REVIEW OF LITERATURE
Domenico Cotugno described a young shoulder whose urine coagulated like soft white of an egg, when heated and he had massive oedema.

Richard bright (1836) was the first physician to demonstrate that the excretion of albuminous urine was a mark of serious renal disease. Bright demonstrated that albuminous urine was an important sign which precedes any clinical feature of structural alteration of kidney.

Renal biopsies indicated that proteinurca is a sign of structural change in the kidney (Iversen and Brum, 1951). Definite histopathological changes were found out associated with proteinuria with the half of height and electron microscope.

Walker et al (1942) measured glomerular filtrate of animals by using nephron puncture technique. They proved that glomerulus was relatively impermeable to the passage of albumin and glomerular filtrate contained very little amount of albumin.

On the molecular level Perguhar and Palade (1961) pioneered the use of combining tracer proteins with the aminonucleoside model to follow passage of proteins through the glomerulus. Further improvement in this area was done by Venkatachalam Karnovsky and Cotran (1969). Tamm and Horsfall (1952) isolated and characterised proteins produced by kidneys. They also discovered urokinase and
secretory IgA. Excretion of low molecular weight proteins in certain diseases has received attention on the kidney as a homeostatic mechanism for reclaiming protein but it is not due to breakdown of glomerular barrier but rather to impairment of reabsorptive process or catabolic process.

The type of protein excreted in renal disease depends upon the specific nature of the disease. Protein excretion pattern associated with renal tubular disease was different from that found in glomerular disease (Butler and Flanagan, 1958).

MECHANISM OF PROTEIN EXCRETION

Tubular Proteinurea

Normal, low molecular weight (<40,000) serum proteins such as beta-2 microglobulins (11,600 mol. wt.), Lysozyme (14,000 mol. wt.) or light chain (<2,000 mol. wt.) are readily filtered by glomeruli but are reabsorbed so efficiently that only trace amount enter the urine. Diseases that selectively damage tubules more than glomeruli, cause excessive excretion of these small proteins with little or no increase in albumin excretion. The resulting proteinuria is usually between 1-3 gm/24 hours and oedema and lipid disorders do not occur because albumin disorders are small. Bence Jones proteins which is probably a dimer of two light chains. Light chains themselves, and myoglobins are example of proteins whose plasma concentration may increase as a consequence of
of disease. If their filtered load rises enough to exceed tubular reabsorptive capacity, overflow proteinuria may occur.

**Glomerular proteinuria**

Normal glomeruli filter very little albumin or globulin. Glomerular capillary endothelium form a barrier penetrated by pores of about 1000 Å diameter that holds back cells and other particles but offers no impediment to most proteins. The glomerular basement membrane traps molecules about 50 Å in effective radius above 100,000 daltons molecular mass. The foot processes (Podocytes) of visceral epithelial cells cover the urinary aspect of glomerular basement membrane and it produces a series of narrow channels through which molecules that traverse the basement membrane must pass.

Anionic molecules, like albumin are filtered less freely than neutral or positively charged molecules of the same size so very little albumin enters the filtrate. Thus charge selectivity appears to be due to anionic glycoproteins that cover the surface of foot processes and contributes to matrix structure of basement memrane. The glycoproteins are anionic because they contain the dicarboxylic amino acids e.g. glutamic, aspartic acid and serine acid. At the pH of blood (7.4) of urine (4.5 to 7.5) carboxylic and zialic acid residues are dissociated and therefore have a negative change. Albumin also carries
an overall negative charge. The negatively charged of glycoproteins repel those of albumin and retard filtration. Glomerular disease can disrupt any of these filtration barriers. Injury limited to polyionic glycoproteins would tend to produce selective losses of anionic proteins, such as albumin. Extensive injury that involves the entire basement membrane, not only its polyionic compartment, may increase losses of very large proteins as well as albumin.

**Quantity of Proteinurea**

Protein excretion is abnormal when the total daily excretion exceeds 150 mg (Reiman and Levinsky, 1971). For any given rate of protein excretion the concentration of protein in a single voided urine sample will vary inversely with the urine flow. However, even at low flow rates the concentration of protein in normal urine does not exceed 10-20 mg/dl. Thus the occurrence of a higher concentration in any specimen of urine implies the existence of proteinurea. Protein excretion above 3.5 gm/24 hour is termed massive proteinurea and usually occurs when glomeruli have been damaged enough to allow plasma proteins, especially albumin, to enter the urine.

The kidneys from patients with nephrotic syndrome usually do not show the inflammatory changes on glomerular lesions typical of nephritis. The presence of rate in the renal tubular cells and in casts
in the urine sediment suggested to early pathologists, that the major pathologic changes of this disorder were in renal tubules. To emphasize this finding Muller (1905) called this condition nephrosis. Researchers however, soon demonstrated that proteins found in the urine of patients with nephrotic syndrome consisting chiefly of albumin were identical to those circulating in the blood and were not of renal tubular origin. Walker (1941) proved that the origin of proteinuria and the prime site of the pathology of nephrotic syndrome lie in the glomerulus.

In some patients it was seen (Berman, 1958) that some patients had only gross proteinuria and lipidurea without oedema, hypercholesterolemia, hypoproteinuria and have been shown on biopsy to have the same kinds of pathologic changes that accompany the more classic syndromes.

In recent years the massive proteinuria alone became to represent the syndrome because massive protein loss connotes serious renal disease whether or not the losses are so disproportionate to nutritional state and hepatic albumin synthesis that hypoproteinemia has developed and oedema and lipid disturbances appeared.

Therefore the useful exact definition of nephrotic syndrome is massive urinary protein excretion (more than 3.5 g/m/24 hour/1.73 m²), the proteins being mainly albumin or generally reflecting the composition of serum proteins.
The other features such as elevated serum cholesterol, lowered serum albumin and oedema were not found in all the cases of nephrotic syndrome, therefore they were described as the variable (although common) findings of nephrotic syndrome (Berman, 1958).

**Hypoproteinemia**

Albumin is the major protein loss in the urine accounting for approximately 70% of the total (Kark, 1958). Therefore, hypoalbuminemia accounts for most of the reduction in the protein concentration in the plasma. Though a degree of hypoglobulinemia may occur.

Even though the hypoalbuminaemia is not a constant finding of the nephrotic syndrome. In one series Schreiner found that hypoalbuminaemia was not present initially in 16 percent of cases. The variable tendency of hypoalbuminaemia was possibly dependent upon the amount and duration of the protein loss.

The loss of proteins in the urine is recognized as one aspect of the overall turnover of the plasma proteins, as they are continually being metabolized and constantly replaced by newly synthesized protein molecules. The normal amount of protein catabolized and that excreted in urine is off set by synthesis. Catabolism and synthesis are both quite dynamic, for in man it has been shown that about one tenth of the plasma mass of the protein is broken down each day.
The albumin is synthesized in liver at about 8-14 g/day for a 70 kg person. It is balanced by normal rates of albumin degradation and it is capable of increasing somewhat in response to increased demand. An important normal control stimulus for albumin production is the oncotic pressure of plasma protein.

Some nephrotic patients seem capable of remaining in albumin balance (with low serum concentration) despite of massive proteinurea. Other are severely hypoproteinaemic even with lesser proteinurea. The poor appetite ill advised dietary protein restriction or malabsorption from edematous bowel may account for some limitation of albumin synthesis, but it appears likely that some other unknown impairment of liver function may be present as well in some nephrotic patients.

Jensen et al (1967), Waldman et al (1972) studied the disturbances in albumin metabolism in nephrotic patients and animals by using the radio-labelled albumin and found that endogenous fractional catabolic rate of albumin was increased in nephrotic patients. A likely explanation for this is increased exposure of albumin to renal tubular catabolic sites.

Katz et al (1963) found that the fractional catabolic rate of albumin of experimentally nephrotic rats was raised, however if a nephrectomy was performed this elevated catabolic rate dropped to a large extent, indicated that the increased catabolism occurred in the
kidney. Therefore in summary it would appear that hypoalbuminaemia is due primarily to the losses in the kidney and that this is augmented by an increased endogenous catabolism by the renal tubules.

**Oedema**

Oedema was the commonest presentation of most of the studies conducted in India and abroad.

The oedema represents the accumulation of visible or palpable excess quantities of interstitial fluid. For the oedema to be generalised, several litres of excess fluid must be present. In order for oedema formation to occur, fluid must move from the plasma across the capillary walls into the interstitial space and the kidneys must retain sufficient quantities of salt and water to account for the body's increased content.

The starling forces (oncotic pressure and hydrostatic pressure) determine the distribution of fluid between capillary and interstitial spaces. The oncotic pressure of plasma helps to retain the fluid inside the capillary. In nephrotic syndrome the oncotic pressure of plasma is decreased due to hypoalbuminemia which helps in the formation of oedema.

Squire (1957) in his large series of cases has found reasonable correlation between occurrence and severity of oedema and degree of hypoproteinaemia, especially albumin concentration. Anasarca and oedema of limbs were found to occur when serum albumin levels
were below 1.6 g% and 1.8 g% respectively and never above the concentration of 3.9 g%.

But there was the lack of definite correlation between occurrence of generalised oedema and serum albumin concentration in some cases studied by Berman et al (1958), Mukerjee (1973) and Shanbhag et al (1973).

Shanbhag found a number of patients even at an albumin concentration of 1.1 to 1.2 g% without any oedema.

This lack of definite correlation between occurrence of generalised oedema and serum albumin concentration was explained by Berman on the basis that apart from albumin concentration, the oedema depends on changes in functional status and dietary habits and ability of kidney to eliminate the salt and water.

The stimuli leading to this renal salt and water retention in nephrotic syndrome is not clearly understood. It might be expected that hypoalbuminemia would produce a contracted plasma volume with reduced central venous pressure, cardiac output and perfusion of kidneys. These stimuli are known to enhance renal salt retention.

**HYPERLIPIDEMIA**

Hyperlipidemia is a common accompaniment of the nephrotic syndrome. Low density lipoproteins and cholesterol are elevated most frequently, but as the plasma oncotic pressure falls to very low levels. very low density lipoprotein (VLDL) and triglyceride also increases.
Abnormal serum lipids have been used in the past to justify terming the nephrotic syndrome a metabolic disease. Schreiner described the hyperlipidemia as a secondary manifestation for the following reasons.

- Some patients do not have hyperlipidemia until weeks or months after the development of the other features of the nephrotic syndrome.
- In nephrotic rats, the prevention of proteinurea inhibits the development of hyperlipidemia.

Hyperlipidemia is not found in all the cases of nephrotic syndrome. Kark (1958) described low or normal levels of serum cholesterol in cases of nephrotic syndrome in generalized disease process and indicated it as a poor prognostic feature.

Sarin and Sarin (1960) studied 50 cases of nephrotic syndrome, out of which only 30 cases had hypercholesterolemia above 250 mg%.

Mukerjee (1973) found the hypercholesterolemia in about 43.1% cases of nephrotic syndrome. The normal cholesterol concentration in nephrotic syndromes has been attributed to inadequate intake of diet due to associated nausea, vomiting and diarrhoea of nephrotic syndrome, presence of oedema and acute onset of salt retention and oedema due to heart failure.

Shanbhag (1973) studied 116 cases and found that the serum cholesterol was lowest in amyloidosis (177.0 mg%)
followed by membranoproliferative and proliferative glomerulonephritis. Highest serum cholesterol level was noted in end stage or sclerosing group.

Ram Singh et al (1987) studied 650 cases of nephrotic syndrome and found that patients of nephrotic syndrome associated with pulmonary tuberculosis has significantly lower serum cholesterol levels (average 152.4±26.3 mg%) as compared with the cases of nephrotic syndrome associated with other glomerulonephritis (average 419.6±45.7 mg%). Further more he found that the mean serum cholesterol level showed a linear inverse relationship with the duration of pulmonary tuberculosis. 40.9% patients of nephrotic syndrome associated with pulmonary tuberculosis showed hypocholesterolemia whereas none of the patients of the nephrotic syndrome associated with nephritis. Thus the hypocholesterolemia could serve as a pointer of associated pulmonary tuberculosis in nephrotic syndrome.

The exact cause of lipid abnormality in cases of nephrotic syndrome is not clear. Several mechanisms have been proposed so far.

Hypoproteinemia

Human studies have shown a fairly good negative correlation between the level of serum albumin and lipids, which have been reversed following the infusion of the albumin (Baxter, Goodman, Allen, 1961). Schreiner also suggested an inverse but not necessarily straight line
relationship between the serum concentrations of cholesterol and albumin.

Stephen K. Newmark et al. (1975) found that in nephrotic patients there was significant inverse correlation between the lipid values and serum albumin but there was no significant inverse relationship between the lipid values and 24 hour urinary protein loss.

It has been suggested that albumin acts as a transport mechanism for the egress of cholesterol from plasma to bile. A deficiency of serum albumin therefore leaves cholesterol trapped in plasma (Rosenman et al, 1956).

According to Valarie Wass et al (1981) the accelerated hepatic lipoprotein production occurs almost certainly as a result of increased protein synthesis by liver in response to abnormal loss of albumin which provides a relatively non specific stimulus for the synthesis of apoproteins and probably other hepatic proteins as well as albumin itself.

Other suggested mechanisms for hypercholesterolemia are changes in the rates of disposal, elimination or interconversion of cholesterol (Baxter et al, 1961). Amount of nephrotic tissue and nature of disease (Hymaen et al, 1958) and thyroid function abnormalities (Peters, JP et al, 1945; Recant et al, 1958; Epstein et al, 1925).
Coagulation and Fibrinolytic Abnormalities

Patients with the nephrotic syndrome are apt to develop deep venous thrombosis and pulmonary artery thrombosis especially when given steroid therapy (Pollak et al, 1956; Levine, 1967). The association of renal vein thrombosis and nephrotic syndrome has been known for many years and a recent study reports a very high incidence especially in patients with membranous glomerulonephropathy (Llach, Arieff, Massry, 1975). It is rather difficult to separate out abnormalities due to nephrotic syndrome per se and the effect of therapy particularly steroids. The following abnormalities however, have been described.

1. The plasma fibrinogen level is raised and there is an inverse correlation with serum albumin and positive correlation with the serum cholesterol level. Both synthetic and catabolic rates of fibrinogen are increased in patients with the nephrotic syndrome due to glomerulonephritis (Takeda and Chen, 1967).

2. Coagulation factors V, VII, VIII, X have been reported to be elevated in both untreated nephrotics and those on treatment but not in remission. Mild thrombocytosis and accelerated thromboplastin generation times were also reported (Kendall, Lohmann and Dossetor, 1971).

3. Reduced plasma and urine fibrinolytic activity has been reported in a group of patient in treatment for the nephrotic syndrome (Wardle, Menon, Rastogi, 1970).
AETIOPATHOGENESIS

The nephrotic syndrome is the condition resulted from the excessive glomerular leakage of plasma proteins in the urine. The defect in the charge or size selective barriers of the glomerular capillary wall can arise as a consequence of a wide variety of disease processes including immunologic disorders, toxic injuries, metabolic abnormalities, biochemical defects and vascular disorders. Thus the nephrotic syndrome is not a single disease entity, but the metabolic expression of a wide variety of underlying disease states. It may be the result of:

a. Primary renal disease or idiopathic.
b. Nephrotic syndrome secondary to other diseases.

Idiopathic Diseases

Nephrotic syndrome is said to be idiopathic if it occurs without a known cause and without any apparent relationship to a systemic disease. They are divided into a variety of histologic classes.

Causes of Nephrotic Syndrome

I. Primary glomerular diseases or idiopathic:
   1. Minimal change disease.
   2. Mesangial proliferative glomerulonephritis.
   3. Membranous glomerulonephritis.
   4. Membranoproliferative glomerulonephritis.
   5. Focal and segmental glomerulosclerosis.
6. Other uncommon lesions:
   - Crescentic glomerulonephritis.
   - Focal and segmental proliferative glomerulonephritis.
   - Unclassifiable lesions.

II. Secondary to other disorders.

A. **Infections**
   

B. **Drugs**
   
   Gold, mercury, pernicillamine, street heroin, probenilid, captopril, Tridone, Mesentoin, Percholate, Antivenum, Antitoxins, and contrast media.

C. **Neoplasia**
   
   Hodgkin's disease, Lymphomas, Leukemia, Carcinomas, Malenoma, Wilms's tumour.

D. **Multisystem diseases**
   
   SEL, Henoch-Schonlein purpura, vasculitis, Good pasture syndrome dermatomyositis, dermatitis, herpetiformis, amyloidosis, sarcoidosis, Sjogren's syndrome, rheumatoid arthritis.

E. **Heridofamilial**
   
   Diabetes mellitus, alport syndrome, sickle cell disease, Fehy's disease, nail patellae syndrome, lipodystrophy, congenital nephrotic syndrome.
F. Miscellaneous

Pre-eclamptic toxaemia, thyroiditis, myxoedema, malignant obesity, renovascular hypertension, chronic interstitial nephritis with vesiculouretric reflux, chronic allograft rejection, bee stings.

Minimal Change Disease

Originally recognised by Muller et al (1905) described in detail by Munk and By Velhard and Fahr. This is also known as lipid nephrosis, nil lesion or foot process disease. This is the commonest cause of nephrotic syndrome in children contributing 77% of cases in the international study of kidney disease in children. Although less but still it is found in 25-30% cases of nephrotic syndrome in adult age group.

Typically patients present with overt nephrotic syndrome, normal blood pressure, normal or slightly reduced GFR and a benign urinary sediment, varying degree of microscopic haematuria are found in upto 20% of cases.

Munk (1913) described the term lipid nephrosis on the basis of tubular changes, included vacuolisation, accumulation of hyline droplets and lipids in the tubular cells and the protenaecous cast in the tubular lumens, but there was no glomerular lesion described.

Tiwari (1987) and Cameron (1974) found following histological changes in the cases of minimal change disease.
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Glomerular sclerosis</td>
<td>11.8 %</td>
<td>42.8 %</td>
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<tr>
<td>Mesangial cellularity</td>
<td>9.5 %</td>
<td>46.0 %</td>
</tr>
<tr>
<td>Tubular atrophy</td>
<td>17.8 %</td>
<td>51.0 %</td>
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<tr>
<td>Interstitial changes</td>
<td>9.5 %</td>
<td>-</td>
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<tr>
<td>Vascular changes</td>
<td>3.6 %</td>
<td>32.8 %</td>
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Electron microscopically there is fusion or effacement of foot processes of glomerular epithelial cells over the surface of the basement membrane. The basement membrane itself is of normal thickness and consists no deposits. There is no cell proliferation, inflammatory infiltrate, fibrosis, or fibrin deposition.

The occasional occurrence of minimal lesion nephrotic syndrome in association with allergic reactions to insect stings, poison ivy, poison oak, or inhaled allergens and usual responsiveness of minimal lesion nephrotic syndrome to corticosteroid or other immunosuppressive therapy suggest a possible immune cause (despite the absence of any glomerular immunoglobulins).

**Membranous glomerulonephritis**

There is diffuse thickening of glomerular capillary wall without proliferation of the cells. The capillary wall thickening is due mainly to deposition of numerous, irregular electron dense deposits between the basement membrane proper and the epithelial cell cytoplasm.
The epithelial cells overlying the deposits have lost their foot processes and are somewhat swollen. It is the combination of sub-epithelial deposits and altered epithelial cytoplasm that given the appearance of a diffusely thickened basement membrane by light microscopy.

This disorder accounts for about 30-40% of cases of idiopathic nephrotic syndrome, blood pressure, GFR, urinary sediments tends to be normal early in the course. Haematuria or hypertension may occur by they are not constant or necessary features. Renal function usually normal on presentation.

Although most cases of membranous nephropathy are idiopathic, a variety of antigens has been identified been claimed to be pathogenic in those particular patients. These include DNA and C type viral antigens in membranous nephropathy associated with SLE, Hepatitis Bs and Be antigens, thyroglobulins, Tumour antigens; (Melanoma and Cancer of lung and colon), malaria tryponormal antigens, and a renal tubular epithelial cells antigen associated with hemoglobinopathies, renal vein thrombosis and renal cell carcinoma. It is also observed after the exposure of heavy metals (Gold, mercury), drugs (Penicillamine, Captopril).

Membranoproliferative Glomerulonephritis

This condition is characterised histologically by both thickening of basement membrane and proliferation of cells. Because the proliferation is predominantly in
the mesangium. A frequently used synonym is mesangio
capillary glomerulonephritis. A number of patients with
this histologic lesion exhibit persistent hypo-complemen-
temia and the disease is also known as hypo-complementemic
glomerulonephritis.

The glomeruli are large and hyper cellular, the
latter due to a prominent increase in mesangial cells.
The GBM is thickened often focally, particularly in the
peripheral loops. The glomerular capillary wall shows
a double contour or tram track appearance in silver or
PAS stains. This is caused by the splitting of basement
membrane because of inclusion within it of processes of
mesangial cells extending into peripheral capillary loops,
so called mesangial interposition.

MPGN is divided into two major subtypes
according to ultrastructural findings.

Type I

Type I is characterised by presence of sub-
endothelial electron dense deposits.

Type II

The lamina dense of glomerular basement membrane
(GBM) is transformed into an irregular, electron dense
structure due to the deposition of dense material in the
GBM proper giving rise to the term dense deposit disease.

MPGN is found in about 7% cases of nephrotic
syndrome. It typically causes nephrotic syndrome in
young adults and adolescents, is usually progresses to end stage renal failure. Most series report a slight female preponderance. Nephrotic syndrome is presenting feature in about 40% of patients. Microscopic haematuria with or without RBC casts is a universal finding. Hypertension is found in about 30-50% cases and up to a third have some degree of azotemia when first seen.

As in most other types of glomerulonephritis no etiologic agent is evident. In few instances the MPGN may be found in association with a variety of clinical conditions in which chronic antigenemia may predispose to glomerular disease. Examples of some such conditions include:

- Shunt nephritis - occurs in patients of ventriculoatrial shunts infected with staph. epidermatitis.
- Some patients with infected endocarditis, chronic active hepatitis and visceral abscesses associated with bacteremia.
- Hepatosplenic form of schistosoma mansoni infection and occasional cases of lupus nephritis or sickle cell nephropathy.

FOCAL AND SEGMENTAL GLOMERULAR SCLEROSIS AND HILTINOSIS

In the course of international study of the effect of corticosteroid therapy in lipoid nephrosis, it was noted that a small proportion of patients responded poorly to steroids. In these patients light microscopic examination of renal biopsies showed that while most
glomeruli were normal, an occasional glomerulus exhibited an area of sclerosis confined to only a segment of the glomerulus. Thus, the lesions were focal in that they involved some glomeruli and segmental in that they involve a segment of the affected glomerulus. Hyline masses were frequently present in the sclerotic areas. Initially the sclerosis involves juxtamedullary glomeruli, subsequently it became more generalised.

Electron microscopy shows, focal basement membrane collapse and denudation of epithelial surfaces. All glomeruli reveal diffuse epithelial foot process effacement. Immunofluorescence reveals nodular deposits of IgM and C3 within sclerotic areas.

Although this is almost certainly a variant of lipid nephrosis, the entity has now been separated from lipid nephrosis.

Patients with this lesion have the nephrotic syndrome but differ from usual patients with lipid nephrosis in the following respects.

1. They have a higher incidence of haematuria and hypertension.
2. They respond poorly to corticosteroid therapy.
3. Many progresses to chronic glomerulitis.
4. Immunofluorescence microscopy shows deposition of IgM and complement in the sclerotic areas of the glomeruli.
5. There is high incidence and recurrence in patients with focal sclerosis, who receives renal transplants.
Mesangial Proliferative Glomerulonephritis

The lesion is characterized by mild to moderate diffuse but distinct increase in the cellularity of the glomerular capillary bed. The peripheral glomerular capillary walls are thin and delicate and extracapillary proliferation is not seen. The precise nature of the proliferating cells is not clearly understood but may represent combinations of proliferating mesangial cells, endothelial cells and infiltrating mononuclear cells. By immunofluorescence a variety of patterns are observed (IgA, IgM, IgG and C3).

This lesion accounts for approximately 10% of instances of idiopathic nephrotic syndrome, in adults. Hematuria either gross or microscopic is commonly observed. Loin pain may be present. Renal function may be modestly decreased at the time of diagnosis but is most often normal. The pathogenesis of this lesion, is unknown and almost certainly result of diverse pathogenetic processes. They are unresponsive to corticosteroid therapy and to evolve with time into those of focal and segmental glomerular sclerosis.

TUBERCULOSIS AND NEPHROTIC SYNDROME

The association between pulmonary tuberculosis and nephrotic syndrome is experienced by many workers from very past. But the etiological relationship between the two has not been established yet. Lendonzy and Bernard (1901) described the tuberculosis as a cause of nephrotic syndrome. Bour and Ducomet (1957) described the relation-
ship between lipid nephrosis and pulmonary tuberculosis.

Mittal et al (1966) studied the renal changes in the pulmonary tuberculosis. They studied 25 cases and found amyloidosis in 2, interstitial nephritis in 1, cloudy swelling in 7 and pyelonephritis in 3 cases. Similar study was carried out by Shah et al (1973). They studied 30 cases and found the membranous glomerulonephritis in 2 cases, amyloidosis in 7 and cloudy swelling in 5 cases.

Jain et al (1986) studied the renal changes in 50 cases of pulmonary tuberculosis. out of which 14 cases had the proteinuria of nephrotic range. They biopsied 12 cases, and found membranous glomerulonephritis in 4 cases, proliferative glomerulonephritis in 2 cases, chronic glomerulonephritis in 6 cases, amyloidosis in 2, pyelonephritis in 7 and cloudy swelling in 3 cases.

Most of these changes except for amyloidosis seem to be nonspecific changes and their aetiologic correlation with pulmonary tuberculosis is debatable.

Of special interest is the present of membranous glomerulonephritis and interstitial glomerulonephritis. It is possible that the initial damage to the kidney parenchyma produced by the tubercle bacilli or its toxins may stimulate release of autoantigens which may perpetuate the process.

Veresnchagin (1958) has incriminated hypersensitivity mediated by tubercle bacilli to be responsible for these changes.
Petrolwala et al (1983) studied 25 cases of nephrotic syndrome out of which 3 cases were associated with pulmonary tuberculosis.

However, many workers of our country and abroad (Sarin and Sarin, 1960; Berman, 1959; Wahi et al, 1962; Prakash, 1965; Johny, KV, 1972; Singh et al, 1987; and Sharma, 1987) found the amyloidosis secondary the tuberculosis as a leading cause of the nephrotic syndrome.

Sarin and Sarin (1960) studied the 50 cases of nephrotic syndrome and found amyloidosis in 33 cases out of which 11 cases were due to pulmonary tuberculosis.

Prakash et al (1965) studied 140 cases of nephrotic syndrome and found the amyloidosis as a second leading cause (32 cases), out of which 11 cases of amyloidosis were secondary to pulmonary tuberculosis.

Johny KV (1972) biopsied 50 cases of nephrotic syndrome and found amyloidosis in 4 cases of which one was due to miliary tuberculosis and one was due to pulmonary tuberculosis and 2 cases were due to other causes.

Singh et al (1987) studied 650 patients of nephrotic syndrome and found associated tuberculosis in 375 patients. They biopsied 97 cases and found amyloidosis in 65 cases. In these 65 cases tuberculosis was the cause in 60 cases. They found that the mean serum cholesterol levels were significantly low (p < 0.001) in those with amyloidosis due to pulmonary tuberculosis.
Sharma et al (1987) studied 250 cases of nephrotic syndrome and found the amyloidosis in 15 cases out of which 9 were secondary due to tuberculosis.

Joel Neugarted et al (1983) described a rifampicin induced nephrotic syndrome and acute interstitial nephritis. They admitted a case of pulmonary tuberculosis with normal renal functions and with no urinary protein. They treated the case with R-cin 600 mg and INH 300 mg daily. After 20 days of starting the therapy the blood urea was 50 mg%, serum creatinine 2.1 mg% and 24 hour urinary albumin was 4.1 gm.

INH and Rifampicin were discontinued on 20th day, after 30 days of discontinuation the 24 hour urinary protein excretion was 3.7 gm and after 100 days of discontinuation of therapy. On light microscopy the glomeruli were normal and the interstitium was oedematous and infiltrated by lymphocyte, plasma cells, neutrophils and eosinophils, and electron microscopy showed the focal but extensive effacement of epithelial cell foot processes and the presence of electron dense deposits in mesangial matrix and in sub-endothelial and paramesangeal sites. Co-existing glomerular lesions and acute interstitial nephritis during rifampin therapy have been reported only rarely (Gabow et al, 1976; Bansal et al, 1970; Manasia and Paul, 1975). Gabow et al (1976) suggested that release of tubular antigens as a consequence of rifampicin induced acute interstitial nephritis may give rise to
supper-imposed immune complex glomerulonephritis.

So it is not clear yet that the association of nephrotic syndrome and pulmonary tuberculosis is due to hypersensitivity to tubercle bacilli, or secondary to amyloidosis or secondary to rifampicin therapy.