11. The symptoms of pyloric stenosis are projectile vomiting, visible peristalsis, constipation, starvation stools, rapid loss of weight and pyloric tumor.

12. Closer observation will reveal, as well, pallor; lividity; loss of turgor; circumoral cyanosis; cold, clammy, cyanotic hands and feet; subnormal temperature, unless obscured by starvation elevation, and spasm not only of the pylorus but often of the larynx, pharynx, esophagus, cardia, and various portions of the intestine. There is also hypertonicity of the skeletal musculature.

13. Irritation of the infant nervous system produces an effect predominantly stimulating. An inhibiting effect is virtually absent.

14. In the treatment, certain points should be observed:

(*a*) Errors in diet or hygiene must be corrected.

(*b*) In every advanced case, saline solution should be given subcutaneously at frequent intervals until enough fluid can be taken by mouth to supply body needs.

(*c*) Atropin, like digitalis, must be active, that is, it must be freshly prepared from the crystals. Once in solution, deterioration is rapid.

(*d*) In the milder cases, the drug may be given by mouth, in the bottle, or, if the patient is breast fed, in a teaspoonful of water before feeding.

(*e*) In the severe cases, the drug should be administered hypodermically until vomiting is controlled.

(*f*) The dose is variable, $\frac{1}{1000}$ grain (or even $\frac{1}{2000}$ grain, in rare instances) at each feeding to a maximum which either controls symptoms or produces the physiologic effect, i. e., flushing, etc. The largest dose used was $\frac{16}{1000}$ grain at each feeding, or $\frac{1}{8}$ grain in twenty-four hours. Beginning with $\frac{1}{1000}$ grain, one should increase the amount at each feeding until the result is obtained, when the dose becomes fixed.

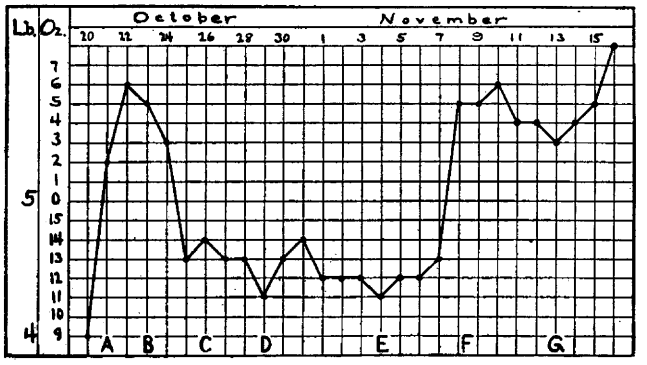

Fig. 5.—Weight curve: *A*, administration of saline solution subcutaneously; *B*, subcutaneous saline stopped; *C*, first three roentgenograms made, after which atropin was begun by mouth; *D*, roentgen ray; *E*, transferred for operation; atropin hypodermically; *F*, obstipation relieved by omission of atropin; *G*, loss due to vomiting when atropin was omitted.

(*g*) Treatment may need to be given only a few weeks, or may be required most of the first year.

(*h*) There are rare cases in which much smaller doses are required to begin with.

15. Occasionally, constipation with severe rectal tenesmus results. The omission of a few doses of atropin relieves this.

16. Infants of this type are practically immune to the harmful effects of atropin.

17. This paper is based on an experience of more than forty cases ranging from a mild spasm to complete stenosis. One of the patients died suddenly; another discontinued treatment and was successfully operated on. The others recovered under atropin treatment, although at least 20 per cent. had been advised that operation would be required.

18. In an illustrative case of so-called congenital pyloric stenosis with complete obstruction, the patient was cured by atropin.

19. Hypertrophic pyloric stenosis is a symptom of the hypertonic infant. It is only an advanced degree of pylorospasm. Most, if not all, cases can be cured by sufficient doses of atropin correctly administered.

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SICKLE CELL ANEMIA

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LOS ANGELES

Recent medical literature contains the records of three patients, all negroes, or negroes with an admixture of Caucasian blood, in whom severe anemia, characterized by certain peculiar morphologic alterations of the red blood cells, was present. The first case was reported by Herrick.[1] Washburn [2] published the records of a patient whose blood showed similar changes, and Cook and Meyer [3] reported the third example of this rare type of anemia.

REPORT OF CASE

The following record is presented in some detail on account of the rarity of the disease:

History.—C. P., a negro, aged 21, was admitted to the Johns Hopkins Hospital, March 15, 1915, complaining of general weakness. The family history was fragmentary, and no evidence was adduced to indicate that any other member of the family had suffered from symptoms similar to his. The patient was born in Virginia and had never been farther than one of the contiguous states. He stated that, as far back as he could remember, he had been weak and sickly and unable to work or play as hard as other persons of his age. He had frequent attacks of tonsillitis during childhood, and gave a history of measles, pertussis, diphtheria and typhoid fever. He denied venereal infection. His present illness began about ten days before admission, with swelling of the ankles, increased thirst and frequent urination, and he stated that during this period he had lost about 40 pounds (18 kg.) in weight.

Physical Examination.—The patient was slender, and very black. There was no axillary hair, and the beard and pubic hair were scanty. There was marked pitting edema of both ankles. The epitrochlear glands were palpable, and there was slight general glandular enlargement. The tonsils and adenoids were moderately enlarged. The sclerae were pale and had a peculiar greenish hue. The mucous membranes were pale. The lingual papillae were not atrophic. There was slight dulness at the right pulmonary apex, but there were no râles. A roentgenogram revealed slight infiltration of the right upper pulmonary lobe. The cardiac impulse was forcible. Cardiac dulness extended 12 cm. to the left, and 4 cm. to the right, of the midsternal line. A loud systolic murmur was present at apex and base. The pulmonic second

1. Herrick, J. B.: Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia, Arch. Int. Med. **6**: 517 (Nov.) 1910.
2. Washburn, R. E.: Peculiar Elongated and Sickle-Shaped Red Blood Corpuscles in a Case of Severe Anemia, Virginia M. Semi-Month. **15**: 490, 1911.
3. Cook, J. E., and Meyer, J.: Severe Anemia with Remarkable Elongated and Sickle-Shaped Red Blood Cells and Chronic Leg Ulcers, Arch. Int. Med. **16**: 644 (Oct.) 1915.

sound was accentuated. The radial arteries were easily palpable. The blood pressure was 105 systolic and 70 diastolic, according to the Tycos sphygmomanometer. The abdomen was

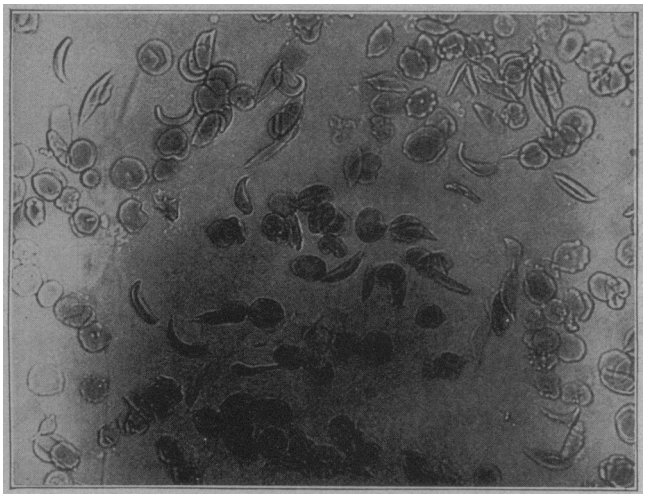

Fig. 1.—Unstained film of blood (high dry).

slightly distended. The liver edge was felt 9 cm. below the costal margin in the right mammillary line. It was smooth and slightly tender. The spleen was not felt, and splenic dulness was not increased. The genitalia were normal. The tendon reflexes were active.

Course Under Observation.—The patient was observed at intervals for nearly two years. The pallor, muscular weakness and edema of the ankles were present constantly. The urine was of low specific gravity, and contained a trace of albumin on each examination. On one occasion, the albumin amounted to 1 gm. per liter, measured by the Esbach albuminometer, and there were numerous hyaline casts. The phenolsulphonephthalein excretion, however, was 72 per cent. in two hours, and the blood urea nitrogen was 6 mg. per hundred cubic centimeters. In March, 1916, the patient was readmitted to the hospital complaining of headache, pain in the upper abdomen and jaundice. He stated that he had had several similar attacks during the last few years. There was marked rigidity and considerable tenderness of the right upper abdomen, and fever to 103 F. The sclerae were yellow, and the urine contained bile. These symptoms subsided in about a week, and the patient was discharged from the hospital. He returned for observation in July, 1916. He had developed deep, "punched out" leg ulcers on both ankles; otherwise his condition was unchanged.

Laboratory Examinations.—The Wassermann reaction was negative with serum on several occasions. Blood cultures taken during the febrile and the afebrile periods remained sterile.

The urinary findings of importance have been given. No parasites or ova were found in blood, urine or stools after repeated searching.

The blood was examined on many occasions, and the results have been summarized in Table 1. Fresh smears demonstrated a moderate leukocytosis without increase of the eosinophils. The blood platelets were not diminished in number.

The red blood cells were reduced in number, and there was marked anisocytosis and poikilocytosis. The characteristic alteration of the blood was marked secondary anemia with a large number of sickle-shaped and oat-shaped and elliptical erythrocytes (Figs. 1 and 2). Each red blood cell contained a normal amount of hemoglobin. By means of a specimen of blood stained by a Romanowsky dye, these changes of morphology were brought out more clearly. An occasional myelocyte and a few nucleated red blood cells were present. Erythrocytes showing diffuse or punctate basophilia were frequently encountered. A differential count of the red blood cells was made, and they were classified as accurately as possible according to shape and size (Table 2). About 25 per cent. of the erythrocytes showed a granuloreticulofilamentous structure when vitally stained with brilliant cresyl blue. The fragility of the unwashed red blood cells was determined by means of solutions of sodium chlorid, of various concentration. Hemolysis began at 0.3 per cent. and was complete at 0.18 per cent. sodium chlorid solution. Differential counts of the unhemolyzed red cells remaining in the tubes of this test demonstrated that the sickle-shaped and oat-shaped cells were more resistant than the more normal erythrocytes. The clotting time of the blood, according to Howell's method, was five minutes and twenty seconds. The blood belonged to Group II, by the Moss classification.

TABLE 2.—DIFFERENTIAL COUNT OF RED BLOOD CELLS IN CASE REPORTED

Cells	Per Cent.
Approximately normal	50.4
Sickle-shaped	3.4
Oat-shaped	14.0
Macrocytes, diameter greater than 10 microns	11.0
Microcytes, diameter less than 6 microns	6.8
Irregular and misshapen	14.4

TABLE 1.—RESULTS OF BLOOD EXAMINATIONS IN CASE REPORTED

Date	R. B. C., Million per Cubic Millimeter	W. B. C. per Cubic Millimeter	Hemoglobin, per Cent.	Color Index	Differential White Blood Count, per Cent.							Nucleated R. B. C. in Counting 250 W. B. C.	
					Polymorphonuclears			Small Mononuclears	Large Mononuclears	Transitionals	Myelocytes	Normoblasts	Megaloblasts
					Neutrophils	Eosinophils	Basophils						
5/ 3/15	2.46	20,700	39	0.8	77.2	0.4	0.8	15.6	4.4	0.8	0.0	8	0
5/17/15	1.95	19,000	40	1.0	59.3	1.0	0.3	23.3	6.7	2.0	7.4	0	0
3/30/16	2.12	14,200	48	1.1	50.0	0.0	2.0	31.2	5.6	3.6	4.8	72	0
4/ 4/16	2.32	12,400	50	1.1	57.5	0.0	0.0	25.0	7.5	1.5	6.0	0	0
4/28/16	2.75	12,600	58	1.0	58.6	1.0	2.0	27.6	4.3	2.0	4.3	3	0
5/15/16	1.96	20,400	48	1.2	41.2	2.0	0.3	32.6	2.0	0.3	1.3	305	4

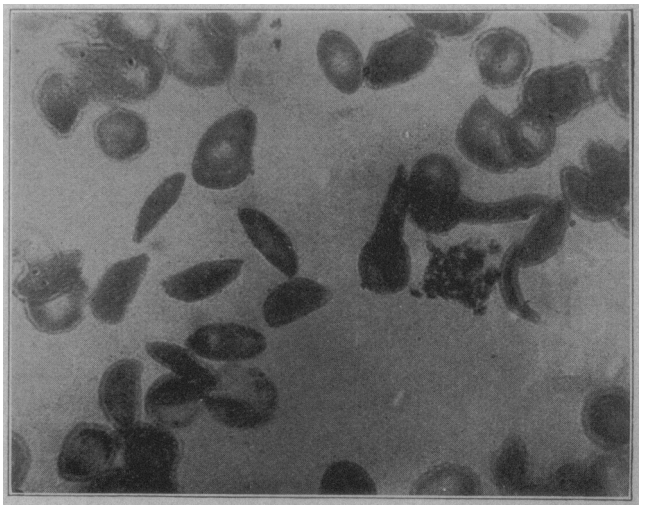

Fig. 2.—Stained film of blood (oil immersion).

COMMENT

The striking feature of the recorded cases is that all four patients were either negroes or mulattoes. Data concerning two are not definite, although they were described as negroes. Of the remaining patients, one was a mulatto and the other a negro without admixture of Caucasian blood. All were less than 30 years of age when the peculiar anemia was first discovered. They were equally divided as to sex. Two were born in Virginia and had never been farther than one of the contiguous states. One had recently come to the United States from the West Indies, and one had never left the immediate vicinity of St. Louis.

The cause of the peculiar type of anemia from which these patients suffered is not known, although a considerable amount of suggestive evidence has been obtained from clinical and experimental investigations. Studies of the blood have thus far failed to reveal the presence of any parasites, and the urine and feces of the patients have been free from metazoan parasites or their ova. Syphilis has also been excluded, as nearly as possible, as a causative factor, by means of the negative histories of the patients and the results of the Wassermann reactions with their serums. No patient gave a history of hemorrhages from any of the mucous surfaces, and no one dated his present symptoms from a previous illness. In each instance, however, the patient stated that he had been weak and unable to work hard as far back as he could remember.

Washburn's patient first developed leg ulcers at the age of five years, and it is probable, therefore, that she had anemia at that time. The family physician of the patient reported by Cook and Meyer stated that each of her brothers and sisters had died in early life of a disease associated with a grave anemia. Emmel [4] made careful studies of the blood of that patient and, in addition to the demonstration of evidences of phagocytosis of erythrocytes in the peripheral blood, he pointed out the interesting circumstance that many of the normal-shaped red blood cells became elliptical or elongated when allowed to remain in physiologic sodium chlorid solution at room temperature. Furthermore, he showed that the erythrocytes of the blood of the patient's father, although apparently normal in other respects, underwent similar changes when subjected to the same experimental conditions. These results have not been confirmed and, therefore, must be evaluated with caution. Nevertheless, they do point to an hereditary or congenital anomaly as the factor of importance in the development of the disease, and this assumption is supported by the history of disability in early life, by the occurrence of the disease only in negroes, and by the reports of Dresbach [5] and Bishop [6] of otherwise healthy, and presumably normal persons whose red blood cells were elliptical. Since two of those persons were brother and sister, it is reasonably certain that the anomaly was congenital.

The symptoms of the malady have been very similar in all the reported cases, and may be very briefly described. The patients all complained of weakness and poor health since early childhood. All had swelling of the ankles associated with leg ulcers probably dependent on the chronic anemia. Two patients had had repeated attacks of abdominal pain associated with fever and jaundice; these symptoms were relieved in one instance by the removal of a number of gallstones.

Physical examination revealed a few abnormalities of some interest. The sclerae were of a peculiar greenish color in three of the reported cases. Two patients had a slight general glandular enlargement with scanty pubic and axillary hair. The spleen was not recorded as palpable in any instance, a fact of considerable importance in differential diagnosis. Otherwise the physical signs were those usually encountered in patients with a severe, long-continued anemia.

TABLE 3.—RESULTS OF BLOOD EXAMINATIONS OF ALL OTHER CASES REPORTED

Reported by	Date	Red Blood Count, Million per Cubic Millimeter	White Blood Cells per Cubic Millimeter	Hemoglobin, per Cent.	Color Index	Differential Leukocyte Count, per Cent.						
						Polymorphonuclears			Small Mononuclears	Large Mononuclears	Transitionals	Nucleated R. B. C.
						Neutrophils	Eosinophils	Basophils				
Herrick.....	1904	2.8	15,250	50	0.9	72	5	0	15	7	0	Present
	1906	2.7	30,500	55	1.0	58	7	0	22	12	0	
Washburn.....	April, 1909	2.0	11,000	50	1.2	63	4	6	25	2	0	
	Sept., 1909	2.4	8,140	51	1.0	64	4	0	27	3	2	Present
	Jan., 1911	2.5	12,400	48	0.9	63	3	2	24	5	1	Present
Cook and Meyer...	Nov., 1914	2.0	10,560	43	1.0	58.4	12.6	0.6	17.8	10.6	0	32 while counting W. B. C.
	Nov., 1914	2.2	10,320	45	1.0	37.5	26	3	30.5	3	0	
	Jan., 1915	2.9	14,200	53	0.9	55	12	2	23	8	0	Present

The abnormalities of the blood are of particular interest and of the greatest importance in the diagnosis of the disease (Tables 1 and 3). There was a marked anemia with a color index near unity. The red blood cells numbered from 2,000,000 to 3,000,000, and the leukocytes from 12,000 to 25,000, per cubic millimeter. The platelets were not thought to be diminished in number, although no counts were made. The blood of two patients showed a slight relative and a marked absolute eosinophilia. A small number of nucleated red cells and an occasional myelocyte were present in every film examined. A few red blood cells showed diffuse or punctate basophilia when the film was stained with a Romanowsky dye. A large number of erythrocytes could be vitally stained with brilliant cresyl blue. There was no increase or decrease of fragility of the red cells, and the clotting time of the blood was normal.

The clinical features and the morphologic alterations of the red blood cells are so characteristic that differential diagnosis was not difficult in the reported cases. The blood picture does not resemble that seen in any of the more common anemias, and it is possible that the disease represents a clinical entity. If that is true, it is of particular interest that up to the present the malady has been seen only in the negro, and, so far as could be ascertained, it is the only disease peculiar to that race.

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4. Emmel, V. E.: A Study of the Erythrocytes in a Case of Severe Anemia with Elongated and Sickle-Shaped Red Blood Corpuscles, Arch. Int. Med. **20**: 586 (Oct.) 1917.

5. Dresbach, Melvin, quoted by Bishop, F. W.: Elliptical Human Erythrocytes, Arch. Int. Med. **14**: 388 (Sept.) 1914.

6. Bishop, F. W. (Footnote 5).