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IMMUNOLOGICAL FACTORS IN THE PATHOGENESIS
OF MINIMAL - CHANGE GLOMERULONEPHRITIS

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<i>TCFC</i>	<i>T-colony forming cells.</i>
<i>THF</i>	<i>Thymic humoral factor.</i>
<i>TIN</i>	<i>Tubulo-interstitial nephropathy.</i>
<i>VLDL</i>	<i>Very low density lipoprotein.</i>
<i>VPF</i>	<i>Vascular permeability factor.</i>

INTRODUCTION

INTRODUCTION

Renal diseases may include damage to the glomeruli, the tubules or the interstitial tissue. It has been recently shown that many types of glomerulonephritis are caused by immunological mechanisms, which appear in one of two forms:

1. Immune complex disease.
2. Antiglomerular basement membrane disease.

(Ghally and Sherif, 1984).

It was suggested that the immunological involvement in such disease, can be mediated either by a humoral immune response, cell mediated immune response or a coordinated response of both limbs of the immune system derived from complementary T and B cell interactions (Prasad et al., 1972).

In contrast, minimal change glomerulonephritis (MCGN), which is the commonest cause of nephrotic syndrome in children, does not show a clear-cut immune basis in its pathogenesis as evidenced by the absence of depositions of immunoglobulins or complement in the glomeruli as judged by immunofluorescent techniques (Wilson et al., 1982).

Recently, it has been suggested that the disease could be produced by a systemic abnormality of T-cell function. This hypothesis was supported by the following observations:

1. The condition responds dramatically to immunosuppressive drugs.
2. Occurrence of MCGN during active Hodgkin's disease.
3. Increased susceptibility of MCGN patients to develop pneumococcal infections.
4. The demonstration of changes in lymphocyte transformation responses, suppressor cell activity and cytotoxicity to human kidney tissue in some patients with MCGN (Shalhoub, 1974 & Chapel and Haeney, 1983).

Giangiacomo et al. (1975) suggested cell-mediated immunity or immuno deficiency on the basis of elevated serum IgM level and reduced serum IgG level in some patients with MCGN.

Association of MCGN with atopy and increased serum IgE level was reported by several authors (Wittig and Goldman, 1970 & Yokoyama et al., 1985).

These facts in mind stimulated us to undertake this work, aiming at studying the role of immunological mechanism in the pathogenesis of MCGN. This includes

review of the literature regarding MCGN and the immunological role in its' pathogenesis. Also, estimation of serum immunoglobulins IgA, IgE, IgG, IgM and complement (C_3) levels in patients with MCGN, selected from the pediatric clinic of renal disease in Ain Shams University Hospital in Egypt.

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REVIEW OF LITERATURE

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ANATOMY OF THE KIDNEY

The following account on the structure of the kidney is based on the description given by Ham (1974) & Leeson and Leeson (1976)

The human kidneys are paired organs, each is bean-shaped, about 10 to 20 cm. in length and 3.5 to 5cm thick, enclosed in a thin fibro connective tissue capsule. On the medial aspect is a depression, the hilum, through which the blood vessels enter and leave, and from which the excretory duct, the ureter leaves.

On cut surface, the kidney is seen to be made up of a "cortex" and "medulla". The former has a brown-red colour and a granular appearance, while the latter is of a lighter grey colour and is radially striated; it consists of several "pyramids". A pyramid is that part of the medulla that projects toward the renal pelvis more as a cone than a pyramid, the distal part of it being called the "papilla". Between adjacent medullary pyramids, cortical material extends between the pyramids to separate them and forms the renal columns (of Bertin). The base of each pyramid does not show a clear demarcation from the dark, brownish, granular cortex of the kidney, since medullary material extends into the cortex as fine, radially oriented rays, the "medullary

rays". Each pyramid with its associated overlying cortex is regarded as a lobe.

The kidney can be considered as a compound tubular gland which secretes urine, each kidney containing a large number of uriniferous tubules. Each tubule consists of two parts, the nephron and the collecting tubule. Each nephron is a thin tube approximately 20 - 50 micron wide and 50mm long and responsible for urine secretion. There are probably 1,300,000 nephrons in each kidney; some estimates run as high as 4,000,000. The nephron consists of four chief parts:-

1. The malpighian or renal corpuscle, which contains the glomerulus.
2. The proximal convoluted tubule
3. The loop of Henle and
4. The distal convoluted tubule.

The collecting tubule is the excretory duct, which conveys urine to the renal pelvis.

RENAL CORPUSCLE:-

It consists of Bowman's capsule and the glomerulus. The Bowman's capsule, which is the epithelium lined dilatation of the nephron is invaginated by a tuft of capillaries, the glomerulus, thus acquiring a cup-shape, which is double walled. There is narrow slit-like space,

the capsular space, between the outer or parietal layer (capsular epithelium) and the inner or visceral layer (glomerular epithelium) which closely invests the capillary tuft.

The glomerulus; consists of a unique type of capillary plexus fed by an afferent and drained by an efferent arteriole, supported by a stalk called the mesangium. The afferent arteriole on entering the glomerulus branches into a few primary branches and these give rise to capillaries that drain to primary branches of the efferent arteriole. The capillaries that hang from each primary branch of an afferent arteriole constitute what might be termed a "lobule". The capillary tuft is made up of no more than eight lobules.

The wall of the capillary loop acts as the glomerular filter and is composed of three elements : the capillary endothelium, the glomerular basement membrane and the epithelial cells.

- Capillary Endothelium: It offers no anatomical barrier to the passage of molecules. With the light microscope they have, a lightly stained eosinophilic cytoplasm and rather densely stained nuclei. These cells line the glomerular capillary have nucleus and cytoplasmic mass lying usually on the mesangial side of the capillary. By

electron microscopy the endothelial cell lining is continuous except for the large numbers of pores or fenestrations, which are up to $1000\text{\AA}$ (100nm) in diameter.

- Epithelial Cells or Podocytes: The visceral layer of epithelium closely invests the capillaries of the glomerulus and is difficult to delineate by light microscopy. These cells do not form a complete sheet over the capillaries, i.e.: there are discontinuities. By electron microscopy, the nuclei of the cells are ovoid and surrounded by small amount of cytoplasm. These cells lie apart from the capillaries, but contact one or more capillary loops by a series of cytoplasmic processes the "major processes" which give rise to delicate "minor processes" which end in numerous "feet" embedded in the basement membrane, and hence the alternative term "podocytes". Between feet, as they extend to attach to the basement membrane are small slit-like spaces, about $250\text{\AA}$ (25nm) wide, referred to as filtration slits or slit pores.

- Glomerular Basement Membrane (GBM): The basement membrane covering the glomerular capillaries is about 0.3 micron in thickness and is continuous between the capillaries but it does not enclose the entire circumference of any single capillary. It is lacking over the mesangial surfaces of the capillaries and is

regarded as the main filter preventing passage of large molecules. On light microscopy, it looks homogenous but electron microscopy allows three layers to be distinguished: a central lamina densa (Ld), with a less dense lamina rara interna (Li) on the endothelial side and a lamina rara externa (Le) on the epithelial side. Chemical studies have revealed that the basement membrane belongs to the collagen family and is a glycoprotein.

THE MESANGIUM:-

It is now accepted that there exists a supporting stalk for the glomerulus known as the "mesangium". It contains cells known as the "mesangial cells", separated by an extensive matrix. The mesangial cells lie usually at the branchings of capillary loops between endothelium and basement membrane and do not contact the capillary lumen. They are stellate in shape and have numerous cytoplasmic filaments. They are both phagocytic and contractile and there is some evidence that they are concerned in maintenance of basement membrane. The mesangium is filled by an amorphous substance made by the mesangial cells and having electron density similar to that of the glomerular basement membrane and it is referred to as "mesangial matrix". The mesangium probably forms part of the reticulo endothelial system.