THE ROLE OF IMMUNOGLOBULIN (E) AND EOSINOPHILS IN SOME KIDNEY DISEASES

THESIS

SUBMITTED FOR PARTIAL FULFILMENT

OF MASTER DEGREE

GENERAL MEDICINE

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CAIRO - EGYPT

1985

ACKNOWLEDGMENT

I would like to express my deep gratitude to Dr. Badawey Labib Mahmoud, Assistant Professor of Medicine, Ain Shams University for his keen supervision, fruitful guidance and patience offered to me during the progress of this work.

I am also endebted to Dr. Nabeel Aziz Shoukry, Assistant Professor of Medicine, Ain Shams University for his generous advice and inspiring opinions and for his leading remarks especially in the practical aspects.

I wish to thank Dr. Mouhamed Ramadan Badar , Assistant Professor of Medicine, Ain Shams University for his kind help and guidance and valuable suggestions.

Finally, I owe my thanks to Dr. Salah Tawfik and Dr. Hala Anwar for thier help during the measurements done in the practical part.

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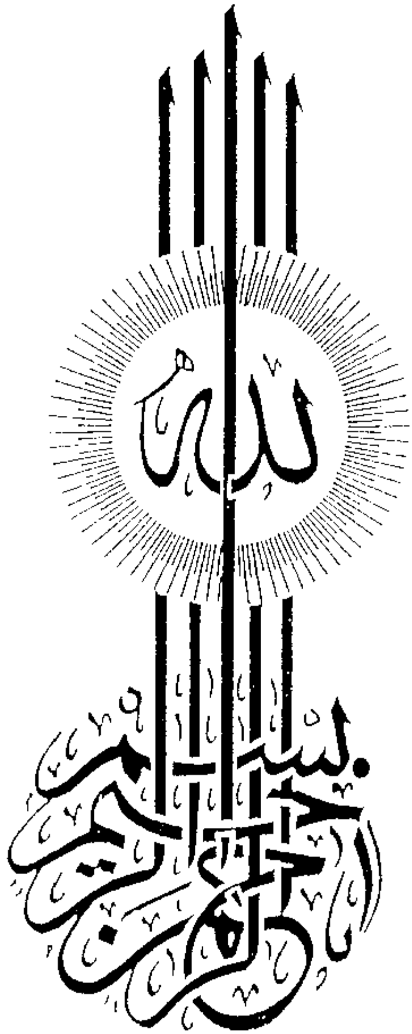
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ABBREVIATIONS

Ab : Antibody

Ag : Antigen

BSA : Bovine Serum Albumin

C : Complement

CMI : Cell Mediated Immunity

C3NeF : C3 Nephritic factor

DH : Delayed Hypersensitivity

ECA : Eosinophil Chemotactic Factor of Anaphylaxis

GN : Glomerulonephritis

GBM : Glomerular Basement Membrane

IC : Immune Complexes

Ig : Immunoglobulin

IgE : Immunoglobulin E

HLA : Human Lymphocyte (Leucocyte) antigen

MHC : Major Histocompatibility Complex

MCGN : Mesangiocapillary glomerulonephritis

P-K reaction : Prausnitz Kustner reaction (for immediate hypersensitivity)

SRSA : Slow Reacting Substance of Anaphylaxis .

INTRODUCTION
and
AIM OF THE WORK

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The recognition of the important role played by aberrant immunologic process in many forms of renal injury, especially those involving the glomerular circulation, constitutes one of the most significant conceptual advances made in the understanding of renal disease during the last quarter century (Glassock and Brenner,1980).

The immunopathogenesis of renal injury particularly the role of the immunoglobulin E which was not put under heavy studies as regards its relation to kidney disease, at the same time, the association of glomerular diseases with abnormal activation of the complement cascade (Wilson 1979) are points to be considered.

In experimantal animals, platelets, basophils, eosinophils and IgE antibody interact to bring about the release of vasoactive amines, at the same time, these complexes possess unique properties of evoking an inflammatory response at the site of deposition (Wilson,1979).

As the role of IgE and eosinophils were not greatly investigated for the purpose of a possible diagnostic value in investigating kidney diseases especially chronic ones.,

So the aim of this work is to elucidate whether there is any relationship between levels of IgE in some kidney diseases mainly attributed to immunological aetiology on one hand and the peripheral count of eosinophils of these patients on the other hand.

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REVIEW

OF

LITERATURE

THE GLOMERULUS , TUBULE , AND INTERSTITIUM :
STRUCTURE - FUNCTIONS ;

a brief review of the structure of the renal glomerulus will be helpful in understanding glomerular disease. The glomerulus is a vascular - epithelial organ designed for the ultrafiltration of plasma. Embriologically, it consists of an invagination of a capillary-containing mesenchymal mass into an epithelium lined sac, the Bowman's space. The epithelium that invests the capillary network (visceral epithelium) is incorporated into and becomes an intrinsic part of the filtration membrane , wheras the parietal epithelium lines the Bowman's space, the cavity in which plasma first collects.

From the capillary lumen to the urinary space, the filtering membrane consists of:

1- A thin layer of fenestrated endothelial cells, each fenestrum being about 70 to 100 nm in diameter.
2- a glomerular basement membrane (GBM) about 320 nm wide, with a central electron dense layer , the lamina densa and peripheral electron lucent layers, the lamina rara interna and externa.
3- Visceral epithelial cells(podocytes). Podocytes are structurally complex cells that possess interdigitating processes embedded in and adherent to the lamina rara externa of the basement membrane (striker;1970)

Adjacent foot processes(pedicles) are separated by 20 to 30 nm wide filtration slits, which are bridged by a thin diaphragm that, when viewed in face, exhibits an orderly structure with multiple repeating rectangular pores each about 4 by 14 nm, in the shape of a zipper (Radwell;1975) The glomerular basement membrane, a network of fibrillar material, is chemically a complex glycoprotein consisting of both relatively neutral collagen like glycopeptides as well as highly acidic sialoglycoproteins. The acidic glycoproteins are oriented towards the lamina rara externa and interna, in close relationship to the endothelial and epithelial cell coats, both of which also contain negatively-charged groups (Venkatchalam;1978)

The main function of the glomerulus is filtration. Two characteristics distinguish glomerular filtration from transcapillary exchange in other organs:

1- The glomerulus almost completely excludes plasma proteins of the size of albumen (MW ± 70 000, radius 3.6 nm) and larger from the filtrate.
2- It exhibits an extraordinarily high permeability to water and small solutes. The latter can be accounted for by the highly fenestrated endothelium and the presence of the epithelial slits, both of which allow free passage of fluid;

Physiologic studies indicate that the filtration of macromolecules across the glomerulus decreases with increasing effective molecular radius, approaching zero at radius of approximately 3.5 nm (Renkin; 1973). There is thus, a size-dependent permability barrier in the glomerulus from studies that emply particles visible under the electron microscope (e.g dextran). it appears that the glomerular basement membrane is the principal structure responsible for this size discrimination, although admittedly a pore of appropriate dimensions (3.5 nm) has not been resolved (Farquhar; 1975). Alterations in the structure and composition of the GBM are thus central to the leakage of proteins and blood cells characteristic of glomerular injury.

In addition to size, clearance studies using dextrans and protein molecules of different isoelectric points demonstrate that the glomerulus can descriminate among molecules according to their charge, allowing greater penetration of neutral and cationic molecules as compared to anionic molecules of the same size (Striker,1970). This charge-dependent restriction is important in the virtual complete exclusion of albumin from the filtrate, since albumin is an anionic molecule with isoelectric point of 4.5.

It is now clear that this charge restriction is dependent of the presence of the negatively charged sialoglycopro - teins, which tend to repel similarly charged molecules. It follows therefore, that any loss of this glomerular polyanion will result in increased filtration of anionic molecules such as albumin and, indeed recent evidence suggest that a defect in the glomerular polyanion may account for albuminurea in some renal disease.

Another important component of the glomerulus is the mesangium, also called the centrilobular or axial region The mesangium forms a branching supportive framework around which the anastomosing capillaries of the individual glomerular lobules ramify. It consists of stellate mesangial cells embedded in a basement membrane-like PAS positive glycoprotein - the mesangial matrix.
Mesangial cells are phagocytic, and the mesangium is thought to have a clearing function for macromolecules that may leak across the glomerulus, they also contain contrctile elements in their cytoplasm; by their contraction they are thought to modulate intraglomerular blood flow under physiologic conditions. In normal glomerulus the mesangial area is narrow and contains a small number of cells and scant matrix. However, mesangial cell hyperplasia and increased mesangial matrix are commonly seen in a variety of glomerular diseases (Robbins; 1979)

The tubules:

The structure of the renal tubular epithelial cells varies considerably at different levels of the nephron and , to a certain extent correlates with the functional capacity of the tubular segment. For example, the highly developed structure of the proximal tubular cells , with their abundant long microvilli (which appear in histologic sections as the brush border), numerous mitochndria , apical canaliculi , and extensive intercellular interdigitations , may be correlated with its major functions: reabsorption of two thirds of filtered sodium and water as well as glucose, potassium, phosphate, amino acids, and proteins. A sodium pump is thought to be located in the basal lateral labyrinth proximal tubular cells; operation of the pump is by the action of membrane-bound Na^+-K^+ ATPase and closely situated mitochondria, which supplies energy through oxidative phosphorylation. It is thus no surprise that the proximal tubule is particularly vulnerable to ischemic damage. Furthermore, toxins are frequently reabsorbed by the proximal tubules, rendering it also susceptible to chemical injury (Robbins; 1979)

The interstitium:

The renal interstitium is an important component of the kidney, since it appears to be the primary site of reactivity in a variety of renal diseases (Robbins; 1979) In the normal cortex, the interstitial space is compact, being occupied by the fenestrated peritubular capillaries and a small number of fibroblast-like cells, Any obvious expansion of the cortical interstitium is usually abnormal , this expansion can be due to oedema or infiltration with acute inflammatory cells, as in acute interstitial diseases, or may be caused by accumulation of chronic inflammatory cells and fibrous tissue, as in chronic interstitial disease (Becker,1968). The amount of mucopolysaccharide in the interstitial tissue of the medulla increases with age and in the presence of ischemia. The kidneys are innervated by both the cholinergic and adrenergic fibres from the autonomic nervous system (Norman; 1982) Nerve endings are present in the smooth muscle cells of the vascular tree and near the tubules, but the glomeruli are not innervated, sympathetic stimulation appears to be another determinat of renin secretion. Lymphatics occur in the renal cortex but not apparently in the medulla. Cortical lymphatics start as capillaries among the tubules and around intertubular arteries, from there, they follow the same course as major renal arteries towards the renal hilus.