# Chapter 8

RENAL AND METABOLIC DISEASE

# Four Types of Renal Diseases
## (With disease progression, other components may become involved)

Based on initial morphologic component affected

- Glomerular
  - Most often immune mediated
- Tubular
  - Result from toxic or infectious substances
- Interstitial
  - Result from toxic or infectious substances
- Vascular
  - Caused by a reduction in renal perfusion that induces morphologic and functional changes in kidney

# Glomerular Diseases

Diseases that damage glomeruli include immunologic, metabolic, and hereditary

Secondary glomerular diseases

- Systemic diseases that initially and principally involve other organs but also affect kidneys

Primary glomerular diseases

- Specifically affect kidneys, often only organ involved
- Primary diseases consist of several different types of glomerulonephritis

# Morphologic Changes in Glomerulus (Mostly Immune Mediated)

Cellular proliferation

- Increased numbers of capillary endothelial, mesangial, and epithelial cells in glomerular tuft

Leukocytic infiltration

- Neutrophils and macrophages attracted by a local chemotactic response

Glomerular basement thickening

- Any process that results in enlargement of basement membrane (immune complexes and diabetes)

Hyalinization with sclerosis

- Accumulation of homogeneous eosinophilic extracellular material

# Clinical Features of Glomerular Diseases

Hematuria

Proteinuria

Oliguria

Azotemia

Edema

Hypertension

- The severity of each feature and the combination present vary depending on the number of glomeruli involved, mechanism of injury, and the rapidity of disease onset

# Nephrotic Syndrome

Group of clinical features that occur simultaneously

Heavy proteinuria (≥3 g/day)

Hypoproteinemia (due to loss of protein in urine)

Hyperlipidemia

Lipiduria

Edema

Urine microscopic

- Mild hematuria and fatty, waxy, and renal tubular epithelial casts

# Types of Glomerulonephritis

Acute glomerulonephritis

Rapid glomerulonephritis

Membranous glomerulonephritis

Minimal change disease

Focal segmental glomerulonephritis

Membranoproliferative glomerulonephritis

Immunoglobulin A (IgA) nephropathy

Chronic glomerulonephritis

- The different types are not disease specific
- Initial presentation may be one type, but can progress into that of another

# Systemic Diseases and (Secondary) Glomerular Damage

## Systemic lupus erythematosus (SLE)

- Autoimmune disorder with immune complex deposits and complement activation

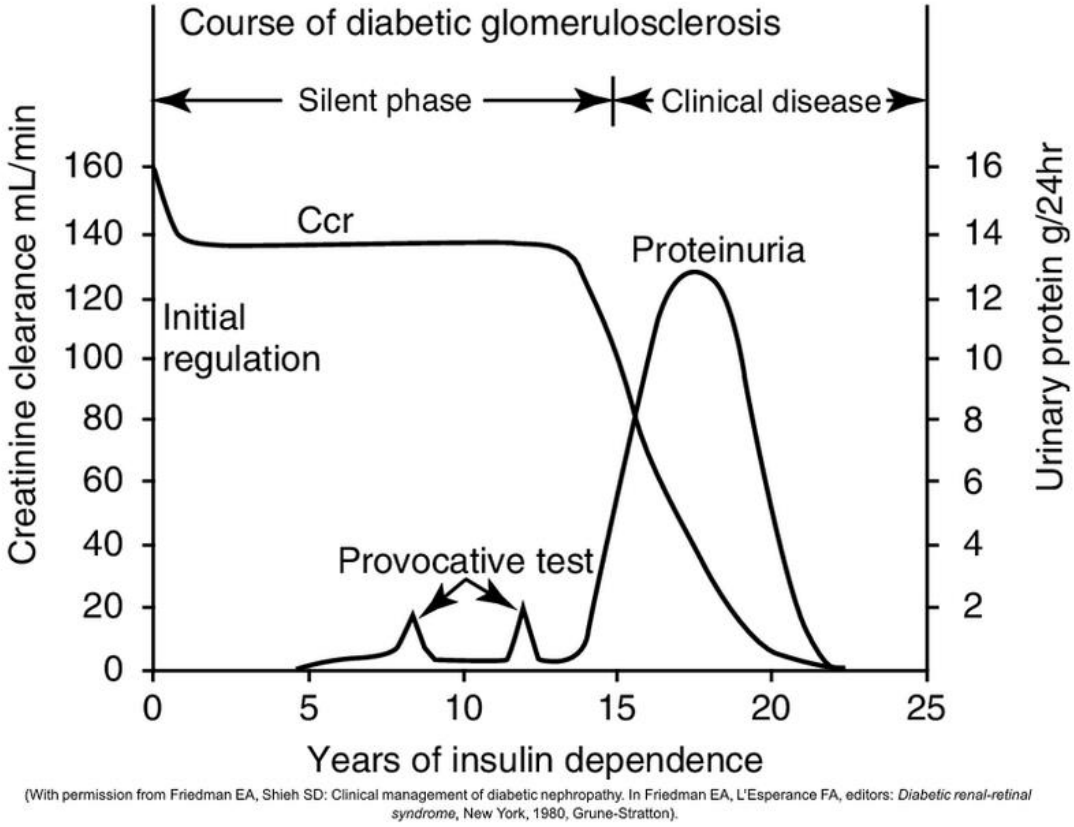
## Diabetes mellitus

- Carbohydrate metabolism disorder leads to glomerular syndrome, hypertension, susceptibility to pyelonephritis

## Amyloidosis

- Systemic disease involving many organs; characterized by deposits of amyloid, a pathologic protein substance
- Leading to proteinuria and nephrotic syndrome

**Figure 8-1.** A composite drawing showing the course of diabetic nephropathy. Exercise and other stress cause intermittent proteinuria before a sustained protein leak, which may lead to nephrotic syndrome. Initial regulation indicates initiation of insulin therapy. (With permission from Friedman EA, Shieh SD: Clinical management of diabetic nephropathy. In Friedman EA, L'Esperance FA, editors: *Diabetic renal-retinal syndrome*, New York, 1980, Grune-Stratton).




(With permission from Friedman EA, Shieh SD: Clinical management of diabetic nephropathy. In Friedman EA, L'Esperance FA, editors: *Diabetic renal-retinal syndrome*, New York, 1980, Grune-Stratton).

# Tubular Diseases

## Acute tubular necrosis (ATN):

- Ischemic ATN
  - Seen in sepsis, shock, trauma
- Toxic ATN
  - From exogenous or endogenous nephrotoxins

## Tubular dysfunction:

- Fanconi's syndrome
- Cystinosis and cystinuria
- Renal glucosuria
- Renal phosphaturia
- Renal tubular acidosis

# Tubulointerstitial Disease/Infections

Urinary tract infections (UTIs)

Acute pyelonephritis

Chronic pyelonephritis

Acute interstitial nephritis

Yeast infections

## BOX 8.2 Causes of Tubulointerstitial Diseases

- Infection
  - Acute pyelonephritis
  - Chronic pyelonephritis
- Toxins
  - Drugs
    - Acute interstitial nephritis
    - Analgesic nephritis
  - Heavy metal poisonings, such as lead
- Metabolic disease
  - Urate nephropathy
  - Nephrocalcinosis
- Vascular diseases
- Irradiation
  - Radiation nephritis
- Neoplasms
  - Multiple myeloma
- Transplant rejection

# Acute and Chronic Renal Failure

## Acute renal failure (ARF)

- Sudden decrease in glomerular filtration rate (GFR), azotemia, and oliguria
- Functional abnormality; but no cellular changes
- Classified as prerenal, renal, and postrenal

## Chronic renal failure (CRF)

- Progressive loss of renal function
- Due to hypertrophy of remaining healthy nephrons, not clinically recognizable until 80% to 85% function lost
- Azotemia, acid-base imbalance, abnormal calcium (Ca) and phosphate ($PO_4$) metabolism

# Renal Calculi

Aggregates of mineral salts in a matrix of proteins and lipids

75% of renal calculi contain calcium

Found primarily in renal calyces, renal pelvis, ureters, or bladder

Absence of natural inhibitors postulated cause

Four factors influence calculi formation:

- Supersaturation of chemical salts in urine
- Optimal urinary pH
- Urinary stasis
- Nucleation or original crystal formation

## TABLE 8.9 Renal Calculi Composition

| Chemical Component | Approximate Frequency |
|---|---|
| Calcium | 75% |
| with oxalate | 35% |
| with phosphate | 15% |
| with others | 25% |
| Magnesium ammonium phosphate | 15% |
| Uric acid | 6% |
| Cystine | 2% |
| All others | <1% |

# Amino Acid Metabolism Disorders

Cystinosis and cystinuria

Maple syrup urine disease (MSUD)

Phenylketonuria (PKU)

Alkaptonuria

Tyrosinuria

Melanuria

# Other Metabolic Disorders

Diabetes mellitus

- Problems with glucose metabolism
- One long-term side effect is glomerular damage and chronic renal failure

Diabetes insipidus

- Decreased antidiuretic hormone (ADH) or nephrons are resistant to ADH
- Results in polyuria

Porphyrias

- Hereditary defects of theme synthesis pathway
- Increased porphyrins and porphyrin precursors in blood and urine

# Inherited Metabolic Disorders

Heelstick blood samples from neonates are used to screen for inherited metabolic disorders

Tandem mass spectrometry (MS/MS) is the analytical detection method used to screen for the substances produced in the many metabolic disorders

## TABLE 8.11 National Newborn Screening Tests in United States[10]

### Recommended Uniform Screening Panel (RUSP)

| 31 Core Conditions | |
|---|---|
| 3-MCC | 3-Methylcrotonyl-CoA carboxylase |
| ASA | Argininosuccinate aciduria |
| BIO | Biotinidase |
| BKT | Beta ketothiolase |
| CAH | Congenital adrenal hyperplasia |
| CBL A,B | Methylmalonic acidemia |
| CCHD | Critical congenital heart disease |
| CF | Cystic fibrosis |
| CH | Congenital hypothyroidism |
| CIT I | Citrullinemia type I |
| CUD | Carnitine uptake defect |
| GA-1 | Glutaric acidemia type I |
| GALT | Transferase-deficient galactosemia (classical) |
| Hb S/S | Sickle cell anemia |
| Hb S/C | Sickle-C disease |
| Hb S/A | S-βeta thalassemia |
| HCY | Homocystinuria |
| HEAR | Hearing screening |
| HMG | 3-Hydroxy 3-methylglutaric aciduria |
| IVA | Isovaleric acidemia |
| LCHAD | Long-chain L-3-hydroxyacyl-CoA dehydrogenase |
| MCAD | Medium-chain acyl-CoA dehydrogenase |
| MCD | Multiple carboxylase |
| MSUD | Maple syrup urine disease |
| MUT | Methylmalonic acidemia |
| PKU | Phenylketonuria |
| PROP | Propionic acidemia |
| SCID | Severe combined immune deficiency |
| TFP | Trifunctional protein deficiency |
| TYR-1 | Tyrosinemia type 1 |
| VLCAD | Very long-chain acyl-CoA dehydrogenase |

| 26 Secondary Target Conditions | |
|---|---|
| 2M3HBA | 2-Methyl-3-hydroxy butyric aciduria |
| 2MBG | 2-Methylbutyryl-CoA dehydrogenase |
| 3MGA | 3-Methylglutaconic aciduria |
| ARG | Argininemia |
| BIOPT-BS | Defects of biopterin cofactor biosynthesis |
| BIOPT-REG | Defects of biopterin cofactor regeneration |
| CACT | Carnitine acylcarnitine translocase |
| CBL C,D | Methylmalonic acidemia (Cbl C, D) |
| CIT-II | Citrullinemia type II |
| CPT-Ia | Carnitine palmitoyltransferase I |
| CPT-II | Carnitine palmitoyltransferase II |
| De-Red | Dienoyl-CoA reductase |
| GA-II | Glutaric acidemia type II |
| GALE | Galactose epimerase |
| GALK | Galactokinase |
| H-PHE | Benign hyperphenylalaninemia |
| IBG | Isobutyryl-CoA dehydrogenase |
| M/SCHAD | Medium/short-chain L-3-hydroxy acyl-CoA dehydrogenase |
| MAL | Malonic acidemia |
| MCKAT | Medium-chain ketoacyl-CoA thiolase |
| MET | Hypermethioninemia |
| SCAD | Short-chain acyl-CoA dehydrogenase |
| TYR-II | Tyrosinemia type II |
| TYR-III | Tyrosinemia type III |
| Variant Hbs | Variant hemoglobins |