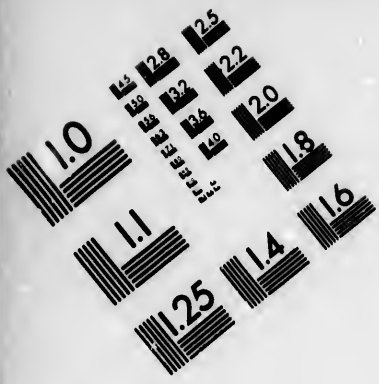

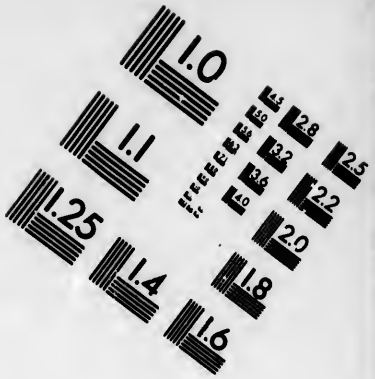

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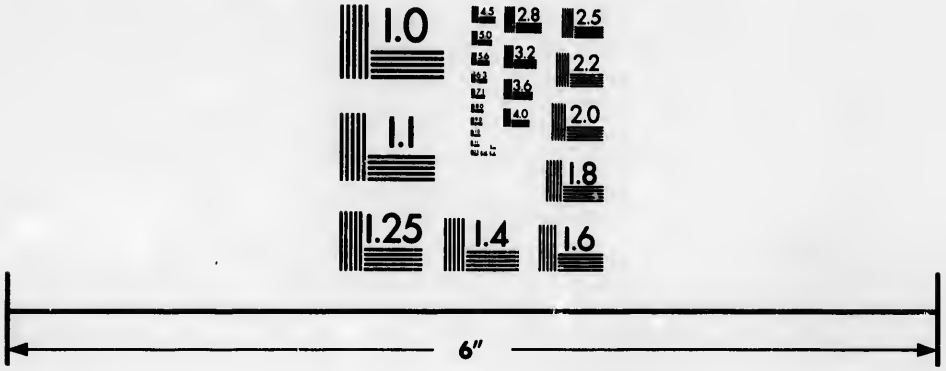

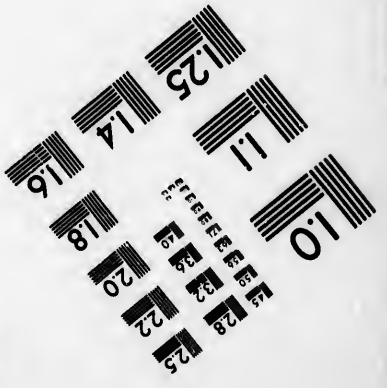

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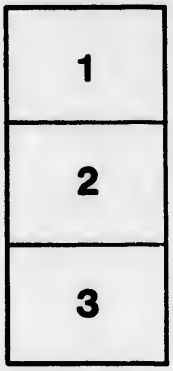
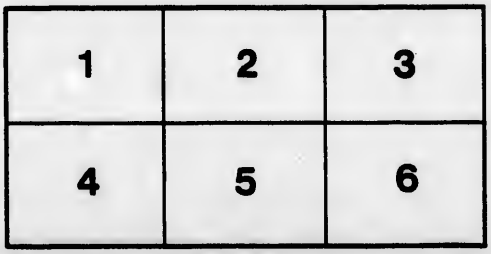
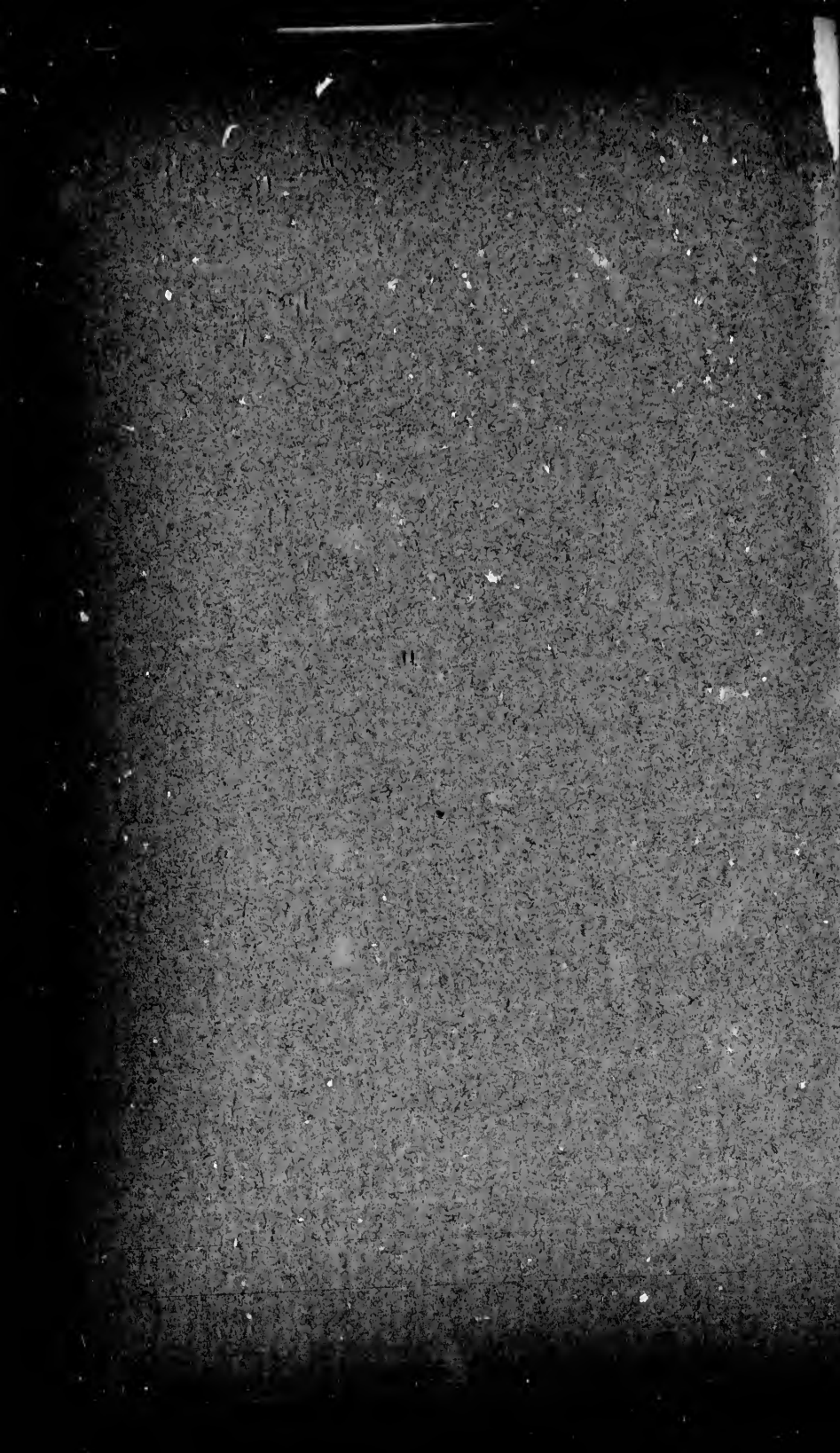




ACUTE LEUKÆMIA IN CHILDHOOD WITH REPORT OF A CASE.

By Thomas McCrae, M. B. (*Tor.*),

Instructor in Medicine, The Johns Hopkins University, and Physician in Charge of the Clinical Laboratory, The Johns Hopkins Hospital.



[From The Johns Hopkins Hospital Bulletin, No. 110, May, 1900, page 102.]

ACUTE LEUKÆMIA IN CHILDHOOD WITH REPORT OF A CASE.

By Thomas McCrae, M. B. (*Tor.*),

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The question of the condition of the blood in the anæmias of early life is such an unsettled one, and cases of acute leukæmia in childhood are so rare that every such case is worthy of report in detail. The present case is as follows:

Male; aged 3 years; anæmia; fever; purpuric rash; blood picture of leukæmia; hæmorrhages; convulsions; death; duration about one month.

J. L., male, aged 3 years, was admitted to the service of Professor Osler, in The Johns Hopkins Hospital on May 11th, 1898. The symptoms to which his parents drew attention, were a slight cough and a peculiar area over the sacrum which had almost a gangrenous appearance. The circumstances connected with his admission to the hospital were rather peculiar. His sister was a patient at the time with a surgical complaint, and he was brought from out of the city to see her. He had some cough and interference with his breathing, probably due to adenoids. For this he was admitted, but at the time it was not thought that he had any serious condition.

Family history.—One uncle on the father's side had died of tuberculosis; otherwise the history was negative. There was no history of lues nor anything suggesting it.

Previous history.—He was a large healthy child at birth. He was not breast-fed, but brought up on various artificial foods, combinations of milk, etc. For two months after birth he did not thrive, but afterwards did well until two years old, when he had fever for some time, the nature of which was unknown. Chicken-pox was the only disease of infancy that he had had. In February of 1898—three months before admis-

sion—he caught cold and had some bronchitis. With this it was noted that there were numerous ulcers over the mucous membrane of the mouth. Since this attack he had some cough and obstruction to his breathing. He did not snore at night, but frequently woke up complaining of being choked. About the same time a peculiar bruised area was noted over the sacrum, which was slightly tender. This was thought to have been due to injury. The area did not increase in size, and there were no others like it elsewhere. Otherwise the boy had seemed to be perfectly well, with good appetite and digestion.

Present illness.—There were no special symptoms of this and only the previous conditions were mentioned. To these his parents had given but slight attention, as the boy was thriving and seemed hearty and strong. It was thought, however, that for a day or two previous to admission he had been more easily tired than ordinarily and was rather peevish. He had also complained of some slight pains in the neighborhood of the joints. The boy's father—who was a physician—was positive that until a few days before admission, the patient had been as well as usual and played about with his ordinary vigor.

Examination showed a very stout boy, large for his age, but with a generally pale flabby look which was very striking. He was very bright and intelligent and showed a lively interest in his examination. The mouth was kept open, and the breathing was noisy. The tonsils were much enlarged and there were numerous adenoids present. The gums and mucous membranes were very pale. The shape of the thorax was normal. There were no rickety nodules. The percussion

note was clear throughout. The breath sounds were everywhere harsh and accompanied by numerous sibilant and sonorous râles. No tubular breathing was heard. The heart sounds were clear and of normal relative intensity. The abdomen was full and prominent. The edge of the liver was felt about 3 cm. below the costal margin. The spleen was palpable and hard, although not enlarged beyond the costal margin. There was no tenderness over the abdomen. There was no glandular enlargement. No œdema or signs of rickets

were present. Over the sacrum was an area about 5 cm. in diameter, dark purple in color and with a bruised, almost gangrenous look. It felt indurated, was slightly tender and was not adherent to deeper structures. No fluctuation could be made out.

The patient remained in the hospital until May 24th, during which time his general condition was as follows:

May 15th. Frequent coughing and constant mouth breathing. His appetite was good and he took his food well.

May 18th. The general condition was worse. There were great irritability and restlessness. At times complaint was made of pains in the legs. A small petechial rash appeared on the legs. It was most marked about the knees.

May 20th. He was very fretful and could only be got to take nourishment with difficulty. At times there were severe paroxysms of coughing. There were periods when he became collapsed with great pallor and a very feeble pulse. The purpuric rash persisted. There were many coarse râles everywhere over the the chest. The liver and spleen were as before. No enlarged glands were felt.

May 22d. The patient was much weaker. There was no pain.

May 24th. The condition was worse. He was very weak and took but little nourishment. In view of his grave condition his parents decided to take him home to Indianapolis. It was learned that he stood the journey well and seemed better for a day.

His subsequent history was obtained from Dr. F. B. Wynn, of Indianapolis, to whom I am also indebted for the account of his blood examination. Dr. Wynn writes as to his condition: "The temperature was from 99° to 100°, pulse 140–160 and very weak, respirations 40–50 with considerable dyspnœa, petechial hæmorrhages, several attacks of epistaxis, and on two days nausea and vomiting." Death occurred on May 30th with convulsions which were thought to be due to cerebral hæmorrhage. There was no autopsy.

While in the hospital, his temperature was elevated, usually to 100° and 100.5°. On May 21st it rose to 103.3° falling gradually to 99° on the morning of the 24th. The pulse varied from 120 to 160, and the respirations were

usually about 40. Dyspnœa was most marked after the attacks of coughing. He did not lose any weight while in the hospital. The urine had a specific gravity of 1.015 to 1.017. The reaction was acid and there was neither albumin nor sugar present. The diazo reaction was not given. Microscopically urates and uric acid were found.

Blood.—The first examination after admission was on May 12th. The hæmoglobin was 35 per cent (v. Fleischl), the red corpuscles 1,680,000, and the white cells 26,000 per cmm. (a ratio of 65 to 1). A differential count of 1000 leucocytes in specimens stained with Ehrlich's triple stain showed :

Polymorphonuclears . .	13.3 per cent.	
Lymphocytes, Small, 41.5	86.5	do.
do. Large, 45.		
Large mononuclears . . .	.2	do.

The red cells did not show any special variation from the normal in either shape or size, and but slight polychromatophilia. No nucleated red cells were seen in counting 2000 leucocytes nor in careful additional search. The lymphocytes showed all variations in size from the smallest up to some which were fully 15 microns in diameter. So many cells were on the border line that the division into small and large is only approximate. The depth of nuclear staining varied much in cells of the same size but the general staining was pale. This was more marked in the larger forms; still, there were but few small lymphocytes with a typical deeply staining nucleus. Cells with nicked or divided nuclei were very rare. The protoplasm about the nucleus was unstained in the majority of the larger forms. One myelocyte was seen. In this, as in the later specimens, there was a marked tendency for the lymphocytes to disintegrate and appear in the stained specimen as shapeless blotches with a pale blue stain. The polynuclear cells in the same specimen would be quite normal. It was found that by making the specimen rather thick, and drawing the covers apart as rapidly as possible, this disintegration could be prevented. Both the small and large lymphocytes showed the tendency to break up.

May 15th. The differential count of 1000 leucocytes showed—

Polymorphonuclears . . .	4.4 per cent.	
Lymphocytes, small, 78.9 large, 16.7	95.6	do.

The general characters of the cells were much as on May 12th. There were still all variations in size between the largest and smallest lymphocytes. No nucleated red cells or myelocytes were found.

May 19th. The hæmoglobin was 32 per cent, red corpuscles 1,760,000, and white cells 60,800 per cmm. (a ratio of 29 to 1). The differential count of 1000 leucocytes gave:

Polymorphonuclears . . .	.4 per cent.	
Lymphocytes, small, 96.6 large, 2.6	99.2	do.
Large mononuclears, . . .	.3	do.
Eosinophiles, ...	.1	do.

The red cells were much the same. No nucleated red cells were found in counting 2000 leucocytes, and in additional search. The lymphocytes were much smaller on the average, and many of them were of the typical small type. No myelocytes were seen.

May 24th. The hæmoglobin and red cells were practically the same as on the 19th, but the white corpuscles had fallen to 21,800 per cmm. (a ratio of 84 to 1). The differential count of 1000 leucocytes showed:

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Polymorphonuclears, . . .	.9 per cent.	
Lymphocytes, small, 89.2 large, 9.4	98.6	do.
Large mononuclears, . . .	.4	do.
Eosinophiles, ...	.1	do.

The general characters of the cells were as before, but the red cells showed somewhat greater variation in staining. No nucleated red cells or myelocytes were seen.

Dr. Wynn very kindly sent me his count taken a few days later in Indianapolis. The hæmoglobin was 30 per cent (Gowers), red corpuscles 1,800,000, and white 36,000 per cmm.

In considering this case a striking feature is the rapid

course. The patient was admitted to the hospital almost accidentally—if one may so term it—on May 11th, and beyond the presence of enlarged tonsils and adenoids he seemed, on superficial examination, to be in ordinary good health. Had it not been for the results of the blood examination, no suspicion of leukæmia would have been entertained. There were no symptoms pointing to acute disease, and his father was sure as to his having been in his normal condition up to a few days before. From the time of admission to the hospital until death was less than three weeks. Including the few days of malaise previously the whole course was not over four weeks. Even when the first blood examination was made, the possibility of the case being one of extreme lymphatism was considered, although the high percentage of lymphocytes (86.5) suggested leukæmia. In his condition any attempt to remove the adenoids and enlarged tonsils was thought unadvisable, even though they caused considerable obstruction. About May 18th the general condition changed and the symptoms were more severe. The blood showed 99.2 per cent of lymphocytes and the hæmorrhagic rash had appeared. The temperature ranged higher and from this to the time of discharge the downward course was rapid. Death, as already noted, occurred on May 30th.

In regard to the blood condition a relatively high proportion of the hæmoglobin to the red corpuscles is seen. The color index on the first examination was slightly over 1, falling a little below it subsequently. A high-color index, while usually characteristic of pernicious anæmia, occurs not infrequently in other blood conditions. In a recent case of lymphatic leukæmia in this hospital the color index was always about 1 during observations extending over a period of two months. In two recent cases of splenic anæmia the same ratio was observed. It will be noted that there was practically no diminution in the number of red cells during the course of the disease. In the stained specimens they showed but little variation from the normal throughout. Variations in the staining were rather more marked. No nucleated red cells were found at any time, although special search was made for them. In all the specimens the same difficulty was found in obtaining satisfactory slides. Unless the covers

were drawn apart very rapidly, the majority of the lymphocytes were irregular masses without any definite outline. They took the stain exactly as the nuclei in the better specimens. This tendency to disintegration may be a feature of the lymphocytes in acute cases. So far as known there are not sufficient observations to speak with certainty on this point. The staining of the nuclei of the lymphocytes showed great variation, although the prevailing stain was a pale one, and this was most marked in the larger forms. The lymphocytes showed increase both absolutely and relatively. The polymorphonuclears showed an absolute reduction. On admission they were 3400 per cmm., but fell later to 240 and 180 per cmm. The eosinophiles were absent in the earlier counts, and 60 and 21 per cmm. were found in the later ones.

Leukæmia is a relatively rare disease in the first decade. Cassel[1] states that among 3000 autopsies in Friedrichshain there were only two instances of leukæmia below the age of ten years. Considering acute leukæmia, however, there seems ground for thinking that it occurs in a somewhat larger proportion. Theodor[2] collected 45 cases of acute leukæmia of which 6 were in the first decade. There were 5 between the ages of 10 and 15 years. Fussell and Taylor[3] have published a series of 56 cases, among which 9 were in this period. Morse[4] in reporting a case in 1898 collected 7 from the literature. There is doubt expressed as to cases reported some years ago, but apparently 13 previously reported cases may be accepted. A recent case in an infant reported by Pollmann[5] is not included, as the condition appears to have been considered congenital. Bloch and Hirschfeld[6] report a case in a boy aged eight months, which was probably acute, but the exact duration was not known. The present case is the fourth to be reported within a year. The previous cases are as follows:

I. Keating[7]. Female, aged 4½ years; epistaxis, fever, hæmorrhagic rash, cervical glands and spleen enlarged. The blood was examined by Dr. Osler. The red cells were normal, no nucleated cells being seen. The whites were very numerous,

there being 50 or 60 in one field. They were largely lymphocytes. Duration 9 weeks; type probably lymphatic.

II. Wadham[8]. Male, aged 5 years; no hæmorrhages, slight fever, cervical glands enlarged, abdominal pain and distention. The type can not be decided from the description given. Duration 8 weeks. Autopsy.

III. Guttmann[9]. Male, aged 10 years; a previous history of enlarged tonsils and adenoids, hæmorrhages, hæmorrhagic rash, no fever, hemiplegia, priapism, spleen and liver enlarged. The blood showed whites to reds as 1 to 1.4. Type was probably lymphatic. Duration 4½ days. At autopsy the thymus was found much enlarged.

IV. Eichhorst[10]. Male, aged 8 years; onset sudden with precordial pain, hæmorrhages, fever, enlarged spleen and liver; no swelling of the lymph-glands. The blood showed 88,000 whites. No nucleated reds were seen. Duration 2 weeks. Autopsy. Lymphatic in type.

V. Müller[11]. Male, aged 4 years; hæmorrhages, ulceration of throat and only the cervical glands enlarged, liver and spleen enlarged, fever. The blood showed 109,000 whites of which 97 per cent were mononuclear, with an acute staphylococcus infection. Shortly before death the leucocytes fell to 6800. Duration 5 weeks. Lymphatic in type. Autopsy.

VI. Müller[11]. Male, aged 4 years; hæmorrhages, hæmorrhagic rash, fever, liver and spleen enlarged. The blood showed 209,000 white cells of which 98 per cent were mononuclear. Duration 4 weeks. Type lymphatic. No autopsy.

VII. Goldschmidt[12]. Male, aged 2½ years; cervical glands enlarged, liver and spleen enlarged, fever, nephritis. Blood picture of leukæmia. Nucleated red cells present. Duration 8 weeks. Autopsy. Lymphatic in type.

VIII. Theodor[2]. Male, aged 4 years; luetic family history, hæmorrhages, cervical glands enlarged, spleen enlarged, liver not; no fever. The white cells were to the reds as 1 to 9. Nucleated red cells were present. Duration 6 weeks. Lymphatic in type. No autopsy.

IX. Cabot[13]. Infant; lymphocytes over 98 per cent, duration 6 weeks, lymphatic in type.

X. Morse[4]. Female, aged 3 years; hæmorrhages, enlarged

tonsils, liver and spleen enlarged, general glandular enlargement. The duration was not more than 7 weeks, and probably less. The type was lymphatic. No autopsy.

XI. Bradford and Shaw[14]. Male, aged 7 years; hæmorrhages, fever, swelling and ulceration of the mouth, cervical glands enlarged, spleen enlarged, liver not. Duration probably 7 or 8 weeks. Autopsy. Lymphatic type.

XII. Haushalter and Richon[15]. Male, aged 7½ years; hæmorrhagic rash, no fever, glands and spleen enlarged, blood cultures yielded streptococci. Duration 8 weeks. Autopsy. Lymphatic type.

XIII. Bradley[16]. Male, aged 8 years; hæmorrhages, hæmorrhagic rash, liver and spleen enlarged. The white cells were 85,000, of which 97 per cent were lymphocytes. There were a few nucleated red cells present (personal communication from Dr. Bradley). Duration 7 weeks. No autopsy Lymphatic type.

It is of interest to compare the symptoms in this series of cases. As in case IX only the blood features and duration are known, it is not considered in the figures given for various other symptoms.

Family history.—There is nothing of any importance under this heading. In only one case was there a luetic history, and two had a tuberculous family history.

Previous history.—Various infections are noted in the previous histories of the cases. One had had meningitis, one measles, one suppurating cervical glands, and three had suffered from some affection of the tonsil[9]. This last is of some importance in connection with the number of instances in which the disease was accompanied by acute tonsillitis.

Sex.—A large proportion of the cases were in males, namely 11 out of 13. This is true of acute leukæmia at all ages. In the series of Fussell and Taylor, among 55 acute cases where the sex was known, 33 were males. The same is found in leukæmia generally in childhood. Thus, Birch-Hirschfeld, among 39 cases below the age of 15 years, found 25 males and 14 females. This applies to cases from the earliest years.

Onset.—This was sudden in many of the cases as might be expected from the rapid course. In one case, No. VIII, the

first symptom was hæmorrhage following a fall from a horse. In four cases hæmorrhage was the first prominent symptom.

Hæmorrhages.—These occurred in 10 cases. The bleeding was from the nose, mouth, stomach, bowels and kidney. In no case did the bleeding seem to have been sufficient to cause death directly. A hæmorrhagic rash was present in 10 cases, of which 9 had also bleeding from a surface.

Fever.—This was noted in 8 cases, its absence in 4, and in 1 there was no note. The temperature was usually not extremely high. The highest was in No. XI, where it rose to 105.4°. In this case blood cultures taken at this time were negative.

Glandular Enlargement.—General enlargement was noted in 4 cases, enlarged cervical glands only in 5 cases, no enlargement in 2, and no note in 2 regarding it. In the cases with enlargement of the cervical glands only, this was usually associated with local throat or mouth conditions such as enlarged tonsils, adenoids or ulceration.

Spleen.—This was enlarged in all the cases. The degree was not great, the edge usually being 3 to 4 cm. below the costal margin.

Liver.—There was enlargement in 8 cases, none in 3, and in 2 the condition was not noted. In no case was the enlargement extreme.

Miscellaneous Symptoms.—Pains in the joints and bones were noted, hemiplegia, priapism, etc., but none in any large proportion of the series.

Blood.—There was marked anæmia in all the cases in which blood examinations were made. Among the eight cases in which the corpuscles were counted the highest count was in No. VI, viz., 2,350,000 and the lowest of 1,000,000 in No. IV. The percentage of hæmoglobin varied from 40 in No. V to 18 in No. II. The degree of anæmia in these acute cases is striking. It suggests the possibility of the development of the disease in children already anæmic. The red corpuscles did not show any rapid fall while the cases were under observation. If such low counts were suddenly brought about by the disease, it would seem probable that the rapid fall would continue with the advance of the other symptoms. If the onset of the disease were attended with such rapid blood destruction, why not the terminal stages? An explanation

may be that these children had been suffering from leukæmia in a more chronic form for some time and that what we consider the whole course was only an acute exacerbation at the termination. The histories of these cases and the consideration of the marked general features do not support this view The question is an interesting one, and may be answered when cases have been observed with blood counts taken prior to the onset of any symptoms.

The high-color index in the present case has already been commented on. A color index over 1 was shown in 4 cases of the series, Nos. IV, V, XIII, XIV. When the color index was below one, as in three cases, Nos. VI, X, XII, it was only about .5. This relation of the hæmoglobin to the red cells divides the cases into one class with the blood of a pernicious anæmia type, and into a second with the characters of a secondary anæmia. As already stated a similar point has been noted in a series of cases of splenic anæmia. So far as can be gathered from the descriptions given, no difference was observed in the shape and size of the red cells in these two groups. In spite of the severe anæmia the red corpuscles as a

rule showed little variation from the normal in their characteristics. This may be due to the acuteness of the condition as in a case of pernicious anæmia at present under observation in which the symptoms developed with great suddenness. It was fully two months after the onset before the red cells showed any special variation in size, shape or staining. In 10 cases of this series it was noted that the red cells showed no marked changes from normal in their general characters. In the remaining 3 cases there was no note on this point. The occurrence of nucleated red corpuscles is an interesting question. The statement is made by some writers that cases of leukæmia in children show more abundant nucleated red corpuscles and that megaloblasts are usually equal in number to normoblasts. The cases of this series do not seem to support the view that nucleated red cells are common in acute leukæmia in childhood. Thus among 11 cases in which full descriptions are given, no nucleated red cells were found in 7, and in the 4 cases where they were found the numbers do not seem to have been large. In only one case, No. VIII, was the

occurrence of megaloblasts noted. In this instance their number increased while the patient was under observation.

White corpuscles.—The number of the leucocytes shows wide variation. There are counts in 8 cases, the highest being 209,000 in No. VI, and the lowest 21,000 in the present case. The characteristics of the white corpuscles are much the same in all the cases. In some only a general account is given but sufficient to recognize the prevailing type of cell. In all there is an absolute and relative increase in the mononuclear elements. The proportion of large to small cells varies in the different cases. There does not appear to be any relation between the varying proportions of large and small forms and the relative acuteness of the disease. The mononuclears in all the described cases showed great variation in their staining. The largest absolute number of mononuclear cells was in No. VI, where they numbered 204,800 per cmm. The absolute number of the polymorphonuclear leucocytes was about normal in most of the cases. The highest number per cmm. was in No. XI, where they were about 15,000 on one occasion and 8800 on another. The lowest number was in the present case, where on admission they were 5400 per cmm., falling later to 240 and 180. Myelocytes were rarely seen and were only noted as of very occasional occurrence.

Type of Leukæmia.—This is apparently lymphatic in 13 cases, and in the remaining case no note regarding the blood is given. This is in accordance with the acute course of lymphatic leukæmia generally as compared with the splenomyelogenous type. There are instances of the latter variety in children.

Duration.—The period of nine weeks has been generally accepted as the limit of time within which a case should be considered acute. While the general features of the case should also be considered in classing a case as acute, still it will be found that nearly all cases with acute features terminate in this time. Müller,[11] in reporting the two cases noted before, has also described a case with a duration of 13 weeks, which, in its general features, might be termed acute. The duration in 4 cases of this series was less than one month, and in 10 was between four and nine weeks.

General features.—These cases show some agreement in

their features beyond the acute course. The disease occurs usually in a male with no special feature in his family or previous history except perhaps a history of throat trouble. This was marked in some instances and suggests possibly something of a causal relationship. In one, No. XII, emphasis is laid on the presence of carious teeth. Possibly, if this condition had been more often looked for, it might have assumed more importance as a possible causal source of infection. Hunter[17] has recently raised the question of a possible association between foci of infection in the mouth—such as carious teeth—and pernicious anæmia, considered as a chronic infective disease. A possible relationship to the so-called "Lymphatic Constitution" must also be considered. This has been discussed by Ewing[18] who considers that there is no direct indication of connection between that condition and leukæmia. That children with the lymphatic constitution are more apt to develop leukæmia we can not say. One of the series, No. III, showed a much enlarged thymus at autopsy.

The onset is usually with moderate suddenness; fever is present in a majority of the cases with hæmorrhages and a hæmorrhagic rash. General glandular enlargement is found in less than half of the cases; in more the cervical glands alone show enlargement. The spleen was enlarged in every case where there are notes of an examination and the liver also in more than half of the series. In all, the anæmia is a striking feature, and the symptoms of the disease may be summed up as a severe anæmia with frequent multiple hæmorrhages, fever, enlargement of the spleen and frequently of the liver. In some cases general glandular enlargement, but in others only of the cervical glands, enlarged tonsils, ulceration of the mouth, pains in the bones, etc., are present. With these is a downward course to a rapidly fatal termination. Guinon and Jolly[19] in discussing the subject divide the cases into three classes:

1. Typical forms: swollen glands; anæmia; terminal hæmorrhages.
2. Hæmorrhagic form: features of an infectious purpura.
3. Pseudoscorbutic: lesions of the mouth, gums and tonsils predominate.

Diagnosis.—This can only be made with certainty through the examination of the blood. In nearly all the cases emphasis is laid on the striking anæmia. This with the severe general symptoms and the occurrence of hæmorrhages should suggest a blood examination. Probably the conditions with which it is most apt to be confounded are: (1) an acute infection with specially marked throat symptoms, and (2) a hæmorrhagic purpura. Bradford in referring to his cases has laid emphasis on the probability of considering an acute leukæmia to be merely an infection unless a blood examination be made. Probably, with more frequent routine work on the examination of the blood, cases will be found more often.

Treatment.—This can only be symptomatic with our present knowledge. In no case does any treatment appear to have been of any service.

In conclusion, emphasis may be laid on the necessity of careful study of the anæmias of early life. The subject at

present is in a rather chaotic state, and only through careful blood examinations can we hope to have the lines drawn more satisfactorily.

REFERENCES.

1. Cassel: Ein Fall von lieno-medullärer Leukämie bei einen achtjahrigen Mädchen. Berl. klin. Wochen., 1898, p. 77.

2. Theodor: Acute Leukämie in Kindesalter. Archiv f. Kinderheilk., 1897, XXII, H. 12, p. 47.

3. Fussell and Taylor: Acute Leukæmia. The Philadelphia Medical Journal, 1899, III, p. 39.

4. Morse: Acute Leukæmia in Childhood. Archives of Pediatrics, 1898, XV, p. 130.

5. Pollmann: Ein Fall von Leukæmie beim Neugeborener. Münch. med. Wochen., 1898, I, p. 44.

6. Bloch and Hirschfeld: Zur Kenntniss des Veränderungen un Centralnervensystem bei Leukämie. Zeit. f. klin. Med., 1900, XXXIX, H. 12, p. 32.

7. Keating: Lymphatic Leukæmia in Children. Amer. Jour. of Obstetrics, 1886, p. 160.

8. Wadham: Case of Leucocythæmia in a Child. Lancet, 1884, I, p. 158.

9. Guttmann: Ueber einen Fall von Leukæmia acutissima. Berl. klin. Wochen., 1891, XXVIII, p. 1109.

10. Eichhorst: Ueber acute Leukämie. Virchow's Archiv, 1892, CXXX, p. 365.

11. Müller: Zur Kenntniss der acuten Leukämie im Kindesalter. Jahrb. f. Kinderh., 1896, Bd. XLIII, p. 130.

12. Goldschmidt: Acuter Leukämie. Munch. med. Wochen., 1896, XLIII, p. 714.

13. Cabot: Clinical Examination of the Blood. 3rd edition. New York, 1898, p. 397.

14. Bradford and Shaw: Five cases of acute Leukæmia. Medico-Chir. Trans., 1898, LXXXI, p. 343.

15. Haushalter and Richon: Leucémie aigue chez un enfant. Archiv de Méd. des Enfants, 1899, June, p. 356.

16. Bradley: A case of acute Lymphatic Leukæmia. New York Med. Jour., 1899, p. 923.

17. Hunter: Further observations on Pernicious Anæmia; a chronic infective disease; its relation to infection from the mouth and stomach. The Lancet, 1900, I, p. 221, et seq.

18. Ewing: The Lymphatic Constitution. The N. Y. Medical Journal, 1897, II, p. 37.

19. Guinon and Jolly: Un cas de leucémie aigue. Rev. mens. des Mal. de l'enfance, 1899, June, p. 262.