CHILDHOOD LEUKAEMIA IN SINGAPORE CHILDREN

By Freda M. Paul, M.B.B.S., M.R.C.P., F.R.F.P.S., D.C.H.

(Department of Paediatrics, University of Singapore)

This paper is based on a hundred cases of childhood leukaemia seen in the Department of Paediatrics in children ten years and under over a ten-year period from the years 1957 to 1967. The Paediatric Unit in General Hospital, Singapore is a 282 bedded unit and together with St. Andrew's Mission Hospital tap the majority of children in Singapore. From questionaires sent by the leukaemic study group it was found that no child with leukaemia was treated at the private hospital on the island and it is highly unlikely that general practioners would treat a child with leukaemia who had at some stage or other had not passed through the Paediatric Unit, General Hospital or the St. Andrew's Mission Hospital so that our figures and disease pattern are fairly representative of childhood leukaemia in Singapore.

INCIDENCE

Deaths attributed to leukaemia at all ages in England and Wales have increased two and half times in the last two decades (Registrar—General Statistics Review 1938 to 1957). Kwa et al show the overall incidence of leukaemia of all types ranged from 2·8 to 3·4 per hundred thousand population in Singapore from 1961 to1965. There was no evidence to indicate a rise over the five year period surveyed here. The figures below represent the incidence of childhood leukaemia seen in the Paediatric Unit, General Hospital, Singapore over a ten year period from the years 1957 to 1967, the incidence being based on the total number of admissions, and as seen below there has been no rise in the incidence of childhood leukaemia.

MORTALITY

Morality rates from leukaemia at all ages obtained from an analysis of death certificates range from 2·2 per hundred thousand in 1961 to 3·4 per hundred thousand in 1965 (Kwa et al). Doll and Court Brown (1961) report from England and Wales that there was an increase in the age-group 0 to 4 years and 15 to 19 years during the last ten years. They attribute this increase to improvement in case finding, accurate certification of deaths, and also to an increase in the number of deaths from childhood leukaemia. In Singapore approximately 4% of our hospital deaths in children under the age of ten years are due to leukaemia in the Department of Paediatrics and there has been no increase in this figure over the last five years. Now when you compare the incidence of leukaemia deaths in Singapore children on the island, again there has been no increase. This is based on the assumption that there are no deaths outside the two hospitals mentioned above due to leukaemia.

INCIDENCE OF CHILDHOOD LEUKAEMIA IN THE PAEDIATRIC UNIT, GENERAL HOSPITAL, SINGAPORE OVER A TEN-YEAR PERIOD (1957 to 1967)

Year	Incidence (based on hospital admissions)
1957	0·23
1958	0·06
1959	0·19
1960	0·19
1961	0·15
1962	0·17
1963	0·19
1964	0·19
1965	0·05
1966	0·14
1967	0·17

Fig. 1. Note that there has been no rise in the incidence of leukaemia among hospital admissions over the last ten years.

INCIDENCE OF CHILDHOOD LEUKAEMIA DEATHS IN THE PAEDIATRIC DEPARTMENT, GENERAL HOSPITAL, SINGAPORE (1963 to 1967)

Year	Incidence of Leukaemia Deaths (based on hospital deaths)
1963	4·58
1964	4·29
1965	2·58
1966	3·30
1967	4·51

Approximately 4% of our hospital deaths in children under the age of ten are due to leukaemia in the department of paediatrics.

INCIDENCE OF LEUKAEMIA DEATHS IN SINGAPORE CHILDREN FROM 1962 to 1965

(based on total deaths in Singapore children under the age of 10.)

Year	Incidence
1962	0·66
1963	0·91
1964	0·49
1965	0·24

Fig 2. There has been no rise in the incidence of leukaemic deaths in children in Singapore.

It would be interesting at this stage to compare leukaemic deaths by age, sex and mortality (in infants per 100,000 liveborn) with a number of countries, and it will be seen that Singapore figures follow very closely Japan and United States of America (non-whites), except for the males in the year 1957 in the age group one to four, when there was a slight increase, as there was a preponderance of males for that year in that age-group.

SEX DISTRIBUTION

In most series of cases of childhood leukaemia there were more males affected than females, *e.g.* in Lightwood's series of cases from the Great Ormond Street Childrens' Hospital, London, (1960) between the years 1951 to March 1957 there were 51 males as opposed to 49 females. In Iverson's series of cases from Denmark (1966) there were 306 boys and 210 girls. In our series of childhood leukaemia here, there are 61 males as opposed to 39 females and when you compare this with the sex distribution of children under the age of ten, the difference in sex distribution is not statistically significant, because the probability is greater than 0·05.

SEX DISTRIBUTION OF CHILDHOOD LEUKAEMIA

	Observed	Expected
Males	61	52·5
Females	39	47·5

$\varepsilon x^2 = 3{\cdot}2$

Difference in sex distribution not statistically Significant ($P > 0{\cdot}05$)

Fig. 4. There is a preponderance of males to females in leukaemic children which is not significant statistically.

DEATHS FROM LEUKAEMIA AND ALEUKAEMIA IN

1959 by sex and age and mortality per 100,000 (in infants per 100,000 liveborn) in a number of countries Extracted from Annual Epidemiological and Vital Statistics (1962 Table 7.3.1. and Table 7.3.2.)

Country	Under One Year	1 to 4 Years	5 to 9 Years
England & Wales	M 2·3	M 5·5	M 4·0
	F 1·7	F 4·5	F 4·1
Denmark	M 5·3	M 6·6	M 6·3
	F 5·6	F 9·8	F 2·7
Sweden	M 1·8	M 8·8	M 3·2
	F 2·8	F 6·8	F 4·1
Canada	M 3·3	M 6·2	M 4·7
	F 4·3	F 6·4	F 3·2
U.S.A. (White)	M 3·2	M 6·0	M 4·9
	F 2·2	F 5·2	F 3·4
U.S.A. (Non-white)	M 2·4	M 3·1	M 1·5
	F 3·4	F 2·6	F 1·5
Japan	M 3·4	M 3·8	M 2·9
	F 4·3	F 3·0	F 2·1
Singapore (1957)	M —	M 5·9	M 2·7
	F 6·7	F 1·6	F 0·9

Fig. 3. Childhood leukaemic deaths in Singapore by age, sex and mortality follow the trends of Japan and USA (non-whites).

AGE DISTRIBUTION

Hewitt (1955) found the peak incidence of cases of childhood leukaemia to be between 2 to 4 years and in Singapore children the peak seems to be between 3 to 4 years and a second peak is seen between 5 to 6 years; if we compare this with the sex distribution there are more males in the 3 to 4 year old period, and more females in the 5 to 6 year old period.

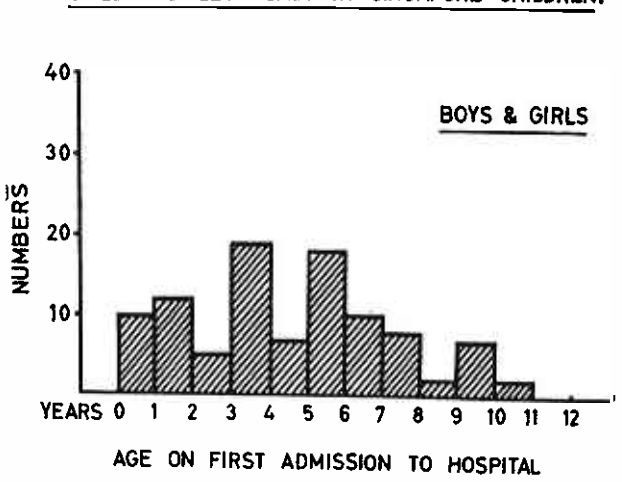


Fig. 5 (a). Note the peak incidence to be between 3 to 4 years with another peak between 5 to 6 years.

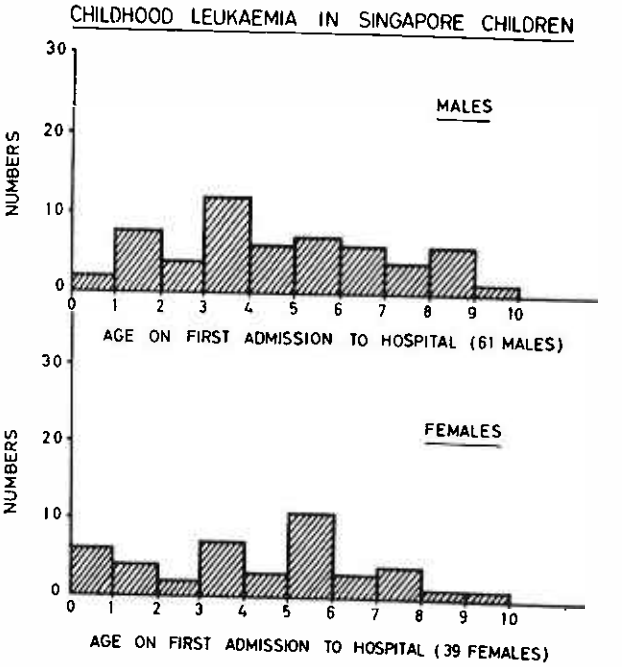


Fig. 5 (b). Note there are more males affected in the 3 to 4 year period and more females in the 5 to 6 years period.

ETHNIC DISTRIBUTION

The ethnic distribution of the cases here followed the general pattern of the general population and the Chinese predominate, who form the majority of the population.

ETHNIC DISTRIBUTION OF LEUKAEMIC CHILDREN IN THE DEPARTMENT OF PAEDIATRICS GENERAL HOSPITAL SINGAPORE

Chinese	-	-	-	82
Malay	-	-	-	9
Indian	-	-	-	6
Eurasian	-	-	-	3
Others	-	-	-	Nil

Fig. 6. The ethnic distribution of the leukaemic cases conforms to the ethnic distribution of the general population.

SEASONAL DISTRIBUTION

Epidemiological studies of leukaemia are very interesting and interest in the distribution in England has been stabilised by reports of clustering together in various communities. In the Liverpool series of cases (1960) seasonal variation was not found but cases tended to occur in the more densely populated areas (Mainwaring).

One gets the impression that admissions of cases of leukaemia always occur in groups, and if you study the cases of leukaemia in children according to the monthly distribution, you will notice a rise in the monthly distribution during the rainy months of October to February and it will be interesting to speculate on the significance of the finding in respect to mosquito borne viruses and the possibility of them inducing leukaemia to those predisposed to leukaemia, but this is only a speculation.

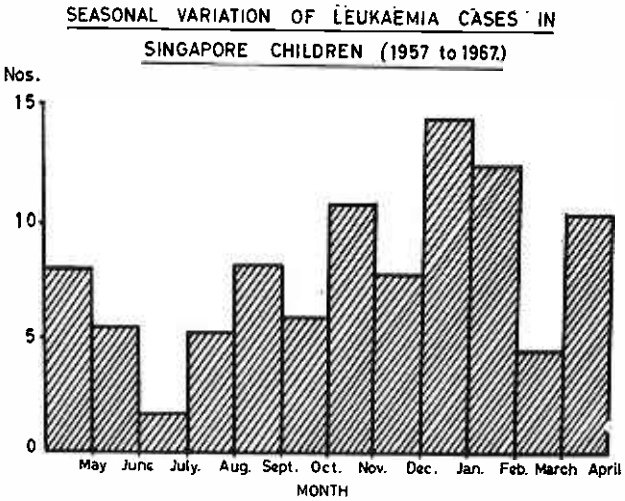


Fig. 7. Note that there is a rise in the monthly distribution of leukaemia during the months of October to February.

CLASSIFICATION OF MATERIAL

The leukaemia study group here has shown that of the 280 cases of leukaemia analysed 77% were of acute variety. On analysis of the 100 cases of childhood leukaemia, 90% of the acute variety 67% being lymphoblastic and 23% being acute myeloblastic leukaemia. Unlike the picture in adults there were only two cases of chronic myeloid leukaemia and only two with undifferentiated stem-cell leukaemia. There were three cases of lymphosarcoma with leukaemic transformation. In two cases the bone marrow was perfectly normal, only to find blast cells 3 months later, and finally there was only one case of mongolism with congenital leukaemia.

CLASSIFICATION OF MATERIAL

1. Acute Leukaemia - -	90%
(a) Acute lymphoblastic leukaemia - -	67%
(b) Acute myeloblastic leukaemia	23%
2. Chronic Myeloid Leukaemia -	2%
3. Stem-Cell Leukaemia - -	2%
4. Erythroid Leukaemia - -	2%
5. Lymphosarcoma with Leukaemic Transformation - -	3%
6. Suspected Acute Leukaemia -	2%
7. Congenital Leukaemia - -	1%

Fig. 8. Note that 90% of the cases are due to acute leukaemia mainly of the lymphoblastic variety.

MORPHOLOGICAL DIFFERENCES BETWEEN A LYMPHOBLAST AND A MYELOBLAST.

Even the expert haematologist and pathologist find it very difficult to distinguish morphologically between a lymphoblast and a myeloblast. The following is a diagramatic representation to show the difference between the two.

The main striking features are as below:

1. The nucleus of the lymphoblast occupies almost the whole of the cell and has a clear nuclear membrane.
2. The number of nucleoli in a myeloblast is larger and always greater than two.
3. Thirdly the cytoplasm has very few granules in a myeloblast but none in a lymphoblast.

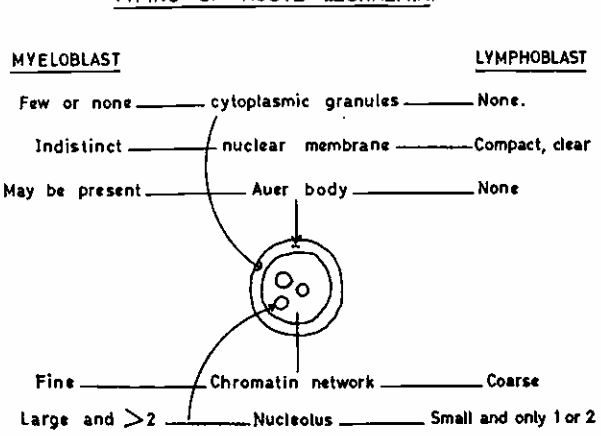


Fig. 9. A diagramatic representation to show the difference between a myeloblast and a lymphoblast.

CONCEPT OF AETIOLOGY

Work by Robert Miller (1966) and others find a wide variety of agents responsible for the etiology of leukaemia. It is difficult for anyone to pinpoint any one of these factors in the etiology of childhood leukaemia here except to say that while one unfortunate child who has the propensity to get leukaemia develops the disease when exposed to any one of these factors, there are many more who escape getting leukaemia even if exposed to these agents.

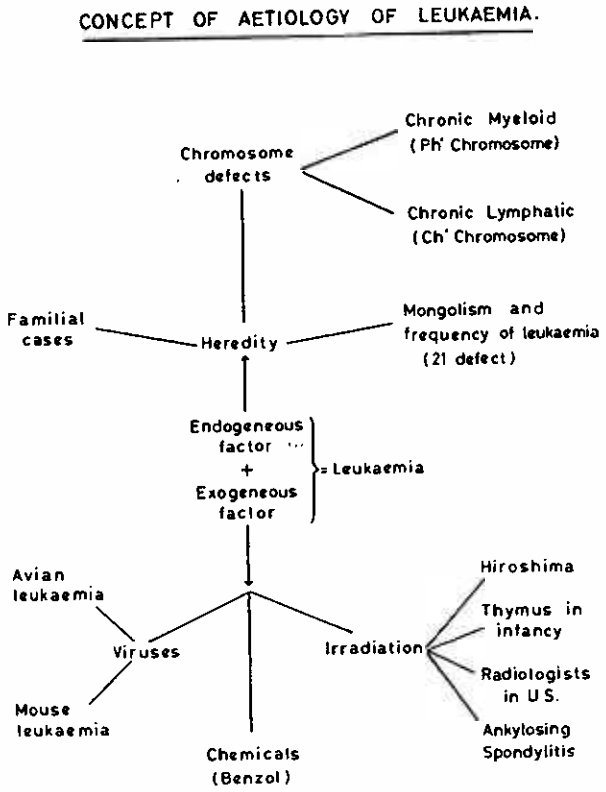


Fig. 10. Summarises the various etiological factors which are known to produce leukaemia, as described by Miller (1966).

ASSOCIATION OF LEUKAEMIA WITH MONGOLISM

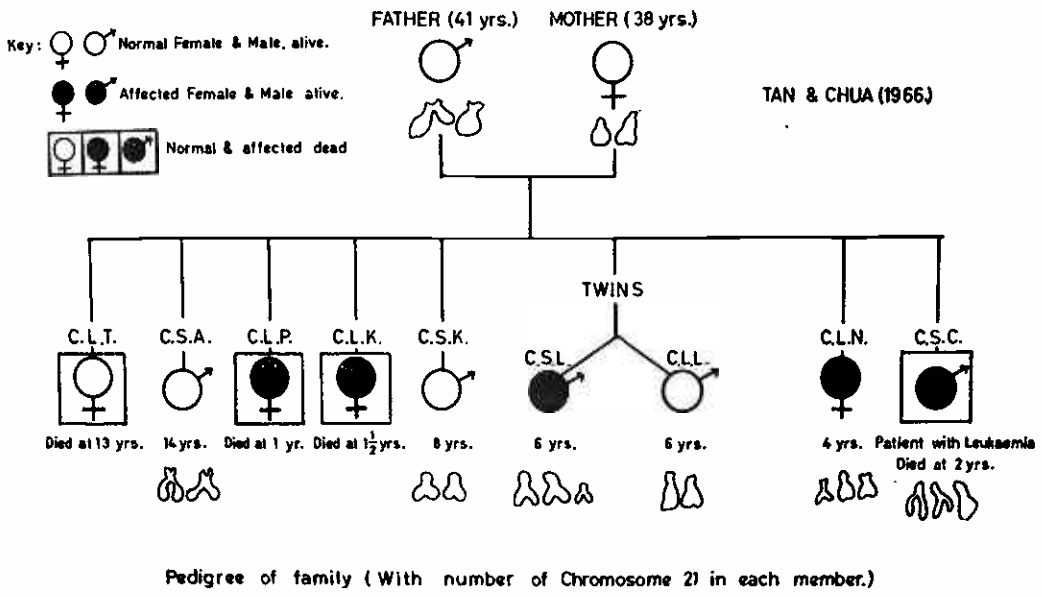
Of particular interest in this series of cases was the association of mongolism with childhood leukaemia. Stewart et al (1958) in a study of 671 cases of leukaemia found 17 mongols giving an incidence of 2·6%. Iverson (1966) in a study of 500 cases found the incidence to be 2·7%. It is cited by Lejeune in 1964 that the incidence of mongolism in leukaemia is fifteen times higher than that of the random childhood population. In our series of cases the incidence of mongolism in leukaemia is 2%. The incidence of mongolism based on the total number of live births is 1 in 800. Therefore the incidence. of mongolism in leukaemic patients is seventeen times greater than the general childhood population under ten in Singapore, and this is significant because the probability is less than 0·001. In the two cases with mongolism one case was particularly unique in that it was a case of familial mongolism with five mongols in one family reported by Tan and Chua in 1966. Two of the mongols have died. Three of the mongols show a regular trisomy 21 karyotype. The mongol that developed leukaemia is one of the twins, the other twin showing a normal karyotype. (See Fig. 11)

CHROMOSOMAL ABNORMALITIES IN CHILDHOOD LEUKAEMIA

In acute lymphoblastic leukaemia the abnormality in number tends to be on the increase *i.e.* hyperdiploidy (See Fig. 12) and is found more constantly in children than in adults. This change in number tends to be constant for the individual but differs from patient to patient. The Ph chromone which is really a deletion of the long arm of chromosome 21 is found in chronic myeloid leukaemia and is found only in the blood and bone-marrow and and may disappear from the blood during remission but remains in the bone-marrow.

CLINICAL FEATURES

Childhood leukaemia presents in a very insiduous and bizzarre manner. The average duration of symptoms is four weeks, and this is the duration of symptoms as put forward by the parents. In most cases the history is actually longer. The main presenting symptoms are fever, pallor, bruising and joint pains. In 80% of cases the children present as a pyrexia of unknown origin. The enlarged liver and spleen are only moderately enlarged. In every case therefore who presents with fever and anaemia it is justifiable to do a simple and quick blood film for abnormal cells. In 18% of cases the children present with joint pains and swelling simulating rheumatic fever and rheumatoid arthritis very closely. As seen below the symptomatology of our cases is no different from that of Lightwood and Iverson of England and Denmark respectively. (See Fig. 15)



Pedigree of family (With number of Chromosome 21 in each member.)

Fig. 11. Family of familial mongolism with leukaemia in one of twins reported by Tan & Chua (1966).

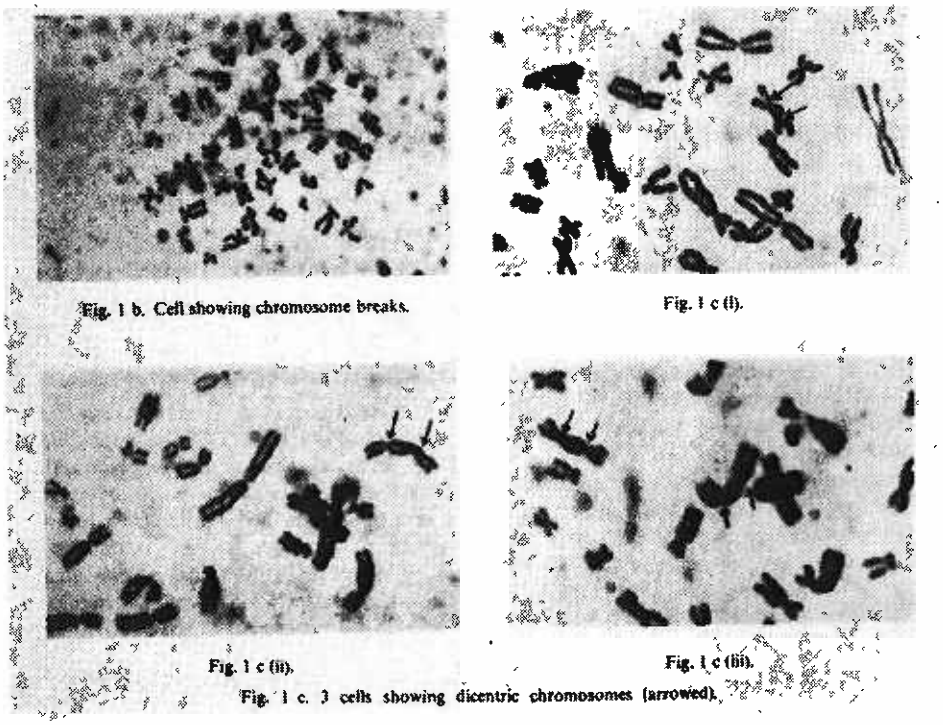


Fig. 12. Chromosomes in acute leukaemia to show ancuploidy, breaks and dicentric chromosomes (Tan and Chua, 1966)

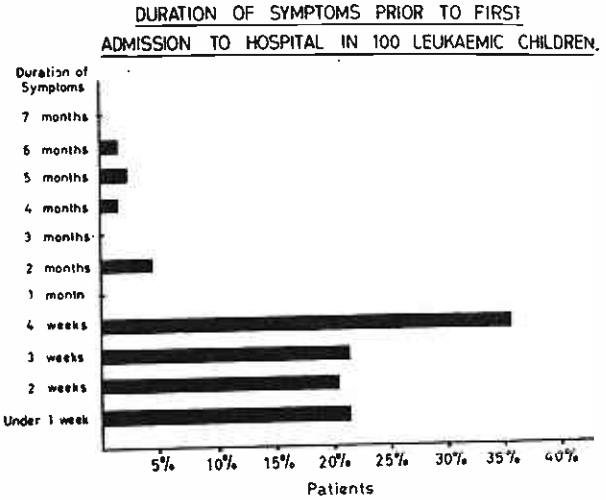


Fig. 13. The majority of our cases arrived late with a history of 4 weeks duration.

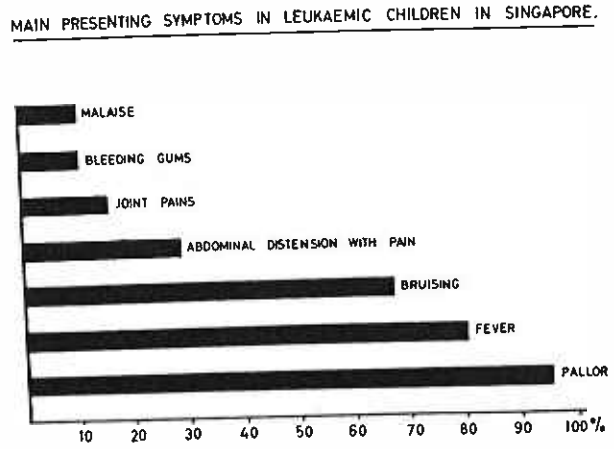


Fig. 14. Note pallor, fever and bruising the main presenting symptoms in leukaemic children.

SOME ATYPICAL PRESENTATIONS OF CHILDHOOD LEUKAEMIA (See Fig. 16)

The atypical presentations of childhood leukaemia are important because they present a problem in diagnosis. It is possible in such cases that the leukaemic process is present in the extramedullary system, like the liver, spleen and lymph nodes before manifesting itself in the peripheral blood or bone-marrow. This may be so because of some anti-leukaemic treatment, usually steroids, which have already been administered. Five of our cases presented with the triad of anaemia, fever and thrombocytopaenia and while on steroid therapy showed evidence of leukaemia. There were three cases of lymphosarcoma presenting with lumps in the neck and abdomen proven by biopsy to be lymphosarcoma and on bone marrow biopsy later showed evidence of leukaemia (See Fig. 17). It is interesting to note in this series that the haemoglobin was maintained in the region of 13 grams. There were two cases of hepatosplenomegaly which showed evidence of erythroid hyperplasia producing erythroid leukaemia. There was one case of a pronounced megaloblastic reaction producing a relative folic acid deficiency owing to tremendous nucleic acid drainage, only to get myeloblastic leukaemia later on (See Fig. 18). Two children presented with rheumatoid arthritis who developed leukaemia and one very interesting case of para-

PRESENTING SYMPTOMS LEUKAEMIC CHILDREN

	England (Lightwood)	Denmark (Iversen)	Singapore
Pallor	54%	82%	98%
Fever	80%	55%	80%
Bone & Joint Pains	37%	26%	16%
Bruising	23%	23%	65%
Bleeding Gums	—	15%	28%
ABD Distension & Pain	—	1 to 2%	13%
Malaise	51%	82% (with pallor)	5%
Swelling of neck	12%	23%	6%
Vomiting	12%	—	4%
Cough	8%	—	6%
Backache	5%	1%	1%
Dyspnoea	5%	—	3%

Fig. 15. Note that the four cardinal symptoms of childhood leukaemia are pallor, fever, joint pains and bruising.

lysis of the legs who was sent to Middleton Hospital as poliomyelitis. Chloroma or the green tumour involving the orbit is very rare, but in this series of cases there were two cases presenting with bilateral proptosis and deposits in the orbit. To prove the point further that the etiology of leukaemia is still unknown, we have had two cases of leukaemia developing under our very eyes, one a case of Thalassaemia Major, developing leukaemia and one a case of Tuberculous Meningitis developing leukaemia. There were two cases of anaemia with cafe-au-lait spots who developed chronic myeloid leukaemia with marked hepatosplenomegaly, but the association between the two is not known (See Fig. 16)

SOME ATYPICAL PRESENTATIONS OF CHILDHOOD LEUKAEMIA

1. Idiopathic thrombocytopaenic purpura, hypoplastic or aplastic anaemia - -	5 cases
2. Lymphosarcoma with leukaemic transformation - -	3 cases
3. Anaemia with erythroid hyperplasia → Erythroid Leukaemia - -	2 cases
4. Megaloblastic Reaction developing into leukaemia - -	1 case
5. Rheumatoid Arthritis developing leukaemia - - -	2 cases
6. Simulating Poliomyelitis -	1 case
7. Bilateral Proptosis → leukaemia	2 cases
8. Obstructive Jaundice → leukaemia	1 case
9. Mongolism with leukaemia -	2 cases
10. Thalassaemia Major → leukaemia - -	1 case
11. Tuberculous Meningitis → leukaemia - -	1 case
12. Cafe-au-lait spots developing chronic myeloid leukaemia -	2 cases

Fig. 16. To show some atypical presentations of childhood leukaemia in this series.

LABORATORY INVESTIGATIONS

In the present material, as most of the cases arrived late, 55% were between 3 to 6 Grams of haemoglobin and below. (See Fig. 19)

In 20% of cases the white cell count was above 100,000 c.mm. while the leucocyte count was below 3,000 per c.mm. in 28% of cases. (See Fig. 20)

The thrombocyte count was low, accompanied with haemorrhages into the skin, but a thrombocyte count below 50,000 per cubic mm. was found in approximately one half of the patients without haemorrhage. (See Fig. 21)

RADIOLOGICAL CHANGES IN CHILDHOOD LEUKAEMIA

(See Figs. 23, 24, 25, 26, 27)

The pathological changes of the bone consist of the following. There is actual infiltration of the marrow with leukaemic cells leading to

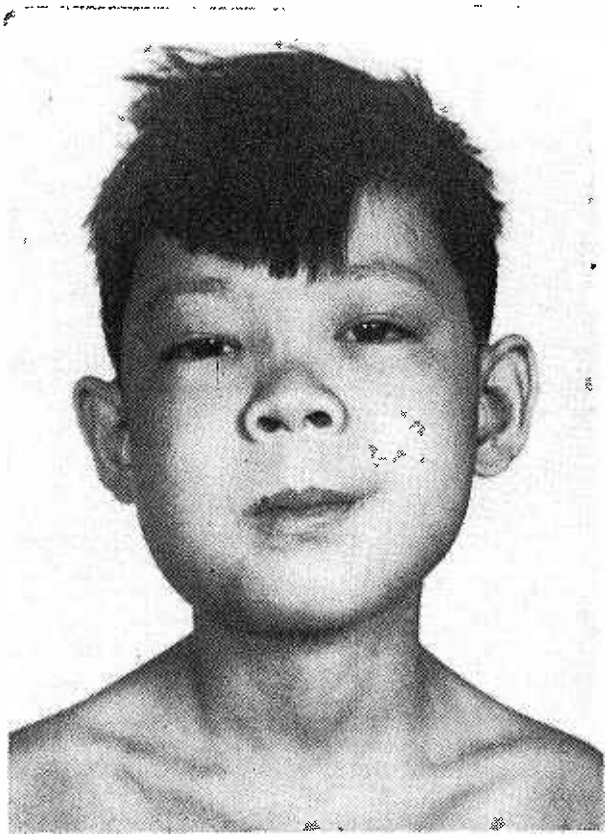


Fig. 17 (a)

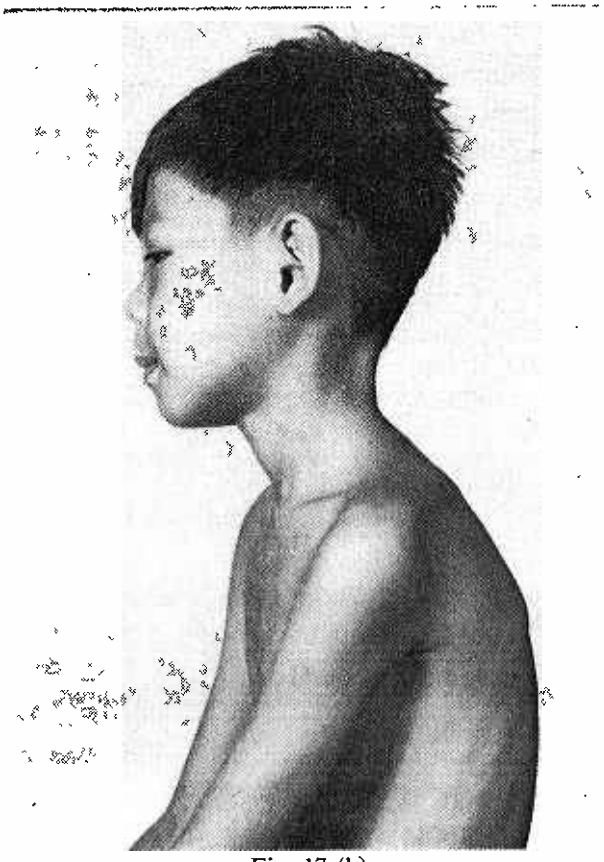


Fig. 17 (b)

Figs. 17 (a) and (b). A case of lymphosarcoma with leukaemic transformation to show swelling of mandible due to leukaemic infiltration. Note lump in neck due to enlarged lymph nodes.

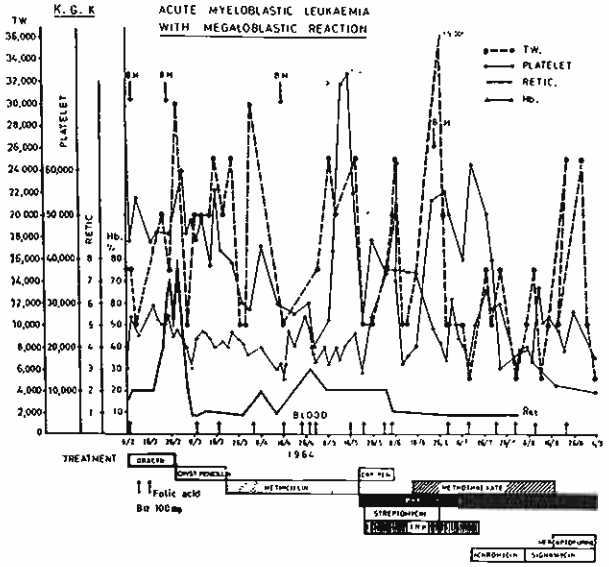


Fig. 18. A case of myeloblastic leukaemia with megoloblastic reaction, presenting as a megaloblastic anaemia.

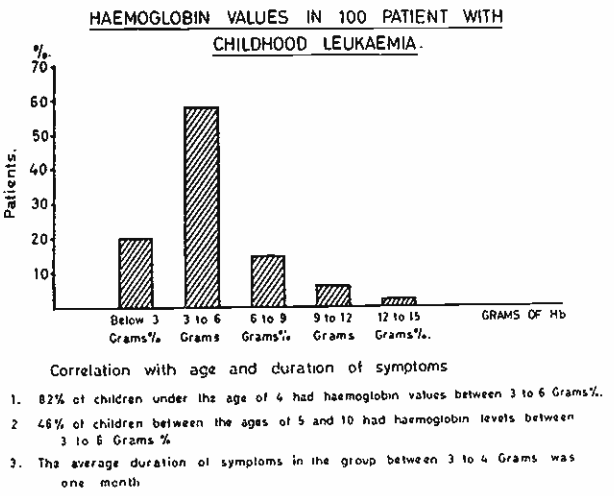


Fig. 19. The majority of the cases had haemoglobin levels between 3 to 6 Grams %.

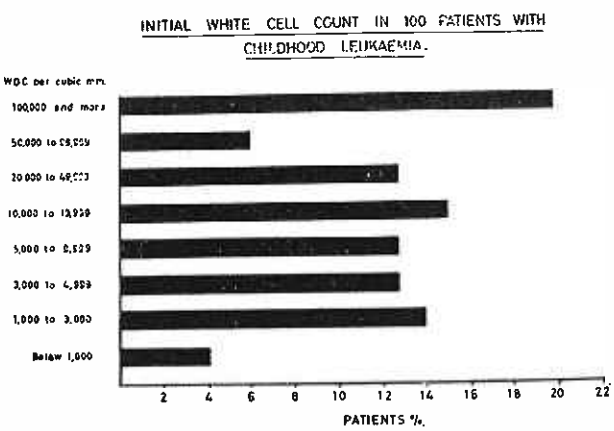


Fig. 20. The majority of the cases had a WBC count above 100,000 per cubic mm.

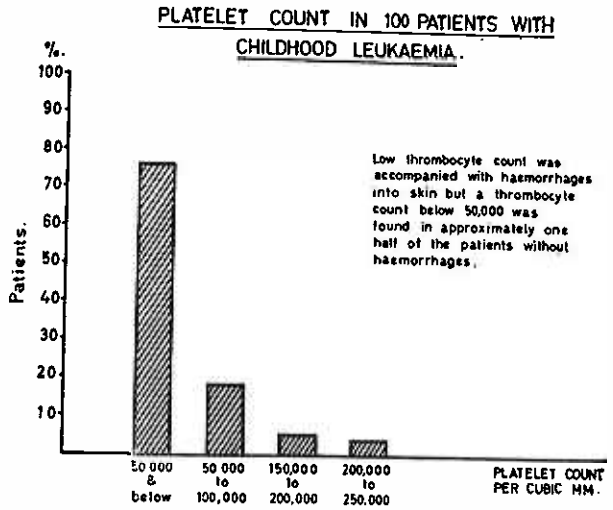


Fig. 21. Low thrombxyle count was accompanied with haemorrhages into the skin but a thrombxyle count below 50,000 was found in approximately one half of the patients without haemorrhage.

rarefaction, and proliferation with the formation of subperiosteal new bone in an attempt to widen the bone for expansion. Degenerative changes may be due to infarcts and produce avascular necrosis of bone and haemorrhage may be responsible for the radiolucent areas in the long bones. The best sites for leukaemic changes are the knees and the shoulder. As seen in Figure 22, in 49 cases where radiographs of the bones were done, metaphyseal translucent areas were found in 40%. The importance of the radiological findings lies in the fact that in doubtful cases of childhood leukaemia the presence of a metaphyseal line is highly diagnostic of acute leukaemia.

Radiological Bone Changes of Acute Leukaemia

The commonest type of leukaemia producing bone changes is acute lymphatic leukaemia. The commonest type of radiological lesions are.

1. DESTRUCTIVE CHANGES
   a) Metaphyseal translucent zone

   b) Focal bone erosions—multiple small erosions eating into cortex→pathological fractures.
   c) Diffuse infiltration—whole bone is rarefied and weakened producing collapse.
2. FORMATIVE CHANGES
   a) Subperiosteal ossification—occurs in metaphyseal region and shaft.
   b) Osteosclerosis—commoner in chronic leukaemia than acute.
3. CHLOROMA

   The "green tumour" in leukaemia, causing erosion of orbital bone.

BONE CHANGES IN 49 cases (Singapore)

Metaphyseal translucent area	-	40%
CORTICAL INVOLVEMENT		
(Erosion) Round translucent area		20%
Sclerosis	- -	4%
Generalised rarefaction	-	4%
PERIOSTEAL INVOLVEMENT		
Irregularity of periosteum	- -	24%
Subperiosteal calcification	- -	3%
SKULL INVOLVEMENT	- - -	3%
VERTEBRAL COLLAPSE	- - -	1%
EFFUSION JOINT	- - -	2%

Fig. 22. Note the radiolucent area along the metaphysis, a characteristic feature so diagnostic of acute leukaemia present in 40% of cases.

TREATMENT

The most gratifying thing about childhood leukaemia is the dramatic response to treatment initially particularly remission induced by steroids. About 90% of our cases of acute lymphoblastic leukaemia will remit, and the criteria for remission are as follows:

1. Abeyance of all signs and symptoms.
2. A sustained haemoglobin level of 11 gms per 100 ml.
3. A disappearance of abnormal cells from the blood and a return to normal of the total and differential leucocyte count.
4. Bone-marrow showing, absence of leukaemic cells less than 10% of blast cells.

Partial remission is an amelioration of symptoms and signs and a blood picture short of the above criteria.

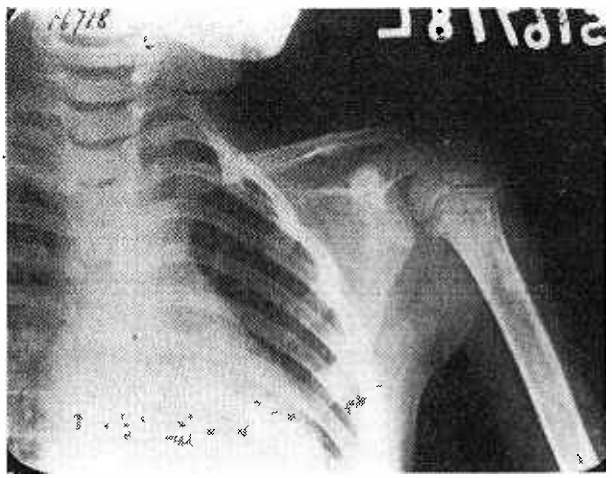


Fig. 23. Note the radiolucent area along the metaphysis so characteristic of acute leukaemia.

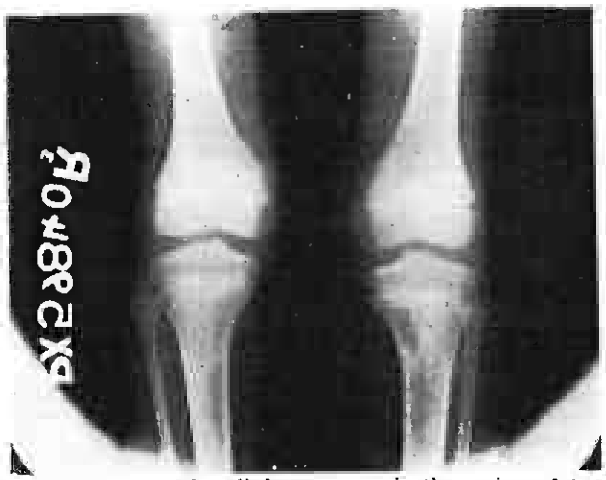


Fig. 24. A round radiolucent area in the region of the tibia, destruction lesions due to leukaemia.

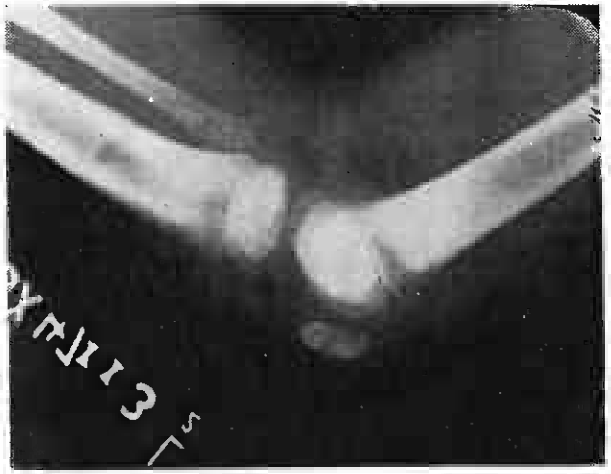


Fig. 25. Subperiosteal ossification with sclerosis of bone so characteristic of leukaemia.

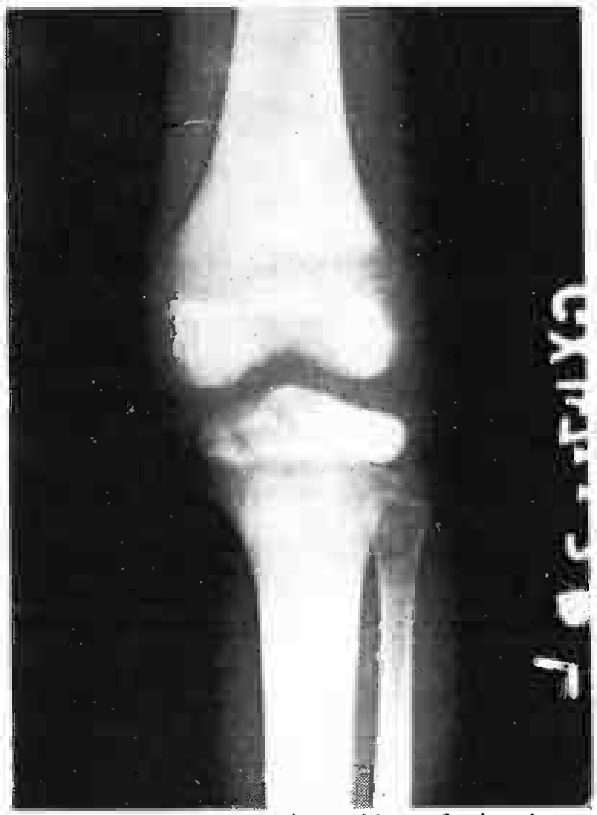


Fig. 26. Dense sclerotic lesions with rarefaction due to leukaemia. Sclerotic lesions are rarer in acute leukaemia.

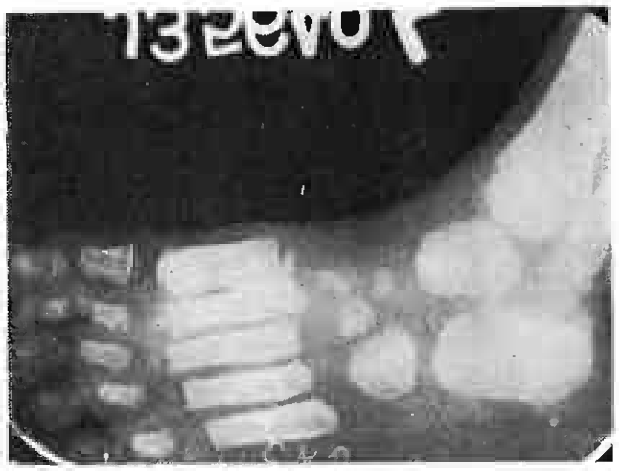


Fig. 27. Periosteal thickening of metatarsal bones due to leukaemia.

It will be seen that Group IV give the best results and with optimum therapy the survival was 18·8 months, which is about the same as most countries. Perhaps the most important part of therapy is supportive therapy, *i.e.* blood transfusions, white cell transfusions and platelet transfusions. Psychologically we keep the child as cheerful as possible in the face of impending death, and with a minimum stay in hospital. The ultimate truth and prognosis is revealed to the parents from the onset. Over zealous treatment can lead to severe side effects of drugs like ulceration of mouth, stomatitis, bleeding, agranulocytosis and alopecia. Fig. 28 shows a typical response of a lymphoblastic leukaemia to treatment, with complete remission initially and a survival of 18 months.

CYCLICAL THERAPY IN LEUKAEMIA

We have had no occasion to use cyclical therapy in leukaemia and this is what we plan to do in our prospective study of childhood leukae-

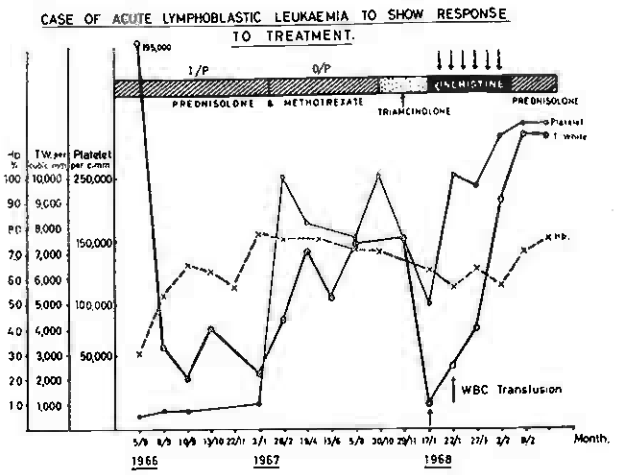


Fig. 28. A typical case of acute lymphoblastic leukaemia to show good response and remission to treatment, with a survival of 18 months.

Below are the list of drugs that we have used in the treatment of childhood leukaemia.

Drug	Dosage	Frequency	Route	Remarks
1. Antimetabolities				
a) Folic acid antagonists				
1) Methotrenate	5 yrs. = 2·5 mgm 5 yrs. = 5 mgm	Daily	Oral	2/52 for effect
2) Aminopterin	5 yrs. = 0·5 mgm 5 yrs. = 1 to 1·5 mgm	Daily	Oral	Not used now
b) Purine antagonists				
1) 6 Mercapto-purine	2·5 mgm/kg	Daily	Oral	2/52 for effect
2) Alkylating agents; Cytoxan	2 mgm/kg	Daily	Oral	2/52 for effect
2. Steroids Prednisolone	10 to 40 mgm	Daily	Oral	2 to 3 days for effect
3. Newer agents				
a) Vincolenco-blastine	0·07 to 0·2 mgm/kg	Weekly	I/V	
b) Vincristine	2 mgm/	Weekly	I/V	
4. Intrathecal Methotrexate	0·3 to 0·4 mg/kg	Every 4 to 5 days for about 3 injections.		

The results of our treatment of childhood leukaemia can be divided into 4 groups:

I. Steroid Therapy				
Long Course of Steroid	No. of Cases 37	Survival in Months		
		Shortest	Longest	Average
		3 weeks	7 months	4·2 months

II. Steroid Therapy + 6 Mercaptopurine				
Long Course Steroid + 6 MP	No. of Cases 12	Survival in Months		
		Shortest	Longest	Average
		13 days	9 months	5·5 months

III. Steroid Therapy + Methotrexate				
Long Course of Steroid + Metho-trexate	No. of Cases 11	Survival in Months		
		Shortest	Longest	Average
		2 weeks	11 months	8·9 months

IV. STEROID THERAPY + 6 M.P. OR STEROID THERAPY AND METHOTREXATE

		Survival in Months		
		Shortest	Longest	Average
Steroids + M.P. or Steroids + Methotrexate	No. of Cases 40 (4 taken home against medical advice)	2 months	28 months	18·8 months

mia. Cyclical therapy means the continuous and consecutive administration of a series of several antileukaemic drugs in recurring limited cycles. The object is to administer each drug for a limited phase and to discontinue it before drug resistance has developed, replacing it with the next drug in the series. Colebatch from Melbourne Childrens' Hospital in a controlled trial has not revealed any clear cut differences between the cyclical and non-cyclical regimes in 38 cases followed up for 14 months.

FUTURE OF CHILDHOOD LEUKAEMIA

What is the future of childhood leukaemia? Many remark that it is a waste of time and labour to give white cell transfusions, a waste of blood when blood can be given for more useful purposes and a waste of money to order expensive drugs like Vincristine. The answer to the question is threefold:

1. Children with leukaemia who remit are indistinguishable from normal children, and as paediatricians we feel it is justified to treat the children to the best of our ability so that they are able to lead happy and full lives.
2. From reported cases of long-term survivals from Boston Childrens Hospital (Mitus et Dameshek) and from cases reported by Burchenal none of those who have survived for eight years or more have subsequently died of leukaemia.
3. Thirdly we live in an era where medical science continues to advance and we live in the hope that someday the cure to childhood leukaemia will be discovered.

ACKNOWLEDGEMENT

I wish to thank Professor Wong Hock Boon, Head of Department of Paediatrics for encouraging me to join the Singapore Leukaemia Study Group and for all his help, to Doctors Herbert Yeo and Tan Kim Ping for help in filling the leukaemia proformas.

REFERENCES

1. Burchenal, J.H. (1965): Proc. Nat. Cancer Conf., 1964. Philadelphia in press B.M.J. P1328 May 1965.
2. Colebatch, J.H. (1965): "Experience with cyclical therapy in leukaemia", Australian Cancer Society Childhood Leukaemia Study Group.
3. Doll, R. & Court-Brown, W.M. (1961): "Leukaemia in children and young adult", Brit. Med. Journ., 1, 5231.
4. Hewitt, D. (1955): Brit. J. Pro. Soc. Med., 9, 81.
5. Iverson, Torben (1966): "Leuiaemia in infancy and childhood", Acta Paediatrica Scandinavia Supplement 167.
6. Kwa, S.B. et al (1968): "Leukaemia in Singapore", Singapore Med. Journal Convention issue.
7. Lightwood, R. Barrie, H., Butler, N.: "Observations on 100 cases of childhood leukaemia", Brit. Med. Journ., 1, 747.
8. Mainwaring, D. (1966): "Epidemiology of acute leukaemia of childhood in the Liverpool area", Brit. J. Prev. Soc. Med., 20, 189 to 194.
9. Miller, Robert, W. (1966): "Etiology of childhood leukaemia", Paediatric clinics of North America Vol. 13, No. 2, page 267.
10. Steward, A. & Hewitt, M.A. (1959): "Epidemiology of human leukaemia", Brit. Med. Bull., 15, 73 to 77.
11. Tan, G. & Chua, T.S. (1966): "Familial Mongolism", Journ. of Singapore Paed. Soc., Vol. 8, No. 2, Oct. P. 90.
12. Turpin, R. & Lejeune, J. (1953a): "Etude D'une famile comportant quatre freres et soeurs mongolic", Sem. Hop. Paris 76, 3978 to 3984.
13. Registrar-General Statistical Review of England and Wales for vear 1938 to 1957 H.M.S.O. (London).