LEUKÆMIA IN INFANCY AND EARLY LIFE.

BY

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During a study of the diseases of the blood in infancy and early childhood, I was struck by the absence in the literature of any analysis of the symptomatology and blood picture of leukæmia covering a large series of cases. The following paper constitutes such an analysis. It is based on the records of 100 cases of leukæmia, consisting of 91 taken from the literature, 8 cases (hitherto unpublished) observed in the Royal Hospital for Sick Children, Glasgow, and one case which I was allowed to study under the care of Professor Monro in the Western Infirmary, Glasgow. All the patients in this series were under 8 years of age. The greatest care has been taken in their selection so that there could be little doubt regarding the diagnosis, and I consider that they permit of an accurate and comprehensive description of the blood picture and symptomatology of the condition. The selection of examples of myelocytic leukæmia was especially difficult because a number of the cases reported as examples of this disease would almost certainly appear to be cases of severe anæmia in childhood or the so-called von Jaksch's Anæmia.

The general symptoms of all varieties of leukæmia are very much alike and they will, therefore, be treated together. The blood pictures will, however, be described separately.

Nomenclature. In this paper the different varieties of leukæmia have been classified according to the most prominent type of abnormal cell found in the blood stream. For purposes of classification the terms "lymphatic" and "myelogenous" are, in my opinion, hardly suitable, as they suggest that in the one case the origin of the disease is in the lymphatic system and in the other in the bone marrow; whereas it is nowadays generally admitted that in both types the pathological process is primarily located in the bone marrow. The terms "lymphocytic" and "myelocytic" have, therefore, been adopted. The third variety of leukæmia, viz. : lymphoidocytic, has been so named in preference to "myeloblastic," as in this type the large lymphoid cells with deeply staining cytoplasm frequently are too primitive to give an oxidase reaction and, therefore, strictly speaking, they cannot be called myeloblasts. They are still undifferentiated leucoblasts. The lymphoidocytes (hæmohistioblasts of Maximov) are multipotential and may differentiate into lymphoblasts or myeloblasts; they are encountered in the blood stream in most cases of leukæmia in childhood.

ÆTIOLOGY.

It is not proposed to enter into a discussion of the special ætiology of leukæmia, even if such were possible. Only the general ætiological features will be considered.

Age. In the following table the age incidence is shown.

TABLE I.

Age in Years	1	2	3	4	5	6	7	8
Lymphocytic	12	13	8	16	8	6	5	2
Myelocytic	7	4	2	0	0	3	0	3
Lymphoidocytic	0	1	2	1	2	2	1	2
TOTAL	19	18	12	17	10	11	6	7

From this table one interesting fact emerges ; namely that there are roughly twice as many cases of leukæmia occurring during the first four years of life as occur during the subsequent four years. In certain of the cases (for details of which see appendix) the age of the infant when it came under observation was less than two months and it is possible that these are examples of congenital leukæmia. Case No. 63 came under my own observation in Professor Findlay's wards and the history seemed to date from birth. In not one of these cases did the mother suffer from leukæmia. It is well known, of course, that women the subject of leukæmia have given birth to normal children and I know of no instance having been reported in which a leukæmic child was born of a leukæmic mother. These facts militate against the theory that leukæmia is infective in origin and are more in keeping with the view that it is related to the malignant processes and is, as Banti calls it, " a sarcoma of the blood."

Sex. In 94 cases the sex was stated and of these 62.87 per cent. were males. This is in accordance with the statements generally made that the disease in adult life is more common in the male subject.

SYMPTOMATOLOGY.

Leukæmia may be either insidious or abrupt in its onset. In the former case the patient gradually becomes less active ; he may be lethargic and somnolent ; he is frequently irritable and suffers from loss of appetite ; he tends to lose weight and, as a rule, he becomes pale. These prodromal symptoms may persist for one or two months and during this stage the diagnosis of the disease is difficult, but, sooner or later, increasing pallor, hæmorrhages, enlargement of the spleen or of the superficial lymphatic glands will appear and suggest some grave disorder of the blood.

When the onset is abrupt the patient may be suddenly stricken down with fever and great prostration. On examination neither the spleen, liver, nor superficial lymphatic glands may show any palpable enlargement and the only symptoms likely to suggest the possibility of leukæmia may be a purpuric rash or a severe attack of epistaxis. However, even in the cases with the most sudden onset, the patient generally lives long enough for the majority of the main clinical features of the disease to manifest themselves.

The following table illustrates the symptoms of leukæmia in the order of their frequency. In a regrettable number of instances no note has been made to indicate the presence or absence of a particular symptom, and it has been assumed that it was absent if not mentioned.

TABLE II.

Analysis of Symptoms.					Present.	Absent.
Enlarged Spleen	..	..	..	..	92	7
Enlarged Glands	..	..	..	..	84	13
Hæmorrhages	..	..	..	..	78	8
Fever	..	..	..	..	70	7
Enlarged Liver	..	..	..	..	70	19
Digestive Disorders	..	..	..	..	44	3
Gingivitis and Stomatitis	..	..	..	..	37	7
Cardiac Murmurs	..	..	..	..	30	9
Enlarged Tonsils	..	..	..	..	24	11
Albuminuria	..	..	..	..	20	20
Œdema	..	..	..	..	19	13
Dyspnoea	..	..	..	..	17	3
Pain	..	..	..	..	16	11
Retinal Changes	..	..	..	..	12	6

In Table 2 it will be observed that there are five chief symptoms, viz. :—splenomegaly, enlargement of the lymph glands, enlargement of the liver, hæmorrhages and fever. The other symptoms, although they may constitute an important part of the general picture in individual cases, are of relatively infrequent occurrence.

(1) *Splenic enlargement.* Enlargement of the spleen *per se* during the first four years of life is of little diagnostic significance for it is well known that in many examples of tuberculosis and syphilis the spleen becomes palpable and may even appear as a very large mass in the abdomen. In the more severe forms of anæmia the spleen is almost constantly palpable, although the degree

of enlargement bears no relation to the severity of the anæmia. Enlargement of the spleen, however, appears to be the most constant feature of leukæmia during childhood and it is therefore advisable to make a blood examination in every case presenting this symptom. The spleen often alters slightly in size during the course of the disease and when its volume diminishes, as it does after a hæmorrhage or an attack of diarrhoea, the parents sometimes offer the opinion that the child is looking better and that its appetite has improved. Again, during the last few days of the illness it is in many instances noticeable that the spleen decreases in size and this alteration may be associated with a similar diminution of the superficial lymphatic glands and with a fall in the white-cell count.

(2) *Glandular Enlargement.* Table 2 also shows that in all but 13 cases there was some degree of glandular enlargement, although in a number of the children the increase was either very slight or limited in extent. The occasional absence of all enlargement, not only of the superficial lymph nodes but also of those more deeply placed, even at post mortem examination, is important since it certainly points to the bone marrow as the site of the primary lesion. Nowadays it is an accepted fact that the blood is never leukæmic until definite changes characteristic of the disease have taken place in the bone marrow, and the occasional instances of leukæmia which arise from time to time showing no enlargement of the glands "go to prove that acute leukæmia, whether lymphoid or myelocytic, is due to changes in the bone marrow, the other hæmopoietic organs being involved, if at all, secondarily." This is in accordance with the opinions expressed by Neumann, Walz, Pappenheim, Brandenburg and others.

When glandular enlargement is present it is most commonly observed during life in the neck. Post mortem the mesenteric glands are almost constantly found to be enlarged, but during life it is not always possible to detect them with certainty. The mediastinal and bronchial glands are also frequently involved and may give rise to distressing symptoms.

(3) *Hæmorrhages.* A petechial rash is one of the commonest symptoms of leukæmia. The eruption may appear all over the body or it may be limited to a small area. Frequently it occurs in the form of successive crops coming on for no apparent reason and bearing no relation to the severity of the disease. The parents sometimes notice that the child "bruises easily" and during the course of the illness large extravasations may take place. Probably the commonest site for these ecchymoses is in the region of the sacrum. Bleeding from the mucous membranes is also common. In the large majority of cases there is hæmorrhage from the gums which occurs as a persistent oozing of blood and may be a prominent factor in the production of the anæmia. Bleeding from the gums may be the principal symptom and lead to a faulty diagnosis of infantile scurvy. Epistaxis is another common symptom and when it takes place it is usually severe, prolonged, and likely to recur. Bleeding from the

bowel is quite common and hæmatemesis occurs in a few cases. Hæmaturia is rare. In this series the percentage of cases in which hæmorrhages occurred is as follows :—Lymphocytic leukæmia, 93·8 per cent. ; Myelocytic leukæmia, 78·6 per cent. ; and Lymphoidocytic leukæmia, 75·0 per cent.

The explanation of this tendency to hæmorrhage is somewhat obscure. The more severe forms of purpura are generally associated with a marked decrease in the number of blood platelets and such is usually found in lymphocytic leukæmia. On the other hand, there is also a marked hæmorrhagic diathesis in the other forms of leukæmia although studies of these in the adult reveal the fact that the platelets may be normal or even increased in number. No figures showing the platelet count in myelocytic leukæmia during childhood are available. However, in most examples of moderately acute leukæmia (and all leukæmias of childhood may be regarded as acute) the bone marrow is so crowded with leucoblastic cells that the megakaryocytes, from which the platelets are understood to be formed, come to be decreased in number. But, even when present, thrombocytopenia constitutes only a partial explanation of the tendency to bleeding, and it would seem not improbable that some abnormal change in the vascular endothelium plays an important role.

(4) *Fever.* Some degree of fever was present in 70 cases of this series ; in 7 cases it was stated to be absent and in 23 it was not mentioned. There is nothing characteristic about the temperature chart of a case of leukæmia. Sometimes the fever is of the continued type, sometimes it is remittent or intermittent and, speaking generally, it is capricious and irregular. Occasionally the temperature may rise to 105° F. At the beginning of the illness in children there is usually some degree of fever, and this is one of the points which makes the clinical picture so similar to that of an acute infectious disease. Towards the termination of the disease the temperature may fall and be accompanied by a decrease in the size of the spleen, liver and lymphatic glands, and a fall in the number of leucocytes in the blood. On the other hand, the patient may die with hyperpyrexia suggesting some toxic action on, or a leukæmic infiltration of, the pons varolii.

The ætiology of the disease being unknown, it is impossible to explain the fever. It may however be that (1) it is a manifestation of the systemic reaction to a specific infection ; (2) it is the result of some secondary infection with pyogenic organisms ; (3) it is due to the digestive disturbances which occur during the course of the illness ; (4) it is due to the action of degenerated leucocytes on the heat centres (Treadgold ²).

(5) *Hepatic enlargement.* Enlargement of the liver was present in 70 instances in this series, and in 19 it was stated that the organ was not enlarged. How accurate these figures are it is difficult to say. In young children the lower border of the liver can usually be felt half to one inch below the costal margin, and it is quite possible that this condition has been recorded as an actual enlargement of the liver in a proportion of the cases. However, in the majority of cases in which a post-mortem examination was performed

the liver was found to be definitely enlarged. The relative frequency of hepatic enlargement in the three varieties of leukæmia was as follows :—Lymphocytic leukæmia, 80·6 per cent; Myelocytic leukæmia, 75·0 per cent.; Lymphoidocytic leukæmia, 66·6 per cent.

(6) *Digestive disturbances.* Symptoms referable to the gastro-intestinal system were present in 44 cases; in 53 cases no note was made, because these symptoms were either absent or not considered significant. Such symptoms were anorexia, diarrhoea, constipation and vomiting. Hæmatemesis and melæna were present in a few patients. The tongue was generally furred and the gums were frequently swollen and bleeding. 37 children in this series suffered from stomatitis and gingivitis. The tonsils were enlarged in 24 cases; in 11 there was stated to be no enlargement and in 65 no reference was made to the condition of the tonsils.

(7) *Cardio-vascular symptoms.* In a considerable number of cases mention was made of the condition of the heart and pulse. The pulse was generally soft, of low tension and increased in rate. The heart was sometimes found to be enlarged, and a murmur or bruit coincident with ventricular systole was heard in a proportion of the cases (30 in this series). Post-mortem examination in no case revealed endocarditis nor was there any record of infiltration of the auriculo-ventricular bundle such as might have produced heart block.

(8) *Genito-urinary symptoms.* In 3 cases it was stated that the kidneys were large and easily palpated (Nos. 25, 28, 32) but with these exceptions there was no clinical note of the size of these organs in any of the series. In several instances post-mortem examination showed a considerable enlargement of the kidneys. Albuminuria was not uncommon but seldom appeared to be present to the same degree as in acute nephritis. The uric acid output was increased, due to the katabolism of the excessive endogenous protein associated with the leucocytosis. Hæmaturia was rare.

(9) *Respiratory symptoms.* Dyspnœa was not an uncommon symptom. It may be due to enlarged glands in the neck pressing on the trachea or larynx. This was the cause of death in Case No. 4. Again, dyspnœa may be due to enlarged bronchial and mediastinal glands pressing on the recurrent laryngeal nerve or on one of the larger bronchi. In infants with leukæmia the tonsils are often enlarged with, presumably, hypertrophy of the nasopharyngeal adenoid tissue, and it is quite possible that these factors play a part in the production of the dyspnœa. Finally, dyspnœa may exist as a manifestation of the severe degree of anæmia which is so constantly present.

A mild bronchitis is probably present in the majority of cases but it usually causes no symptoms of importance. Some degree of œdema of the lungs is always present and is associated with the anæmia. Pneumonia may occur at any time during the course of the disease, but, as a rule, it is not associated with the usual reactions seen in the healthy subject and, not infrequently, it may be discovered only at the post-mortem examination.

(10) *Skin*. One of the most constant features of leukæmia is the occurrence of hæmorrhages either into or beneath the skin. These phenomena have already been described. Sweat rashes are not uncommon in childhood and when present in cases of leukæmia probably bear no relation to the disease. Herpes occurred in one of this series (Case No. 20) and ulceration of the skin occurred in Case No. 17. Oedema of the skin and subcutaneous tissues was present in 19 instances. The oedema may be generalised and associated with ascites or it may be limited to the face or ankles. In a proportion of cases tumours may be present in the skin, the condition called "Nodular leukæmia" by Ward (³) who has collected a number of examples. According to Ward the nodules probably arise from the scattered foci of lymphoid tissue which occur throughout the meso- and hypo-blastic tissues. The nodules do not appear in the epiblastic tissues such as the epidermis or the central nervous system, although they frequently grow from the subjacent fibrous tissue of the skin (Case No. 54) and the dura mater. The cutaneous nodules differ greatly in size and colour. They may be as small as a pin's head or as large as a cricket ball and their colour is dependent upon their depth from the surface and whether or not they have been the seat of interstitial hæmorrhages. The nodules may be present throughout the alimentary canal. Finally, they occur in connexion with the bones, particularly the bones of the head and it is these tumours which frequently have the green colour which has been responsible for their having been named Chloroma (Cases Nos. 89, 95). In some cases the usual greenish colour may be absent; in others it may fade very rapidly after removal of the tumour, but it can sometimes be brought back by immersing the tissue in hydrogen peroxide. The nodules, wherever placed, may become smaller in size or even disappear suddenly. Chloromata may occur with any of the three types of leukæmia, but they seem to be most commonly associated with the lymphocytic and lymphoidocytic varieties.

(11) *Retinal changes*. It is unfortunate that in 82 of this series no mention has been made of the appearances of the fundus oculi. In 6 it was stated that there was no abnormality and in 12 certain changes were observed. The commonest lesion consisted of one or more small retinal hæmorrhages (11 cases). In one case pallor of the disc and fundus was noted and in another, in addition to retinal hæmorrhages, there was a neuro-retinitis.

COURSE OF THE DISEASE.

The duration of leukæmia in infancy is always short and, therefore, the disease must be regarded as a uniformly acute process at this time of life. Seldom, are remissions of the symptoms observed. Once the disease has developed, the patient passes steadily downhill and within 2 or 3 months death takes place. The following figures show the average duration of the illness in 73 per cent. of this series:—

Lymphocytic leukæmia	..	..	..	2.0 months.
Myelocytic leukæmia	..	..	..	4.3 ..
Lymphoidocytic leukæmia	..	..	..	2.1 ..

The apparent relative chronicity of the disease in the myelocytic form is largely to be accounted for by the protracted course of case No. 78, in which it is stated that the child lived for 2 years after leukaemia had developed.

The figures in this series seem to show that in children the average duration of the illness varies but little whether the large or small lymphocytes dominate the blood picture, or whether the case is a definite lymphoidocytic leukaemia.

THE BLOOD.

(a) *Lymphocytic Leukaemia.*

Seventy per cent. of this series were examples of lymphocytic leukaemia. The blood flows easily from a prick in the finger or lobe of the ear. It is paler and more watery than in the healthy subject and, as a rule, it does not show the normal tendency to rapid coagulation.

Serum. The serum may appear quite normal, or it may contain a moderately large quantity of fat, as in Case No. 56. In none of the cases in this series was the Wasserman reaction said to be positive. A positive Widal reaction was obtained in Case No. 6. In some examples the serum may be frankly jaundiced. In 7 cases a streptococcus was said to have been cultivated from the blood and in Case No. 57 I isolated a streptococcus which multiplied rapidly under anærobic conditions but which, although it survived, grew less freely under ærobic conditions. It must be remembered, however, that streptococci may be isolated quite frequently during the terminal stages of many illnesses in childhood.

Red Cells. The total red cell count is always decreased and towards the end of the illness it may fall below a million per cubic millimetre (Cases No. 8, 13, 40, 54, 64). The average red cell count was 1,946,000. Irregularity in size and shape of the corpuscles is present and polychromasia and basophile stippling are common features. Nucleated red cells are generally present but, as a rule, they are scanty in number. The erythrocytes stain well and the average hæmoglobin content in this series was 31 per cent., which gave a colour index of 0.816.

White cells. In this series there was a leucocytosis in 58 cases; in 8 the total white cell count was either decreased or within normal limits; and in 4 no note was made. The average leucocyte count was 210,245 per c.mm.

It would appear that in those cases in which the onset is not very sudden and in which the patient does not seem to be seriously ill the white cell count is high and may even exceed a million per cubic millimetre (Cases No. 10, 31, 41, 52). When the onset is abrupt and the patient is prostrated and obviously in a perilous condition the white cell count may not be raised and, in fact, there may even be a definite leucopenia (Cases No. 17, 22, 30, 54, 58, 62, 65). During the last few days of the illness the leucocyte count almost always falls and this is regarded as a grave factor in the immediate prognosis,

The one constant feature about the blood in lymphocytic leukæmia is the high *relative* increase of the lymphocytes. Whatever the total white cell count may be, the lymphocytes are always relatively in excess of normal and in this series averaged 94 per cent.

Characters of Lymphocytes. The type of lymphocyte which dominated the blood picture was noted in 52 of this series. In the majority of cases (61·54 per cent.) the micro- and meso-lymphocytes were the predominating cells. In these forms the nucleus stains deeply and the cytoplasm is scarcely visible. In some examples (38·46 per cent.), however, the large lymphocytes were present in the greatest proportions. Such cells have a rather paler nucleus than the small forms and in it one or two nucleoli may be observed. The cytoplasm is not abundant and seldom if ever contains the azurophil granules which are so commonly seen in the lymphocytes of healthy blood.

In films from every case of lymphocytic leukæmia lymphoidocytes may be found. Sometimes they are present in quite large numbers and the blood picture represents an intermediate stage between lymphocytic and lymphoidocytic leukæmia.

A large number of the lymphocytes seen in a film of lymphocytic leukæmia present some abnormality which leads to their being regarded as pathological cells in contradistinction to the healthy lymphocytes which appear in a simple lymphocytosis. Such abnormalities consist of extreme scantiness of the cytoplasm, vacuolation of the cytoplasm, changes in the nucleus indicative of karyolysis and the familiar "shadow" or "basket" cells which are found so often in cases of leukæmia with a high cell count. The latter forms represent the penultimate stage of the lymphocytes which have undergone cytolysis, although in a certain proportion they are due to a breaking up of the already fragile lymphocytes in the making of a very thin film.

(b) *Myelocytic Leukæmia.*

Red Cells. The average total red cell count in this series was 2,114,800 which is about the same as that observed in the lymphocytic variety. The average hæmoglobin content was 31·8 per cent, giving a colour index of 0·76.

White Cells. The average white cell count was 139,020 per c.mm. This figure is much lower than that obtained in the cases of lymphocytic leukæmia in this series. In no case was there a leucopenia.

Apart from the clinical features of these cases, the characteristic which compelled a diagnosis of leukæmia was the high proportion of myelocytes present in the blood films (average 32 per cent.). Such a myelocytosis is not observed in any other condition in infancy or childhood. Further, post-mortem examinations were performed in 58 per cent. of these cases and the diagnosis was stated to have been confirmed by the appearances observed.

The following figures represent the average differential count of the white cells obtained from this series :—

Polymorphonuclears	..	..	..	..	38.7%
Eosinophils ..	..	..	..	..	3.6%
Lymphocytes	..	..	..	..	25.0%
Myelocytes	..	..	..	..	32.0%

It is somewhat remarkable that no mention has been made of the proportion of basophils because myelocytic leukæmia essentially consists of an absolute increase of *all* the cells of the granular series.

There is one interesting fact to be learned from these figures, viz. : that in myelocytic leukæmia in infancy and early childhood there is a large *absolute* lymphocytosis which accompanies the increased output of the normal and abnormal cells of the granular series.

(c) *Lymphoidcytic (Myeloblastic) Leukæmia.*

In this series there were 11 cases.

Red Cells. The average red cell count was 2,066,400 per c.mm. The hæmoglobin content was 31 per cent. and the colour index was 0.775.

White Cells. In this form of leukæmia the white cell count was low in comparison with the other varieties : the average here being 47,962 per c.mm. The average proportion of lymphoidocytes (or myeloblasts) present in a differential count was 58 per cent. A leucopenia was observed in cases No. 91 and 93. An average differential count gave the following figures :—

Polymorphonuclears	..	..	..	..	9.3%
Eosinophils ..	..	..	..	..	2.0%
Lymphocytes	..	..	..	..	22.5%
Myelocytes	..	..	..	..	4.6%
Lymphoidocytes	..	..	..	..	58.0%

The lymphoidocytes are regarded as being the parent cells of both the granular and non-granular series and thus they may differentiate into myeloblasts or lymphoblasts. The lymphoidocytes do not give a positive oxydase reaction and if the preponderating cell in a blood film from such a case gives this reaction it indicates that differentiation is taking place towards the granular series and only then is it justifiable to apply the term myeloblastic leukæmia.

SUMMARY.

An analysis has been made of the clinical features of 100 cases of leukæmia occurring in children under 8 years of age. It is shown that the symptomatology of all three varieties of the disease is more or less the same and that the commonest features are enlargement of the spleen, lymphatic glands and liver, along with some degree of fever and various forms of hæmorrhage. The disease runs an acute course and the patient rarely lives more than 2 months after the diagnosis has been made,

The blood picture shows a marked degree of anæmia and a leucocytosis in all forms of the disease. The leucocytosis is highest in lymphocytic leukæmia and lowest in lymphoidocytic leukæmia, although in either of these varieties an actual leucopenia may be present. 19 cases of myelocytic leukæmia have been analysed and it is shewn that, in addition to a very high myelocyte count, there is also a large absolute lymphocytosis.

In conclusion, it gives me much pleasure to acknowledge with gratitude the encouragement and kindly criticism which I have received from Professor Leonard Findlay at whose suggestion this investigation has been made.

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TABLE I.

(see over)

TABLE I.
CASES OF LYMPHOCYTIC LEUKÆMIA.

No.	Author.	Sex.	Age in Months.	Duration in Months.	Enlarged Spleen.	Enlarged Liver.	Enlarged Glands.	Fever.	Hemorrhages.	Retinal Changes.	Dyspnoea.	Digestive Symptoms.	Albuminuria.	Heart Murmurs.	Stomatitis.	Pain.	Edema.	Enlarged Tonsils.	P.M. Examination.	Red Cell Count.	Hb. %.	White Cell Count.	Lymphocytes. %	Predominant Type of Lymphocyte.
1	Savory	M	54	1½	—	—	+	+	+	+	+	+			+			+	—	2,157,000	35	356,000	96	Large
2	Geissler, Japha...	M	60	3	+	+	+	+	—											1,580,000		34,250	97	
3	Chisholm. . .	M	42		+		+		+														98	
4	Larabee .. .	F	1½	1	+	—	+		+		+	+							—	4,392,000	60	918,000	99	Small
5	Babonneix, Tixier	F	18	2	+		+	+	+		+	+	+		—				+	2,950,000	70	43,600	91	Large
6	Rocaz .. .	M	48	1	+		+	+	+			+	+		+				+	1,816,000	30	244,000	96	
7	McCaw .. .	F	20	1½	+	+	+	+	+				+						—	2,200,000	38	818,000	99	
8	Glimski .. .	M	12		+	—	+		+			+			+		+		+	918,760	21	180,416	94	
9	Churchill .. .	M	48	1	+	+	+	+	+		+	+	—	+					+	2,740,000	40	52,000	99	
10	Véeder .. .	F	17		+	+	+	+	+				+	—	+				+	3,370,000	55	1,330,000	99	Small
11	Bezy .. .	F	84		+	—	+	+	+		—	+	—			+			+	3,000,000		20,000	95	Large
12	Strauss .. .	M	13	1	+	+	+	+	+			—	—					—	+	2,008,000	25	208,000	97	
13	Condat .. .	F	48		+	+	—	—	+			+			+		+		—	660,000	20	148,000	91	Small
14	Hutchison .. .	F	72	3	+	+	+	+	+	+					+					1,200,000	10	170,000	98	Small
15	Carpenter .. .		42	1	+	+	—			+			+							1,568,000	15	130,000	99	Small

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16	Surmont, Debon	..	..	42	4	+	—	+	+	+	+	+	+	+	+	+	+	+	+	2,433,500		14,375	99	Small
17	Nobel	..	..	18		+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,700,000	25	6,400	79	
18	Comby	..	..	F 48	4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	2,164,000		70,680	97	
19	Johnson	..	..	M 24	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,200,000		517,000		Large
20	Whiphan, Leatham	..	..	F 24	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	3,000,000	42	20,000	98	Large
21	"	"	..	M 57	½	+	+	+	+	+	+	+	+	+	+	+	+	+	+	2,196,000	58	22,800	72	
22	Moussous	..	..	M 42	4	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,143,600	21	5,580	99	Small
23	McCrae	..	..	M 36	1	+	—	+	+	+	+	+	+	+	+	+	+	+	+	1,760,000	32	60,800	99	Small
24	Forbes, Langmead	..	..	M 18	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,106,000	15	83,000	91	Small
25	"	"	..	M 15	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,000,000	30	29,000	92	Small
26	"	"	..	M 24	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,200,000	20	196,840	98	Small
27	"	"	..	F 12	1½	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,000,000		60,000	93	Small
28	"	"	..	F 7		+	+	+	+	+	+	+	+	+	+	+	+	+	+	2,000,000		321,000	99	Large
29	"	"	..	M 36	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,340,000	32	14,000	96	Small
30	"	"	..	F 42	6	+	—	+	+	+	+	+	+	+	+	+	+	+	+	2,550,000		7,500	96	Small
31	"	"	..	M 30	2½	+	+	+	+	+	+	+	+	+	+	+	+	+	+	3,000,000	35	1,000,000	97	Small
32	"	"	..	F 39	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+		38			
33	"	"	..	F 48	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	2,284,000	45	61,000	99	
34	Chaney	..	..	F 60	6	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,500,000	21	19,000	100	Small
35	"	..	..	M 54	1½	+	—	+	+	+	+	+	+	+	+	+	+	+	+	2,500,000	45	304,000	96	Small
36	Cheney	..	..	M 84	4	+	—	+	+	+	+	+	+	+	+	+	+	+	+	2,000,000	15	480,000	96	Small

TABLE I (Contd.).
CASES OF LYMPHOCYTIC LEUKÆMIA.

No.	Author.	Sex.	Age in Months.	Duration in Months.	Enlarged Spleen.	Enlarged Liver.	Enlarged Glands.	Fever.	Hæmorrhages.	Retinal Changes.	Dyspnoea.	Digestive Symptoms.	Albuminuria.	Heart Murmurs.	Stomatitis.	Pain.	Œdema.	Enlarged Tonsils.	P. M. Examination.	Red Cell Count.	Hb. %.	White Cell Count.	Lymphocytes. %	Predominant Type of Lymphocyte.	
37	Bradford, Shaw	..	M 84	2	+	—	+	+	+	+	+	+	+	+	+	+	—	—	+	+	1,480,000	31	34,400	99	Large
38	Muller ..	..	M 48	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+			109,600	97	Large
39	„ ..	..	M 48	1	+	+	—	+	+	+	+	+	+	+	+	+	+	+	—	—			209,000	98	Large
40	Vermehren ..	..	F 3	3	+	+	+	+	+	+	+	+	—	+	+	+	+	+	—	—	739,000		260,000	99	Small
41	Lommell ..	..	M 1	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,282,000		1,240,000		Small
42	Mennacher ..	..	M 11	5	+	+	+	+	+	+	+	+	+	+	+	+	—	—	+	+	4,900,000	40	258,000	73	Small
43	McWeeney, Farnan ..	..	F 36		+	—	+	+	+	+	+	+	—	—	+	+	+	+	—	—	1,540,000		136,400	97	Large
44	Kakels ..	..	M 18		+	+	+	+	+	+	+	+	+	+	+	+	+	+	—	—	2,046,000		682,000	94	Small
45	Morse ..	..	F 36	$\frac{1}{2}$	+	+	+	—	+	+	+	+	+	+	+	—	—	+	+	—	2,024,000	25	87,400	94	Small
46	Myers ..	..	M 51	2	+	+	+	+	+	+	+	—	—	+	—	—	—	+	+	+	1,424,000	25	32,000	97	Small
47	Holskaw ..	..	M 11	1	+	+	+	+	+	+	+	+	+	+	+	—	—	+	+	+	3,200,000		109,000	99	Small
48	Smith ..	..	M $1\frac{1}{2}$	$\frac{1}{2}$	+	+	+	+	+	+	+	+	+	+	+	—	—	—	—	—	2,624,000		189,000	91	Small
49	Lehndorf..	..	M 48	1	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	1,690,000	27	69,000	92	Large
50	„ ..	..	F 16	2	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	2,800,000		80,500	92	Large
51	Flesch ..	..	M 48	$\frac{1}{2}$	+	+	+	+	+	+	+	+	+	+	+	+	+	+	—	—	3,000,000		380,000	96	Large

TABLE II.
CASES OF MYELOCYTIC LEUKÆMIA.

No.	Author.	Sex.	Age in Months.	Duration in Months.	Enlarged Spleen.	Enlarged Liver.	Enlarged Glands.	Fever.	Hæmorrhages.	Retinal Changes.	Dyspnoea.	Digestive Symptoms.	Albuminuria.	Heart Murmur.	Stomatitis.	Pain.	Œdema.	Enlarged Tonsils.	P.M. Examination.	Red Cell Count.	% Hb.	White Cell Count.	% Polymorphs.	% Eosinophils.	% Lymphocytes.	% Myelocytes.	% Lymphoidocytes.
71	Morse ..	..	..	12 1	+	+	+	—	+										—	2,900,000		48,000	46	6	31	21	
72	Lehndorf ..	..	..	18 2	+	+	+	+	+				+	+	+		+		+	1,600,000	22	32,000	53	1	33	12	
73	Berghinz ..	..	..	96 4	+	+	+	+									+		—	2,000,000		800,000	59	2	9	27	
74	Karsner..	..	..	30 6	+	+	+		+	+	+	+	—	—	—	—	—		+			19,000					
75	Falconer ..	..	..	72	+	—	+	+	—	—				+		—			—	2,260,000	45	146,970	47	5	2	36	
76	Stewart, Campbell ..	..	..	72 3	—		+	+	+						+				+	750,000		40,000	45	3	25	27	19
77	Whipham ..	..	..	18	+	+	+	+	+											4,080,000	80	63,400	32	2	5	26	
78	Charon, Gratia..	..	..	96 24	+	+					+								+	880,000	39	305,000	49			37	
79	Ginsberg ..	..	..	30 4	+	+	+		+										+		55						
80	Cassell ..	..	..	96	+	—	—		—		+					+			—	3,550,000	40	500,000	30	12		69	
81	Goodall ..	..	..	2½	+	+	—		+			+		—	+				+	1,100,000		75,000	26	1	24	48	
82	Carpenter ..	..	..	12	+	+	—		+											2,900,000		48,000	47	1	31	21	
83	Zylberlast ..	..	..	6 3	+	—	—		—		+	+	—			—			+	2,720,000	35	39,370	32	3	49	26	
84	Menetrier, Aubertin ..	..	..	4	+	+	—		—										—	Whites to red s=1.4			24		25	42	
85	Weilclerc ..	..	..	14 ½	+	+	+	+											+	3,317,000		28,000	9	4	41	17	
86	Hirschfeld ..	..	..	72 ¾	+	+	+	+		+		+	—	+	+		—		+	800,000		59,000	60		18	23	
87	Benjamin Sluka ..	..	..	6 1	+	—	+	+	+			+					+		+	1,500,000	30	120,000	27		31	42	
88	Delfosse ..	..	..	12	+		+	+	+											1,400,000		25,000				33	
89	R.H.S.C. ..	..	..	13 2½	+	+	+	+	+	—			+	+		+	+	—	+	2,080,000	20	115,000					

LEUKÆMIA IN INFANCY AND EARLY LIFE

TABLE III.
CASES OF LYMPHOIDOCYTIC LEUKÆMIA.

No.	Author.	Sex.	Age in Months.	Duration in Months.	Enlarged Spleen.	Enlarged Liver.	Enlarged Glands.	Fever.	Hæmorrhages.	Retinal Changes.	Dyspnoea.	Digestive Symptoms.	Albuminuria.	Heart Murmurs.	Stomatitis.	Pain.	Oedema.	Enlarged Tonsils.	P. M. Examination.	Red Cell Count.	% Hb.	White Cell Count.	% Polymorphs.	% Eosinophils.	% Lymphocytes.	% Myelocytes.	% Lymphoidocytes.	
90	Panton, Tidy	..	..	14	—	—	—	+	—	—	—	+	—	—	—	+	+	—	—	—	1,930,000	20	13,800	1	1	1	98	
91	Ross	..	..	34	+	+	+	+	+	+	—	+	—	+	+	—	—	—	+	—	2,377,000	30	6,900	1	23	—	75	
92	„	..	..	39	+	+	+	+	—	—	—	—	—	+	—	—	—	—	—	—	1,800,000	28	17,200	19	19	—	38	
93	„	..	..	66	+	+	+	+	+	—	—	—	—	+	+	—	—	—	+	—	2,650,000	30	1,132	2	10	2	86	
94	Dallas	..	..	20	+	—	+	—	—	—	—	—	—	—	—	—	—	—	—	—	2,253,000	25	36,452	30	49	—	21	
95	Esser	..	..	96	+	+	+	+	+	—	—	—	—	+	—	—	—	—	+	—	840,000	35	8,700	21	1	5	24	
96	Horwitt	..	..	60	+	+	+	+	+	—	—	—	—	—	—	—	—	—	—	—	1,000,000	—	140,000	2	—	—	98	
97	Bass	..	..	96	+	+	+	+	—	—	+	—	—	—	—	—	—	—	—	—	2,080,000	41	134,400	5	15	—	80	
98	Purser	..	..	36	—	—	+	+	—	—	—	—	—	—	+	—	—	—	—	—	2,800,000	50	78,000	—	—	—	—	
99	Nanta and Loubet	..	..	84	+	—	—	+	+	—	—	+	—	—	+	+	—	—	—	—	2,900,000	—	20,000	—	—	—	77	
100	Stirnemann	..	..	36	—	—	+	+	+	—	—	+	—	+	+	—	—	—	—	—	2,100,000	20	70,000	3	2	43	7	44

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