IMMUNE COMPLEX DISEASES

THESIS

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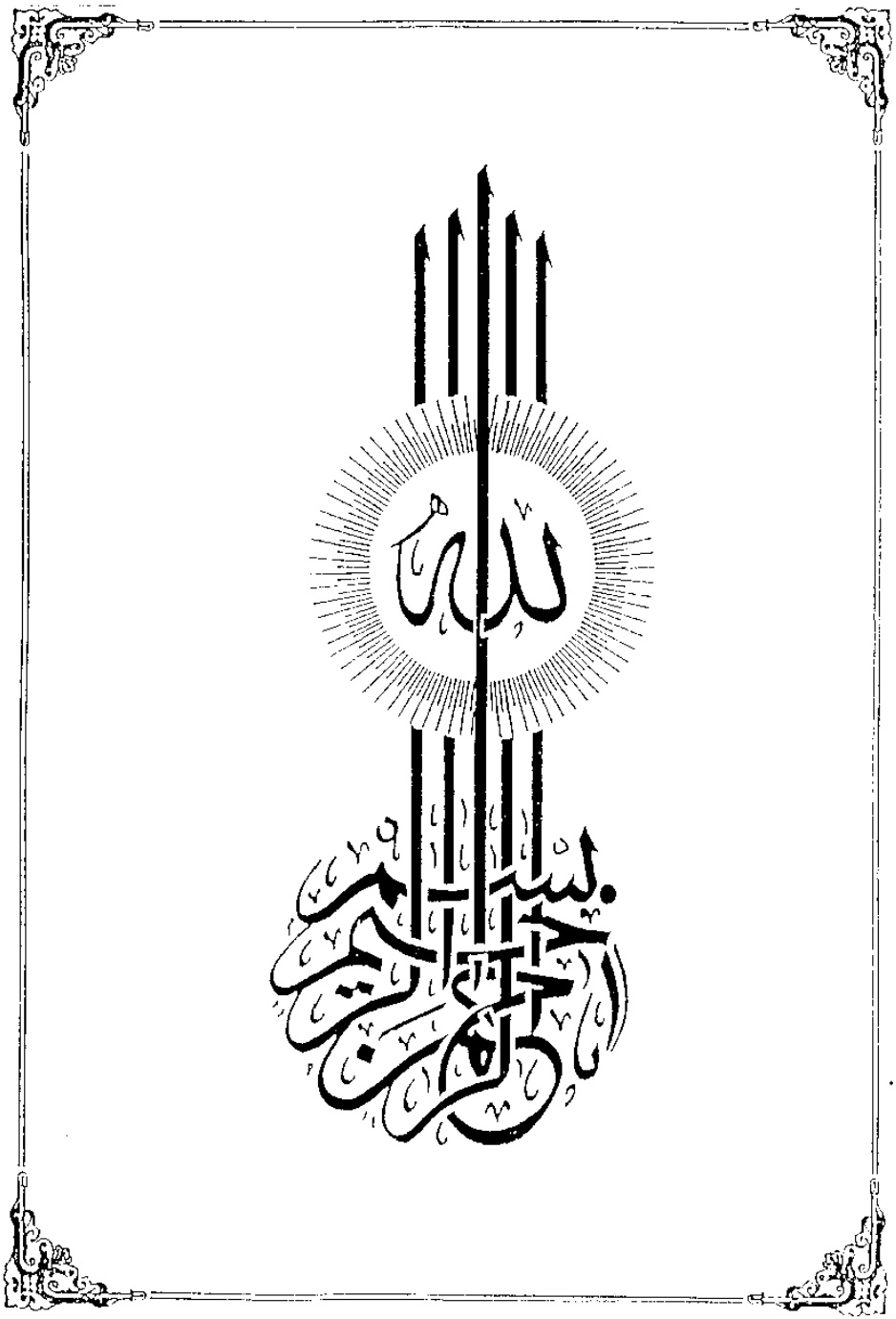

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In the following thesis we will discuss the various immune complex diseases in the various organs of the body and its immunologic pathogenesis.

It also include a chapter about the methods used for detection of immune complexes, we will know that many diseases that was believed to be due to various causes are attributed to immune complex pathogenesis.

HISTORICAL BACKGROUND OF IMMUNOLOGY

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(Foster WD, 1970) & (Fudenberg Hetal, 1976)

Immunology is relatively a young branch of medical science. For many years immunology was studied as part of microbiology and progress in the field consisted mainly of application of what had been learned about immunologic phenomena of the problem of diagnosis and control of bacterial infections. The explosive increase in fundamental information has made immunology an independent branch of medical science.

Jenner started medical immunology by introducing vacination with cowpox in (1796) as means of protection against smallpox. Later, as a consequence of the work on microbes by louis Pasteur (1822-1895) and his collaborates. They investigated the possibility of protection against infection by vaccination of attenuated strains of microorganisms. The idea of using attenuated strains of microorganisms was confirmed by Pasteur when he studied vaccination against anthrax (1881).

Richet and Hericourt concluded in (1888) that the blood of an animal immunized with staphylococci confined

partial protection against subsequent inoculation with these microorganisms. The specificity of the protective effects of immunization had already been observed by Pfeiffer in (1889).

The term antigen was introduced to designate any substance capable of inducing a reaction against itself and the illogical term antibody to designate the factor present in the serum pocessing this activity. The precepitin reaction was described later by Kraus in (1897) with microbial culture supernates and the serum of immunized animals. The term sensetizer was used by Bordet to denote the thermostable serum component reacting in the lysis of bacteria. In (1900) Bordet established the reaction which he designated alexine (complement) fixation. In (1901) he described this general principle which is still valid and useful and which was first applied by Wassermann. Neisser and Bruck in (1906) in the diagnosis of syphilis.

At the close of the 19th century all the immunologic phenomena observed to that time supported the view that they were defensive mechanisms. It had already been shown by Wassermann and von Dugern that second challenge of a previously immunized individual by the same antigen increased the antibody activity in its serum. Thus the fact of

immunologic memory had to be explained. The phenomenon of anaphylaxis was then discovered by Charles Richet and Portier in (1902).

The next year Arthus described what is now known as Arthus phenomenon. i.e. the local necrotic lesion produced by injecting antigen into previously immunized animal. At the begining of the 20th century Von pirquet studied serum sickness. He suggested that this reaction had a direct connection to the presence of antibodies to the injected serum in the animal.

Hay fever was a recognized disease entity for a long time, but until the beginning of this century, it was belcived to be due to toxic substances in polliens. Shortly thereafter Wolf-Eisner suggested that hay fever might be a hypersensitivity reaction. The role of histamine and related substances in inflammatory and anaphylactic reactions was studied by Dal and Laidlaw in (1910). Lewis (1927) explained tripple response in skin reactions and Riley and West (1953) discovered that histamine is present in mast cells and is released by the breakdown of these cells.

Identification of Immunoglobulins

Felton was the first to obtain purified preparations of antibodies. The practical isolation of pure antibodies from sera was achieved by Heidelbarger and Kendall (1936).

As a result of studies with ultracentrifugation (1937) and with electrophoresis in liquid media (1938) it became clear that antibodies belong to that globulin fraction of the serum proteins pocessing slow mobility and designated (gamma) globulins.

Studies on the cellular aspect of immunology had confirmed the role of white blood corpuscles in the formation of antibodies.

Pfeiffer and Marx found that antibodies appear earlier in the spleen, lymph nodes and bone marrow than in the blood.

Recent Period of immunology

In (1948) Astrid Fagraeus showed that it is through the development of plasma cells that the actual synthesis of antibodies takes place. In (1953) Grabar and Williams demonstrated that immunoglobulins are heterogenous and detected the existance of IgA.

The central role of the thymus in immunologic process was first clearly established by experimental studies performed by I.f.A.P Miller in London in (1961 - 1962).

The last few decades have seen the emergence of new branches in immunology.

1) Immunopathology studies of pathologic processes have in many ways helped to understand normal ones.
2) Immunogenetics has included analysis of amino acid sequences in immunoglobulins, histocompatability antigens and genetic markers on immunoglobulins.
3) Tumour immunology: Include the absence of various normal components on tumour cells, the appearance of antigens present normally in foetal life or in tissues other than that ones in which tumour has developed and existance in some tumours of neoantigens.
4) Transplantation immunology Emerged from work on acquired tolerance. Since regection of grafts is an immunologic phenomenon dependent mainly on the thymus. Chemical substances and antithymocytes immune sera are being used as immunosuppressive agents.

5) Immunologic Disorders: Concerned both with broad spectrum and antigen selective immunodeficiency and method of immune therapy for these disorders.

Further the development of technics and instruments with development of immunologic methods have made possible the discovery of entire new fields of study and have made large contributions to immunology and other branches of seience.

Immune mechanisms in tissue damage:

Traditionally it has been thought that a major stimulus to the development of these immune responses is protection against micro-organisms which threaten the welfare of the host. It is clear however that these protective immune responses also may prove deleterious to the host as in the case of autoimmune disorders. Thus immune responses to an infecting organism may eradicate the organism but at the same time produce significant pathologic or even lethal effects in the host. Pathogenetic mechanisms that produce both beneficial and deleterious effects will be described as immune mechanisms, that cause tissue damage.

Various immune mechanisms involved in the production of tissue damage were classified in (1963) by Gell and Coombs into 4 basic types

Type I Anaphylactic

Type II Cytotoxic

Type III Arthus type and antigen antibody complexes

Type IV Delayed hypersensitivity.

Type I Reactions

Type I reactions are produced by pharmacologically active substances released from tissue cells such as basophils and mast cells following reaction between antigen and specific antibody adsorbed to the tissue cell membrane. Depending on the mode of application of antigen, the clinical features may be systemic or local.

Type II Reactions

Type II reactions are classically considered to be cylotoxic in character and involve the combination of IgG or IgM antibodies with antigen determinants on a cell membrane.

Alternatively a free antigen or hapten may be adsorbed to a tissue component or cell membrane and antibody subsequently combines with this adsorbed antigen. Complement fixation frequently occurs in this situation and

leads to cell damage. There are situations however particularly in the experimental studies where the combination may in fact lead to stimulation of the cell. Some examples are long acting thyroid stimulator (LATS). antilymphocyte antisera and anti immunoglobulin antisera.

Type III Reactions

These reactions are secondary to localization of antigen antibody complexes in tissue and inflammation is the main feature. Classical reaction of this type are the Arthus reaction and serum sickness similar sequences of events occur in both examples and also in immune complex diseases, now increasingly recognized in clinical medicine. The pathogenesis of the characteristic inflammatory lesions in type III reactions in summarized in the following table.

Pathogenesis of inflammatory lesions in type III reactions:-

1) Formation of antigen-antibody complexes (generally in antigen excess).
2) Fixation of the complement by the complexes.
3) Release of complement components chemotactic for leucocytes.
4) Damage of platelets causing release of Vaso active amines.