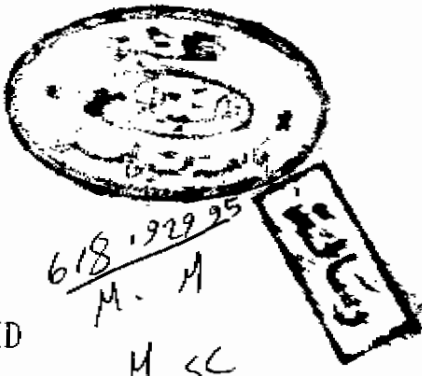
SURVEY OF TUBERCULOSIS IN INFANCY AND CHILDHOOD

A Thesis Submitted for the Partial Fulfilment of

Master Degree in Paediatrics



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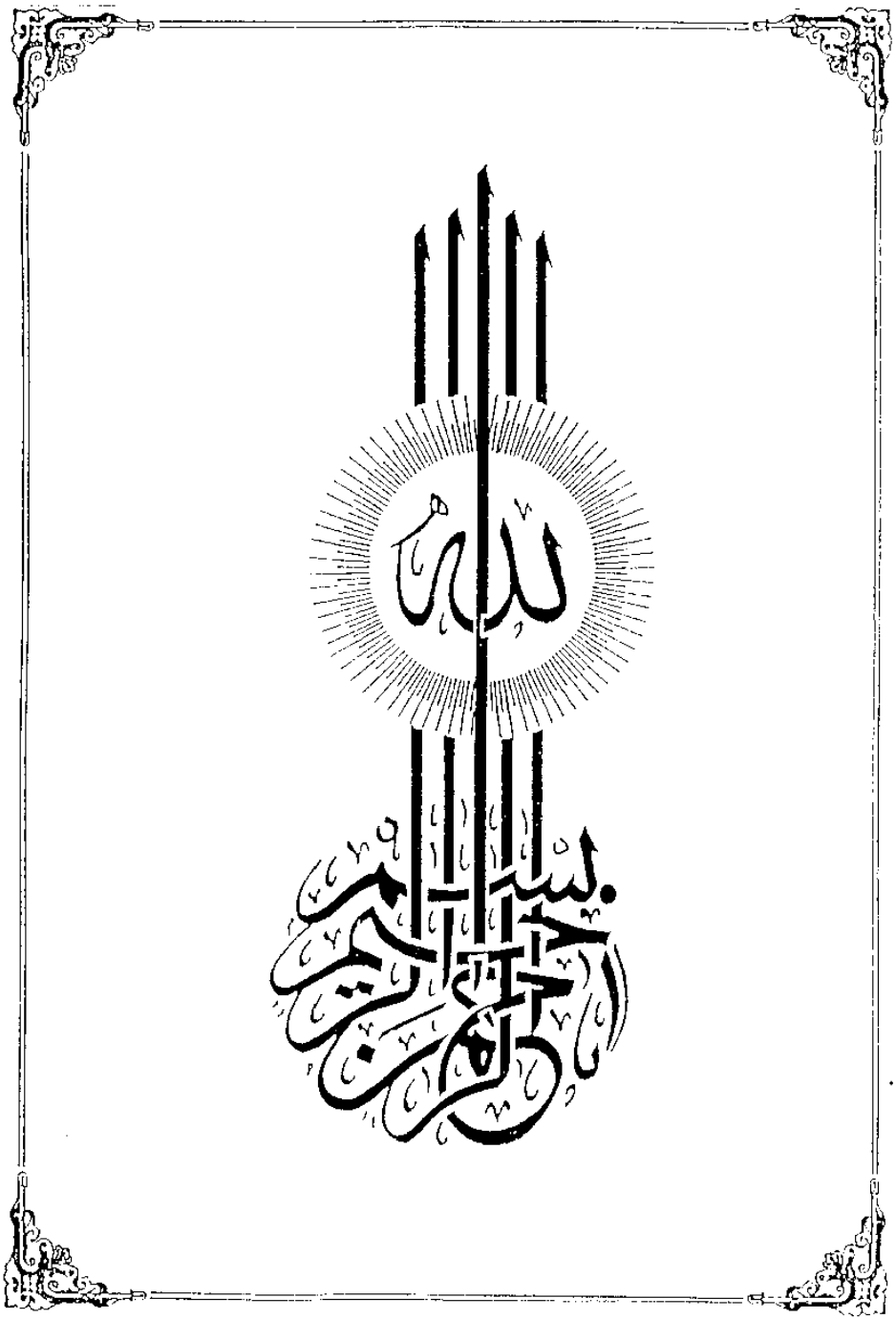

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TUBERCULOSIS IN INFANCY AND CHILDHOOD

INTRODUCTION

Inspite of the marked decrement in the incidence of tuberculosis in most developed countries, as a result of improved socio-economic and hygienic level as well as a consequence to advances in antituberculous therapy, tuberculosis is still one of the principal causes of suffering and death in developing countries including Egypt.

Tuberculosis affects all age groups especially infants and children. In infancy, it has a high fatality because of tendency to occurence of acute haematogenous forms of the disease, miliary tuberculosis and tuberculous meningitis.

In the paediatric age group, all types of tuberculosis are detected including pulmonary tuberculosis and extra-pulmonary tuberculosis which affects many organs as lymph nodes, bones and joints, genito-urinary tract, serous membranes (Pleura, pericardium and peritoneum), meninges and intestine. Congenital tuberculosis also do occur. That is why we were stimulated to carry on this survey which is concerned with ; pathogenesis, pathology, clinical manifestations of various forms of the disease, ways of prevention and treatment of tuberculous lesions in infancy and childhood.

REVIEW OF LITERATURE

Tuberculosis is as old as man kind. It existed in ancient Egypt as revealed by traces of Pott's disease in skeletons and mummies.(Morse et al, 1964).

A disease that was probably tuberculosis was known as early as 1000 B.C. Hippocrates described the symptoms of a malady called phthisis, meaning to waste away, and recognised nodules of the lungs as a feature of the disease. He also thought of the contagiousness of tuberculosis. (Harris & McClement, 1977).

There is an excellent description of the symptomatology and pathology of consumption(Tuberculosis) in the Arabic manuscripts: Al- Canon by Ibn-Sina (A.D. 1036), and Al-Hawi Fil-Tib by Al-Razi (A.D. 925). (Al-Damluji & Bignall , 1976).

In the middle ages, tuberculosis was thought to be a constitutional and familial disease. The pathological changes cast in lungs, glands, and bones were shown when cadavers of the sufferers were dissected. In 1819 Laennac, who was the first to use the stethoscope, described the

physical findings in cavitory tuberculosis.(Al-Dalmuji & Bignall, 1976).

Koch (1882) isolated the tubercle bacillus and attributed the infection to it. A few years later, three types of tubercle bacilli were shown to be pathogenic to man and animals ; namely human, bovine and avian. In the beginning of the present century many other mycobacteria responsible for disease in man and animals were discovered.

Tuberculin was introduced by Koch (1890) while he was searching for a therapeutic agent in tuberculosis. His discovery opened new era towards a better understanding of the hypersensitivity reactions in human tissues.

Two French scientists, Calmette and Guerin (1922) succeeded in attenuating tubercle bacilli by growing them on culture media, and after 30 passages, the organisms lost their virulence to monkeys, guinea pigs and rabbits. The vaccine was first tried as a preventive measure against tuberculosis by their colleague Weill-Halle in the same year.

The Story of chemotherapy started when gold preparations were used in the 1920 s along with cod liver oil,

vitamins and calcium. Modern chemotherapy began in 1935 when it was discovered that sulfones were capable of reversing an established infection in animals and man (Hudson & Sellors, 1963).

In 1944 Waksman discovered streptomycin and in 1945 Feldman and Hinshaw proved that streptomycin exerted a superior effect on the human form of M. tuberculosis in the guinea pig. Impressive results were obtained when the drug was used in human disease, particularly in miliary and meningeal tuberculosis. Soon it was found that the arrest of disease is temporary and the appearance of drug resistance and deafness tempered the initial optimism.

Youmans et al (1947) introduced para-amino salicylic acid as a powerful antituberculous drug. Combination of P.A.S.A. with streptomycin gave hopes of a specific cure and prevention of drug resistance.

In 1952 isonicotinic acid hydrazide was discovered and in 1958, the World Health Organisation advised its use in chemoprophylaxis in tuberculosis(Al-Damluji & Bignall, 1976).

Epidemiology :

Infants and children are most frequently infected from an adult case. More illness occurs among the contacts of sputum-positive than of sputum-negative persons. When infection takes place in an infant it is usually possible to locate the source since the infant is relatively static. (Hudson & Sellors, 1963).

Overcrowding, close contact with infected persons, and poverty with its accompanying social ills, all favour transmission of the disease.(Shah et al, 1971).

While genetic factors may be involved, environmental influences are far more important. Malnutrition and concomitant infections are two important factors which lower the resistance and make children, especially those under one year, prone to infection.(Udani & Maddocks, 1978).

In 1951 Rich postulated that the development of active tuberculosis depends on four factors ;

1- The magnitude of the infecting dose.
2- The virulence of the organism.
3- The native ability of the individual to develop acquired resistance.
4- The route of entry into the body.

The most important factor which determines the fate of a tuberculous lesion in the human body is the ability to develop acquired resistance following primary infection (whether it is natural or by B.C.G. vaccination)(Rich,1951).

The maintenance of tuberculin hypersensitivity is of importance in the control of tuberculosis so that factors causing a decline or reversion of a positive tuberculin reaction can influence the incidence of the disease. Many observations have shown that certain infections temporarily reduce tuberculin hypersensitivity. Starr & Berkovitch(1964) noted that with measles. Wellman & Wetton (1963) found that hypersensitivity was depressed by the measles virus vaccine and also by a number of other viral vaccines including trivalent polio-virus vaccine. Schick & Dolgin (1963) observed similar changes after giving prednisone.

World Health Organization(1964) estimated that there were approximately 15 million persons in the world suffering from active tuberculosis from which 3 millions die annually. Three quarter of the cases are in the developing countries. (Almenda 1964).

The two commonest measures of tuberculosis are annual mortality rates based on death certificates and annual incidence based on notifications. In many countries both

are unsatisfactory and incomplete. Prevalence surveys by mass x-ray, tuberculin test, or bacteriological examination have been used, but are expensive and limited in scope. The most important of these is the sputum examination to detect infectious cases, but this is perhaps the most difficult to supervise and standardize especially in children . A tuberculin survey, which measures prevalence of infection, is simpler and it is possible through analysis of infection rates to make a rough estimate of the number of cases of active tuberculosis which should be expected(Udani & Maddocks, 1978).

In Egypt, tuberculosis is still a major health problem. Incidence of infection as revealed by tuberculin positive reactors below the age of 15 year is 20-30 percent (Awad et al, 1978). Annual infection rate of 4 to 5 percent was estimated in Egypt in 1960 by El-Mohandis and Sakr.

In India, it was found that as many as 40 percent of the population were tuberculin positive by the age of 14 year and nearly 55 percent by the age of 20 year(Udani et al,1974).

The extrathoracic type of tuberculosis(mainly C.N.S., miliary and disseminated tuberculosis) is responsible for nearly 70% of deaths in children, while 30% of deaths are due

to the intrathoracic type. (Udani et al , 1974).

The annual reported number of new cases of pulmonary tuberculosis declined steadily in U.S.A. between 1962 and 1972 while the number of reported cases of extrapulmonary tuberculosis remained stable. Extrapulmonary tuberculosis can occur at any age but the very young and very old are more prone to dissemination(Hoeprich, 1977).

BACTERIOLOGY

Tuberculosis is caused by Mycobacterium Tuberculosis of the order Actinomycetales. Human and bovine strains account for almost all cases in man though there is evidence that the avian strain may also infect man. (Dragsted,1949). The majority of cases of pulmonary tuberculosis are of the human type whilst the bovine type is more common in abdominal tuberculosis and tuberculosis of bone.

The tubercle bacillus is a slender bacillus about 4 microns in length and 0.4 micron in diameter. The organisms are straight or slightly curved, occuring singly, in clumps, or in strands aligned in a parallel fashion. They stain either uniformly or in beaded pattern. When the organisms are stained with aniline dyes, such as carbolfuchsin in Ziehl-Neelsen method, the red colour is not removed even with mineral acids, thus the organisms are said to be acid fast. The bacillus is rich in lipids that are contained in and adjacent to the cell wall. These lipids account for the acid fast property of the bacillus, and its relative resistance to destruction by some physical and chemical agents that are lethal to other microorganisms. The tubercle bacillus is a strict aerobe, the organisms show a distinct predilection for the upper regions of the lung where PO_2 is higher than elsewhere. The tissue PO_2 in other organs

correlates well with the prevalence of tuberculosis in extrapulmonary sites. (Hinshaw and Murray,1980).

The tubercle bacillus grows on Lowenstein solid medium and Dubos fluid medium. Colonies of the bacillus grow slowly and usually require 3 to 6 weeks to appear. Colonies are wrinkled, dry and creamy in colour.

The natural route of infection is by the respiratory or alimentary tract but it may occur through the skin, mucosa of the mouth, tonsil or eye.(Miller, 1953).

The most common route for the entry of bacilli is the respiratory tract, the vehicle is either droplets from the breath of infected persons, or by dust carrying dried bacilli. Infection via the alimentary tract results from swallowing infected materials as milk, floor dust contaminating any food, sucking of finger or contaminated article, or using utensils of diseased individuals.(Griffith and Denaro,1955).

Demonstration of tubercle bacilli remains the cornerstone for diagnosis of an active case of tuberculosis. Bacilli can be detected in the sputum, laryngeal swab, tracheal and bronchial lavage, gastric lavage and body fluids(cerebrospinal,

pleural, pericardial and peritoneal fluid). Bacilli can be detected also in urine and faeces, by direct examination , culture methods or animal inoculation. (Mitchison, 1972).

Animal inoculation is the most sensetive and conclusive test for the detection of the tubercle bacillus in any suspected material. The material prepared for culture can be used at the same time for animal inoculation. A suitable inoculum is injected subcutaneously in the thigh of a guinea pig, which is highly susceptible to experimental infection with both human and bovine types. A local swelling appears at the site of injection in one-two weeks ; at first hard, it may later caseate and ulcerate. The lymph glands draining the site of inoculation become involved by lymphatic spread and later the lymph glands in other parts of the body are also affected. The animal begins to lose weight and dies in 6 to 16 week. At autopsy there is a picture of generalised tuberculosis. The spleen is enlarged and shows greyish white tuberculous nodules. Similar nodules appear in the liver, but it is of rare occurence in the lungs. Films prepared from any of these lesions, stained with Ziehl-Neelsen will show plenty of acid fast tubercle bacilli.(Abdel-Aziz, 1973).