IMMUNOLOGIC ORCHITIS AND ITS RELATION TO MALE INFERTILITY

Thesis

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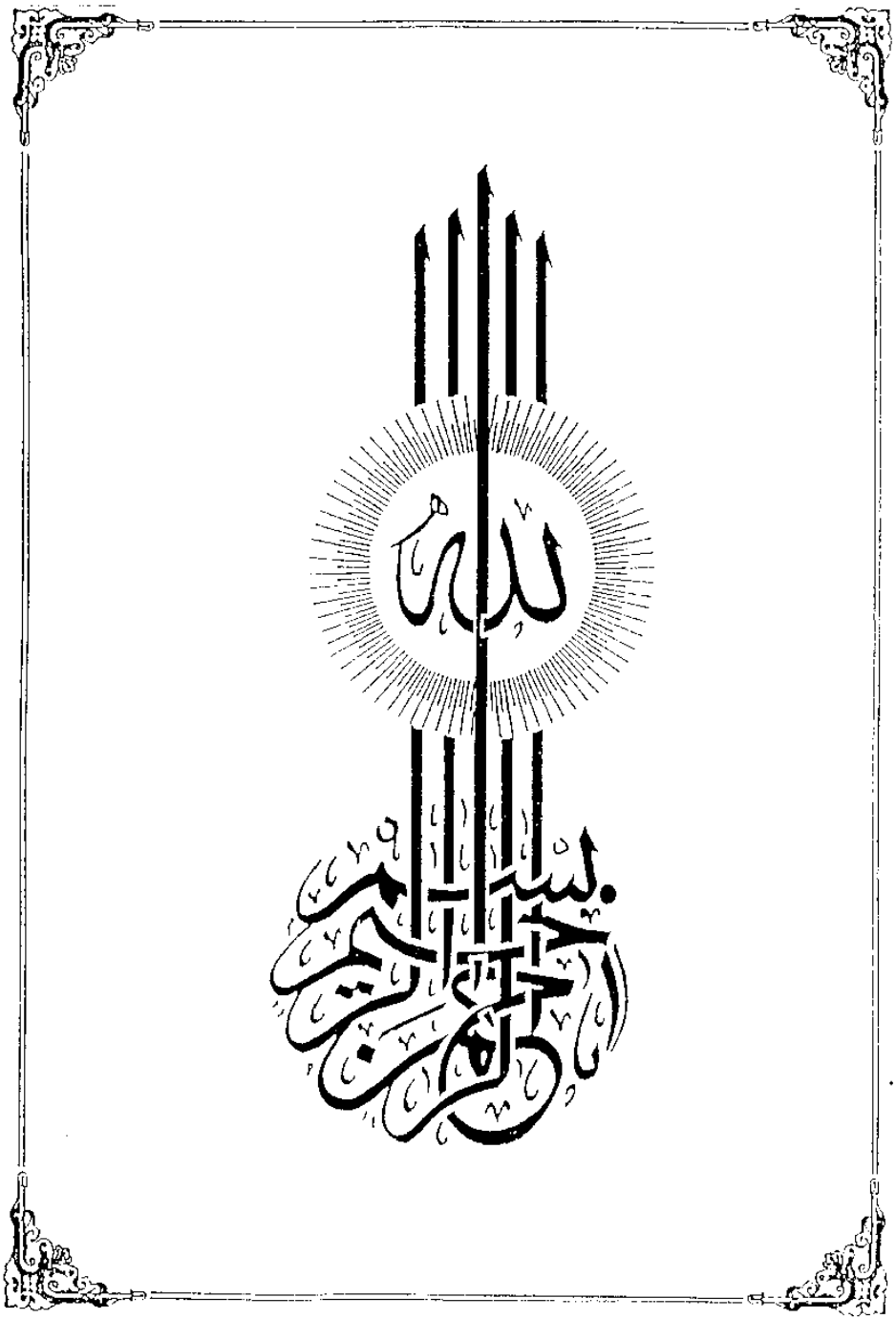

THIS WORK IS DEDICATED TO
MY PARENTS AND MY WIFE

C O N T E N T S

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INTRODUCTION
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Testicle is the factory of sperm formation in the body and any abnormality in testicular tissue leads to abnormal spermatogenesis.

Immunologic reactions against testicular tissue lead to its destruction and disturbance of its function. Infertility due to immunologic orchitis stands to be an interesting research subject .

In this thesis we will throw a light on immunologic reactions that occur against testicular tissue , and its sequilae.

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REVIEW OF LITERATURE

1. BASIC IMMUNOLOGY

The immune system :

One of the characteristic features of the adult vertebrate is its ability to distinguish between its own normal constituents (self) and those of external or foreign origin (non-self). Damaged or degenerated tissue components are included in this group of non-self substances. The reaction to foreign substances involves the elimination of the foreign material, and is an important homeostatic mechanism . Because the response is a protective mechanism, it has been called the immune response. The immune response is a reaction to foreign material which results in the formation of antibodies which may be either immunoglobulins or cell - bound. Two separate systems are involved. The lymphoid tissue associated developmentally with thymus is responsible for the production of cell bound antibodies , while the immunoglobulins are synthesized in cells which are associated with the gut (Walter and Israel, 1979).

The cells of immune system are the macrophages and lymphocytes. Macrophages have an essential role in concentrating and presenting antigens to lymphocytes. They determine which T-cells will be induced to stimulation by

various antigens. They secrete active mediators that regulate type and magnitude of T and B lymphocyte responses. Also they play a key role in antigen processing (Unanue , 1972).

Lymphocytes are the antigen specific cells acting via receptors on the surface membrane of every immunocompetent cell. Each receptor is specific and various classes of lymphocytes express their own specificity (Katz, 1983).

Two distinct types of lymphocytes have been identified ; T lymphocytes and B lymphocytes.

T lymphocytes :

They are 2 main types, regulatory and effector T lymphocytes. Regulatory T lymphocytes include helper and suppressor cells. T and B lymphoyctes can act independently as well as in co-operation to produce an immune response. Sepcific antigen receptors exist on the surface of both T-cells and B-cells. Certain antigens can directly stimulate the B-cells to produce plasma cells and antibody ; other antigens require the interactions of T-cells (helper cells) which provide specific and non specific helper substances that will allow the B-cell to mature to produce

antibody. A separate population of T-lymphocytes can also act to suppress the immune response i.e. suppressor T - lymphocytes. This appears to involve active processes in the suppression of helper T-cells (Bellanti, 1978).

Effector T-lymphocytes are responsible for cell mediated immune reactions as delayed cutaneous hypersensitivity and rejection of foreign tissue grafts (Cerrotini and Brunner, 1974). Cytotoxic T lymphocytes referred to as "killer cells" are responsible for these cell mediated reactions (Kimball, 1983).

B lymphocytes :

They are classified into various subclasses on the basis of the different immunoglobulins they senthesize . B-lymphocytes senthesize all classes of circulating immunoglobulins (IgM, IgG, IgA and IgE) (Moller, 1973).

The immune response is either humoral immune response or cell mediated immune response.

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Humoral Immune Response :

It happens by synthesis and release of antibodies by B lymphocytes and plasma cells on antigenic stimulation. The proteins that function as antibodies are called immunoglobulins.

Immunoglobulins are glycoprotein molecules that combine specifically with the antigen. They are found in variable proportions in extravascular fluids , and exocrine secretions (Lanim, 1976).

IgG is the major immunoglobulin of the secondary immune response and its importance is due to its ability to diffuse into almost of the body tissues to interact with the antigen (Thaler et al., 1977).

It can perform various biological functions according to its subclasses. IgG_1 and IgG_3 can cross the placenta, fix complement and bind to macrophages. IgG_2 does not cross the placenta nor it strongly fix complement or bind macrophages. IgG_4 can cross the placenta and does not significantly fix complement (Thaler et al., 1977).

IgM is the major Immunoglobulin of the early part of the primary humoral response. It has the greatst capacity for complement fixation than the other immunoglobulins (Metzger, 1970). It is present in high concentrations at the secretory surfaces as a secretory IgM (Goodman , 1983). It does not cross the placenta.

IgD is normally present in serum in trace amounts. It has a special antibody activity against certain antigens, including insulin, penicillin, milk proteins, diphtheria toxoid, nuclear antigens and thyroid antigens . IgD (with IgM) is the predominant immunoglobulin on the surface of human B lymphocytes (Goodman and Wang, 1978).

IgE is involved in the allergic diseases. It comprises only 0.004 % of the total serum immunoglobulin but binds with very high affinity to mast cells. Upon combination with certain specific antigens called allergens, IgE antibodies trigger the release from mast cells of pharmacologic mediators responsible for the characteristic wheal and flare skin reactions evoked by exposure of the skin of allergic individuals to allergens (Goodman and Wang, 1978).

IgA is the major immunoglobulin of the secretory immune system and it is the dominant immunoglobulin in the external secretion. It plays a key role in providing initial protection against external pathogens (Lanim, 1976).

Immunoglobulins in addition to binding specifically to antigens, initiate some other biological activities independent of the antibody specificity. They direct blind processes i.e. transfer across membranes, cell binding immunoglobulins and complement fixation (Spiegelberg , 1974).

Complement fixation :

The complement system is the primary humoral mediator of antigen-antibody reactions. It consists of chemically and immunologically distinct plasma proteins capable of interacting with each other, with antibody and with cell membranes.

After activation of the system these interactions lead to the generation of biologic activity which ranges from lysis of a spectrum of different kinds of cells , bacteria and viruses to mediation of inflammatory processes.

Complement is also able to enlist the participation of other humoral and cellular effector systems and induce histamine release from mast cells, migration of leucocytes, phagocytosis and release of lysozomal constituents from phagocytes (Cooper, 1983).

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