Chapter 34 - RENAL FUNCTION

I. The Kidneys

A. Anatomy

B. Function

1. Excretory
2. Regulatory - maintenance of homeostasis
3. Endocrine - active vitamin D, prostaglandins, erythropoietin, renin.

C. Formation of Urine

D. Renal Dialysis

E. Kidney Transplantation

II. Tests of Renal Function – Table 34-1

A. Renal Clearance and Glomerular Filtration Rate

1. Defined as the quantity of blood or plasma completely cleared of a substance per unit of time - units will be vol/time (mL/min)

$$C = (U_{conc} \times V)/P_{conc}$$

2. May reflect GFR only or tubules only or a mixture of both forms of clearance.
   a. GFR - inulin cleared by nephron only
      1. Must be freely filtered by the nephron
      2. Must <u>not</u> be reabsorbed, metabolized or secreted in the tubules
   b. Tubular clearance - PAH often used

B. Glomerular Permeability – Table 34-2,3.

1. **Fractional clearance of dextran**
   Clearance of dextran/Clearance of inulin
2. **Protein - normally < 150 mg/day**
3. **Proteinuria – etiology & differential diagnosis. See table 33-4 for etiology. See Table 34-18 for collection protocol for urinary proteins**

    1. **An abnormality in the glomerular basement membrane**
    2. **Decreased tubular reabsorption of filtered Proteins – lysozyme for PCT, variety of proteins (RBP, A1M, see Chap. 19) useful for assessing tubular damage**
    3. **Increased plasma concentrations of freely filtered proteins – Bence Jones proteins, myoglobin (causes renal damage – can cause acute renal failure in crush injuries)**
    4. **Decreased entry of proteins into tubules as a result of tubular epithelial cell damage**
    5. **Assessment**
        a. **Measurement of total urinary protein**
            1. **Method of indicators - dipstick**
               FP = alkaline pH, dyes, antibiotics
               FN = + charged proteins
        b. **Electrophoresis of urinary proteins**
        c. **Measurement of selective clearance of protein of different molecular sizes**
            1. **Microalbuminuria - elevated excretion of albumin when urinary protein is < 150 mg/d. Predictive of development of proteinuria in diabetics MW = 66,000**

2. Ig/albumin ratio - glomerulo-nephritis

C. Glomerular Filtration Rate – Most commonly used is creatinine clearance rate because it is simpler than inulin (IV admin) or radionuclides. Cystatin C reported as a better endogenous marker still not commonly used.

1. 4-, 12- or 24-hr timed urine collection used. Nonprotein nitrogen chromogens found in serum & can cause underestimation of GFR, while secretion of creatinine in tubules causes overestimation – this causes creatinine clearance rate to agree closely with inulin clearance rate. When more accurate methods are used to measure serum creatinine, agreement worsens. Patients who have lost ½ - 2/3 normal renal function should have GFR measured with inulin or radionuclides.
2. Preparation: hydrate with 600 mL water, withhold tea, coffee & drugs on day of test.
3. Sources of error – recoding of timing, vigorous exercise during the test, proper hydration (urine flow must be 2 mL/min), retention of urine in bladder (4 hour test).
4. Reference range: 105 ± 20 ml/min (males); 95 ± 20 ml/min (females). More accurate test show an increase of12 ml/min. Decreases with age.

D. Nonprotein Nitrogen Compounds

1. Urea – from urea cycle in liver
   a. prerenal azotemia

b. postrenal azotemia
c. sUrea N/sCreat
    1. Low – acute tubular necrosis, low protein intake, starvation, severe liver disease
    2. High (with normal creatinine) – catabolic tissue breakdown, prerenal azotemia, high protein intake (esp. uremic patients), GI hemorrhage
    3. High (with elevated creatinine) – postrenal obstruction or prerenal azotemia + renal disease
d. Reference: 7 – 18 mg Urea N/dL or 15 – 39 mg Urea/dL or 2.5 – 6.4 mM urea in serum. Values tend to be slightly higher in males, higher if high-protein diet is eaten.

2. Creatine – produced in kidneys, liver & pancreas & transported by blood to tissue. Produced by transamidation of arg & gly. Is phosphorylated to high-energy compound. Creatinine is degradation product – excreted via kidney.
    a. Depends on muscle mass. Higher in high protein diets. Fairly constant excretion in the same individual – parallels production in absence of renal disease
    b. Reference intervals: Serum: 0.6 – 1.1 mg/dL (females), 0.7 – 1.2 mg/dL (males). Urine: 11 – 20 mg/ d per kg body weight (females), 14 – 26 mg/d per kg body weight (males). Decreases with age.

3. Uric Acid – major catabolic product of purine

nucleosides. Endogenous sources produce 300 jg/d while dietary sources contribute 400 mg/d. End-product in humans (lower primates & mammals produce allantoin). 75% excreted in urine, remainder in GI tract where bacteria convert to allantoin.

- **a. Renal Handling:**
  1. **Freely filtered through glomerulus**
  2. **98-100% absorbed in PCT**
  3. **Subsequent secretion into DCT**
  4. **Further secretion later in DCT – 6 to 12% of filtered load is excreted in urine**
  5. **pK_a is 5.6, so at higher urine pH's urate is major form (soluble) while a low pH's uric acid (insoluble) is major form**
- **b. Clinical Significance:**
  1. **Hyperuricemia**
     - **a. Decreased excretion – Primary: idiopathic. Secondary: chronic renal failure, increased renal reabsorption, decreased secretion, lead poisoning, organic acids, low dose salicylate, thiazide diuretics**
     - **b. Increased formation – Primary: increased purine synthesis, inherited metabolic disorder. Secondary: excess dietary purine, increased nucleic acid turnover, malignan;cy, psoriasis, cytotoxic drugs, altered ATP metabolism, tissue hypoxia, alcohol**
  2. **Hypouricemia – severe liver disease, defective reabsorption, overtreatment**

with allopurinol or uricosuric drugs.

E. Urinalysis – Dipstick testing (qualitative & semiquantitative) for protein, leukocyte esterase (WBC), nitrite, pH, free hemoglobin, bilirubin. Also measure specific gravity, report color & foaming. Spin down sediment and examine for WBC, presence of renal cells, RBC, crystals, casts (tubular structures of packed RBC, WBC or other material formed in renal tubules), etc.

III. Renal Function and Acid-Base Disorders

A. Amino acids

B. Renal Tubular Acidosis – characterized by hyperchloremia, normal anion gap, & urinary $[HCO_3^-]$ and $[H^+]$ inappropriate for plasma pH. Caused by decreased reabsorption in PCT or decreased urinary acidification in DCT. Four types:
   1. Proximal renal tubular acidosis (PRTA, Type II RTA
   2. Distal renal tubular acidosis (DRTA, Type I)
   3. Hyperkalemic DRTA
   4. Selective aldosterone deficiency (DRTA, Type IV)
   5. Can have combine RTA I & II (Type III)
   6. Fractional bicarbonate excretion useful for diagnosis:
      $\{([HCO_3^-]_{urine}/[HCO_3^-]_{plasma})/([creat]_{urine}/[creat]_{plasma})\} \times 100\%$
      PRTA excretion 10 – 15%, DRTA excretion<10%
   7. NH_4Cl loading: used to assess DRTA if pH of fasting overnight urine > 5.5. Use $CaCl_2$ if liver disease present.

IV. Water Homeostasis

A. Urine volume – sources

B. Control of osmolality

1. **ADH**
2. **Countercurrent multiplier system (see fig. 34-3)**

C. Diseases associated with disturbances of the concentrating system – diabetes insipidus (lack of ADH production or lack of receptor action leading to excessive water loss). SIADH (excessive production of ADH. See Table 34-12

D. Quantitative measurement of water excretion

1. **Solute excretion rate = U_{osm} x V x 1000**
2. **Osmolal clearance = C_{osm} = U_{osm} x V/P_{osm}**
3. **Free Water clearance, C_{water} = V – C_{osm}**
4. **Negative free water clearance, Tc_{water} = C_{osm} – V**

E. Assessment of Renal Concentrating Ability

1. **Measurement of specific gravity**
2. **Urine osmolality measurements (see Chap. 25)**
3. **Ratio of serum sodium to serum osmolality**
4. **Ratio of urine osmolality to serum osmolality**

V. Renal Diseases and the Role of the Laboratory

A. Renal Failure: see Tables 34-5,6 for symptoms & signs. Progress to end stage renal failure, can be acute or chronic

1. **End-stage renal disease and the pathophysiology of uremic syndrome. See Table 34-9 for biochemical characteristics - retained nonprotein nitrogen compounds, acid-base abnormalities, carb intolerance, abnormal lipid metabolism, altered endocrine function**
2. **Acute renal failure (ARF) – see table 34-7 for etiology. Lab monitors electrolyte disturbances & fluid status. Polyuric phase because**

glomerular function recovers before tubular function.

3. Chronic renal failure (CRF) – progressive loss of functioning nephron units. Major causes diabetes mellitus, renal vascular disease and glomerulonephritis.
4. Glomerular diseases
    a. Acute nephritic syndrome
    b. Rapidly progressive glomerulonephritis
    c. Chronic glomerulonephritis
    d. Autoimmune nephritis
    e. Interstitial nephritis
    f. Nephrotic syndrome
        1. minimal change disease, focal-segmental membrano-proliferative
5. Cystic Renal Disease – polycystic kidney disease – genetic.
6. Tubular diseases
    a. Fanconi syndrome
    b. Selective inherited defects in amino acid transport
        a. RTA
7. Diabetic nephropathy – see table 34-10 for stages, functional changes, structural changes, alterations in GFR & blood pressure.
8. Hypertensive nephropathy – measurement of renal vein renin. Atherosclerosis, arterio-sclerosis, idiopathic hypertension
9. Urinary tract obstruction – prostate enlargement, fibroid may block excretion
10. Renal Calculi – see table 34-11 for promoters, inhibitors & predisposing risk factors of stone formation.
    a. Chemical analysis may aid in

diagnosis since composition of stone may indicate cause – patients with hypercalciuria and Ca oxalate stones may develop kidney infections resulting in the deposition of $MgNH_4PO_4$ on surface of stone (mixed stone). Analysis confirms infection resulted after stone formation. IR & X-ray diffraction used in large medical centers.

b. Hypercalciuria may be absorptive, resorptive or renal

11. Pseudohypoparathyroidism – receptor defect in kidney. Inherited.
12. Toxic nephropathy – see Table 34-13 for listing of nephrotoxins

VI. Renal Replacement Therapy – see fig. 34-4, 34-5 for survival rates for patients receiving transplants, hemodialysis, or peritoneal dialysis & diagram of hemodialyzer. Table 34-14 – lab support for renal replacement therapies

A. Hemodialysis
B. Peritoneal Dialysis
C. Renal Transplantation
    1. Preop assessment
    2. Postop assessment
    3. Immunosuppression therapy