ACUTE LYMPHOBLASTIC LEUKAEMIA IN PAEDIATRICS

An Essay

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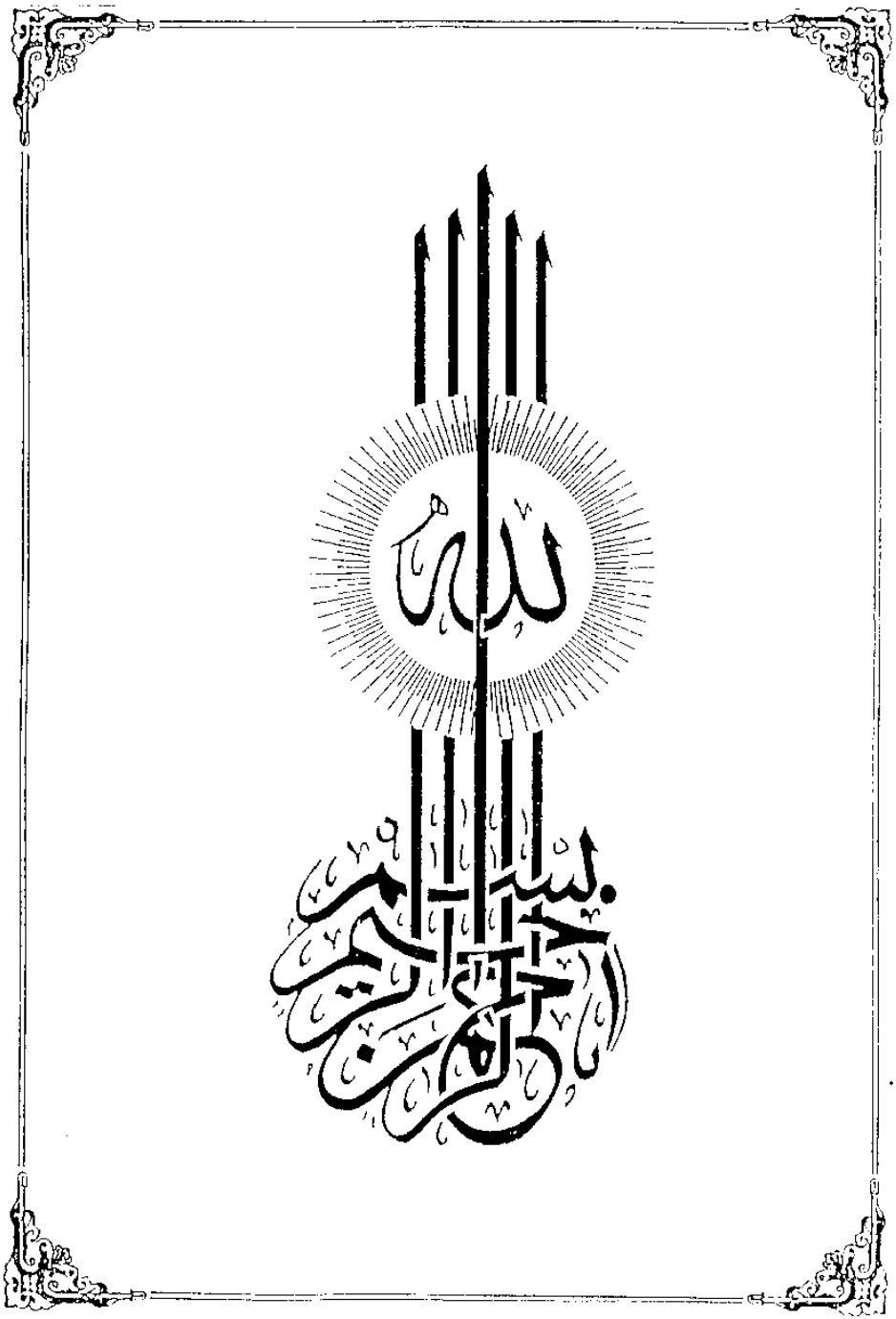

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ABBREVIATIONS AND SYMBOLS

ADM	adriamycin (doxorubicin)
ALL	acute lymphoblastic leukaemia
AMLL	acute mixed lineage leukaemia
ANLL	acute non-lymphoblastic leukaemia
Ara-C	cytosine arabinoside
ASP	L-asparginase
BMT	bone marrow transplantation
CALLA	common acute lymphoblastic leukaemia antigen
CD	cluster differentiation
CFU-C	colony forming unit-culture
CFU-S	colony forming unit-spleen
CML	chronic myeloid leukaemia
CNS	central nervous system
CPA	cyclophosphamide
CRT	cranial radiation therapy
CSpRT	cranio-spinal radiation therapy
CSF	cerebrospinal fluid
CT	computerized tomography
Cylg	cytoplasmic immunoglobulin
DNA	deoxyribonucleic acid
DNR	daunorubicin (daunomycin)
EBV	Epstein-Barr virus
ER	E-rosette test
FAB	French-American-British cooperative working group
G6PD	glucose 6-phosphate dehydrogenase
HLA-DR	human leucocyte antigen D-related locus
HTA	human thymocyte antigen
HTLV	human T-cell leukaemia lymphoma virus
Ig	immunoglobulin(s)
IM	intramuscular
IT	intrathecal
IV	intravenous
LDH	lactate dehydrogenase
MoAb	monoclonal antibody
6-MP	6-mercaptopurine

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MTX	methotrexate
PAS	periodic acid Schiff
Ph^1	Philadelphia chromosome
PRD	prednisone
RNA	ribonucleic acid
SmIg	surface membrane immunoglobulin
TDT	terminal deoxynucleotidyl transferase
TF-X	thymus factor X
TG	thioguanine
VCR	vincristine
VM-26	podophyllotoxin (teniposide)

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INTRODUCTION

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INTRODUCTION

Leukaemia is a disorder which has apparently unrestrained proliferation of the white blood corpusles in the absence of a demonstrable stimulus (Altman & Schwartz, 1983). It is a comparative newcomer among the major known diseases, as its recognition as a distinctive disease has had a history of little more than 100 years.

The first accurate description of a case of leukaemia was given in 1827 by Velpeau. However, it was not recognised as a definite entity until its description in 1845 by Bennett in Scotland and by Virchow in Germany. Based on the observation of very large proportion of abnormal colourless globules which simulated pus cells, Bennett termed the condition "suppuration of the blood", while Virchow termed it "white blood" as he could not find any evidence of suppuration. In 1847, Virchow introduced the term "leukaemia", while Bennett introduced the term "leucocythaemia" in 1852.

Within 12 years of recognition of leukaemia, the two chief varieties of chronic as well as the acute form had been described, and the main clinical and pathologic features tabulated.

In 1870, Neumann reported that the bone marrow was an important site for the formation of blood corpuscles in health and disease, and suggested that there might, in fact, be a myelogenous leukaemia.

In 1879, Gowers subdivided leukaemia into splenic leucocythaemia and lymphadenosis.

In 1893, Kundrat used the term lymphosarcoma for a primary affection of lymph nodes which spread to neighbouring structures in the fashion of malignant

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diseases and considered it a separate entity from leukaemia. It was not long, however, before Turk in 1903 recognised that there were close connections betweeen lymphosarcoma and leukaemia. He grouped them together in one system of lymphomatoses. By 1914 the distinct entities of leukaemia had all been described.

Despite improved methods of classification, progress toward determining its cause and treatment remained dormant until the past several decades (Gunz & Henderson, 1983).

In the last decade there have been major advances in the treatment of childhood malignancy. The dramatic improvement in the outlook for children with acute lymphoblastic leukaemia (ALL) is perhaps most noteworthy. Whereas 20 years ago the major concern was the developing of better methods of inducing complete remission, today much of the focus has shifted to issues facing long-term survivors (Poplack et al., 1985).

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EPIDEMIOLOGY

Incidence
Age distribution
Sex distribution
Geographical distribution
Leukaemia clustering
Social distribution
Seasonal distribution
Familial incidence

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EPIDEMIOLOGY

Incidence

ALL constitutes about 30% of childhood malignancies, being the most common paediatric cancer. Young and Miller (1975) calculated the risk for developing ALL to be 4,2 per 100,000 children for white Americans. They reported that it is almost twice as common in white than in non-white American children.

El-Balkainy et al. (1984) reported that, among patients at the National Cancer Institute, Cairo, ALL was the second paediatric malignancy after Hodgkin's disease with a ratio 1:1.3, respectively.

Khalifa et al. (1982) reported an incidence of 23.3 per 100,000 of out-patients attending the Children's Hospital at Ain Shams University.

Age Distribution.

The peak incidence occurs in the 3 to 5 years age group, being rare before the age of one year (Khalifa et al., 1982; Altman & Schwartz, 1983).

Sex Distribution

Boys are more commonly affected than girls, starting from the first year of life and becomes most prominent for children of ages 6 to 15 years, of whom approximately two-thirds of patients are boys (Young & Miller, 1975). Also, Khalifa et al. (1982) reported a male: female sex ratio of 2:1.2 (Figure 1).

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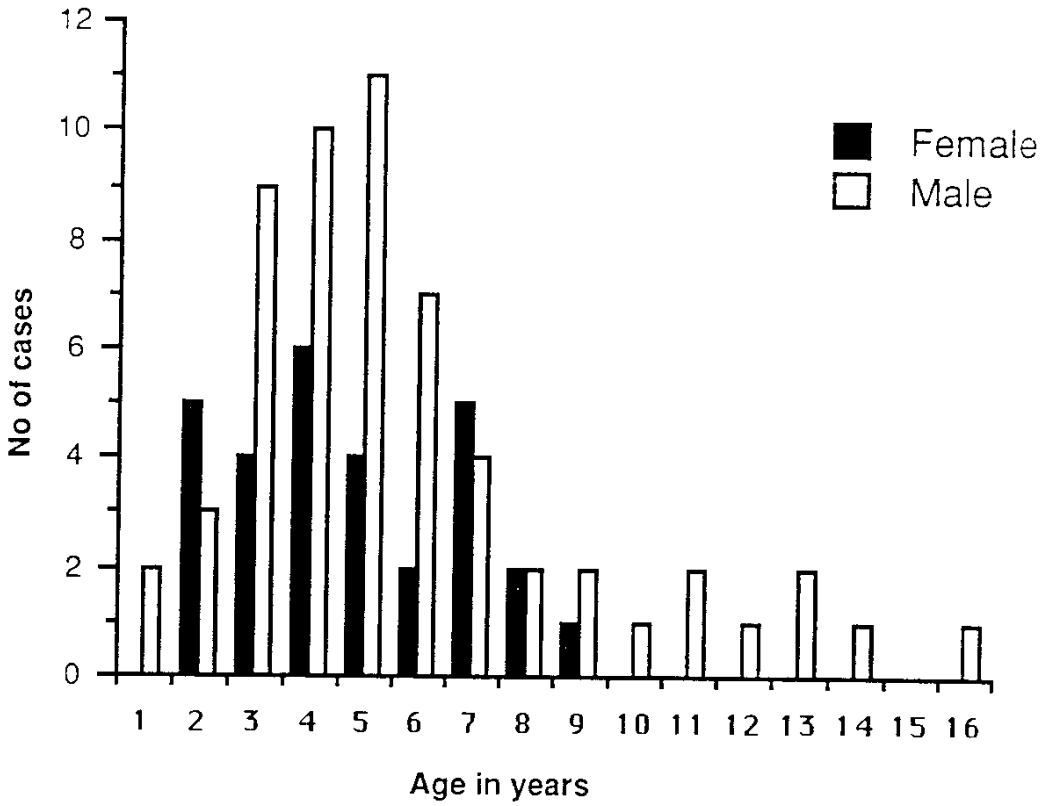

Fig. 1. Incidence of ALL according to age and sex *(From: Khalifa et al., 1982).*

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Geographical Distribution

The correlation between the development of age peak and major periods of industrialisation arouse the suggestion that this phenomenon reflects different times of exposure to a new environmental leukaemogens. For example, this peak age phenomenon was first noted in England in the 1920s, in the United States in the 1940s, and in Japan in the 1960s but has not been seen in relatively unindustrialised countries (Miller, 1979).

No difference in the incidence have been reported in relation to geography or between urban (industrialised) and rural areas (Catovsky, 1981).

Leukaemia Clustering

There has been considerable interest in reports of "leukaemic clusters", the occurrence of a greater than expected number of leukaemia cases within a given geographical area or time period. Although the demonstration of bona fide clustering would have had profound epidemiologic implications, most studies have been unable to confirm this phenomenon and it can be attributed to chance (Corbett & Schey, 1982).

However, Hamza et al. (1982) reported clustering of ALL cases in Egypt, with high prevalence in Cairo and Port-Said governorates. They also reported that this phenomenon was proved statistically to be a real rather than an apparent one.

Social Distribution

A higher incidence has been observed among high socioeconomic class, when compared with the lower class. Ramot and Magarth (1982) reported that after 1967,

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a change occurred in the ratio of Burkitt's lymphoma to leukaemia among Arab children; the incidence of ALL was low. Beginning in the mid 1960s, the incidence of ALL rose to 4 per 100,000 per year, and a young age peak appeared. This transformation of leukaemia incidence among Arab children occurred over 8 years concurrent with socioeconomic changes toward a more Western economy in the region. The authors used this observation to suggest that environmental factors played an important role.

Seasonal Distribution

There is no consistent correlation of leukaemia frequency with months of births or months of onset of clinical symptoms (Altman & Schwartz, 1983).

Familial Incidence

The prevalence of ALL was found to be higher in families of affected children (Miller, 1967; Gunz et al., 1975). The risk was calculated to be four times greater among siblings and non identical twins of leukaemic children than in the general paediatric population (Drapper et al., 1975). Those at highest risk are identical twins of affected children, the risk being maximum before the first year of life (about 25%) then it returns to that of the general paediatric population after the age seven (Miller, 1967).

Progeny of survivors of childhood ALL do not show increased risk (Li et al., 1979), neither do infants born to mothers with leukaemia (Miller, 1979).

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