Original Articles.

THE RELATION OF CHRONIC ENLARGEMENT OF THE SPLEEN TO ANEMIA IN INFANCY.*

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THE objects of this paper are to consider the relation of chronic enlargement of the spleen and anemia in infancy to each other, and whether or no there is any justification for the recognition of the special forms of anemia known as the "splenic anemia of infancy" and "anemia infantum pseudo-leukemika." Before taking up these subjects it may be well to consider briefly the peculiarities of the blood in infancy, both in health and disease, and the conditions under which chronic enlargement of the spleen occurs at this age.

The blood of infants under two years normally differs in certain of its characteristics from that of adults. The hemoglobin, although relatively high for a short time after birth, is, during the rest of childhood, relatively low. The number of red corpuscles is about the same or a little larger than in adults, averaging a little over five millions per cubic millimeter. During the first weeks of life there is more or less variation in the size and shape of the red cells, and nucleated forms are not very unusual. The number of white corpuscles per cubic millimeter is somewhat larger than in adults, averaging from ten thousand to fourteen thousand. The relative proportions of the various forms of leucocytes are also considerably different. The limits are roughly as follows: Small mononuclear, 50% to 70%; large mononuclear, 5% to 15%; polynuclear neutrophils, 30% to 40%; eosinophiles, 1% to 10%; that is, the proportion of mononuclear forms is about three times as great as in adult life, while that of the polynuclear neutrophils is only one half as large. The mononuclear cells, moreover, are not merely lymphocytes, but vary much, not only in the size of the cell as a whole, but also in the size of the nucleus and in the amount of protoplasm.

Blood changes develop more easily and more frequently as the result of various morbid conditions and diseases in infants than in adults. All the changes seen in the blood of adults as the results of disease are exaggerated in infancy. The tendency is always to revert to a younger or to the fetal type of blood. All forms of blood disease in infancy are apt to be associated with splenic enlargement. As the result of this tendency to exaggeration of changes and to reversion to a younger type of blood, the red corpuscles show much greater variety in size and shape and many more nucleated forms than under similar pathological conditions in the adult. Leucocytosis also develops more rapidly and to a greater degree. Its type, moreover, is not constant, as in adults, in whom the increase of white cells is largely in the polynuclear neutrophils. In infants the increase is sometimes in the lymphocytes, sometimes in the large mononuclear forms, sometimes in the polynuclear neutrophils, and sometimes, even, in the eosinophiles. Leucocytosis is more apt to occur in blood conditions associated with splenic enlargement than in

those without it. Myelocytes occur in less severe conditions and in greater numbers than in adults. An increase in the number of eosinophilic cells, even if considerable, seems to be of little significance. The percentage of hemoglobin is almost always relatively low.

Chronic splenic tumor is much more common in infancy than in later years, occurring not only under the same conditions as in adults, but in many others not associated in them with splenic enlargement. It is, as in adults, an almost constant accompaniment of leukemia, pseudo-leukemia, cirrhosis of the liver and malaria. These conditions, with the exception of malaria, are extremely rare in infancy. Malaria, however, is not at all uncommon. In it the splenic tumor develops early, attains considerable size and persists a long time. Enlargement of the spleen from amyloid change occurs in association with amyloid changes in other organs as in adults and from the same causes. Malignant disease of the spleen is almost unknown in infancy, but does occur. If so, it is usually congenital or secondary to malignant disease elsewhere. Primary endothelial hyperplasia of the spleen (Bovaird) has not yet been seen under two years.

In adults chronic diseases are not, as a rule, associated with enlargement of the spleen. Many of the chronic affections of infancy, however, especially those in which cachexia is marked, are accompanied by enlargement of the spleen. It is in this class that the enlargements of the spleen in syphilis and rachitis probably belong. It is almost invariably enlarged in the hereditary syphilis of infancy. This enlargement is usually due to an increase in the stroma and to thickening of the blood vessels, but may in rare instances be due to gummatous changes. Enlargement of the spleen occurs very commonly in rickets. Its direct dependence on the disease *per se* is, however, doubtful. In tuberculosis the enlargement, unless due to amyloid changes, is usually slight. It is especially common in conditions associated with anemia, all forms of which, whether primary or secondary, may be associated in infancy with enlargement of the spleen.

Before going further it may be well to attempt to define what is meant by the terms "splenic anemia of infancy" and "anemia infantum pseudo-leukemika." Certain authors, usually English, have apparently considered chronic enlargement of the spleen *per se* as sufficient to justify the use of the term "splenic anemia." Most of the others have, however, evidently used the term to describe the clinical complex more commonly known as "anemia infantum pseudo-leukemika." There can be but little doubt that the terms "splenic anemia of infants," "anemia splenica infantile," "anemia splenica infettiva dei bambini" and "anemia infantum pseudo-leukemika" have been applied to practically identical conditions and may be considered as synonymous. No two authors are agreed as to just what are the pathognomic symptoms, physical signs and blood condition of anemia infantum pseudo-leukemika. A combination of the descriptions of Von Jaksch, Luzet and Alt and Weiss describes it as well, perhaps, as anything. (Dr. A. H. Wentworth¹ has

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¹ Boston Med. and Surg. Journ., 1901, cxlv, 374, 402, 435, 461, 488.

No.	Spleen.	Liver.	Glands.	Red Corpuscles.	Hb.	White Corpuscles.	Small Mononuclear.	L'rge Mononuclear.	Polynuclear Neutrophils.	Eosinophiles.	Myelocytes.	Morphological Changes.	ETIOLOGY.					Results.
													Rickets.	Syphilia.	Improper Food.	Gastro-enteric Disorders.	Miscellaneous.	
1.	1	4	?	1,250,000	15%	10,300	67.0	2.0	28.0	2.0		Marked.	+		Yes.	Yes.		Died in one month.
2.	2	N.	+	3,288,000	42%	4,800	49.0	5.0	45.0	1.0		{ One normoblast to one macroblast.	+		Breast.	Yes.		{ Lost in one month. Probably died.
3.	2	N.	+	4,510,000	57%	15,900	44.0	3.5	47.0	5.5		Slight. Normoblasts.	+		Breast.	Yes.		Died in seven months.
4.	2 x 5	N.	++	2,296,000	25%	16,850	34.4	19.8	44.4	0.4	1.2	{ Moderate. Six normoblasts to one megaloblast and one microblast.	++		Yes.	Yes.		{ Well in two and one half years. Spleen not palpable. Liver normal.
5.	2 x 4	3	?	5,072,000	65%	16,600	40.0	18.0	41.0	1.0		Slight.	+		Yes.	Yes.		Lost. Prob'ly did well.
6.	3 x 4	N.	+	1,736,000	25%	4,200	69.0	5.0	25.0	1.0		Marked.	0		Yes.	Yes.		Died in one month.
7.	3 x 6	N.	+	3,708,000	30%	18,520	81.0	4.0	64.0	1.0		{ Marked. Normoblasts.	+		Yes.	Yes.	Pertussis.	{ Lost in one month. Probably did well.
8.	3 x 4	3	+	5,380,000	65%	15,625	43.0	2.0	54.0	0.5	0.5	Slight.	++		?	?		{ Lost in two weeks. Probably did well.
9.	3 1/2	N.	+	950,000	19%	27,000	52.0	13.0	32.0	0.5	2.5	{ Marked. Twenty-four normoblasts to twenty-one megaloblasts and eight microblasts.	0		?	?	Pertussis.	Died in five days.
10.	4 x 8	N.	+	5,158,000	68%	15,200	51.0	5.0	40.0	4.0		{ Moderate. Occasional normoblast.	+++		Yes.	Yes.		{ Well in six years. Spleen just palpable. Liver normal.
11.	4	6	+	5,650,000	75%	11,800	82.0	8.0	51.0	9.0		Slight.	++		?	?		{ Well in seven months. Spleen not palpable. Liver—4 1/2 cm. below ribs.
12.	Umb.	2	+	3,564,000	60%	16,250	31.0	8.0	60.0	1.0		{ Marked. Megaloblasts.	+		?	Yes.		{ Alive in eight months. Doing well. Spleen not palpable. Liver normal.
13.	Umb.	3	+	5,800,000	?	15,000	43.0	2.0	55.0				++		Breast.	Yes.		Died soon. Meningitis.
14.	Umb.	3	+++	2,553,000	55%	8,200	44.0	4.0	50.0	1.0	1.0	Moderate.	+		Breast.	Yes.		{ Well in six months. Spleen? Liver?
15.	Umb.	5	+++	4,340,000	60%	31,500	29.5	9.9	56.5	0.8	3.8	{ Very mark'd. Eleven normoblasts to eighty-nine macroblasts. Nuclear figures.	+		Yes.	Yes.		Died in two months.
16.	Umb.	5	+	4,408,000	58%	47,220	36.5	9.5	50.5	1.0	2.5	{ Moderate. Thirteen normoblasts to eighteen macroblasts and one microblast.	+++		Yes.	Yes.		Lost. Probably died.
17.	Umb.	6	++	4,200,000	65%	13,400	42.0	11.0	45.0	2.0		Moderate.	+	Yes.	Yes.	Yes.		Lost. Probably recov'd.
18.	A. S. S.	N.	?	3,558,000	60%	12,400	28.0	10.0	55.0	7.0		{ Moderate. Megaloblasts most numerous.	++		Yes.	Yes.		{ Well in seven years. Spleen? Liver?
19.	A. S. S.	3	+	4,000,000	40%	18,750	34.4	12.6	51.0	0.2	1.8	{ Marked. Sixteen normoblasts to nine megaloblasts.	+++		Yes.	Yes.		{ Well in eighteen mos. Spleen not palpable. Liver—3 cm. below ribs.
20.	A. S. S.	5	++	3,750,000	55%	16,200	50.0	6.0	39.0	5.0		Slight.	+	Yes.	Yes.	?		{ Lost in two weeks. Probably recovered.
21.	A. S. S.	+++	+	3,720,000	65%	10,700	30.0	4.0	65.0	1.0		Slight.	+		Yes.	Yes.		{ Well in seven months. Spleen not palpable. Liver—3 cm. below ribs.
22.	A. S. S.	3	+	3,750,000	50%	29,600	30.0	18.0	48.0	2.0	2.0	{ Marked. Eight normoblasts to twelve macroblasts and seven microblasts.	++		Yes.	?		Died in three days.

+ = slight; ++ = moderate; +++ = marked.

recently reviewed the literature of this condition very thoroughly.)

It is a form of severe progressive anemia of infants whose symptoms and clinical course correspond to the picture of leukemia. There is marked enlargement of the spleen and more or less enlargement of the liver. The superficial lymph nodes are usually enlarged. The course is less rapid and the prognosis better than in leukemia. The blood condition is as follows: Constant diminution in the number of red corpuscles with a more or less marked diminution in the amount of hemoglobin; poikilocytosis; very many nucleated red cells, chiefly normoblasts, many of these of abnormal form and showing karyokinetic figures; more or less polychromatophilia of the nucleated red cells and many of the non-nucleated; pretty marked leucocytosis, always polymorphous.

Pathological examinations have been few in these cases, and, as a rule, very incomplete. The lesions which have been described in the spleen are almost entirely those of chronic hyperplasia, affecting various parts of the organ in different degrees in individual cases. The livers showed congestion and slight increase in the connective tissue. In some cases there was a slight infiltration of lymphoid cells and in others slight degenerative lesions.

I have notes, with complete examinations of the blood, on twenty-two cases of chronic enlargement of the spleen in infancy, as well as notes without examinations of the blood on a number of others. For lack of a better basis I have arranged them "primarily" according to the size of the spleen, and secondarily according to the size of the liver.

CASE I.—Joseph C., eleven months old, was admitted to the Infants' Hospital Jan. 3, 1901. He had had the breast alone for six months, after that a varied diet. He had always vomited a great deal. The history was otherwise imperfect.

He was well developed, fairly nourished and flabby. The skin was in good condition. There was marked pallor of the skin and mucous membranes. The fontanelle was level. There were two lower incisors. There was a moderate rosary. The cardiac impulse was in the fifth space $1\frac{1}{2}$ cm. outside the nipple line. The upper border of cardiac dullness was at the lower border of the second rib, the right border 3 cm. to the right of the median line, the left $7\frac{1}{2}$ cm. to the left of the median line. The first sound over the whole precordia was continued into a soft, blowing murmur. The second pulmonic sound was the louder. The lungs were negative. The spine showed a marked curve of weakness. The upper border of liver flatness was in the fifth space. The lower border was palpable 4 cm. below the costal border in the nipple line. The spleen was palpable 1 cm. below the costal border. There was a slight umbilical hernia. There was a slight enlargement of the epiphyses at the wrists. The extremities were otherwise normal except for slight edema of the feet and legs. There was no edema of the hands, but a little of the eyelids.

Urine: Pale, clear, acid, 1017, no albumin. Blood: extremely watery and streaky, coagulation very slow; hemoglobin, 15%; red corpuscles, 1,250,000; white corpuscles, 10,300; small mononuclear, 67%; large mononuclear, 2%; polynuclear neutrophiles, 29%; eosinophiles, 2%. There was marked variation in the size and shape of the red corpuscles. There was a tendency to small forms rather than to large. No nucleated forms were seen in two slides.

In spite of careful feeding, iron and arsenic, he failed steadily in weight, strength and color. The temperature was slightly elevated. There was almost no vomiting. The movements were clay-colored. The edema of the face increased.

He died Feb. 3, 1901.

CASE II.—William F., aged ten months, came to the Out-Patient Department of the Infants' Hospital May 17, 1898. There was no history of tuberculosis in the family or of exposure to it. He had nothing but breast milk, but was fed irregularly. A rough analysis of the breast milk showed a specific gravity of 1031 and 2.6% fat. The proteids must, therefore, have been about normal or a little low. He began to lose weight, strength and color at seven months, and had failed steadily since then. He had had no fever. The bowels moved once daily. He vomited a little almost every day.

He was poorly developed and nourished. Pallor was marked. The head was negative. There were two teeth. He held up his head, but was unable to sit alone. There was a moderate rosary. The heart and lungs were normal. By auscultatory percussion the stomach was distended. The liver was normal. The spleen was palpable 2 cm. below the costal border. The extremities were normal. There was a slight general enlargement of the lymph nodes.

Blood: Hemoglobin, 42%; red corpuscles, 3,288,000; white corpuscles, 4,800; small mononuclear, 49%; large mononuclear, 5%; polynuclear neutrophiles, 45%; eosinophiles, 1%. There was moderate variation in the size and shape of the red corpuscles. One macroblast and one normoblast were seen in counting 100 white cells.

When last seen, June 22, 1898, the symptoms had continued, and he had failed steadily in every way. He presumably died shortly after.

CASE III.—Joseph E., five months old, came to the Out-Patient Department of the Infants' Hospital May 9, 1898. He had never had any food but breast milk. He vomited after almost every nursing. The bowels were constipated. He had never gained.

He was small but not much emaciated. The pallor was marked. The head was negative. He was unable to hold it up. There was a marked rosary. The heart was normal except for a systolic murmur over the whole precordia. A few râles were heard here and there in both chests. The abdomen was lax. The liver was normal. The spleen was palpable about 2 cm. below the costal border. The epiphyses at the wrists were slightly enlarged. The extremities were otherwise normal. There was a slight general enlargement of the lymph nodes.

Blood: Hemoglobin, 57%; red corpuscles, 4,519,000; white corpuscles, 15,000; small mononuclear, 44%; large mononuclear, 3.5%; polynuclear neutrophiles, 47%; eosinophiles, 5.5%. There was but little variation in the size of the red corpuscles and very little in their shape. One normoblast was seen in counting 400 whites.

He died Nov. 25, 1896 "of the same trouble."

CASE IV.—Joseph M., was admitted to the Infants' Hospital in May, 1900, when sixteen months old. He had been fed on condensed milk and malted milk, and had never done well. He had always had vomiting and diarrhea off and on, and had never gained.

He was small, thin and markedly pale. The fontanelle was small and much sunken. There were eleven teeth. The costal cartilages were much depressed, making the front of the chest flat. There was a moderate rosary. The heart and lungs were normal. There was a loud systolic blow in the neck. The abdomen was lax. The liver was normal. The spleen was palpable about 2 cm. below the costal border over a distance of 5 cm. The edge was sharp and the notch distinctly felt. The extremities were normal. There was a moderate general enlargement of the lymph nodes, especially of those in the right side of the neck.

Blood: Hemoglobin, 25%; red corpuscles, 2,296,000; white corpuscles, 16,850; small mononuclear, 34.4%; large mononuclear, 19.6%; polynuclear neutrophiles, 44.4%; eosinophiles, 0.4%; myelocytes, 1.2%. The red corpuscles were somewhat irregular in size, shape and color, but poikilocytosis was not marked. In counting 250 white corpuscles, 6 normoblasts, 1 microblast and 1 normoblast were seen. After a few weeks of observation he was discharged to die.

He was seen Sept. 8, 1902, two and one half years later. He was then well and strong and of good color. The liver was normal. The spleen was not palpable.

CASE V. Francis K., aged sixteen months, was admitted to the Infants' Hospital Jan. 12, 1901. He was well until

he was weaned at fourteen months and put on general diet. After that he was constipated, vomited occasionally and lost weight pretty steadily. When weaned he could stand and walk with the aid of a chair. At entrance he was unable to stand.

He was well developed and nourished, but slightly flabby and rather pale. The fontanelle was 3 cm. in diameter. The head was not otherwise abnormal. There were twelve teeth. The spine showed a slight curve of weakness. There was a slight rosary and slight flaring of the lower chest. The heart showed nothing abnormal excepting a faint systolic murmur in the pulmonic area. There was a venous hum in the neck. The lungs were normal. The upper border of the liver flatness was at the fifth rib. The lower border was palpable 3 cm. below the costal border. The spleen was palpable 2 cm. below the costal border and was 4 cm. in width. The abdomen was negative. There was slight enlargement of the epiphysis at the wrists.

Urine: Normal color, alkaline, no albumin. Blood: Hemoglobin, 65%; red corpuscles, 5,072,000; white corpuscles, 16,600; small mononuclear, 40%; large mononuclear, 18%; polynuclear neutrophiles, 41%; eosinophiles, 1%. There was moderate variation in the size of the red corpuscles, but little in their shape. No nucleated forms were seen. No abnormal forms of white cells were seen, but there was great variation in the size of the mononuclear cells, very few of them being small.

He was discharged Jan. 19, 1901, improving in every way. He did not vomit, his movements were normal, and he was gaining in weight. Nothing further is known as to the progress of the case.

CASE VI. Alice F., aged five months, came to the Out-Patient Department of the Infants' Hospital June 22, 1897. She had always been fed on sterilized milk or condensed milk. She had always vomited and had undigested movements. She had gained fairly steadily in weight.

She was fairly developed and nourished and very pale. The heart was normal except for a systolic murmur over the whole precordia. The lungs were normal. The liver was normal. The spleen was palpable 3 cm. below the costal border and was 4 cm. wide. There was a slight umbilical hernia. There was a general enlargement of the lymph nodes more marked in those of the groin.

Blood: Hemoglobin, 25%; red corpuscles, 1,736,000; white corpuscles, 4,200; small mononuclear, 69%; large mononuclear, 5%; polynuclear neutrophiles, 25%; eosinophiles, 1%. There was marked variation in the size and moderate variation in the shape of the red corpuscles. No nucleated forms were seen.

Nothing further is known as to the progress of the case, except that she died July 20, 1897.

CASE VII. Helen G., ten months old, came to the Out-Patient Department of the Infants' Hospital July 2, 1897. She was about a month premature. She was nursed for five months, and then given condensed milk with cereals. She had never been strong, and had always been constipated. She was brought because of fever, crying and sleeplessness for a month.

She was well developed and nourished, but of a very pale, lemon-yellow color. She had no teeth. There was a slight rosary. There was a slight systolic murmur over the whole precordia. The lungs were normal. The liver was not enlarged. The spleen was palpable 3 cm. below the costal border and was 6 cm. wide. There was a slight general enlargement of the lymph nodes.

Blood: Hemoglobin, 30%; red corpuscles, 3,708,000; white corpuscles, 18,520; small mononuclear, 31%; large mononuclear, 4%; polynuclear neutrophiles, 64%; eosinophiles, 1%. There was marked variation in the size and shape of the red corpuscles, many of them being very large. Five normoblasts were seen in counting 500 whites.

She was last seen July 29, 1897, and at that time was doing well in every way.

CASE VIII. Joseph D., aged twenty-one months, was admitted to the Infants' Hospital June 9, 1902. No history came with him.

He was well developed and nourished, but flabby. The anterior fontanelle was 2 cm. in diameter. The frontal and parietal eminences were somewhat enlarged. There were twelve teeth. There was a marked rosary and a slight

retraction of the ribs at the insertion of the diaphragm. The heart and lungs were normal. The level of the abdomen was much above that of the thorax. The liver was palpable 3 cm. below the costal border. The spleen was palpable 3 cm. below the costal border and was 4 cm. wide. The surface was smooth, the edge sharp, the notch palpable. The extremities were normal excepting for considerable enlargement of the epiphyses at the wrists. There was a slight general enlargement of the lymph nodes.

Blood: Hemoglobin, 65%; red corpuscles, 5,380,000; white corpuscles, 15,625; small mononuclear, 43%; large mononuclear, 2%; polynuclear neutrophiles, 54%; eosinophiles, 0.5%; myelocytes, 0.5%. There was slight variation in the size and shape of the red corpuscles. No nucleated forms were seen.

He was lost sight of, and nothing is known as to the further history.

CASE IX. Sylvia V., aged eleven and one-half months, entered the Infants' Hospital May 27, 1899. Nothing was known as to her history except that she had had whooping cough in February. There was not much cough at that time but the appetite was poor, she vomited occasionally and had a sore mouth.

She was markedly emaciated and very pale. There was a systolic murmur over the whole precordia. There was an occasional rale in both chests. The liver was normal. The spleen was palpable about 3½ cm. below the costal border. There was a slight general enlargement of the superficial lymph nodes. The body and extremities were covered with a fine purpuric eruption. The eyelids were puffy. There were a few hemorrhagic spots in the mouth. There was no edema of the extremities.

Blood: Markedly pale and yellow. Hemoglobin, 19%; red corpuscles, 950,000; white corpuscles, 27,000; small mononuclear, 52%; large mononuclear, 13%; polynuclear neutrophiles, 32%; eosinophiles, .5%; myelocytes, 2.5%. There was marked variation in the size and moderate variation in the shape of the red corpuscles. In counting 500 white cells, 22 megaloblasts, 8 microblasts, 24 normoblasts and 12 atypical nucleated red cells were seen.

She took but little food and vomited a great deal. The movements were fairly normal. The temperature rose steadily and she died June 1, 1899.

CASE X. Sadie C., aged twenty months, came to the Out-Patient Department of the Infants' Hospital, June 20, 1896. She was fed at first on the breast, but was soon given patent foods and then put on a general diet. She had always had more or less trouble with the digestion. She could sit and stand alone, but was unable to walk.

She was fairly developed and nourished, but flabby and pale. She had a large, square, flat head. The fontanelle was nearly closed. There were eleven teeth. There was a marked curve of weakness. There was a very marked rosary, pigeon breast and marked retraction of the ribs at the insertion of the diaphragm. The heart and lungs were normal. The liver was not enlarged. The spleen was palpable about 4 cm. below the costal border and was 8 cm. wide. The abdomen was large and soft. There was marked enlargement of the epiphyses at the wrists and moderate bow-legs. There was a slight general enlargement of the lymph nodes.

Blood: Hemoglobin, 68%; red corpuscles, 5,158,000; white corpuscles, 15,200; small mononuclear, 51%; large mononuclear, 5%; polynuclear neutrophiles, 40%; eosinophiles, 4%. There was considerable variation in the size and shape of the red corpuscles. Macrocytes were numerous. An occasional normoblast was seen.

She was seen Oct. 7, 1902, when a little more than seven years old. She was then perfectly well. The tip of the spleen was just palpable.

CASE XI. Minnie B., eighteen months old, was admitted to the Infants' Hospital Jan. 1, 1902. No history came with her.

She was fairly developed and nourished, but flabby and rather pale. The fontanelle was nearly closed. The parietal eminences were enlarged. There were twelve teeth. There was a slight rosary and flaring of the lower ribs. The heart and lungs were normal. The upper border of the liver flatness was at the fifth rib, the lower border was palpable 6 cm. below the costal border. The spleen was palpable 4 cm. below the costal border. The surface was

smooth, the consistency firm, the edge rounded and the notch distinct. The epiphyses at the wrists and ankles were enlarged and there was slight bow-legs. There was a slight general enlargement of the lymph nodes.

Urine: Normal, acid, 1012, no albumin. Blood: Hemoglobin, 75%; red corpuscles, 5,650,000; white corpuscles, 11,800; small mononuclear, 32%; large mononuclear, 8%; polynuclear neutrophils, 51%; eosinophiles, 9%. There was very slight variation in the size of the red corpuscles and none in their shape or staining reaction. No nucleated cells were seen.

She was seen Aug. 7, 1902. She was then perfectly well. The liver was palpable 4-2 cm. below the costal border in the nipple line. The spleen was not palpable.

CASE XII. Catherine A., twelve months old, was admitted to the Infants' Hospital April 23, 1902. She had been fed on patent foods after the first two months. Her appetite had been poor. She had always vomited and had had bad movements.

She was fairly developed and nourished, but pale. The frontal eminences were a good deal enlarged. The anterior fontanelle was 2 cm. in diameter and somewhat depressed. There was no craniotabes. There were two teeth. There was a purulent discharge from the left ear. There was a moderate rosary. The heart was normal. There was an occasional moist rale in both lungs. The level of the abdomen was above that of the thorax. The liver was palpable 2 cm. below the costal border. The spleen was palpable, running out from beneath the costal border just inside the left nipple line, downward to the level of the umbilicus and then backward into the flank. The surface was smooth and hard and the edge sharp. The notch was not made out. There was slight enlargement of the epiphyses at the wrists. There was a slight general enlargement of the lymph nodes.

Urine: pale, no albumin. Blood: hemoglobin, 60%; red corpuscles, 3,564,000; white corpuscles, 16,250; small mononuclear, 31%; large mononuclear, 8%; polynuclear neutrophils, 60%; eosinophiles, 1%. There was marked variation in the size, shape and staining reaction of the red corpuscles. One megaloblast was seen while counting 100 whites.

She remained in the hospital about two weeks. While there she had very little fever and the lungs cleared up. The movements became normal and vomiting ceased.

She was seen Dec. 19, 1902, eight months later. Her general condition was much improved. She was scarcely able to sit up alone. The liver was normal. The spleen was not palpable.

CASE XIII. Sam S., eight months old, was admitted to the Infants' Hospital, May 11, 1902. He had always been breast-fed, but for the last three months had had more or less vomiting and been constipated.

He was fairly developed and nourished. Pallor was moderate. The fontanelle was level and 2 cm. in diameter. There were no teeth. There was a marked rosary and slight flaring of the lower chest. The heart and lungs were normal. The upper border of liver flatness was in the sixth space. The lower border was palpable 3 cm. below the costal border in the nipple line. The spleen was palpable, running out from beneath the costal border in the anterior axillary line, downward to the level of the umbilicus and upward into the flank behind the posterior axillary line. The surface was smooth, the edge sharp, the notch palpable. The abdomen was much enlarged, but lax. There was marked enlargement of the epiphyses at the wrists. There was a slight general enlargement of the lymph nodes.

Urine: high, acid, trace of albumin. Sediment: many pus cells and rarely a hyalin and granular cast. Blood: hemoglobin, 00%; red corpuscles, 5,800,000; white corpuscles, 15,000; small mononuclear, 43%; large mononuclear, 2%; polynuclear neutrophils, 55%; eosinophiles, 0. Typical signs of meningitis developed a little later, and the child died after an illness of a few days.

CASE XIV. Helen P., seven months old, was admitted to the Infants' Hospital in January, 1902. Although she was breast-fed up to two weeks before entrance she had never done well after the first month. She had always vomited, had usually been constipated, but

sometimes had had diarrhea. For the last two weeks she had been fed on Eskay's food.

She was small and poorly nourished. The skin was desquamating. There was a marked yellowish pallor. The fontanelle was level. There was a venous hum in the neck. There was a very slight rosary. The heart area was normal. The first sound over the whole precordia was continued into a blowing murmur, loudest and longest at the pulmonic area. The lungs were normal. The upper border of liver flatness was at the fifth rib. The lower border was palpable 3 cm. below the costal border. The spleen was palpable, running out from behind the costal border about midway between the anterior axillary line and the nipple line, forward and downward to the level of the umbilicus in the nipple line, and backward into the flank. The surface was smooth and hard, the edge sharp, the notch palpable. The abdomen was negative. There was a considerable general enlargement of the lymph nodes. There were a few purpuric spots on the head, face and legs, and a fine purpuric rash on the arms.

Urine: straw colored, slightly acid, no albumin. Blood: hemoglobin, 55%; red corpuscles, 2,553,000; white corpuscles, 8,200; small mononuclear, 44%; large mononuclear, 4%; polynuclear neutrophils, 50%; eosinophiles, 1%; myelocytes, 1%. There was moderate variation in the size and shape of the red corpuscles with a tendency to large, but not to oval forms. There was moderate variation in the staining characteristics of the red corpuscles.

She remained in the hospital about two weeks. She took her food poorly and vomited a good deal. The movements, however, were fairly normal. She lost weight steadily. At the time of discharge the blood showed: Hemoglobin, 70%; red corpuscles, 3,260,000; white corpuscles, 13,125. She was heard from in August, 1902. She was then "perfectly well."

CASE XV. Alice C., ten months old, was brought to the Out-Patient Department of the Infants' Hospital July 14, 1897. She had always been fed on various "infant foods." She had never thrived, and had gained little or no weight. During the last few weeks she had lost both weight and strength. She had always vomited a good deal. She had had diarrhea for the first few months but since then had been constipated, the movements being normal in color. Bunches were noticed in the neck and groins at five months; they had not increased markedly since. Depressed fontanelle, dryness of the skin and nocturnal fever had been present for three months. A tumor was first noticed a week before she came to the hospital. It had increased somewhat in size during this time.

She was poorly developed and emaciated. The skin was dry and brownish. The frontal bones were considerably lower than the parietal. The fontanelle was depressed and small. The frontal eminences were large. There were no teeth. There was a slight rosary. The heart and lungs were normal. There was dullness under the upper part of the sternum, but none at the root of the lungs. The upper border of liver flatness was at the sixth rib. The lower border was palpable 5 cm. below the costal border. The edge of the liver was firm and sharp. The spleen was palpable, running out from under the ribs in the left nipple line downward to the umbilicus and then backward into the flank just above the anterior-superior spine. The surface was smooth, the consistency firm, the notch palpable. There was marked enlargement of all the superficial lymph nodes.

Blood: hemoglobin, 60%; red corpuscles, 4,340,000; white corpuscles, 31,500; small mononuclear, 29.5%; large mononuclear, 9.9%; polynuclear neutrophils, 56.5%; eosinophiles, 0.3%; myelocytes, 3.8%. There was very marked variation in the size and shape of the red corpuscles. Nucleated forms were very numerous. Of 100 nucleated cells 89 were macroblasts and 11 normoblasts. Six macroblasts showed nuclear figures. Many of the nucleated and some of the non-nucleated forms were polychromatophilic.

She was again seen Aug. 9. At that time the spleen had diminished considerably in size. She died Sept. 18. The mother wrote that she had had a hemorrhage from the bowels for two weeks before death, and that "the bunch in the side could not be felt."

CASE XVI. Charles G., ten months old, came to the Out-Patient Department of the Infants' Hospital July 11, 1898. He had been fed on the breast and condensed milk at home and had had cows' milk at a day nursery. He had always had more or less diarrhea and vomiting, varying in severity from time to time. At times he seemed sick, at others not. He was always backward, and his head perspired profusely at night. There had been a gradual increase in the size of the abdomen for two months.

He was fairly developed but poorly nourished. His color was fair, the skin dry. The anterior fontanelle was large. There was no craniotub. There was a purulent discharge from the nose. He had two teeth. He could hold up his head, but was unable to sit alone. There was a marked rosary and flaring of the lower ribs. The heart and lungs were normal. The liver flatness began at the eighth rib in the scapular line; the lower border was palpable 5 cm. below the costal border. The spleen could be felt running out from under the ribs in the nipple line, directly downward to the level of the umbilicus, backward at a right angle into the flank and upward in the posterior axillary line. The edge was sharp and hard, the surface smooth. The abdomen was considerably enlarged and rather tense. The epiphyses at the wrists were considerably enlarged, but the extremities were otherwise normal. There was a slight general enlargement of the lymph nodes.

Blood: hemoglobin, 58%; red corpuscles, 4,408,000; white corpuscles, 47,220; small mononuclear, 36.5%; large mononuclear, 9.5%; polynuclear neutrophiles, 50.5%; eosinophiles, 1%; myelocytes, 2.5%. There was moderate variation in the size and staining qualities of the red corpuscles, but very little in their shape. In counting 500 white corpuscles, 12 normoblasts, 1 microblast and 18 macroblasts were seen.

He was soon lost sight of, and nothing is known as to the further history of the case.

CASE XVII. Maude M., eight months old, was admitted to the Infants' Hospital May 14, 1899. She undoubtedly had congenital syphilis. There was no further history.

She was small, pale and poorly nourished. The head was somewhat flattened, the frontal and parietal eminences enlarged. The anterior fontanelle was 3 cm. in diameter and bulging. The superficial veins of the scalp were considerably enlarged. The nares were occluded, and there was considerable purulent discharge. The mouth was open, and the mouth and throat dry. There were no teeth. She held her head up feebly, but could not sit alone. There was a very slight rosary. The heart and lungs were normal. The lower border of the liver was palpable 6 cm. below the costal border. The spleen could be felt coming out from behind the ribs in the anterior axillary line running downward to the level of the umbilicus and backward under the ribs at about the posterior axillary line. The surface was smooth, the edge sharp, the notch palpable. The abdomen was rather large. The extremities were normal except that the skin of the soles was dry and cracked. There was a general enlargement of the lymph nodes including the post-auricular and epitrochlear, to the size of beans.

Blood: hemoglobin, 65%; red corpuscles, 4,200,000; white corpuscles, 13,400; small mononuclear, 42%; large mononuclear, 11%; polynuclear neutrophiles, 45%; eosinophiles, 2%. There was moderate variation in the size of the red corpuscles, but little in their shape and staining reaction. No nucleated forms were seen.

She was discharged May 19, 1900. Nothing further is known as to the history of the case.

CASE XVIII. Minnie L., seventeen months old, was admitted to the Infants' Hospital Nov. 13, 1895. She had never been nursed, but had been fed on condensed milk. She did not vomit. The bowels moved once in three or four days. The movements were large, hard, whitish, foul and contained a little mucus. A hard lump had been noted in the abdomen for two months. It was as large when first discovered as at admission. She had been pale for a long time, and had lost flesh rapidly in the last three months. She was just beginning to sit up alone.

She was fairly developed and emaciated. There was

marked pallor with a yellowish tinge. The fontanelle was not closed. She had four teeth badly decayed. There was a moderate rosary. The heart and lungs were normal. The liver was normal. The spleen reached nearly to the median line, and extended to about 1 cm. above the anterior-superior spine. The abdomen was full and tense. There was an umbilical hernia. There were a few purpuric spots on the abdomen. The epiphyses at the wrists and ankles were enlarged.

Urine: normal. Blood: hemoglobin, 60%; red corpuscles, 3,556,000; white corpuscles, 12,400; small mononuclear, 28%; large mononuclear, 10%; polynuclear neutrophiles, 55%; eosinophiles, 7%. There was marked variation in the size and shape of the red corpuscles. Macrocytes were more numerous than microblasts. There was a moderate number of nucleated red corpuscles, macroblasts being the most numerous. There was an occasional free nucleus. There were no abnormal forms of white cells.

She was heard from July 29, 1902, when about eight years old. She was said to be perfectly well in every way.

CASE XIX. Jennie R., ten months old, was admitted to the Infants' Hospital June 1, 1901. She was breast-fed for five weeks, after that she was fed on a modified milk prepared at home. This mixture was a weak one and was not changed for seven months. During this time she had no gastro-enteric disturbances, but had gained weight very slowly. From this time until entrance, although still on a stronger modified milk, she had more or less disturbance of the bowels.

She was fairly developed and nourished. There was moderate pallor of the skin and mucous membranes. The anterior fontanelle was 3 cm. in diameter and level. The head was flattened on top and behind. There were two teeth. She sat alone, feebly. There was a moderate rosary. There was slight retraction of the chest at the insertion of the diaphragm. The heart and lungs were normal. The abdomen was distended. There was a slight umbilical hernia. The upper border of the liver flatness was at the upper border of the fifth rib; the lower border was palpable 3 cm. below the costal border. The spleen was felt running out from beneath the ribs in the anterior axillary line, downward just to the right of the umbilicus, then downward and backward to just above the anterior-superior spine and backward into the flank. The surface was smooth; the consistency was firm; the notch was palpable in the nipple line. The spleen was apparently somewhat tender. The epiphyses at the wrists were enlarged. The extremities were otherwise normal. There was a slight general enlargement of the lymph nodes.

Urine: pale, acid, 1010, no albumin or sugar. Blood: hemoglobin, 40%; red corpuscles, 4,000,000; white corpuscles, 18,750; small mononuclear, 34.4%; large mononuclear, 12.6%; polynuclear neutrophiles, 51%; eosinophiles, 0.2%; myelocytes, 1.8%. The red corpuscles showed marked variation in size, shape and staining reaction. There was no tendency to large forms, but a slight tendency to oval forms. Sixteen normoblasts and 9 megaloblasts were seen in counting 500 white corpuscles.

She was put on a stronger milk and beef juice, and was given maltine and iron and syrup of the iodide of iron. The temperature remained normal, she took her food fairly well and did not vomit. There was a tendency to constipation.

On June 16 the tip of the spleen only reached 3 cm. to the left of the umbilicus. The examination of the blood on this date was as follows: hemoglobin, 65%; red corpuscles, 5,132,000; white corpuscles, 18,580; small mononuclear, 23%; large mononuclear, 6%; polynuclear neutrophiles, 69%; eosinophiles, 1%; myelocytes, 1%. There was moderate variation in the size and shape of the red corpuscles with slight variation in their staining reaction. There was a slight tendency to large and oval forms. In counting 500 whites, microblast, 2 normoblasts and 10 megaloblasts were seen.

She had measles in the latter part of June. After that her improvement was even more rapid than before. The spleen was not palpable after Aug. 1.

The examination of the blood Aug. 16 was as follows:

Hemoglobin, 65%; red corpuscles, 5,175,000; white corpuscles, 17,000; small mononuclear, 48%; large mononuclear, 3%; polynuclear neutrophiles, 45%; eosinophiles, 4%. There was slight variation in the size and very little in the shape of the red corpuscles. There was none in their staining reaction. No nucleated forms were seen.

She was seen Nov. 29, 1902, eighteen months after her admission. She was then perfectly well in every way. The lower border of the liver was palpable 3 cm. below the costal border. The spleen was not palpable.

CASE XX. Gladys W., five months old, was admitted to the Infants' Hospital April 29, 1902. The father undoubtedly had syphilis. There had been no miscarriages. The first child was well. This was the second child. She was normal at birth and was breast-fed. She developed snuffles at six weeks. She began to be pale at two months, and at the same time a fine rash appeared on the skin. Since she was three months old she had vomited a good deal, at times had had diarrhea, and had lost weight steadily.

She was small and poorly nourished. The anterior fontanelle was level. The posterior fontanelle was not quite closed. The superficial veins of the scalp were enlarged. Snuffles were marked. There was a slight rosary. The heart and lungs were normal. The liver was palpable 5 cm. below the costal border. The spleen was palpable, running out from behind the ribs in the anterior axillary line, forward to the left parasternal line at the level of the umbilicus, and downward and backward to the anterior-superior spine, filling up the whole flank. The surface was smooth, the edge sharp, the notch indistinctly palpable at about the level of the umbilicus. The abdomen was large and tense. There was an umbilical and a right inguinal hernia. The palms and soles were desquamating. There was a moderate general enlargement of the lymph nodes.

Blood: hemoglobin, 55%; red corpuscles, 3,750,000; white corpuscles, 16,200; small mononuclear, 50%; large mononuclear, 6%; polynuclear neutrophiles, 39%; eosinophiles, 5%. There was very little variation in the size of the red corpuscles and none in their shape. There were no nucleated forms.

She improved rapidly on anti-syphilitic treatment, and was discharged May 12. Nothing is known as to the further history of her case.

CASE XXI. John C., seventeen months old, was admitted to the Infants' Hospital April 21, 1902. He was the first child. He was fed on the breast for five months and then was given strained rolled oats. He had vomited occasionally and had lost some weight. The history was very indefinite.

He was well developed and fairly nourished. His color was good. The fontanelle was closed. There was a slight rosary. The heart was normal. The lungs were normal. The lower border of the liver almost touched the anterior-superior spine, reached to within 2 cm. of the umbilicus and passed under the left costal border in the left nipple line. The spleen was palpable, running out from beneath the costal border in the anterior axillary line directly downward to the level of the anterior-superior spine and backward into the flank. The surface was smooth, the density increased, the edge sharp, the notch not palpable. The abdomen was large and lax. The epiphyses were considerably enlarged at the wrists and moderated at the ankles. The legs were slightly bowed. There was a slight general enlargement of the lymph nodes.

Urine: Pale, 1008, no albumin. Blood: Hemoglobin, 65%; red corpuscles, 3,720,000; white corpuscles, 10,700; small mononuclear, 30%; large mononuclear, 4%; polynuclear neutrophiles, 56%; eosinophiles, 1%. There was a little variation in the size and none in the shape of the red corpuscles. No nucleated forms were seen.

He was seen Nov. 29, 1902, seven months later. He was then a large fat, healthy-looking baby. The liver was palpable 3 cm. below the costal border. The spleen was not palpable. His color was exceptionally good.

CASE XXII. Stanley A., negro, fourteen months old, was admitted to the Infants' Hospital May 21, 1902. There had been no other children or miscarriages. He

was breast-fed up to six months and was then put on Mellin's Food. He had had no gastro-enteric disturbances. He had had a cough off and on for two months.

He was small and poorly nourished. The head was much flattened on top and the forehead prominent. The anterior fontanelle was 3 cm. in diameter. The bridge of the nose was flattened. There was marked snuffles. There was marked pallor of the mucous membranes. There was a slight rosary, and the sides of the chest were somewhat flattened. The heart was normal. The lungs were normal except for an occasional moist rale. He sat up, but feebly. The liver was palpable 3 cm. below the costal border in the nipple line. The spleen was felt running out from beneath the ribs just outside the left nipple line downward and forward to 2 cm. below and about 1 cm. outside the navel, then back into the deep abdomen. The anterior border, tip and a portion of the lower and external borders were easily made out. It then disappeared into the deep abdomen. The anterior edge was rather sharp, the surface smooth, the notch distinct. It was not tender. The whole spleen was easily movable. The abdomen was generally enlarged but lax. There was a slight enlargement of the epiphyses at the wrists. There were knock-knees. There was a moderate talipes valgus on both sides. There was a slight general enlargement of the lymph nodes. There were no ragjades and no fissures or mucous patches about the anus. There was pigmentation on the face and about the anus as if there had been an eruption at some time. The soles were dry and desquamating.

Urine: High, acid, 1022, no albumin. Blood: Hemoglobin, 50%; red corpuscles, 3,750,000; white corpuscles, 29,600; small mononuclear, 30%; large mononuclear, 18%; polynuclear neutrophiles, 48%; eosinophiles, 2%; myelocytes, 2%. There was marked variation in the size and shape of the red corpuscles, but no tendency to oval or large forms. There was a slight general polychromatophilia. In counting 200 white cells, 7 microblasts, 8 normoblasts and 12 macroblasts were seen. There was marked polychromatophilia of the nucleated forms. The most striking thing in the blood was the large number of large mononuclear cells with large, feebly staining nuclei and a small amount of feebly staining protoplasm.

The temperature at entrance was 101° F. It began to rise the next day without any apparent cause. The physical examination was entirely negative. The temperature reached 107° F. on May 24, and the child died that night.

ILLUSTRATIVE CASES OF SECONDARY ANEMIA IN INFANCY.

CASE XXIII. George T., eleven months old, was admitted to the Infants' Hospital March 6, 1902. He was premature, at seven months. He had always been fed on undiluted cows' milk. He had always cried a great deal, vomited after feeding, and had always been constipated. He had never gained.

He was poorly developed and nourished. There was marked pallor of the skin and mucous membranes. There was a slight rosary. The heart and lungs were normal. The liver was normal. The spleen was not palpable. The abdomen was negative. There was a slight enlargement of the epiphyses at the wrists and ankles. There was a moderate general enlargement of the lymph nodes.

Urine: normal, acid, no albumin. Blood: hemoglobin 25%; red corpuscles, 2,600,000; white corpuscles, 15,000; small mononuclear, 63%; large mononuclear, 3%; polynuclear neutrophiles, 33%; eosinophiles, 1%. There was marked variation in the size of the red corpuscles but none in their shape or staining reaction. No nucleated forms were seen.

He was seen Nov. 24, 1902, nearly eight months later. There has been no improvement in any way. The spleen was not palpable.

CASE XXIV. Joseph B., twenty-two months old, was seen July 22, 1897. His digestion had always been very feeble and he had always been pale. He had had bronchitis in the winter and more or less nasal discharge

since then. For two weeks he had been running a moderate temperature, and the pallor had increased.

He was well developed and nourished, but very pale. There was a slight rosary and a slight general enlargement of the lymph nodes. The physical examination was otherwise negative.

Blood: hemoglobin, 42%; red corpuscles, 4,560,000; white corpuscles, 29,720; small mononuclear, 45.5%; large mononuclear, 6%; polynuclear neutrophils, 47.5%; eosinophiles, 1. There was much variation in the size and shape of the red corpuscles. No nucleated forms were seen.

He evidently entirely recovered.

CASES OF ANEMIA AND SPLENIC TUMOR WITHOUT EXAMINATION OF THE BLOOD, BUT WITH RECOVERY.

CASE XXV. William F., eighteen months old, was seen in consultation with Dr. J. P. Torrey of Andover, July 29, 1899. He had always been very pale, but had been well in other ways.

He was well developed and nourished. Pallor was marked. The anterior fontanelle was closed. He had sixteen teeth. There was a slight rosary. The heart was normal. The liver was normal. The spleen reached nearly to the umbilicus. The surface was hard, the edge thin, the notch palpable. The abdomen was negative. The extremities were normal. The cervical lymph nodes were slightly enlarged, the others not.

He was treated with iron and arsenic. Dr. Torrey wrote Oct. 29, 1899, three months later, that the spleen was no longer palpable.

Dr. Torrey examined him again in December, 1902. The boy was then in good health, but still somewhat pale. The spleen was not enlarged.

CASE XXVI. Wolff S., thirteen months old, was admitted to the Infants' Hospital March 14, 1899. He had always been improperly fed and had always suffered from disturbances of digestion.

He was poorly developed and nourished. The fontanelle was 6 cm. in diameter. There was a marked rosary. The heart and lungs were normal. The liver was palpable almost as low as the umbilicus in the right nipple line. The spleen was palpable at the level of the umbilicus. The epiphyses at the wrists and ankles were enlarged. There was a moderate anterior bowing of the tibiae. There was a moderate general enlargement of the lymph nodes.

He was seen Aug. 7, 1902, three and one-half years later. At that time he was perfectly well. The liver was normal. The spleen was not palpable. There was no enlargement of the lymph nodes.

CASE XXVII. Max S., twenty-two months old, was seen at the Out-Patient Department of the City Hospital in February, 1897. He had been very sick during the summer of 1896 with diarrhea. The abdomen had been distended, and Dr. Deering had found an enlarged spleen. He had had more or less disturbance of digestion since that time, and a few weeks before coming to the hospital had had a sharp attack of fermental diarrhea from which he was recovering.

He was well developed and nourished and moderately pale. There was a slight rosary but no other evidences of rickets. The liver was normal. The spleen was palpable about 5 cm. below the costal border. The blood was not examined at that time.

He was seen again in May, 1897, three months later. At that time he was in very good condition and of good color. The tip of the spleen was just palpable. The blood at that time showed hemoglobin, 105%; red corpuscles, 5,160,000; white corpuscles, 5,000; small mononuclear, 30%; large mononuclear, 1%; polynuclear neutrophils, 62%; eosinophiles, 7%. There was a very little variation, in the size of the red corpuscles but none in their shape. No nucleated forms were seen.

THE RELATION OF ENLARGEMENT OF THE LIVER TO THAT OF THE SPLEEN.

In estimating the size of the liver in infancy it

must be remembered that it is normally proportionately larger than in adult life. While under normal conditions it usually does not extend more than 2 or 3 cm., it may extend as much as 4 cm. below the costal border. Only six of the livers in this series were larger than this (11, 15, 16, 17, 20, 21.) Two (17, 20) of these cases had congenital syphilis. In general the largest livers were associated with the largest spleens. In three (18, 19, 22) of the five (18, 19, 20, 21, 22) cases, however, in which the spleen reached to the anterior superior spine, the liver was not enlarged. Enlargement of the liver was, therefore, evidently not dependent upon that of the spleen nor enlargement of the spleen on that of the liver.

THE RELATION OF ENLARGEMENT OF THE LYMPH NODES TO THAT OF THE SPLEEN AND LIVER.

There was a general enlargement of the lymph nodes in every case in which their condition was noted. The greatest enlargement was found in cases in which the spleen was much enlarged (14, 15), but they were moderately enlarged in a case in which the spleen was only slightly enlarged (4), and they were only slightly enlarged in three (19, 21, 22) of four cases (19, 20, 21, 22) in which the spleen was the largest. There was no evident relation between the size of the lymph nodes and that of the liver. They were much enlarged with both normal (14) and enlarged (15) livers, and slightly enlarged with both normal (2) and enlarged (21) livers. The enlargement of the lymph nodes could not have been due, therefore, to that of the spleen or liver. Enlargement of the lymph nodes is, moreover, almost invariably found in all conditions of malnutrition in infancy. Hence it must be regarded here, as elsewhere, merely as a manifestation of malnutrition.

THE RELATION OF THE NUMBER OF RED CORPUSCLES AND THE AMOUNT OF HEMOGLOBIN TO THE SIZE OF THE SPLEEN.

The number of red corpuscles bears no constant relation to the size of the spleen. This is evident if the cases are arranged according to the number of red corpuscles and compared with the arrangement according to the size of the spleen. The arrangement according to the number of red corpuscles, beginning with the largest number, is 13, 11, 8, 10, 5, 3, 16, 15, 17, 19, 22, 20, 21, 7, 12, 18, 2, 14, 4, 6, 1, 9. The two smallest counts were in two cases in which the enlargement of the spleen was slight (9, 1); the largest, 5,800,000, was in a case (13) in which the spleen reached to the umbilicus. In five cases (5, 10, 8, 11, 13) there were over five million red corpuscles, while in five others (3, 15, 16, 17, 19) there were over four million. The lowest count in the cases in which the spleen reached to the anterior-superior spine (18) was 3,556,000, while the lowest in those in which the spleen reached to the umbilicus (14) was 2,553,000.

There was no evident relation between the number of red corpuscles and the size of the liver.

The diminution in the amount of hemoglobin was always relatively greater than that in the number of red corpuscles. The hemoglobin, however, is

always relatively low in infancy, and a relatively great diminution in the amount of hemoglobin is characteristic of the anemias of infancy. The color index in these cases bears no relation to the size of the spleen or liver.

THE RELATION OF THE NUMBER OF WHITE CORPUSCLES TO THE SIZE OF THE SPLEEN.

The arrangement of the cases according to the number of white corpuscles, beginning with the minimum, is as follows: 6, 2, 14, 1, 21, 11, 18, 17, 13, 10, 8, 3, 20, 12, 5, 4, 7, 19, 9, 22, 15, 16. Accepting 14,000 as the normal limit of white corpuscles, there was no leucocytosis in eight (6, 2, 14, 1, 21, 11, 18, 17). Four of these cases (14, 17, 18, 21) were among those in which the spleen was largest. Of fourteen cases in which the number of white corpuscles was increased, the spleen was but little, or moderately, enlarged in seven (3, 4, 5, 7, 8, 9, 10), and much enlarged in seven (12, 13, 15, 16, 19, 20, 22). The largest leucocytosis (47,220) was in a case in which the spleen reached to the umbilicus (16) and the next largest (31,500) in another case in which the spleen reached to the umbilicus (15), but in one case in which the spleen reached to the umbilicus (14) there were only 8,200 white cells, and in the case with the next to the largest spleen there were only 10,700.

It is evident that there was no constant relation between the number of leucocytes and the size of the spleen. The largest spleens were sometimes unaccompanied by leucocytosis, and there was sometimes a marked leucocytosis when the spleen was only slightly enlarged. The largest leucocytoses were usually found, however, in connection with the largest spleens.

THE RELATION OF THE NUMBER OF WHITE CORPUSCLES TO THE SIZE OF THE LIVER.

There was no evident relation between the size of the liver and the number of white corpuscles. There were only 10,700 white cells in the case with the largest liver (21), while the two cases in which the leucocytosis was largest showed only a slight enlargement of the liver (15, 16). Leucocytosis was also marked in cases with normal-sized livers (9, 22).

THE RELATION OF THE NUMBER OF WHITE CORPUSCLES TO THE SIZE OF THE LYMPH NODES.

There was no evident relation between the size of the lymph nodes and the number of white corpuscles. In the two cases in which the enlargement of the lymph nodes was greatest (14, 15) there were 8,200 and 31,500 white corpuscles, respectively. There were, moreover, 47,220 white corpuscles in a case in which the enlargement was slight (16).

THE RELATION OF THE NUMBERS OF RED AND WHITE CORPUSCLES TO EACH OTHER.

The numbers of red and white cells have no constant relation to each other; for example, in one case (16) there were 4,200 white, and 1,736,000 red cells, and in another (2) 4,800 white and 3,288,000 red. In one case (16) with 4,408,000 red corpuscles there were 47,220 white, while in another (17) with 4,200,000 red corpuscles there were only 13,400.

THE RELATION OF THE MORPHOLOGICAL CHANGES IN THE RED CORPUSCLES TO THE OTHER SIGNS.

In a very general way the degree of the morphological changes varied with the number of red corpuscles, the more marked changes occurring in the cases with the smallest numbers of red corpuscles. There were many exceptions to this rule, however. The changes were, on the whole, more marked in the cases with leucocytosis.

There was no correspondence between the degree of the morphological changes and the size of the spleen. The morphological changes were most marked in four cases (1, 6, 7, 9,) in which the spleen was not much enlarged, and in four (12, 15, 19, 22) in which the spleen was much enlarged.

The morphological changes varied, therefore, rather with the number of red and white corpuscles than with the size of the spleen; that is, they formed a part of the pathological changes in the blood and were not connected with those in the spleen.

Certain peculiarities are worth noting. In some cases the morphological changes were marked while there was a comparatively slight diminution in the number of red cells. Nucleated cells were present in cases in which there was little or no diminution in the number of red corpuscles; for example, normoblasts with 5,158,000 red corpuscles (10), and megaloblasts with 4,340,000 (15) and 4,000,000 (19) red corpuscles. In several of the cases which recovered (12, 18, 19) large nucleated red corpuscles were very abundant. These changes are, of course, merely examples of the tendency of anemia in infancy to revert to the fetal type of blood.

There was no correspondence in the amount of the enlargement of the liver and of the spleen. There was no correspondence in the degree of enlargement of the lymph nodes and of the liver and spleen. There was no constant relation between the diminution in the number of red corpuscles and the size of the spleen and liver. There was no constant relation between the number of leucocytes and the size of the spleen and liver, although the largest leucocytoses were usually found in connection with the largest spleens. There was no constant relation between the number of leucocytes and the degree of enlargement of the lymph nodes. There was no constant relation between the number of red and white corpuscles. The morphological changes in the red corpuscles did not vary with the size of the spleen, but in a very general way, with many exceptions, with the number of red and white corpuscles, showing that they were a part of the pathological blood condition and not connected with the condition of the spleen. The degree of the morphological changes was in a general way a guide as to the severity of the anemia. Very marked changes did not necessarily point to a fatal outcome, however, as several cases (12, 18, 19) in which they were most marked recovered. They merely show the tendency of the blood in the anemias of infancy to revert to the fetal type. The hemoglobin was always relatively low, as it almost always is in the anemias of infancy. The condition of the blood in Cases 23 and 24, in which there was no enlargement of the spleen, shows that there is nothing characteristic about the blood

changes found in infancy in association with splenic tumor. The conclusion seems justified, therefore, that the enlargement of the spleen, liver and lymph nodes developed independently of each other, and that they were not directly connected, either as cause or effect, with the changes in the blood.

Granting that this conclusion is correct, the association of these conditions suggests that they are all the results of some common cause.

ETIOLOGY.

Rickets was present in all but two of the cases (6, 9). Neither of these had very large spleens, but they ranked first and third as regards the severity of the anemia. The rachitic changes were slight in eleven (1, 2, 3, 5, 7, 12, 14, 15, 17, 20, 21), moderate in six (4, 8, 11, 13, 18, 22), and marked in three (10, 16, 19). The enlargement of the spleen and changes in the blood were considerable in two (16, 19) of the three cases in which the rachitic changes were marked, but no greater than in other cases (15, 21) in which they were slight. It is evident, therefore, that the rickets was not the direct cause of these pathological conditions, but was itself a symptom of some common cause. Further evidence that rickets was not etiologically responsible for these conditions is the fact that 80% of the children under two years of age at the clinic from which these cases were taken show more or less marked signs of rickets, while these conditions are comparatively rare.

Disorders of the gastro-enteric tract were present in every case in which data were obtained. In two of those without data the food had been unsuitable. There was a history of improper food in all but four (2, 3, 13, 14) of the cases with data on this point. These cases were fed on the breast, and all had gastro-enteric disturbances. It is probable, therefore, that in these cases too the food, even if it was breast milk, was unsuitable. Diseases of the gastro-enteric tract, whether or not due to improper food, are not always followed by anemia and enlargement of the liver and spleen, and therefore cannot be the direct cause of these conditions. Disorders of the gastro-enteric tract, do, however, always cause disturbances of nutrition, and it is to these disturbances of nutrition that they probably owe their etiological importance.

Two (17, 20) of the cases had syphilis. It was in both associated with rickets, improper food and gastro-enteric disturbances. No especial importance can be attributed to it, therefore, as a general etiological factor. It undoubtedly acts chiefly by disturbing nutrition.

Prematurity and pertussis, each present in one case (7, 9), probably acted in the same way.

Disturbances of nutrition in infancy may produce various results. Rickets and scurvy are undoubtedly peculiar manifestations of disturbances of nutrition. In other instances disturbances of nutrition produce atrophy, anemia or enlargement of the lymph nodes, liver or spleen. Why disturbances of nutrition in one case cause rickets, in another atrophy and in another anemia or enlargement of the lymph nodes or spleen is not known. The fact that they do cause all these various conditions explains the peculiar combinations in which these conditions are found and their evident independence of each other.

CONCLUSIONS.

It seems justifiable to conclude, therefore, that when anemia, splenic tumor and enlargement of the liver or lymph nodes are found in association in infancy they are in no way dependent on each other, but are all manifestations of a common cause — disturbance of nutrition; that there is nothing characteristic about the blood changes found in association with enlargement of the spleen, as similar changes are found when there is no enlargement of the spleen; that the anemia is secondary rather than primary; that there is no justification for placing the cases of anemia in infancy associated with enlargement of the spleen or liver in a class by themselves and calling it "anemia infantum pseudo-leukemika," or "splenic anemia of infancy"; that these terms should be dropped from our nomenclature.

PROGNOSIS.

The ultimate fate of these cases is of some interest. Seven disappeared from view after a short time; two (12, 16) of these probably died; five (5, 7, 8, 17, 20) probably recovered; two (17, 20) of these were syphilitic.

Seven are known to have died; one (13) of meningitis, and six (1, 3, 6, 9, 15, 22) without complications. They died after three days, five days, one month, one month, two months and seven months. The blood changes were marked in all of these cases. They included most of the severest cases. The spleens were very large in three (13, 15, 22), but comparatively small in the others.

One (12) was doing well after eight months. Seven (4, 10, 11, 14, 18, 19, 21) were well after six months, seven months, seven months, 18 months, two and one-half years, six years, seven years. The blood changes were moderately severe in these cases. Nucleated reds were numerous in five, megaloblasts predominated in two. Nucleated red corpuscles and megaloblasts are, therefore, evidently not of so much importance in prognosis in infancy as in later life. Five of these cases (12, 14, 18, 19, 21) were among those with the largest spleens, and two (10, 11) of the others had considerably enlarged spleens. Two of the largest spleens were not palpable after seven and eight months (21, 12). Others were found absent after seven months (11), eighteen months (19), two and one-half years (4), and seven years (18). One (10) was just palpable after six years. In three cases in which the spleen was much enlarged, although the blood was not examined, it was not palpable after three months (25), five months (27) and three and one-half years (26). One (21) very large liver was of normal size after seven months, another (11) moderately enlarged, one was still slightly enlarged after seven months. The improvement in the blood condition during recovery is seen in Cases 19 and 27.

The prognosis in these cases depends, therefore, more on the condition of the blood than on the size of the spleen. Recovery may take place even when the changes in the blood are very severe. The size of the spleen has no influence on the prognosis. The largest spleens may return to the normal size in a few months.