomaly may be present (though I must say it is rare) of a red face and general superficial hyperæmia with a very low blood count. During this session there has been under my care in Ward E a patient with what we have termed *anæmia rubra*. With a blood count of about 2,000,000 per c.mm. from ear-tip or finger-tip, he was as red as a beet, and it was not until his blood had fallen to nearly 1,200,000 that he began to present a typical picture of pernicious anæmia. On admission, with his blood at a little above 2,000,000, and looking the healthiest patient in the ward, he had nucleated red blood corpuscles. In the cyanosis of emphysema and the ordinary forms of heart disease, the number of red blood corpuscles per cubic millimetre is not, as a rule, much increased, and rarely reaches the limit of polycythæmia, which, as suggested by Cabot, may well be placed at 7,000,000. Occasionally most extraordinary cyanosis occurs in adherent pericardium, as in a case reported by me (*Archives of Pediatrics*, 1896) and in the case reported by Lorrain Smith and McKisack (*Transactions Pathological Society*, London, 1902). In the latter the blood count was 6,000,000.

Polycythæmia. There are two classes of polyglobulism—*relative*, in which the condition is due to a diminution in the quantity of the plasma of the blood, and *true*, in which there is an actual increase in the number of blood corpuscles. Much work has been done of late years on the subject. Relative polycythæmia is very common. It may be caused by a deficient amount of fluids ingested, which possibly may be the cause of polycythæmia of the newborn; more frequently

it is caused by loss of liquids, either by (*a*) sweat; (*b*) diarrhœa (by far the most common); (*c*) increased diuresis. (*d*) In another group of cases there is loss of liquids by secretion or transudation, as in narrowing of the pylorus with dilatation of the stomach, and in the constant loss of liquids from the blood in recurring ascites. It is interesting to note that in some of these cases the polycythæmia is of a high grade and may persist for months or even for years. It is not necessarily associated with cyanosis, as in cases of dilated stomach and in diarrhœa. There is also a toxic polycythæmia described in poisoning by phosphorus and carbon monoxide, which, too, is probably relative. The polycythæmia of vasomotor disturbances, such as has been determined by Becker, Thayer, and others after the cold bath and after violent exercise, also comes in this class. Where the much-discussed polycythæmia of high altitudes should be placed is by no means certain. While a number of observers hold that there is new-formation, the lack of oxygen acting as a stimulus, others believe that it is relative, and due to increased elimination of fluids from the body, or that it is entirely due to a large number of corpuscles in the peripheral circulation. Others, again, think it is entirely due to the effects of decreased atmospheric pressure. The microcytes, poikilocytes, and nucleated red blood corpuscles point to new-formation, but the question is still under discussion.

True Polycythæmia. Vaquez and his pupil, Quiserne (*Thèse*, Paris, 1902), limit to this class the condition in which with an increased formation there is a continued increase in the number of red blood corpuscles in the circulating blood. It is met with where there is difficulty in proper aëration of the blood, as in high altitudes, or in heart disease, congenital and otherwise; and also in the obscure cases of the form here under consideration. The polyglobulism is regarded as a mode of adaptation to the new conditions and a sort of functional reaction of the organism. Belonging to this group is the polycythæmia so readily studied in congenital heart disease, and described by Krehl, Gibson, and others. The figures often reach as high as 8,000,000 or 9,000,000, rarely so high as in the form discussed in this paper.

It is by no means easy to offer a satisfactory explanation of the polycythæmia with cyanosis here under consideration. It does not seem possible to connect it in any way with the moderate grade of enlargement of the spleen, and yet there are one or two observations in the literature which are of great interest in this connection. Rendu and Widal (*Bull. et mém. Soc. méd. des hôpitaux*, 1899, 3 s., xvi. 528) report the case of a policeman who had an attack of vomiting without apparent cause, with dyspnœa. The temperature was normal. Red blood corpuscles, 6,200,000; leucocytes, 6000. This count gradually

diminished. On examination, skin subicteric; cyanosis of face and hands marked, to a less degree all over the body. A tumor, evidently the spleen, reaching from diaphragm to iliac crest. Eventually ulcers developed on tongue and the liver became enlarged. Autopsy: Spleen adherent to diaphragm, fibrous on section, and filled with caseous masses.

Moutard-Martin and Lefas (*Société des hôpitaux*, 1899) have also reported a case of a woman, aged forty-nine years, with pain in the left hypochondriac region, emaciation, no ascites, no cyanosis, with enlarged spleen, slight albuminuria. The red blood corpuscles were 8,200,000, the leucocytes 31,428. At the autopsy the spleen weighed 750 grammes and contained large caseating nodules.

With our imperfect knowledge of the physiology of polycythæmia it would be premature to discuss at any length the pathology of this remarkable group of cases. We need:

1. A careful study of all forms of chronic cyanosis with polycythæmia, particularly those associated with heart disease and emphysema. (It is to be noted that the cases here reported have the highest blood count on record, much higher than the average in congenital heart disease or in dwellers at great altitudes.)

2. A more accurate study of the blood in this class of cases—the volume, the viscosity, the state of the plasma and the serum, the amount of hæmoglobin, the specific gravity, and the diameter of the corpuscles. As increased viscosity of the blood, with resulting difficulty of flow, seems the most plausible explanation of cyanosis, it is especially important to test the viscosity by accurate physical methods and to determine the relation of the number of corpuscles to the viscosity of the blood.

3. The relation of the splenomegaly to the cyanosis and polyglobulism should be carefully observed. It may not be anything more than the effect of the chronic passive congestion.

Future investigation will determine whether we have here in reality a new disease. The clinical picture is certainly very distinctive; the symptoms, however, are somewhat indefinite, and the pathology quite obscure.