ALLERGIC REACTIONS DURING ANESTHESIA

Thesis

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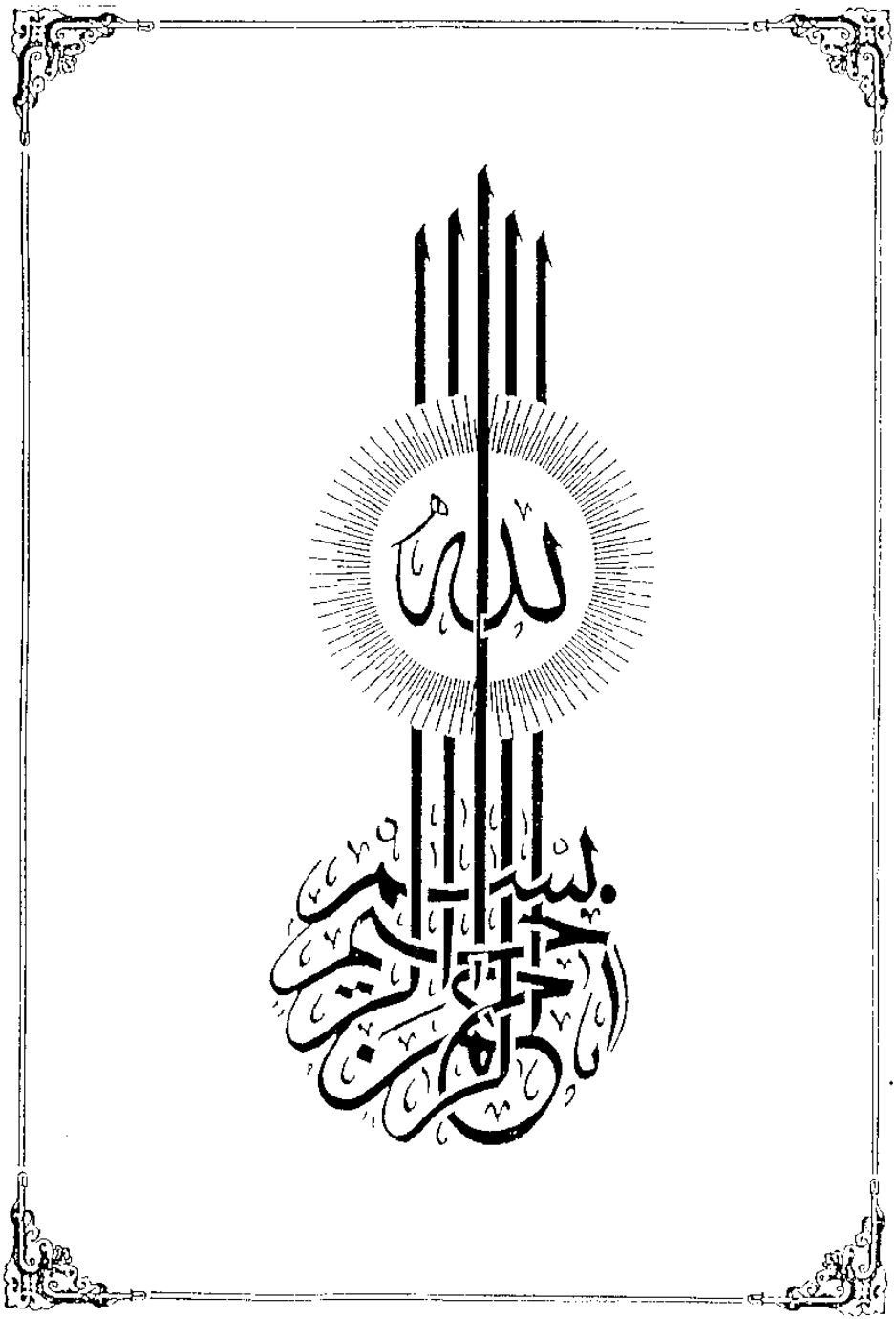

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INTRODUCTION

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The immune system represents a series of complex cellular and humoral elements that function to protect the body against external micro-organisms and toxins as well as internal threats from neoplastic cells.

The immune system can also respond inappropriately to drugs and other foreign substances to cause hypersensitive (allergic) reactions. Allergic reaction observed during anesthesia and in the intensive care unit may represent different aspects of the immune response.

Hypersensitivity reactions in anesthetic practice are of increasing interest as other complications which were once common, but have been avoided by improved techniques. At the same time continuous study of the mechanisms and predisposing factors has not reduced their frequency. Reports by Levy M. in 1979 showed that the incidence of allergic reaction during anesthesia seems to be steadily increasing due to a widespread employment of drugs during the intraoperative period as well as to cross sensitivity between drugs.

The anesthesiologist represents one of the few physicians who personally administers a variety of agents including anesthetic drugs, antibiotics and blood products.

Because any parenterally administered agent can cause death from an allergic reaction, anesthesiologists must diagnose and treat the acute cardiovascular and pulmonary changes that occur in anaphylaxis, the most severe form of an allergic reaction.

PATHO-PHYSIOLOGY OF ALLERGIC REACTIONS

PATHO-PHYSIOLOGY
Of Allergic Reactions

An allergic reaction following the administration of a drug can occur unpredictably in any patient.

The drug responsible for eliciting an allergic reaction is referred to as an allergen or antigen. Despite the unpredictability of an allergic reaction, there is an agreement that patient with history of chronic atopy (bronchial asthma, drug allergies, food sensitivities) are more likely to experience allergic reaction to drugs administered intravenously during anesthesia (Van Arsdel, 1982, Altman, 1981).

Increased susceptibility in atopic patient is due to a genetic predisposition to produce increased amount of IgE.

In these patients the concentration of IgE antibodies is usually chronically elevated, while in normal persons these are present in trace amount.

The response of immune system to foreign materials can be divided into two broad categories:

1. The celllular immune response

Which is mediated by cells of reticuloendothelial system and is especially effective against invading micro-organisms, cancer cells and foreign tissues.

2. The humoral immune response

Which is provided by the circulating antibodies of blood plasma.

The immune system is characterised by two main basic features which are memory and specificity.

Initial exposure to an antigen evokes specific antibody production (primary response) and the antigen is eliminated by contact with these antibodies. The primary response leaves the host prepared for further exposure to the same or sometimes closely related antigen. Re-exposure results in a more rapid and profound secondary response.

The mechanisms of antigen destruction by components of the immune system can be considered to occur in four stages. The immune system must first discriminate between endogenous and exogenous proteins.

Failure of this mechanism results in antibodies directed against host tissues and these auto antibodies may be responsible for a wide variety of auto immune diseases.

The immune system must then localize and destroy the foreign invaders. These are the processes that involve not only antibodies and lymphocytes but also several plasma proteins that together form a defense mechanism termed the complement system.

Introduction of the foreign antigens with components of the immune and complement systems produces biologically active substances that amplify immunologic recognition. Such substances enhance local vascular permeability and vascular stasis and chemotactically attract phagocytic circulatory cells to the local sites of immune reactions; these processes produce a localized inflammatory response and recruited cells then ingest and degrade the antigens.

By immune response we mean the development of specifically altered reactivity following exposure to antigen (Herbert and Wilkinson, 1977).

Antigens are classified into true antigens and incomplete antigens or "Haptens".

Many classifications were made for defining the mechanisms of immune response. Gell and Combs first proposed a scheme in 1963 for classifying immune response. Although the classification is an old one, yet it is useful for understanding hypersensitivity mechanisms. They classified immune responses into four types as shown in (Table 1).

There are five major classes of immunoglobulins (Ig) found in humans. Each class of immunoglobulin is functionally and structurally different. Each molecule of immunoglobulin (Ig) has four polypeptide chains, two heavy (H chains) and two light (L-chains) held together by three disulphide bonds.

The heavy chain contains the specific antigenic determinant of the molecule, consequently each class of immunoglobulin has a unique heavy chain. The two species of light chains are designated Kappa (K) and Lambda (λ). The five species of heavy chains designated alpha (α), gamma (γ), delta (Δ), epsilon (ε) and mu (μ); which characterize the five major classes of immunoglobulins respectively, namely IgA, IgG, IgD, IgE and IgM (Powell and McConkey, 1982).

Immuno-globulin Class	Serum Concentration (mg/100ml)	Molecular Weight	Half Life (days	Characteristic Properties
IgG (total)	Range (900-1800)			*Precipitins
IgG_1	900	146,000	23	*Antitoxins
IgG_2	300	146,000	23	*Complement fixation (except IgG_4)
IgG_3	100	165,000	8-9	
IgG_4	50	146,000	23	*Late Antibody *Placenta transfer (except IgG_2)
IgA	156-294	160,000	6-8	*Mucous membrane surface protection
IgM	67-134	900,000	5	*Agglutinins *Opsonins *Early Antibody
IgD	0.3-0.4	184,000	2.8	*On surface of B-lymphocyte
IgE	0.0001-0.0007	196,000	2.5	*Antibody to Allergens

(Ketchum, 1984)

The following table shows the difference between the immunoglobulins as regard molecular weight, serum concentration, half life in serum and characteristic properties.

Mechanisms for Allergic Reactions:

The four mechanisms responsible for an allergic reaction during or after administration of a drug are:

1. Anaphylaxis (type I hypersensitivity, immune-mediated hypersensitivity).
2. Classic pathway activation of the complement system.
3. Alternate pathway activation of the complement system.
4. Anaphylactoid (pharmacologic, direct histamine release) (Beaven, 1981).

Anaphylaxis: (Type I hypersensitivity)

Anaphylaxis takes place after previous exposure to the drug or chemically related substances and the production of antibodies. The reaction is produced by pharmacologically active mediators released by degranulation of mast cells or

basophils, following interaction between specific antigens and antibodies of IgE on the surface of tissue mast cells or blood basophils.

Anaphylaxis requires previous exposure to the drug or a chemically similar substance and the production of antibodies. Since drugs below a critical molecular size do not seem able to induce drug-specific antigen formation, i.e., not competent to induce an antibody response on their own, these are termed incomplete antigens or "Haptens".

Haptens or incomplete antigens are substances usually simple chemicals which are unable alone to induce an immune response, so the drug (hapten) must combine with a macro molecule such as a protein and sensitization occurrs to the drug-protein complex, the provoked response is finally specific for the hapten (Weir, 1977). In case the intact drug is not compatible to bind to protein, it is possible that a degradation product of the drug with a chemically reactive group can combine with the protein.

This hapten-protein complex induces a B-lymphocyte to proliferate and differentiate into a clone of plasma cells capable of synthesizing and secreting thousands of identical IgE antibodies to that particular drug. Mast cells present