Essay on

RECENT ADVANCES IN NEPHROTIC SYNDROME

By

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A C K N O W L E D G E M E N T

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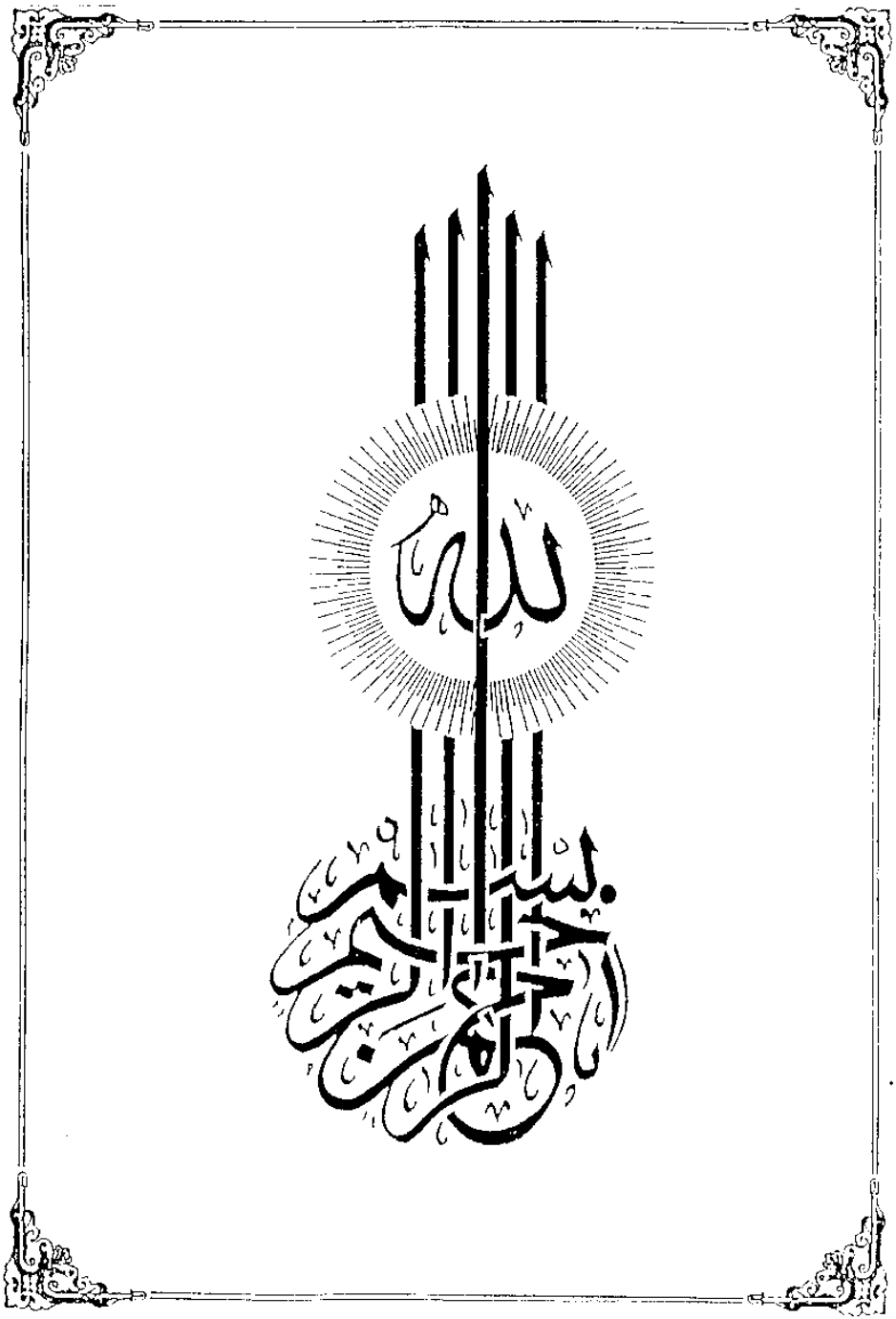

C O N T E N T S

THE NEPHROTIC SYNDROME

"NEPHROSIS"

Nephrotic syndrome is a renal disease mostly of a primary origin and involving mainly the glomerulus, and is characterised by gross edema, heavy proteinuria, hypercholesterolaemia and a chronic course with remissions and relapses over a period of many years with tendency to develop bacterial infections.

In this essay we are going to discuss in short the ultra structure, physiology of the kidney and developmental changes which occur during early infancy before proceeding to the discussion proper of nephrotic syndrome including its etiology, clinical manifestation of different types, laboratory data, differential diagnosis, prognosis and finally its management.

Ultra Structure of the Kidney

The nephron is the anatomic and functional unit of the kidney, there is about one million nephrons in each kidney, and each nephron is composed of a glomerulus and unbranched tubule which joins a collecting duct to drain into the renal pelvis, and it is arranged in a manner that the distal tubule is adjacent to the glomerular stalk at such a point the tubular surface become in contact with the afferent and efferent arterioles, together these structures form the juxta glomerular apparatus which is involved in renal sodium regulation and production of Renin.

The Glomerulus:

The glomerulus (average diameter, 110 to 160 u) is the filtering apparatus of the nephron and, as such, initiates the formation of urine. The adult numbers of glomeruli are present by the time the fetus attains a weight of 2 to 2.5 kg. The glomerulus consists of an intricate spherical-shaped, convoluted capillary network, arising from the afferent arteriole. The walls of the capillaries of this network form a membrane across which the process of filtration occurs. Under electron microscopy (Fig. 1) this membrane is seen to have three layers: (1) an inner layer of endothelial cells which are continuous with the endothelial cells of the afferent arteriole;

(2) the glomerular basement membrane proper, which is an uninterrupted highly convoluted membrane about 1200 Å in thickness. It is formed of a glycoprotein consisting of a nonfibrillar collagen-like protein and two different carbohydrate complexes, one a disaccharide and the other a heteropolysaccharide; these are linked with specific amino acid residues in the protein chains. Under the electron microscope the glomerular basement membrane appears as an amorphous matrix, but a layering into a dense central zone and less dense inner and outer zones has been described with the use of certain fixation techniques; (3) an outer layer of large visceral epithelial cells with extensive cytoplasmic projections which subdivide into foot processes and are in direct contact with the glomerular basement membrane. Covering and between these cytoplasmic extensions is a carbohydrate-rich polyanionic mucoprotein, the negative charge of which is derived primarily from the carboxyl groups of sialic acid. Histochemical techniques with such stains as Alcian blue or colloidal iron are required to demonstrate this material.

In addition to the endothelial and epithelial cells of the glomerular basement membrane, there is a third cell type - the mesangial cell. These cells lie centrally within the glomerulus and have cytoplasmic extensions which are in contact with the endothelial cells. In disease they may

extend between the endothelial cell and the glomerular membrane. Mesangial cells are believed to function in a manner analogous to cells of the reticulo-endothelial system and probably remove macromolecular substances from the circulation.

Bowman's capsule surrounds the glomerulus. Its basement membrane is continuous with the basement membrane of the proximal convoluted tubule and is lined on its inner aspect by the parietal epithelial cells (Vaughan and Mckay, 1975).

Under the electron microscope the endothelium is seen to be fenestrated and pseudopodia of the epithelial cells are seen to form slits along the capillary wall. The normal separation of the foot processes of the epithelial cells is lost during excessive proteinuria such as occurs in nephrotic syndrome, and the gaps or pores are seen in the endothelial lining, however the basement membrane between the endothelial cells and epithelial cells does not contain visible pores (Fig. 2).

The total area of glomerular capillary endothelium across which filtration occurs in man is about 1.5 sq.m.

The proximal convoluted tubule is about 15 m.m. long and 55 u.m. in diameter. In man its walls is made up of a single layer of cells that inter-digitate with one another; the luminal edges of the cells have a straight

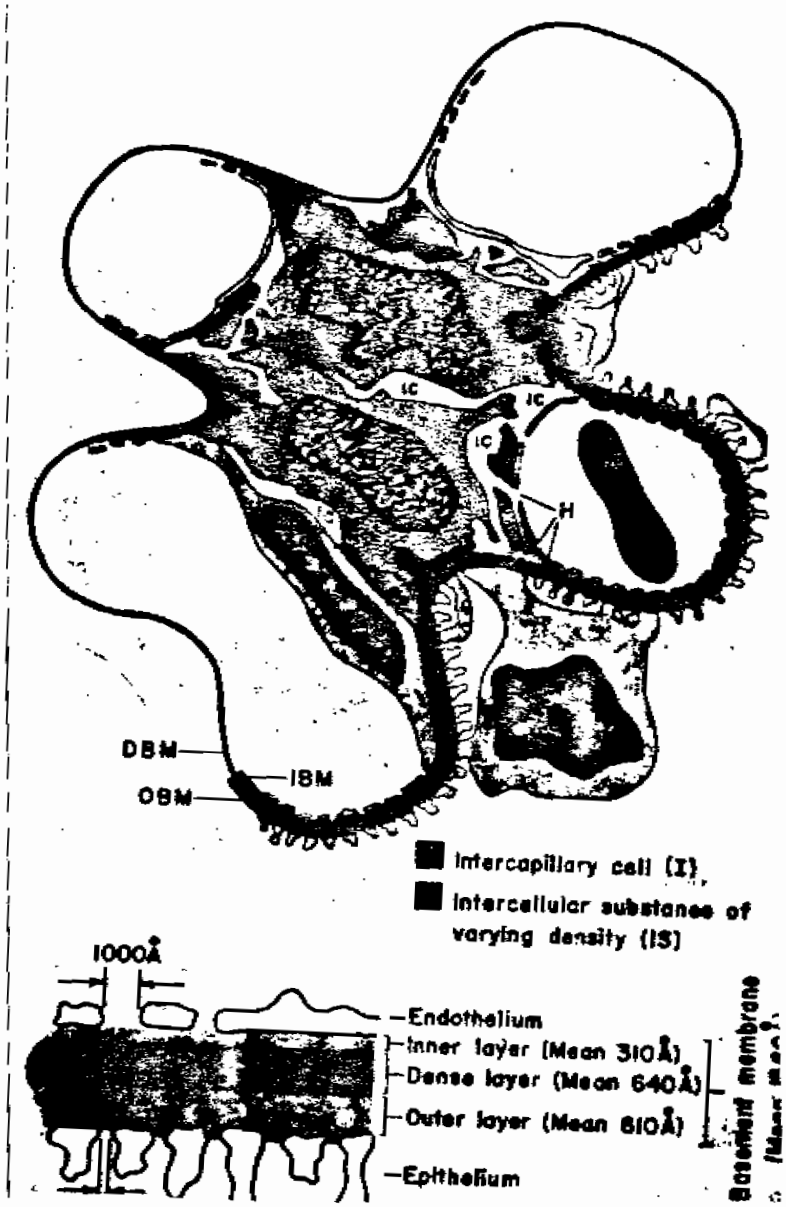

Figure 1: Glomerular lobule with its centrolobular region (mesangium). Measurements of the peripheral basement membranes based on a study of rats. Abbreviations: DBM, dense layer of basement membrane (lamina densa); OBM and IBM, outer and inner layers, respectively, of basement membrane; Ep, epithelium; End, endothelium; IC, intercapillary channel; H, holes or gaps in endothelium; RBC, red blood cell. (From H. Latta, A.B. Maunsbach and S.C. Madden: J. Ultrastruct. Res., 4: 455, 1960, after Vaughan and Mckay, Nelson Text Book of Pediatrics, 1975).

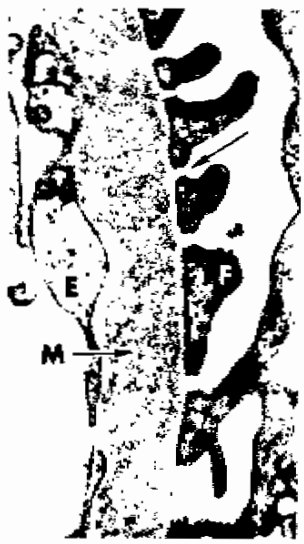

Figure 2: Glomerular capillary wall showing foot process of podocytes, F, filtration slit membrane (arrow), basement membrane, M, and fenestrated endothelium, E. (x40,000.) (From W.A.D. Anderson Text Book of Pathology.

brush border due to the presence of innumerable microvilli.

The convoluted portion of the proximal convoluted tubule (pars convoluta) drains into the straight portion (pars recta) which forms the first part of loop of Henle; the proximal tubule terminates in the thin segment of the descending limb of the loop of Henle which has an epithelium made up of attenuated flat cells.

The nephrons with glomeruli in the outer portion of the renal cortex have short loops of Henle whereas those with glomeruli in the juxta medullary region of the cortex have long loops extending down into the medullary pyramids; in human only 15% of the nephrons have long loops.

The total length of the thin segment of the loop varies between 2-14 m.m. in length, it ends in the thick segment of the ascending limb which is about 12 m.m. in length. The ascending limb of the loop of Henle doubles back to the glomerulus of the nephron from which the tubule arose and passes close to its afferent arteriole, at this point some of the cells of the juxta glomerular apparatus are piled up around the tubule and tubular epithelium is modified histologically to form the macula densa which is arbitrarily designated as the point where the loop of Henle ends and the distal convoluted tubule begins.

The distal convoluted tubule is about 5 m.m. long, its epithelium is lower than that of the proximal tubule and although there are a few microvilli there is no distinct brush border. The distal tubules coalesce to form collecting ducts which are about 20 m.m. long and pass through the renal cortex and medulla to empty into the pelvis of the kidney at the apices of the medullary pyramids.

The total length of the nephron including the collecting ducts ranges from 45-65 m.m. (Ganong, 1975).

Blood Vessels of the Kidney:

The afferent arterioles are short straight branches of the inter-lobar arteries; the efferent arterioles break up into the capillaries which supply the tubule before draining into the renal vein. The arterial segments between glomeruli and tubules are thus technically a portal system; and the glomerular capillaries are the only capillaries in the body that drain into arterioles.

The capillaries draining the tubules of the cortical nephrons form a peritubular network, but the efferent arterioles from the juxta medullary glomeruli drain into a network of vessels that form a hair pin loops (the vasa recta), these loops dip into the medullary pyramids alongside the loops of Henle (Fig. 3).

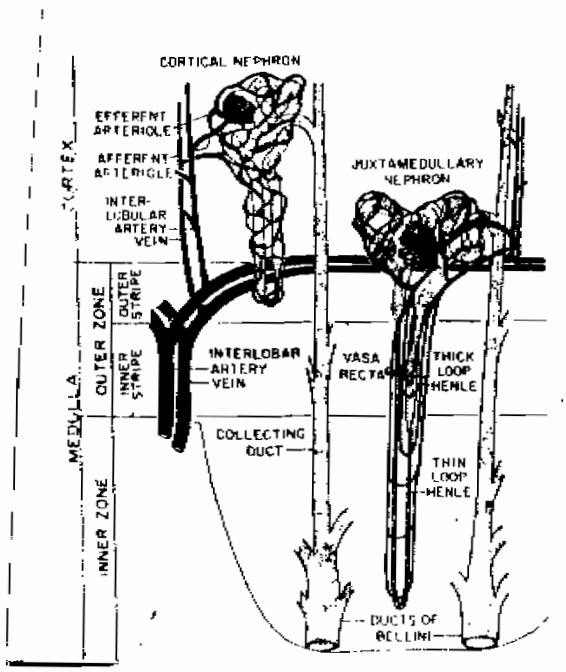

Figure 3: Comparison of the blood supplies of cortical and juxtamedullary nephrons. (From Pitts, R.F.: Physiology of the kidney and body fluids, 3rd ed., Chicago, Year Book Medical Publishers, Inc., 1974, Used by permission, after Vaughan and Mckay, Nelson Text Book of Pediatrics, 1975).

The efferent arteriole from each cortical glomerulus break up into capillaries that generally supply the same nephron, but in the case of juxta medullary nephron the capillaries may supply a number of different nephrons.

In man the total surface of the renal capillaries is approximately equal to the total surface area of the tubule both being about 12 sq.m.

Lymphatics:

The kidney has an abundant lymphatic supply which drains into the thoracic duct into the venous circulation in the thorax.

Renal Capsule:

The renal capsule is a thin but tough structure, if the kidney becomes edematous the capsule limits the swelling of the kidney and the tissue pressure (renal interstitial pressure) rises and this decreases the glomerular filtration rate, and is claimed to be a factor in enhancing and prolonging the anuria in the lower nephron syndrome.

Innervation of the Renal Vessels:

The renal nerves travel along the renal blood vessels as they enter the kidney they contain many sympathetic efferent fibers and few afferent fibers of unknown function, there also appears to be cholenergic component but

its function is uncertain.

The sympathetic innervation comes from 12th thoracic to the second lumbar segments of the spinal cord.

The sympathetic fibers are predominately vasoconstrictor in function and are distributed to the afferent and efferent arterioles, however nerve fibers can also be demonstrated ending in close proximity to the renal tubular cells and the juxta glomerular cells (Ganong, 1975).