REVIEW ON THE RELATIONSHIP BETWEEN BLOOD PLATELETS AND ALLERGY

Thesis
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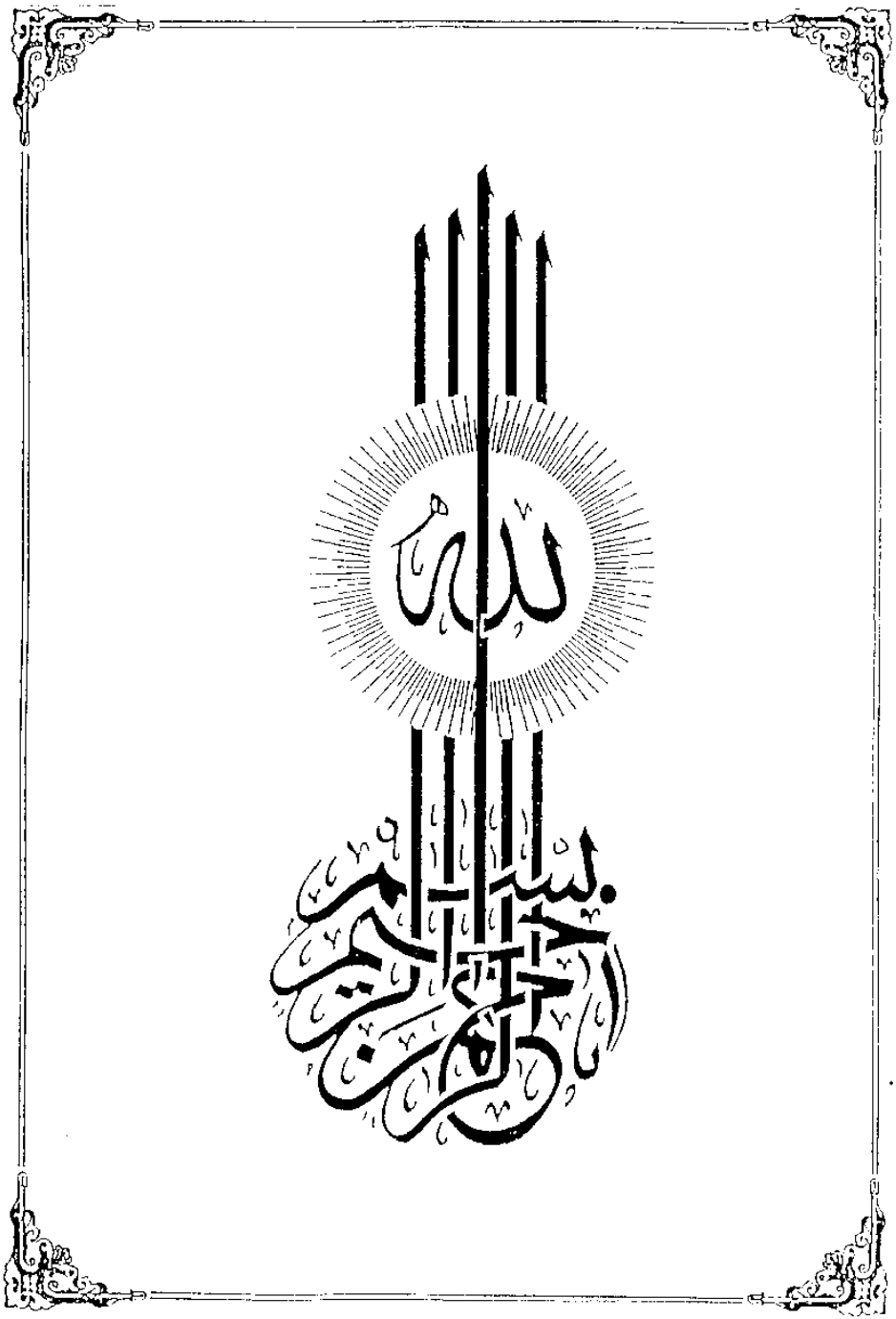
DEDICATED TO MY PARENTS

WHO GAVE TOO MUCH AND RECEIVED TOO LITTLE



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CONTENTS

INTRODUCTION AND AIM OF WORK

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Data reporting a role played by platelets in the induction of allergy are accumulating. An ether-linked analogue of phosphatidylcholine was described as a platelet-activating factor by Benveniste et al. (1972). It is now referred to as PAF-acether and was implicated as an important mediator in the induction of bronchial asthma (Morley et al., 1984). Day et al. (1975) showed that intradermal injection of supernatants from activated human platelets, but not leucocytes, induced delayed, sustained responses.

Sodium cromoglycate was shown to inhibit this response (Basran et al., 1983). This inhibitory action of sodium cromoglycate extends the relationship between the platelets and skin to cover all the allergic reactions in the human body.

This review aims at collection of literature covering this subject and evaluation of the possible role of platelets in the induction of allergic attacks.

HYPERSENSITIVITY

* CLASSIFICATION OF HYPERSENITIVITY REACTIONS
* ANAPHYLAXIS
* LOCAL ANAPHYLAXIS (ATOPY)
* TARGET CELLS OF IG-E MEDIATED ALLERGIC REACTIONS
* MEDIATORS OF IMMEDIATE HYPERSENSITIVITY
* APPROACHES TO TREATMENT OF TYPE I HYPERSENSITIVITY

HYPERSENSITIVITY

Stimulation of the immune response results in a wide variety of hypersensitivity responses. An understanding of these responses and their potential treatment can be facilitated by a classification that emphasizes mechanisms of hypersensitivity. The classification discussed below is based on the familiar classification originally proposed by Gell and Coombs (Beall, 1983).

Gell and Coombs (1968) suggested a classification of four types of hypersensitivity reactions based on the mechanism of tissue destruction and the immunologic reactants involved. Some types of immune tissue damage do not fit into the Gell and Coombs classification. So, Roitt (1974) has proposed a type V designation to include the reaction typified by antibody against thyroid cells that presumably stimulates these cells in a manner similar to a thyroid-stimulating hormone. Another type has emerged from type IV is antibody-dependent cellular cytotoxicity (ADCC), in which cytolysis of antibody-coated-target cells by non-immune effector cells occurs.

Types, I,II,III,V depend on the interaction of antigen with humoral antibody and tend to be called "immediate" type reactions although some are more immediate than others. Type IV involves receptors bound to the lymphocyte surface and

because of the longer time course this has been referred to as "delayed" type sensitivity (Roitt, 1974).

In immunology, the terms "allergy" and "hypersensitivity" are customarily used as synonyms (Barrett, 1980).

The term "allergie" was proposed by Von Pirquet (GK allos "other" + ergon "work") in 1906 to denote an immune deviation from the original state or a "changed reactivity" of an individual. An allergic individual is the one who deviated from the expected immunologic response. Von Pirquet included all forms of altered immunologic responsiveness, encompassing reactions to toxins, bacteria, and other infectious agents, pollen hay fever, and urticaria produced by foods (Frick, 1982).

Classification of Hypersensitivity Reactions

1. Type I, Hypersensitivity (Immediate)

Type I, immediate allergy is mediated by antibodies which sensitize mast and basophil cells. When this antibody combines with its specific allergen, mediators of tissue reaction such as histamine and slow reacting substance (SRS.A) are released (Roitt, 1977). The consequences of the released of these mediators depend on the location of the excited mast cells and hence, on the route by which antigen reaches the body.

Antigen absorbed through mucous membranes promotes local reactions, such as itching, nasal congestion, and sneezing of allergic rhinitis or the bronchospasm and increased secretions of asthma. Systemically administered antigen can cause mediator release from mast cells in many organs and in consequence, generalized reactions such as anaphylaxis (Beall, 1983).

So the term immediate hypersensitivity denotes an immunologic sensitivity to antigen that manifests itself by tissue reactions occurring within minutes after the antigen has combined with its appropriate antibody. Such a reaction may occur in any member of a species (anaphylaxis) or only in certain predisposed or hyperreactive members (atopy) (Frick, 1982).

2. Type II, Hypersensitivity (Cytotoxic sensitivity)

Antibodies damage cells or tissues when they react with an antigen on those cells or tissues. The antigen may be a normal part of a cell surface, it may be revealed after alteration of the surface, or it may be a chemical or viral particle that has become fixed to the tissue. Antibodies are usually of the IgG or IgM type. Damage to the tissues occurs either through activation of the complement system or through macrophages activated by the binding of antibody to their Fc receptors. This latter process is one form of antibody-dependent cell-mediated cytotoxicity (Beall, 1983).

There are many examples of these cytotoxic or cytolytic reactions which are brought about by an immune reaction to a foreign substance which becomes attached to the cell membranes of erythrocytes, leucocytes or platelets. One of the best known examples of this phenomenon is Sedormid (apronal) purpura (Weir, 1981).

Type II, hypersensitivity reactions are difficult to control. Prevention (e.g. in the use of RhoGAM to clear Rh-positive cells from the susceptible mother to prevent sensitization) appears to be the best form of therapy. Antibody titres can be decreased slightly with large doses of corticosteroids or cytotoxic agents. This can work in those conditions where antibody production is short-lived. Removal of the antibodies and possibly of the antigen by plasma pheresis may also be effective if rebound increase in antibody formation can be prevented with cytotoxic agents and if there is reason to believe that stimulation of production of the abnormal antibody will subside (Beall, 1983).

3. Type III, Hypersensitivity (Immune complex diseases)

This type of reaction is due to the presence of precipitating antibodies forming complexes by combination with its antigens in the circulation or interstitial fluids. Soluble toxic immune-complexes will be formed with a moderate excess of antigen. Such complexes fix the first component of complement and by enzymatic activation of the third component. This leads to the release of a fragment of C_3

termed C_{3a} which is an anaphylatoxin and which in turn is capable of causing histamine release with a subsequent tissue reaction. This is the theoretical basis of the non homocytotropic IgG-dependent asthmatic response. The aggregate of immune-complex plus activated complement is chemotactic for polymorpho-nuclear neutrophil cells. The ingestion of the enzymatic immune-complexes leads to destruction of the neutrophil possibly other macrophage cells with the liberation of their cytoplasmic lysosomes into the tissues with consequent tissue damage. Also platelets may be aggregated with two consequences, they provide further source of vasoactive amines and may also form microthrombi which can lead to local ischaemia. It has been found that corticosteroids exert a protective effect on the phospholipid membrane of the lysosomes and this may explain at least in part how they exert their marked inhibitory effect on type III reaction (Roitt, 1977).

There are two types of reaction which fall into this category: serum sickness which is a systemic form and the Arthus reaction which is a local form (Weir, 1981).

Numerous methods of detecting immune complexes are available. Most of these methods for detecting immune complexes are dependent upon detection of aggregated antibody and, hence, do not identify the antigen involved (if one is present) in aggregating the antibody. In general, ways of detecting immune complexes rely on the physical means or on

the activation of complement components. Large amounts of immune complexes can be recognized as cryoglobulins. Immune complexes can also be precipitated from the serum with appropriate concentrations of polyethylene glycol. Immune complexes can be detected more sensitively by their binding to CIq or to the lymphoblastoid cell line, the Raji cell, which has C_{3b} receptors that can be used to detect immune complexes binding C_{3b}. The Raji cell assay and CIq binding are the most widely used of these methods.

Attempts to control immune complex disease have usually made use of anti-inflammatory compounds, particularly corticosteroids. Cytotoxic drugs, such as azathioprine and cyclophosphamide, have also been used. These agents probably inhibit the cellular response to the immune complexes and hence, ameliorate hypersensitivity (Beall, 1983).

4. Type IV, Hypersensitivity (delayed)

This reaction appears within 24-48 hours and may persist for several days. It consists of a firm induration surrounded by oedema of the skin and underlying tissues. The area of induration may be vesicular or necrotic according to the intensity of the reaction. This reaction is mediated by thymic derived T-lymphocytes bearing specific receptors on their surfaces. These T lymphocytes are stimulated by contact with antigen and release lymphokines which recruit non sensitized lymphocytes to the test site.

This type of reaction is taken as evidence of the capacity of the T cell lymphocytes system of the body to react and of the body to resist infection. There is general acceptance that the delayed hypersensitivity is mediated by cells and not by circulating antibodies (MacFarlane, 1969).

The activities of lymphokines (protein materials) are usually expressed either on other T-cells or on macrophages. A prominent example is the expression of macrophage inhibitory factor, a material that inhibits the migration of macrophages and may possibly account for the accumulation of mononuclear cells in the local tuberculin skin test site. Some of the T cells that encounter antigen are also triggered to cytotoxic activity. Such cytotoxic activity may be expressed directly by the T cell or through a secreted cytotoxic lymphokine, lymphotoxin (Beall, 1983).

The classic examples of type IV hypersensitivity are the reactions encountered in contact dermatitis where the allergens are introduced by patch test and the reaction to tuberculin introduced into the skin by scratch or prick test or by intracutaneous test.

The type IV reaction is characteristic of the allergy of infection and is elicited by protein antigenic components of the infecting agent.

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