TUBERCULIN REACTIVITY OF SCHOOL STUDENTS IN SUEZ GOVERNORATE

Thesis
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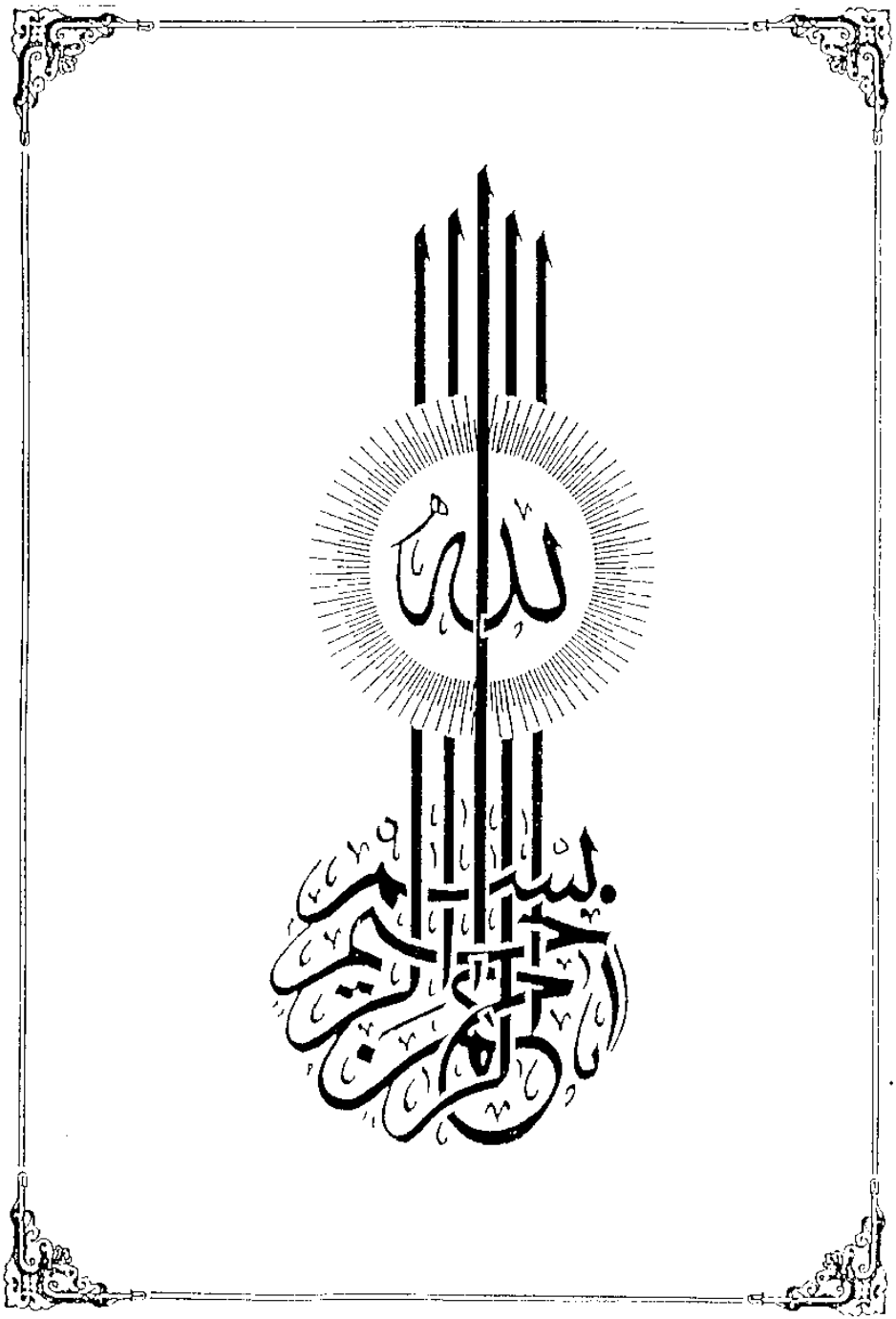

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INTRODUCTION

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In the performance of the tuberculin test, diluted tuberculin is introduced into the body and the result may provide evidence of presence or absence of tuberculous infection in the individual. The test is of immense value in human, and has at least three important applications:

1. Estimation of the extent of tuberculous infection in a community if all its members, or at least a substantial proportion of them, have been tested by tuberculin.

2. Defining a group of infected persons as the test may assist in tracing the source of the infection to one or more persons suffering from active open tuberculosis.

3. Excluding or confirming the presence of tuberculous infection in a sick patients as the tuberculin test may be helpful in establishing the diagnosis ***[Pagel et al., 1964].***

Several methods of applying the test have been extensively used, but those most commonly employed today utilize the skin. The introduction of tuberculin into the conjunctiva, the peritoneum, or the subcutaneous tissues is now seldom adopted in human medicine. **(*Pagel et al., 1964*).**

The basis of tuberculin test is the fact that, coincident with the development of primary tuberculous lesion, the patient becomes hypersensitive to a protein fraction of the tubercle bacillus. The tuberculous aller gy develops within 4 - 6 weeks of 1ry infection and is of cell mediated type, thus when a sensitised person is exposed to tuberculo-proteinwhether in a skin test or through a second infection, a delayed type hypersensitivity reaction occurs. (***Walter and Israel, 1978***).

Intradermal testing with standarized antigen prepared from mycobacterium tuberculosis is the broadly applicable means of detecting latent infection with this organism. It is assumed that a person having a "positive" reaction to 5 Tuberculin units [TU] of purified protein derivative (PPD) not only has been infected with M. tuberculosis but continues to harbor viable bacilli and has relative resistance to acquisition of a new infection with the same species of mycobacterium. It is well established, however, that the cutaneous reaction to tuberculin may decrease overtime, resulting in an apparently negative test, and that in some persons, This sensitivity may be recalled by the application of a second or booster, test. ***"Gordin et al., 1991"***.

AIM OF THE WORK

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The aim of this work is to determine tuberculin reactivity in BCG vaccinated and non vaccinated students in primary, preparatory and secondary schools in Suez Governorate using Mantoux method of tuberculin test including age group 6 - 18 years.

REVIEW OF LITERATURE

Immunology of Mycobacterium Tuberculosis.

Tuberculosis stimulates many responses in the immune system that involve both non specific immunity expressed by polymorphonuclear neutrophils, monocytes and macrophages, and specific immunity expressed by both the cellular and the humoral immune systems.*(Edward and Kirkpatrik, 1986)*.

Hinshaw (1980) stated that immunity in tuberculosis is either native or acquired and it's the latter which intimately associated with allergy. There is no sure clinical method to test or measure immunity other than a patient ability to recover from disease.

Immunological Basis of Tuberculin Reaction.

When PPD is injected intradermally, it is first taken up by macrophages which present this injected antigen to T.lymphocytes. These T-lymphocytes respond by dividing, differentiating and releasing lymphokines. The macrophages accumulate at the site through the release of macrophage chemotactic factors. The macrophages ingest and destroy the injected PPD, so that, elimination removes the stimulous for further lymphokines production, permitting the tissues to return to normal.

T.lymphocytes also, generate Lymphokines that attract basophils and cause local mast cells to degranulate. Histamine derived from these cells enhances the migration of mononuclear cells into the lesion.*(Tizard, 1984).*

The Tubercle Bacilli:

Mycobacteria posses a thick lipoidal wall which has a dual effect. First, the wall render the organism impermeable, protecting it from an adverse environment, such as antibody or that found within phagocytic cells. Second, the cell wall components share in the induction of certain activities, some of which are helpful to the host in its effort to contain progression of disease, some of which cause tissue destruction. Virulent factors that permit the organism to escape the host's defence include:

a- Sulphatides, which are produced by mycobacteria and prevent the release of lysosomal enzymes into the phagosomes, and these present phargolysosomal fusion inside the macrophages which is an essential step in killing intracellular mycobacteria.

b- Mycosides, which form a shield around the organism .

c- The toxic cord factor.

(Chaparas, 1982)

I. Initial interaction between macrophages and mycobacteria:

In tuberculosis there is monocytopoiesis and premature release of monocytes occurs from the bone marrow. These monocytes are attracted to sites of inflammation, and mature into macrophages. These macrophages in tuberculous granuloma will then:

1. Become activated.
2. Leave the granuloma by lymphatic vessels.

(Dannenberg et al.,1975)

OR

3. Ingest tubercle bacilli.

If these macrophages are incapable of killing the tubercule bacilli, the bacteria replicate, and lyse the macrophages with release of bacilli from the disintegrated macrophages. The products of cells and bacterial debris are chemoattractans for circulating monocytes and polymorphs and in time the monocyte become the primary cell type at the site of the lesion ***"Lowrie, 1983"***

Lenzini et al., (1977) mentioned that macrophages once activated, they exhibit profound morphological changes; increased the number of mitochondria and lysosomes, increased activity, increased oxygen consumption, spreading, and phagocytosis and increased tuberculocidal activities.

Ewards and Kirkpatrik (1986) suggested that activation of macrophages is dependant upon the presence of lympokines.

II. Role of lymphocytes in cellular immunity to mycobacterial infection:

Dannenberg and tomashefski (1988) stated that the tubercle bacilli attract macrophages and lymphocytes to the site of infection. The macrophages process and present antigen to T-lympocytes (With receptors for the antigen); and also, produce the monokine, interleukin 1.

The antigen specific T cells respond by becoming activated and produce lymphokines. These lymphokines include chemotactic factors for macrophages and lymphocytes, macrophage - activating factors (such as y interferon), and mitogenic factors such as interleukin-2 which, like interleukin 1, also, causes T-cells to divide. Additional macrophages and lymphocytes are attracted to the site, where they, too, become activated and divide. Following infection, the tubercle bacilli multiply at the site of implantation and travel to the regional. lymph nodes, where a proliferative response occurs involving the T-lymphocytes (***Lefford, 1981***).

When lymphocyte replication reaches its peak, histological tubercles appear in the lymph nodes and the host exhibits delayed

hypersensitivity to tuberculin and become immune to tubercle bacilli. ***(North et al, 1972).***

Thus, in primary tuberculosis, the lesion at the site of infection may be invisible, while the draining lymph nodes are grossly enlarged ***(Lefford and Gregor, 1974).***

A work was done by ***Crowle and May, 1981; and perumal, 1981***, revealed that immunity to tuberculosis is lymphokine mediated i.e. the products of T-lymphocytes of immune subjects when exposed to mycobacterium tuberculosis will bring about the intracellular inhibition of growth of this bacterial species inside the macrophages. They added that the moiety of the immune lymphokines that are responsible for the inhibition of mycobacterial growth inside the macrophages is called ***"Mycobacterial growth inhibitory factor"***

Cahall and Youmans 1975; speculated that a lymphokine is produced by T-lymphocytes, when stimulated by mycobacterial antigen, that would either directly inhibit the growth of tubercle bacilli inside the infected macrophages or would indirectly inhibit their growth by some action on the macrophages. Of interest is their observations that:

(1) For inhibition of intracellular growth of virulent tubercle bacilli by the lymphocyte product, the infected macrophages had to be exposed to this material for at least three days. Less time