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STUDY OF THE BLOOD IN RICKETS

BY

JOHN LOVETT MORSE, A.M., M.D.

[*Reprinted from Medical and Surgical Reports of the
Boston City Hospital, 1897*]



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A STUDY OF THE BLOOD IN RICKETS.

BY JOHN LOVETT MORSE, A.M., M.D.

THE blood of infants under two years differs in certain of its characteristics from that of adults. The number of red corpuscles is about the same or a little larger, averaging a little over 5,000,000 per cubic millimetre. The number of white corpuscles per cubic millimetre is somewhat larger, averaging from 10,000 to 12,000. The relative proportions of the various forms of leucocytes are also considerably different. The limits, as given by Gundobin, are as follows :

| | |
|------------------------------------|-------------|
| Small Mononuclear | 50 % - 70 % |
| Large Mononuclear | 6 % - 14 % |
| Polynuclear Neutrophiles | 28 % - 40 % |
| Eosinophiles | 1 % - 10 % |

That is, the proportion of mononuclear, or unripe, forms is about three times as great as in adult life, while that of the polynuclear neutrophiles, or over-ripe, form is only 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. Finally, an increase in the number of eosinophilic cells, even if considerable, seems to be of less significance.

Anæmia of various sorts is very common in children. It develops more easily and more frequently as the result of various morbid conditions and diseases in them than in adults. This is because the tissue changes in them are more rapid, as the old tissues have not only to be nourished and replaced, but new ones formed. Hence any disturbance

of nutrition is more serious and results in more rapid and significant changes in the blood.

The classification of the anæmias of children is at best a vexed one. That of Monti is the most complete, but seems unnecessarily complicated. They, as those of adults, may be roughly divided into the primary and secondary, the primary being subdivided into simple anæmia, chlorosis, and pernicious anæmia. Chlorosis with its typical symptom complex and blood is not a disease of early childhood. Warner, however, has noted that "in the simple anæmias of childhood the percentage of hæmoglobin is diminished to a much greater extent than that of the red globules." I have also noted this in the anæmia secondary to various diseases. Although cases of the so-called progressive pernicious anæmia have been reported in young children, they are all open to criticism, and it is very doubtful if the condition occurs in them. The simple and secondary anæmias may be divided into the mild and severe forms (anæmia levis and anæmia gravis). In the former the diminution in the specific gravity, hæmoglobin, and number of erythrocytes is slight, and the red corpuscles show no histological changes. In the latter the diminution in the specific gravity, hæmoglobin, and number of red corpuscles is marked, and the histological changes in the red cells are often considerable. The differences, however, are merely in degree, and only show a greater or less amount of disturbance of the blood-forming organs. Either may or may not be accompanied by leucocytosis. In all but the mild anæmia without leucocytosis the spleen may be enlarged. It is to these cases that the term "splenic anæmia" has been applied. They do not merit a special name, however, as there is nothing characteristic in the blood condition, and an enlarged spleen may be associated with a normal condition of the blood.

Much confusion exists concerning the so-called anæmia infantum pseudo-leukæmica. The description of this blood condition, as given by Luzet and Alt and Weiss, is as follows: Constant diminution in number of erythrocytes; constant more or less marked diminution in hæmoglobin; poikilocytosis; very many nucleated red cells, mostly of

abnormal form and many showing karyokinetic figures; polychromatophilia of the nucleated red cells and of many of the non-nucleated; pretty marked leucocytosis, always polymorphous. In addition there is always splenic tumor and more or less enlargement of the liver. Those who consider this blood condition characteristic are divided as to the limitations of the disease. Some, who consider it always primary, would rule out those cases in which it develops secondary to rickets, syphilis, or other anæmias, while others would include them. Others think that there is nothing characteristic in the blood condition, but that it is merely a very severe anæmia, and not typical of any disease. Fischl has found the same type of blood in cases of rickets both with and without splenic enlargement. Moreover, cases of progressive anæmia with enlarged liver and spleen do not always show this condition of the blood. Whether the condition known as anæmia infantum pseudo-leukæmica is to be considered as a separate disease or as merely a severe form of anæmia gravis with leucocytosis must therefore be left for the future to determine.

It is generally recognized that leucocytosis develops more quickly and to a higher degree in children than in adults. While in adults the increase of white cells is almost entirely in the polynuclear neutrophiles, this is not the case in children. In them the leucocytosis is sometimes due to the increase of lymphocytes, sometimes to that of the large mononuclear forms, sometimes to that of the polynuclear neutrophiles, and sometimes even to that of the eosinophiles. According to Weiss, the lymphocytes are much increased proportionately in affections of the gastro-enteric tract, while the mononuclear cells of all sorts, as well as the transition forms, are proportionately increased in those of the respiratory tract. When there are complicated tissue changes and severe organic disturbances, the proportions of the various forms of leucocytes show wide variations. He concludes that the proportions of the leucocytes correspond to certain tissue conditions and alterations, and are thus characteristic for certain diseases only in so far as quite definite tissue changes occur in these diseases. As the same pathological changes occur in many diseases, and different ones in the

same disease, it is evident that the same histological blood condition is not always to be found in the same disease.

Monti has found that in normal children there is a constant relation between the specific gravity of the blood and the amount of hæmoglobin. They vary directly. This relation is not constant in disease, however, and may vary in various ways.

Although the blood must have been examined in many cases of rickets, the literature of the subject is very meagre. No work worthy of mention seems to have been done in this direction before the beginning of the present decade. Since then, however, several observers have reported short series of cases, although no one seems to have undertaken a systematic investigation of the subject.

Monti found all the forms of anæmia described by him in his classification in rhachitis. As a rule, he found the more severe forms in the severe cases. No definite connection between the clinical course of the cases and the condition of the blood could be made out, however. A greater proportion of the severe than of the mild forms showed splenic tumor. A greater proportion of the cases with splenic tumor showed leucocytosis than did those without. Certain cases with very large spleens showed no leucocytosis, however, and others without splenic enlargement showed a high grade. He concludes that "rickets as such does not cause any peculiar anæmia, but that according to the severity of the rhachitic process and the associated involvement of the blood-forming organs very different forms and gradations of chronic anæmia may occur."

Felsenthal examined the blood in 12 cases of rhachitis between the ages of 9 months and 2 years, 9 of which were mild cases with little or no enlargement of the spleen, while 3 were severe and had large, hard spleens. He obtained the same results in all. The number of red corpuscles was normal or almost normal, and there was no evident relation between the number of corpuscles and the severity of the case. The hæmoglobin was diminished in all cases, and always to a greater extent than the red corpuscles. The number of white corpuscles was always increased. He considered the oligochromæmia as the most striking feature.

He found that the red corpuscles often showed a considerable variation in size, and that nucleated forms, mostly normoblasts, and never very numerous, occurred in the severe cases. The majority of the white corpuscles were small and large mononuclear.

Weiss examined the blood in 6 cases. He found that all cases of severe rhachitis show a typical leucocytosis, the principal part of which is to be attributed to an increase of the mononuclear cells. The transition forms are also numerous, so that the polynuclear cells appear relatively diminished.

Gundobin found the same condition in the blood of rickets as in that of other forms of retarded development. He concludes that rickets as rickets causes no peculiar pathological change in white cells, and that any change in them is dependent on concurrent involvement of the internal organs.

Luzet thinks that the blood in rickets associated with splenic enlargement may show all stages from mild anæmia to leukaemia. He thinks the splenic tumor causes leucocytosis, increases the anæmia, and makes the prognosis more gloomy.

Rotch reports the results of the examination of the blood in two cases of rhachitic anæmia, one without and one with splenic tumor. The diminution of red corpuscles and of hæmoglobin was more marked in the latter. It showed no leucocytosis, however, while the former did.

Hock and Schlesinger have found that the specific gravity of the blood in rickets is entirely independent of the severity of the rhachitic process, but varies with the anæmia. Felsenthal and Bernhard have also shown that it varies with the amount of hæmoglobin.

I have examined the blood in twenty cases of active, uncomplicated rickets in infants under two years of age. The blood was in every case taken from the lobe of the ear, and examined with a Thoma-Zeiss apparatus. It was diluted (1-200) with a 3 per cent. salt solution colored with methylene blue. The red corpuscles in one-tenth of a cubic millimetre and the white corpuscles in two cubic millimetres were counted. The hæmoglobin was estimated with a von

Fleischl instrument. Cover-slips were in all cases made at the same time, hardened in equal parts of alcohol and ether, and stained with Ehrlich's "triple stain." A differential count of at least 500 white corpuscles was then made, the classification recommended by Ehrlich being used. As far as possible the blood was taken about noon, and in most cases about three hours after food. The cases may be roughly divided into three groups according to the severity of the process: those in which the manifestations are mild; those in which they are more severe, but in which there is no splenic enlargement; and those in which there is splenic tumor. The first group comprises 9 cases; the second, 4; and the third, 7. The data of the individual cases are as follows:

MILD CASES.

I. Male. Negro. Eight months.

Breast for six weeks. Mellin's food since.

Marked sweating of head for two months. Always little cough. Bowels usually regular.

W. D. and N. Flabby. Holds up head. Head of good shape. Anterior fontanelle widely open. No teeth. Sits alone feebly with marked kyphosis of weakness. Moderate rosary. Moderate retraction of ribs at diaphragm with flaring below. Heart and lungs normal. Abdomen large but soft. Liver normal. Spleen not palpable. No enlargement of epiphyses. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 60% |
| Red Corpuscles | 4,170,000 |
| White Corpuscles | 9,600 |
| Small Mononuclear | 34% |
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 61% |
| Eosinophiles | 1% |

No irregularity in size or form of red corpuscles.

II. Female. Irish. Seven months.

Breast for three months. Then Horlick's malted milk.

Head sweats. Restless at night. Tendency to diarrhoea.

F. D. and N. Flabby. Pale. Holds up head. Head normal. No teeth. Sits alone feebly with moderate kyphosis of weakness. Moderate rosary. Heart and lungs normal. Abdomen full and soft. Liver and spleen normal. Slight enlargement of epiphyses at wrists. Slight general glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 57% |
| Red Corpuscles | 4,200,000 |
| White Corpuscles | 9,300 |
| Small Mononuclear | 36% |
| Large Mononuclear | 3% |
| Polynuclear Neutrophiles | 60% |
| Eosinophiles | 1% |

No irregularity in size or shape of red corpuscles.

III. Female. Negro. Seven months.

Breast for five months. Condensed milk since.

Head sweats. Rolls head. Kicks off clothes. Vomits occasionally.

Large, fat child. Head normal. No teeth. Sits alone with fairly straight back. Slight rosary. Heart and lungs normal. Abdomen little full and tense. Liver and spleen normal. Slight enlargement of epiphyses at wrists. Little bowing of tibiae. Slight general glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 60% |
| Red Corpuscles | 5,048,000 |
| White Corpuscles | 14,770 |
| Small Mononuclear | 61% |
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 33% |
| Eosinophiles | 2% |

Moderate variation in size of red corpuscles, many being large. No poikilocytosis. One normoblast seen in two slides. Several of the large mononuclear leucocytes very large and containing a very large nucleus.

IV. Male. Irish. Thirteen months.

Breast for ten months. Now arrow-root and milk.

Pertussis at seven months. Sits, creeps, and stands alone.

W. D. and N. Flabby. Pale. Head a little large. Fontanelle normal. Six teeth. General kyphosis of weakness. Moderate rosary. Heart and lungs normal. Abdomen soft and not distended. Liver and spleen normal. Considerable enlargement of epiphyses at wrists. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 67% |
| Red Corpuscles | 4,936,000 |
| White Corpuscles | 18,800 |
| Small Mononuclear | 24% |
| Large Mononuclear | 14% |
| Polynuclear Neutrophiles | 58% |
| Eosinophiles | 4% |

V. Female. Negro. Thirteen months.

Breast off and on. Mellin's food for eight months. Then milk. Also a little "table food."

Never well. Very fussy. Head sweats a good deal. Cannot creep or stand.

W. D. and N. Flesh firm. Head rather large, but of fair shape. Fontanelle three-quarters of an inch square. No teeth. Sits almost straight. Moderate rosary. Heart and lungs normal. Abdomen large and rather tense. Large umbilical hernia. Liver and spleen not enlarged. Moderate enlargement of epiphyses at wrists. Slight knock-knee. Some general glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 48% |
| Red Corpuscles | 5,024,000 |
| White Corpuscles | 17,900 |
| Small Mononuclear | 47% |
| Large Mononuclear | 8% |
| Polynuclear Neutrophiles | 44% |
| Eosinophiles | 1% |

Very slight variation in size and shape of red corpuscles.

VI. Male. Irish. Twenty-two months.

Still on breast. General diet since fourteen months.

Always well. Does not stand.

F. D. and N. Flabby. Pale. Frontal and parietal eminences large. Fontanelle one-half inch square. Ten teeth. Sits with fairly straight back. Marked rosary. Slight retraction at diaphragm. Heart and lungs normal. Abdomen, liver, and spleen not enlarged. Cannot stand. Epiphyses at wrists and ankles much enlarged. Anterior bowing of femora and outward of tibiæ. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 70% |
| Red Corpuscles | 5,144,000 |
| White Corpuscles | 10,700 |
| Small Mononuclear | 52% |
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 42% |
| Eosinophiles | 2% |

No variation in size or shape of red corpuscles.

VII. Male. Negro. Seventeen months.

Still on breast. General diet since twelve months.

Always fairly well. Head sweats. Fussy.

F. D. and N. Flabby. Head rather large. Fontanelle nearly closed. Six teeth. Sits fairly straight. Moderate rosary. Heart and lungs normal. Abdomen rather large, but soft. Small umbilical hernia. Liver and spleen normal. Cannot stand. Epiphyses at wrists large. Slight bowing of tibiæ. Slight general glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 64% |
| Red Corpuscles | 5,102,000 |
| White Corpuscles | 14,000 |
| Small Mononuclear | 49% |
| Large Mononuclear | 6% |
| Polynuclear Neutrophiles | 43% |
| Eosinophiles | 2% |

No variation in size or shape of red corpuscles.

VIII. Female. Negro. Eight months.

Condensed milk, one month; cow's milk, three months; malted milk, four months.

Head sweats a great deal. Sleeps poorly. Diarrhoea for long time.

F. D. and N. Rather flabby. Head normal. No teeth. Cannot sit alone. Moderate rosary. Heart and lungs normal. Abdomen not enlarged. Liver and spleen normal. Epiphyses at wrists enlarged. Tendency to knock-knee. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 67% |
| Red Corpuscles | 4,840,000 |
| White Corpuscles | 10,200 |
| Small Mononuclear | 53% |
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 41% |
| Eosinophiles | 2% |

A very little variation in size, but none in shape of red corpuscles.

IX. Male. Negro. Fourteen months.

Never nursed. Oatmeal and milk. Then general diet.

Head sweats. Restless at night. Always little cough. Constipation. Weak. Tries to stand.

F. D. and N. Head large, flat on top. Anterior fontanelle not widely open. Two teeth. Back straight. Marked rosary. Sternum prominent. Marked drawing-in at diaphragm. Heart and lungs normal. Abdomen large and soft. Liver and spleen normal. Epiphyses at wrists considerably enlarged. Knock-knee. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 62% |
| Red Corpuscles | 5,528,000 |
| White Corpuscles | 9,000 |
| Small Mononuclear | 32% |
| Large Mononuclear | 16% |
| Polynuclear Neutrophiles | 51% |
| Eosinophiles | 1% |

A good deal of variation in the size of red corpuscles. Numerous microcytes and macrocytes. Moderate poikilocytosis. Numerous very large mononuclear cells with large pale nucleus and wide pale protoplasm.

SEVERE CASES.

X. Female. Irish. Six months.

P. D. and N. Pale. Craniotabes. Moderate rosary. Heart and lungs normal. Abdomen large and soft. Liver extends 4 centimetres below costal border. Spleen not palpable. Epiphyses at wrists large. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 65% |
| Red Corpuscles | 4,704,000 |
| White Corpuscles | 13,800 |
| Small Mononuclear | 48% |
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 48% |
| Eosinophiles | 0% |

Moderate variation in size of red corpuscles. Slight poikilocytosis.

XI. Male. Italian. Two months.

Condensed milk.

Small and emaciated. Skin dry. Pale. Sutures open and bones movable. Slight rosary and retraction at diaphragm. Heart and lungs normal. Abdomen soft. Liver and spleen normal. No enlargement of epiphyses. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 52% |
| Red Corpuscles | 3,508,000 |
| White Corpuscles | 9,200 |
| Small Mononuclear | 69% |
| Large Mononuclear | 5% |
| Polynuclear Neutrophiles | 25% |
| Eosinophiles | 1% |

Marked variation in size of red corpuscles. Macrocytes much more numerous than microcytes. Marked poikilocytosis. Three macroblasts and two normoblasts seen in counting 500 whites.

XII. Male. Italian. Nineteen months.

Breast for a year. General diet since.

Sweats a good deal. Diarrhœa for a month. Quiet. Sits alone. Cannot creep or stand.

P. D. and N. Much hair. Pale. Head rather large, but not abnormal in shape. Anterior fontanelle open, one-half inch in each diameter. Four teeth. Marked general kyphosis, not disappearing on suspension. Marked rosary. Heart and lungs normal. Abdomen very large, tense, and tympanitic. Liver and spleen normal. Epiphyses at wrists large. Large glands in groins only.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 67% |
| Red Corpuscles | 5,296,000 |
| White Corpuscles | 7,200 |
| Small Mononuclear | 29% |
| Large Mononuclear | 17% |
| Polynuclear Neutrophiles | 53% |
| Eosinophiles | 1% |

Slight variation in size of red corpuscles. Occasional microcyte and macrocyte. A very little poikilocytosis. Numerous very large mononuclear white cells.

XIII. Male. Negro. Two years.

Brought for "general weakness." Head sweats. Tendency to looseness of bowels. Sits alone. Cannot creep or stand.

P. D. and emaciated. Head large and forehead square. Anterior fontanelle open, an inch in each diameter. Ten teeth. General kyphosis of weakness. Pigeon breast. Marked rosary. Slight retraction of chest at diaphragm. Heart and lungs normal. Very large abdomen.

Umbilical hernia. Liver and spleen normal. Epiphyses at wrists large. Inguinal glands enlarged, others not.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 64% |
| Red Corpuscles | 4,604,000 |
| White Corpuscles | 5,500 |
| Small Mononuclear | 39% |
| Large Mononuclear | 15% |
| Polynuclear Neutrophiles | 45% |
| Eosinophiles | 1% |

Very little variation in size and none in shape of red corpuscles.

CASES WITH SPLENIC TUMOR.

XIV. Female. Irish. Nine months.

Breast and general diet.

Constipation. Losing weight. Restless at night. Kicks off clothes.

Head sweats. Sits alone.

F. D. and N. Flabby. Rather pale. Parietal eminences very large, frontal somewhat so. Fontanelle almost closed. No teeth. Sits straight. Slight rosary. Heart and lungs normal. Abdomen little full. Liver extends an inch below costal border. Spleen just palpable. Epiphyses at wrists a little large. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 77% |
| Red Corpuscles | 4,724,000 |
| White Corpuscles | 22,000 |
| Small Mononuclear | 63% |
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 31% |
| Eosinophiles | 2% |

A little variation in size and shape of red corpuscles.

XV. Male. Norwegian. Twenty months.

Always cow's milk. Now fair diet.

Measles at one year. Very few digestive symptoms. Constipation. Sat up at nine months. Just beginning to creep. Doesn't stand. Brought because he cries when stood on feet. Not tender to touch.

F. D. and N. Flabby. Pale. Large head. Fontanelle widely open. Sixteen teeth. Sits with marked kyphosis in lower dorsal region, which is only partially obliterated on suspension. Small chest. Marked rosary. Heart and lungs normal. Abdomen large and soft. Liver large. Spleen palpable. Epiphyses enlarged at wrists and ankles. Anterior and lateral bow-legs. General glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 73% |
| Red Corpuscles | 4,448,000 |
| White Corpuscles | 14,400 |
| Small Mononuclear | 49% |
| Large Mononuclear | 6% |
| Polynuclear Neutrophiles | 40% |
| Eosinophiles | 5% |

Moderate variation in size of red corpuscles, but no microcytes or macrocytes. Very little poikilocytosis.

XVI. Male. Italian. Nine months.

Breast and general diet.

Measles and diphtheria at six months, followed by running ear. Subject to attacks of vomiting and diarrhœa. Head sweats badly. Sits alone.

F. D. and N. Flabby. Pale. Large square head. Fontanelle very widely open, but not tense. No teeth. Back straight. Small chest. Marked rosary. Heart and lungs normal. Abdomen large and tense. Liver normal. Spleen palpable. Epiphyses at wrists and ankles enlarged. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 60% |
| Red Corpuscles | 4,068,000 |
| White Corpuscles | 14,500 |
| Small Mononuclear | 34% |
| Large Mononuclear | 3% |
| Polynuclear Neutrophiles | 56% |
| Eosinophiles | 7% |

No variation in size or shape of red corpuscles.

XVII. Female. Irish. Fifteen months.

Now on milk and cracker only.

Brought because of "weakness in legs." Sits alone. Doesn't creep.

F. D. and N. Pale. Head a little large. Fontanelle almost closed. Seven teeth. Back straight. Marked rosary. Heart and lungs normal. Abdomen full. Liver normal. Spleen distinctly palpable. Large epiphyses at wrists. Legs held loosely and rotated outward at hips. Tendency to talipes varus. No spasm. Knee-jerks present and equal. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 64% |
| Red Corpuscles | 4,936,000 |
| White Corpuscles | 11,900 |
| Small Mononuclear | 39% |
| Large Mononuclear | 6% |
| Polynuclear Neutrophiles | 48% |
| Eosinophiles | 7% |

Moderate variation in size of red corpuscles. A few macrocytes and numerous microcytes. Slight poikilocytosis.

XVIII. Male. Irish. Five months.

Never gained. Cries constantly. Sleeps very little. Frequent vomiting. Constipation.

Small, but not much emaciated. Marked pallor. Head negative; can hold it up. Cannot sit alone. Marked rosary. Systolic murmur over whole præcordia. Heart otherwise normal. A few râles here and there in both chests. Abdomen lax. Liver normal. Spleen palpable below costal border, as large as last phalanx of thumb. Epiphyses at wrists slightly enlarged. No glandular enlargement.

| | |
|-----------------------------|-----------|
| Hæmoglobin | 57% |
| Red Corpuscles | 4,519,000 |
| White Corpuscles | 15,900 |
| Small Mononuclear | 44% |

| | |
|------------------------------------|-----|
| Large Mononuclear | 4% |
| Polynuclear Neutrophiles | 47% |
| Eosinophiles | 5% |

A very little variation in size and shape of red corpuscles. One normoblast seen in counting five hundred white corpuscles.

XIX. Female. Russian. Twenty months.

Breast and patent foods at first. Now general diet. Always digestive disturbances. Very restless at night. Sits and stands; cannot walk.

F. D. and N. Flabby. Pale. Large, square, flat head. Anterior fontanelle nearly closed. Eleven teeth. General kyphosis of weakness. Pigeon breast. Marked retraction at diaphragm. Very marked rosary. Heart and lungs normal. Abdomen large and soft. Liver not enlarged. Spleen palpable below costal border, seven centimetres laterally and three centimetres vertically. Marked enlargement of epiphyses at wrists. Moderate bowing of both femora and tibiae. No glandular enlargement.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 68% |
| Red Corpuscles | 5,518,000 |
| White Corpuscles | 15,200 |
| Small Mononuclear | 51% |
| Large Mononuclear | 5% |
| Polynuclear Neutrophiles | 40% |
| Eosinophiles | 4% |

Considerable variation in size of red corpuscles. Numerous macrocytes. Moderate poikilocytosis. Occasional normoblasts.

XX. Female. Irish. Seventeen months.

Condensed milk and barley-water.

Pale for a long time. Rapid loss of flesh in last three months.

Tumor in abdomen noted two months ago, as large then as now. Just beginning to sit up alone. No vomiting. Constipation.

F. D. and emaciated. Marked pallor with yellowish tinge. Fontanelle not closed. Four teeth. Rosary. Heart and lungs normal. Abdomen very full and tense. Umbilical hernia. Liver not enlarged. Spleen fills left half of abdomen, reaching nearly to median line and to within half an inch of anterior superior spine. No ascites. Epiphyses enlarged. No glandular enlargement. Purpuric spots on abdomen. Urine negative.

| | |
|------------------------------------|-----------|
| Hæmoglobin | 60% |
| Red Corpuscles | 3,556,000 |
| White Corpuscles | 12,400 |
| Small Mononuclear | 28% |
| Large Mononuclear | 10% |
| Polynuclear Neutrophiles | 55% |
| Eosinophiles | 7% |

Marked variation in size of red corpuscles. Many macrocytes and microcytes, the former being the more numerous. Moderate poikilocytosis. Moderate number of nucleated red corpuscles, megaloblasts being the most common form. Occasionally free nuclei. No abnormal forms of white corpuscles.

The results of the blood examinations are more evident, perhaps, in the following table :

| No. | Age in Months. | Type of Disease. | Hæmoglobin. | Erythrocytes. | Leucocytes. | Small Mononuclear. | Large Mononuclear. | Polynuclear Neutrophils. | Eosinophiles. | Morphology of Erythrocytes. |
|-------|----------------|------------------------------|-------------|---------------|-------------|--------------------|--------------------|--------------------------|---------------|---|
| 1 . . | 8 | mild | 60% | 4,170,000 | 9,600 | 34% | 4% | 61% | 1% | Normal. |
| 2 . . | 7 | " | 57% | 4,200,000 | 9,300 | 36% | 3% | 60% | 1% | Normal. |
| 3 . . | 7 | " | 60% | 5,048,000 | 14,770 | 61% | 4% | 33% | 2% | Moderate variation in size. Normoblasts. |
| 4 . . | 13 | " | 67% | 4,936,000 | 18,800 | 24% | 14% | 58% | 4% | Nearly normal. |
| 5 . . | 13 | " | 48% | 5,024,000 | 17,900 | 47% | 8% | 44% | 1% | Nearly normal. |
| 6 . . | 22 | " | 70% | 5,144,000 | 10,700 | 52% | 4% | 42% | 2% | Normal. |
| 7 . . | 17 | " | 64% | 5,102,000 | 14,000 | 49% | 0% | 43% | 2% | Normal. |
| 8 . . | 8 | " | 67% | 4,840,000 | 10,200 | 53% | 4% | 41% | 2% | Slight variation in size. |
| 9 . . | 14 | " | 62% | 5,528,000 | 9,000 | 32% | 16% | 51% | 1% | Considerable variation in size. Moderate poikilocytosis. |
| 10 . | 6 | severe | 65% | 4,704,000 | 13,900 | 48% | 4% | 48% | 0% | Moderate variation in size. Slight poikilocytosis. |
| 11 . | 2 | " | 52% | 3,508,000 | 9,200 | 69% | 5% | 25% | 1% | Marked variation in size. Marked poikilocytosis. Macroblasts and normoblasts. |
| 12 . | 19 | " | 67% | 5,290,000 | 7,200 | 29% | 17% | 53% | 1% | Slight variation in size. Slight poikilocytosis. |
| 13 . | 24 | " | 64% | 4,604,000 | 5,500 | 39% | 15% | 45% | 1% | Nearly normal. |
| 14 . | 9 | spleen palpable | 77% | 4,724,000 | 22,000 | 63% | 4% | 31% | 2% | Nearly normal. |
| 15 . | 20 | " | 73% | 4,448,000 | 14,400 | 49% | 0% | 40% | 5% | Moderate variation in size. Slight poikilocytosis. |
| 16 . | 9 | " | 60% | 4,068,000 | 14,500 | 34% | 3% | 56% | 7% | Normal. |
| 17 . | 15 | " | 64% | 4,936,000 | 11,900 | 39% | 0% | 48% | 7% | Moderate variation in size. Slight poikilocytosis. |
| 18 . | 5 | spleen considerably enlarged | 57% | 4,519,000 | 15,900 | 44% | 4% | 47% | 5% | Slight variation in size. Slight variation in shape. Rarely a normoblast. |
| 19 . | 20 | " | 68% | 5,158,000 | 15,200 | 51% | 5% | 40% | 4% | Considerable variation in size. Moderate poikilocytosis. Occasional normoblast. |
| 20 . | 17 | spleen very large | 60% | 3,556,000 | 12,400 | 28% | 10% | 55% | 7% | Marked variation in size. Moderate poikilocytosis. Numerous nucleated forms. |

An analysis of these cases shows that the number of red corpuscles was in all cases normal or but slightly diminished; that the percentage of hæmoglobin was always diminished, and always proportionately more so than that of the red corpuscles; that there was a leucocytosis in a little more than half the cases; that this leucocytosis occurred more frequently in those cases with splenic tumor than in those without; that the amount of the leucocytosis was independent of the presence, or absence, or size of the splenic tumor; and that the histological changes in the red corpuscles increased, as a rule, with the severity of the case, being most marked in those with splenic tumor.

The approximately normal number of red corpuscles and the absolutely and relatively diminished proportion of hæmoglobin agrees with the results obtained by Felsenthal. It must be remembered, however, as has already been noted, that this condition is not an uncommon one in the anæmias of childhood.

The results as regards the white corpuscles do not agree with those of Felsenthal, who found a leucocytosis in every case, but rather corroborate Monti's conclusions that leucocytosis may or may not be present, and that it is more frequent in the cases with splenic tumor. They also confirm his observation that certain cases with very large spleens have no leucocytosis, as the case with the largest spleen had but little more than the normal number of white corpuscles. The average of the different forms of leucocytes in the nine cases without leucocytosis gives the following proportions, which are somewhat different from those given by Gundobin for normal blood:

| | |
|------------------------------|-----|
| Small Mononuclear | 43% |
| Large Mononuclear | 8% |
| Polynuclear Neutrophiles . . | 47% |
| Eosinophiles | 2% |

The average proportions in the eleven cases with leucocytosis, as well as in the six cases with enlarged spleens, are:

| | |
|------------------------------------|-------|
| Small Mononuclear | 45% |
| Large Mononuclear | 5%—6% |
| Polynuclear Neutrophiles | 45% |
| Eosinophiles | 4%—5% |

That is, almost the same as in the cases without leucocytosis.

These results do not agree with those of Weiss and Felsenthal, who found the increase in the mononuclear and transition forms, but rather with Weiss's general statement that when there are complicated tissue changes the increase may be in any or all of the different forms of leucocytes. It is noticeable that eosinophilic cells are considerably more numerous in the cases with splenic tumor. The association of nucleated forms and of variations in the size and shape of the red corpuscles with an almost undiminished number is of interest.

Conclusions.—The results obtained in these cases, together with those obtained by others, seem to justify the following conclusions: Most cases of rickets are accompanied by anæmia. This anæmia may be of any form and of any grade of severity. The severity of the anæmia varies in a general way with the severity of the process. The most common form is that in which the number of red corpuscles is normal or nearly normal, and the percentage of hæmoglobin both absolutely and relatively diminished. The anæmia may or may not be accompanied by leucocytosis. Leucocytosis occurs more frequently in the cases with splenic tumor than in those without. It may be due to an increase in any or all of the varieties of white corpuscles. The specific gravity varies with the amount of hæmoglobin. Finally, there is no form of anæmia found in rickets which may not be found in other conditions, and no form of anæmia found in other conditions which may not be found in rickets.

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