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Chapter 27: Renal Function

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Renal functions

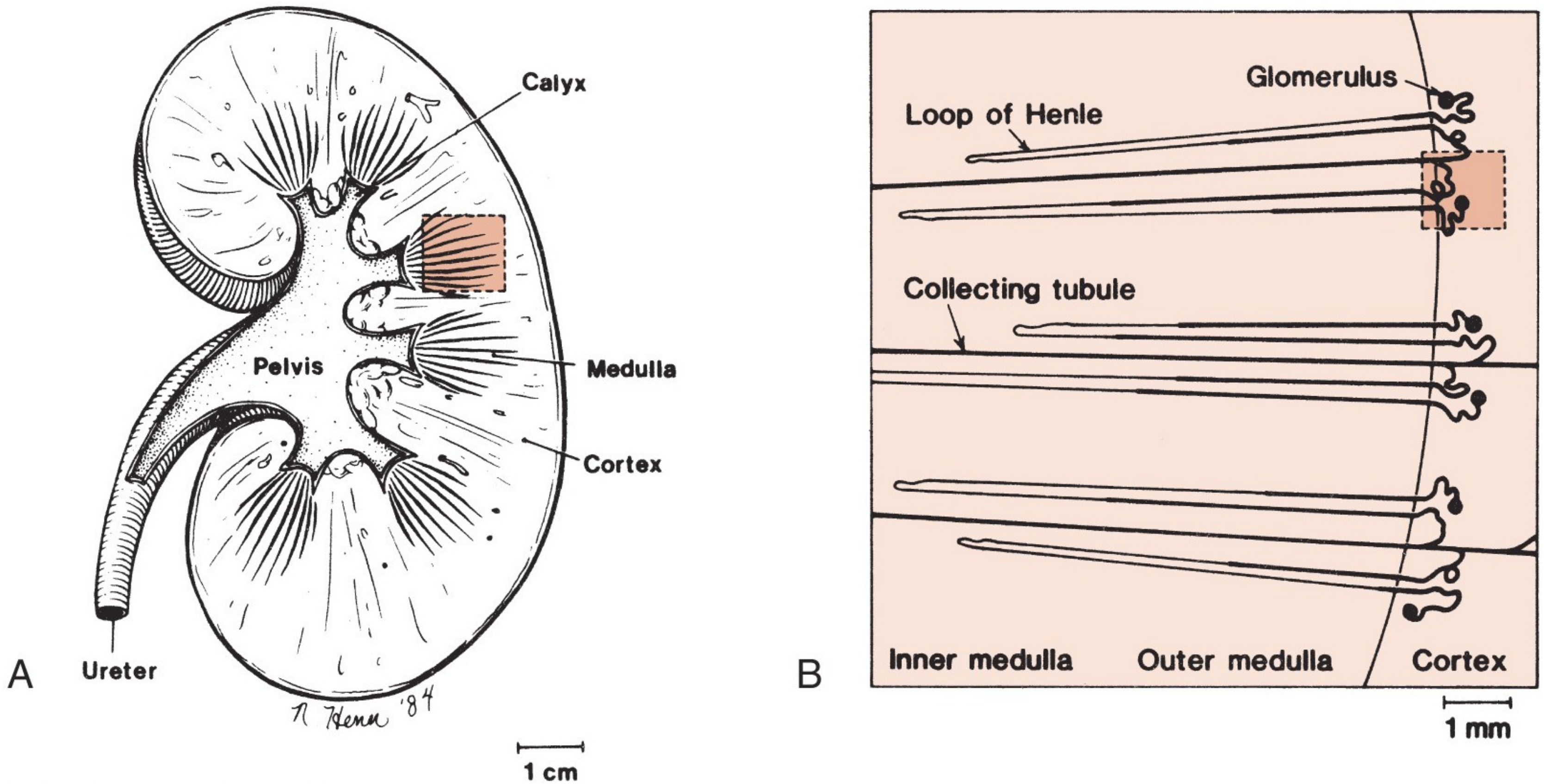
TABLE 27-1 KIDNEY FUNCTIONS
Urine formation
Fluid and electrolyte balance
Regulation of acid–base balance
Excretion of the waste products of protein metabolism
Excretion of drugs and toxins
Secretion of hormones
Renin
Erythropoietin
1,25-Dihydroxy vitamin D_3
Prostaglandins

Renal Functions and Anatomy

- Anatomy
  - **Kidneys:** paired, bean-shaped organs located retroperitoneally on either side of spinal column
  - **Two regions:** cortex (outer) & medulla (inner)
  - **Bilateral ureters:** thick-walled canals, connecting kidneys to bladder
  - **Nephrons:** functional units of kidneys; approximately 1 million are found in each kidney

Renal Functions and Anatomy (cont'd)

- Anatomy of the kidney

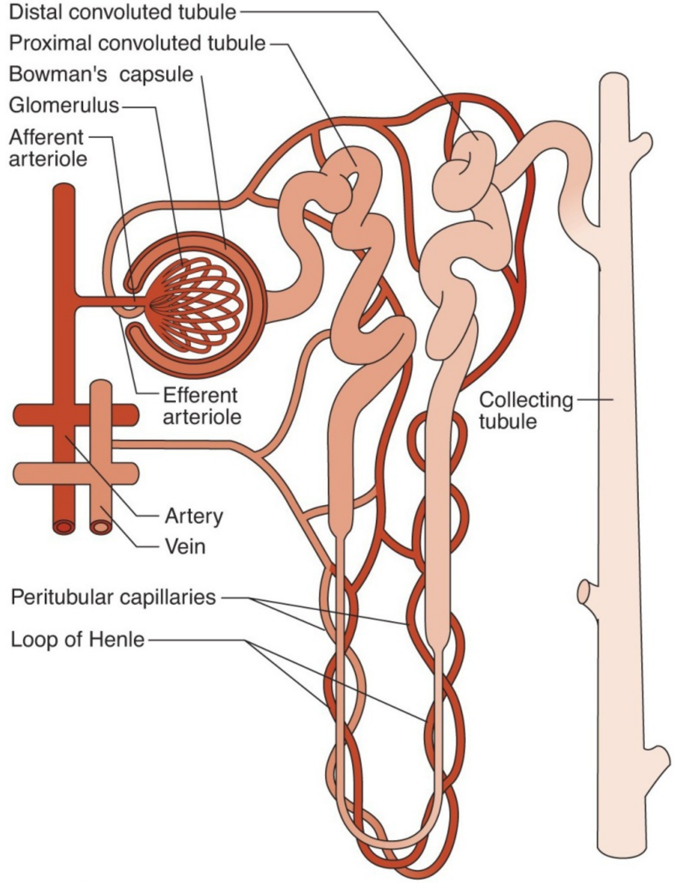


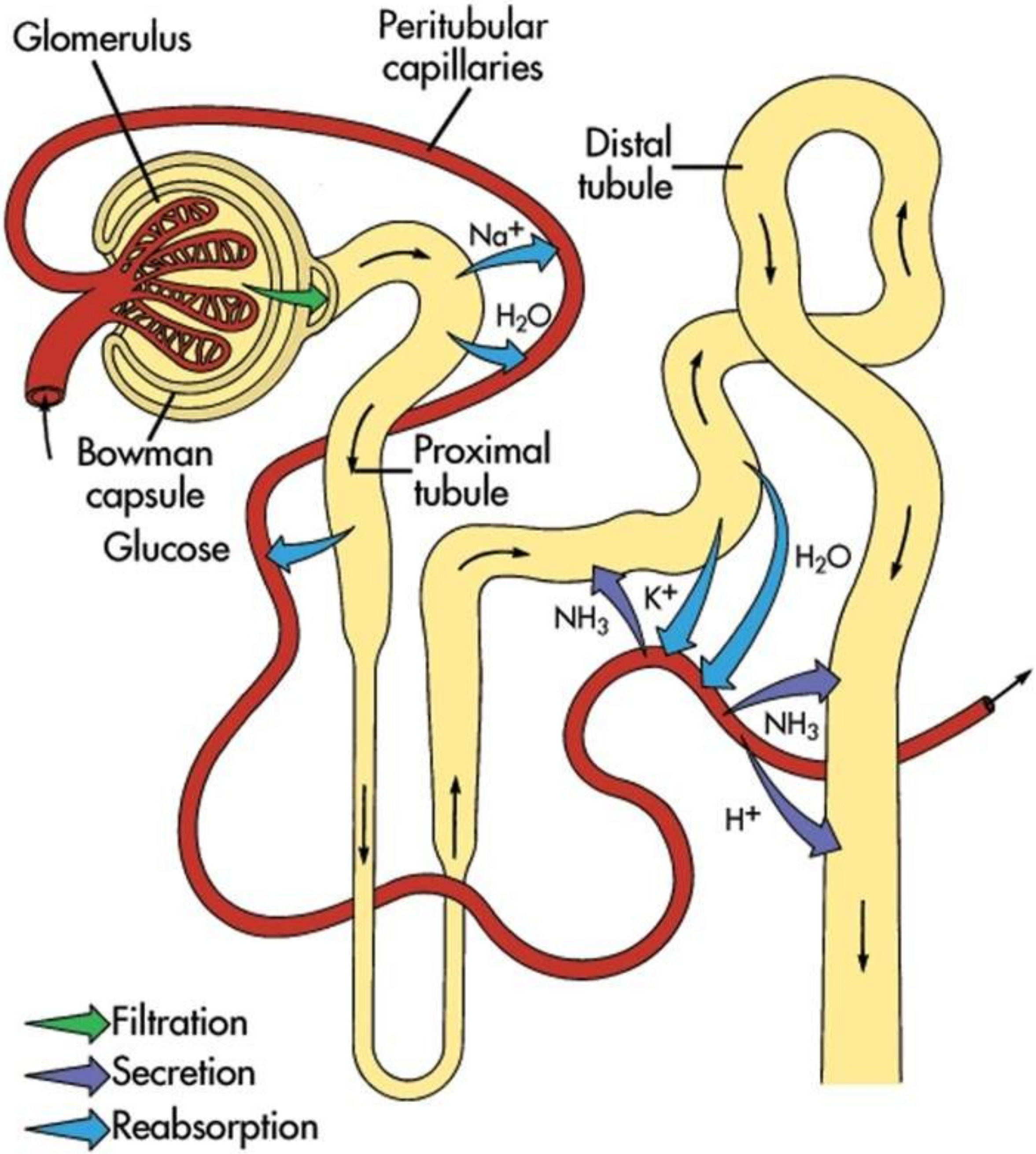
Renal Functions and Anatomy (cont'd)

- Anatomy
  - Five basic parts of nephron:
    - 1) **Glomerulus:** a capillary tuft surrounded by expanded end of renal tubule
    - 2) **Proximal convoluted tubule:** located in cortex
    - 3) **Loop of Henle:** comprising descending & ascending limbs
    - 4) **Distal convoluted tubule:** located in cortex
    - 5) **Collecting duct:** formed by 2 or more distal convoluted tubules as they pass through cortex & medulla

Renal Functions and Anatomy (cont'd)

- Representation of a nephron and its blood supply





(From Thibodeau GA, Patton KT: *Anatomy & physiology*, ed 5, St Louis, 2003, Mosby.)

Renal Physiology (cont'd)

- Water, Electrolyte, and Acid–Base Homeostasis
  - Electrolyte balance
    - **Chloride:** passively reabsorbed as a counter-ion when sodium is reabsorbed in proximal convoluted tubule
    - **Phosphate, calcium, & magnesium**
  - Acid–base balance
    - Regeneration of bicarbonate ions
    - Excretion of metabolic acids
    - Reaction with ammonia
    - Reaction with monohydrogen phosphate

Renal Physiology (cont'd)

- Endocrine Function
  - Kidneys synthesize the following:
    - **Renin:** catalyzes synthesis of angiotensin
    - **Erythropoietin:** acts on erythroid progenitor cells in bone marrow, increasing number of red blood cells
    - **1,25-Dihydroxy vitamin D_3:** active form of vitamin D; determines phosphate & calcium balance & bone calcification
    - **Prostaglandins:** increase renal blood flow, sodium & water excretion, & renin release; oppose renal vasoconstriction

Pathophysiology

- Glomerular Diseases
  - Acute glomerulonephritis
    - Large, inflamed glomeruli with a decreased capillary lumen
    - Abnormal laboratory findings usually include rapid onset of hematuria and proteinuria (usually albumin and generally < 3 g/d)
    - Decreased GFR
    - Elevated BUN, creatinine, oligouria, sodium and water retention
  - Chronic glomerulonephritis
    - Glomerular scarring & eventual loss of functioning nephrons
    - Gradual development of uremia may be first sign.
  - Nephrotic syndrome
    - Associated with massive proteinuria, hypoalbuminemia, edema, hyperlipidemia, & lipiduria
    - This defect almost always yields several abnormal findings, such as massive proteinuria (>3.5 g/d) and resultant hypoalbuminemia.

Pathophysiology (cont'd)

- Tubular Diseases
  - Result in decreased excretion/reabsorption of certain substances or reduced concentrating capability
  - **Renal tubular acidosis:** disorder affecting acid–base balance
- Urinary Tract Infection
  - **Infection:** in either kidneys or urinary bladder. Bacteriuria (as evidenced by positive nitrite dipstick findings for some organisms), hematuria, and pyuria (leukocytes in the urine, as shown by positive leukocyte esterase dipstick)
  - **Obstruction:** in upper or lower tract .The clinical symptoms of advancing obstructive disease include decreased urinary concentrating capability, diminished metabolic acid excretion, decreased GFR
- Renal Calculi (kidney stones)
  - Formed by combination of various crystallized substances

Renal calculi or kidney stones

TABLE 27-2 TYPES OF KIDNEY STONES

STONE COMPOSITION	CAUSE OF STONE FORMATION
Calcium oxalate	Hyperparathyroidism
	High urine calcium
	Vitamin D toxicity
	Sarcoidosis
	Osteoporosis
Magnesium ammonium phosphate	Infectious processes
Calcium phosphate	Excess alkali consumption
	Infection with urease-producing organisms
Uric acid	Gout
	High levels of uric acid in blood and urine
Cystine	Inherited cystinuria

Pathophysiology (cont'd)

- Renal Failure
  - **Acute renal failure:** sudden, sharp decline in renal function
  - **Chronic renal failure:** gradual decline in renal function over time
  - **Renal hypertension:** caused by decreased perfusion to kidney
  - Therapy of acute renal failure
    - **Dialysis:** removal of waste from blood by external, synthetic membrane
  - Therapy of end-stage renal disease
    - Dialysis & transplantation

Renal failure

- Acute kidney injury (AKI) is a sudden sharp decline in renal function as a result of an acute toxic or hypoxic insult to the kidneys

- AKI is subdivided into 3 types:
  - Pre-renal AKI
  - Intrinsic AKI
  - Post-renal AKI

- **Pre-renal AKI:**
  - Defect lies in the blood supply before it reaches the kidney.
  - Causes include cardiovascular system failure and consequent hypovolemia.
- **Intrinsic AKI:**
  - Defect involves the kidney.
  - Most common cause is acute tubular necrosis; vascular obstructions/inflammations and glomerulonephritis.
- **Post-renal AKI:**
  - The defect lies in the urinary tract after it exits the kidney.
  - Occurs as a consequence of lower urinary tract obstruction or rupture of the urinary bladder

Routine Kidney Function Tests

- Routine KFTs
  - Serum creatinine (Cr)
  - Creatinine clearance
  - Serum urea
- Both serum Cr and Cr clearance are used as kidney function tests to
  - Confirm the diagnosis of renal disease
  - Give an idea about the severity of the disease
  - Follow up the treatment

Analytic Procedures

- Clearance Measurements
  - Evaluation of renal function depends on measurement of waste products in blood that accumulate when kidneys begin to fail.
  - **Clearance:** rate at which creatinine & urine are removed from blood into urine
  - **Creatinine:** endogenous metabolic product synthesized at a constant rate & cleared only by glomerular filtration
  - **Creatinine clearance rate:** standard lab method to determine glomerular filtration rate (GFR)
  - **Estimated glomerular filtration rate:** used to predict GFR; is based on serum creatinine, age, body size, gender, & race; does not require urine collection (variable formulas)

Creatinine (Cr)

- Creatine is synthesized in the liver from Arg, Gly & Met
- Creatine is transported to muscles and forms Creatine phosphate, that is used as an energy source
- Creatinine is a waste product of creatine
- Cr is released into circulation at relatively constant rate
- Daily excretion of Cr is reasonably stable

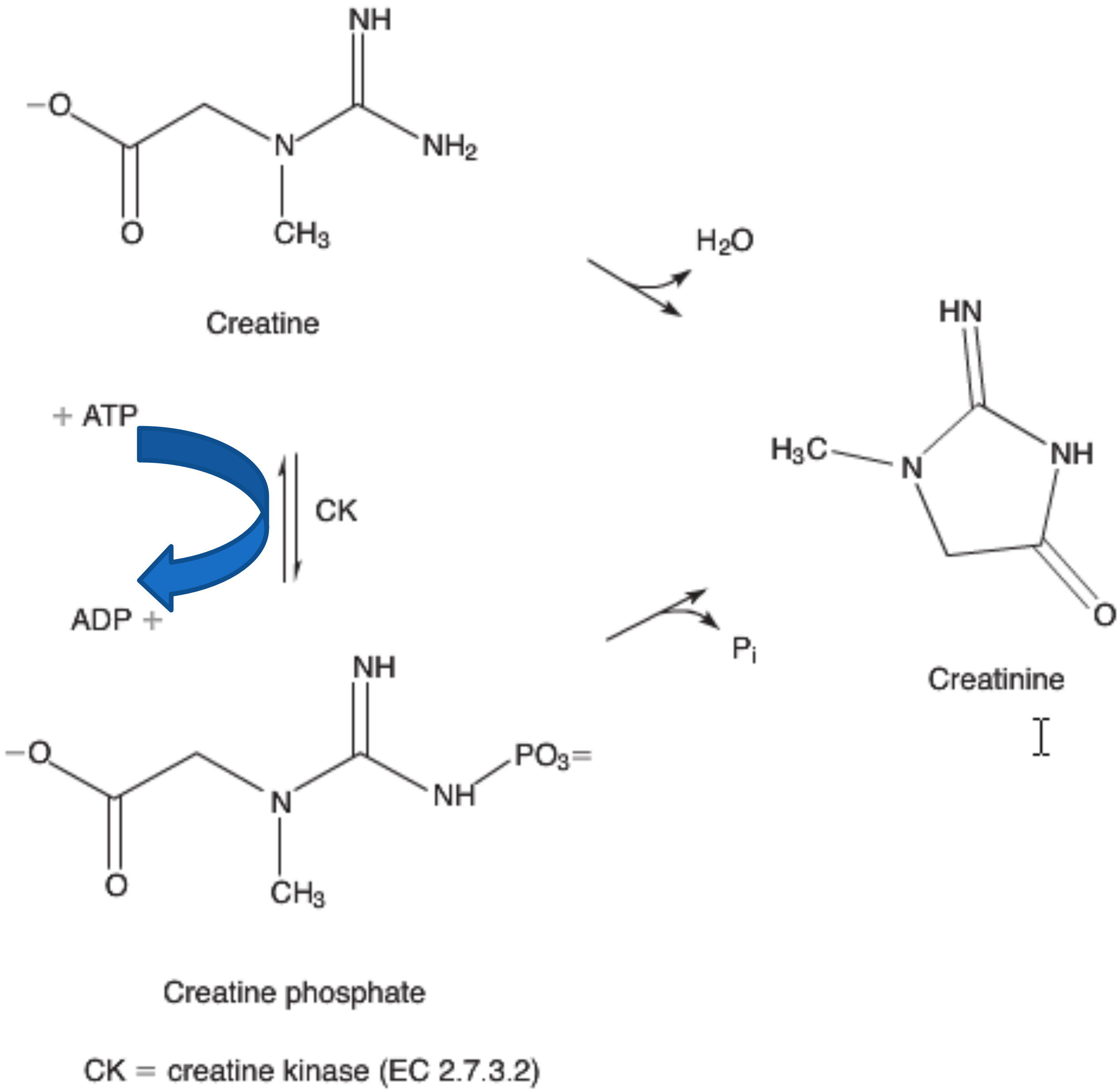


FIGURE 12-4 Interconversion of creatine, creatine phosphate, and creatinine.

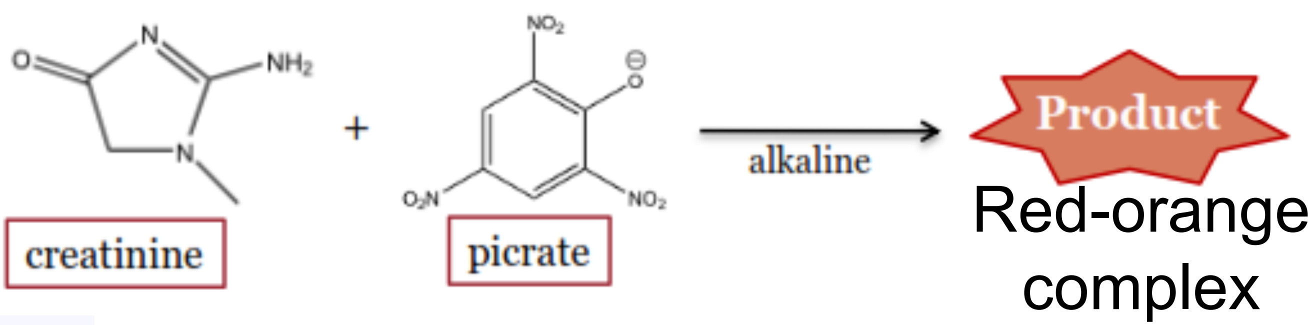
- Cr is cleared essentially only by glomerular filtration
- It is not reabsorbed and is only slightly secreted by the proximal tubule
- Serum levels are higher in males than in females due to the direct correlation with muscle mass.
- Analysis of Cr is simple and inexpensive using colorimetric assays

Clinical applications of Cr

- Clinical applications of Cr:
  - To determine the sufficiency of kidney function
  - To determine the severity of kidney damage
  - To monitor the progression of kidney disease
- Cr concentration is a function of:
  - Relative muscle mass
  - The rate of creatine turnover
  - Renal function

Lab test for Creatinine

- Jaffe reaction/ Alkaline picrate:
- Creatinine + picric acid in alkaline sol → red orange complex
- Interferences:
  - Acetoacetate, acetone, glucose, pyruvate, ascorbate



- Specimens for creatinine measurement
  - Serum, plasma or urine

- Interference:
  - Hemolyzed and icteric samples should be avoided especially with Jaffe rxn
  - Lipemic samples may give erroneous results

Reference range

CREATININE

Adult	Plasma or serum	Jaffe method	Enzymatic method
Male		0.9–1.3 mg/dL (80–115 µmol/L)	0.6–1.1 mg/dL (53–97 µmol/L)
Female		0.6–1.1 mg/dL (53–97 µmol/L)	0.5–0.8 mg/dL (44–71 µmol/L)
Child		0.3–0.7 mg/dL (27–62 µmol/L)	0.0–0.6 mg/dL (0–53 µmol/L)
Adult	Urine, 24 h		
Male		800–2,000 mg/d (7.1–17.7 mmol/d)	
Female		600–1,800 mg/d (5.3–15.9 mmol/d)	

Analytic Procedures (cont'd)

- Clearance Measurements
  - **Urea:** does not provide full clearance assessment & is no longer widely used
  - **Cystatin C:** a low-molecular-weight protein produced by nucleated cells; levels remain stable if kidney function is normal
  - Biologic variation
    - Random fluctuation around homeostatic setting point, either within an individual or between individuals
    - For creatinine, within-subject variation is less than between-subject variation, making it more helpful in monitoring an individual.

Creatine Clearance

- The glomerular filtration rate (GFR) provides a useful index of the number of functioning glomeruli.

- It gives an estimation of the degree of renal impairment by disease

Accurate measurement of GFR

- Accurate measurement of GRF by clearance tests requires determination of the conc in plasma and urine of a substance that is:
  - Freely filtered at glomeruli.
  - Neither reabsorbed nor secreted by tubules.
  - Its concentration in plasma needs to remains constant throughout the period of urine collection.
  - Better if the substance is present endogenously.
  - Easily measured
- Creatinine meets most of these criteria.

Cr Clearance Changes with Age

- Creatinine clearance is usually about 110 ml/min in the 20-40 year old adults.
- It falls slowly but progressively to about 70 ml/min in individuals over 80 years of age.
- In children, the GFR should be related to surface area, when this is done, results are similar to those found in young adults.

Cr clearance: the specimen

- Two specimens: a 24-hour urine & a blood specimen that is drawn during the 24-hour urine collection or not more than 24 hours before or after the urine collection.
- The lab may add 6mol/L HCl or boric acid to the container as preservative.
- The patient is instructed to collect the 24hr-urine as follows:
  - Void and discard the urine.
  - Start timing the 24-hour period immediately after voiding
  - Collect all the urine voided for the next 24 hours. Keep the urine in a cool place.
  - At 24 hours, void and add this urine to the collection container.
  - Bring the urine to the laboratory as soon as possible.

Ref: Clinical chemistry: a laboratory perspective. By Wendy Arneson & Jean Brickell, ©2007. Publisher: F.A. Davies. Chap6 /Page 205

Calculation of Cr Clearance

- Clearance is the volume of plasma cleared from the substance excreted in urine per minute.
- It could be calculated from the following equation:
- Clearance (ml/min) = $(U \times V)/P$
  - **U** = Concentration of creatinine in urine μmol/l
  - **V** = Volume of urine per min
  - **P** = Concentration of creatinine in serum μmol/l

Cr clearance for **pediatric** patients

- Several formulas are available to estimate Cr clearance.
- **Schwarz formula** estimates Cr clearance from serum Cr for pediatric patients:
- Creatinine clearance = (k X Ht) X S.Cr
- where k= 0.45 if age <1 year, k =0.55 if age1-12 years; Ht = height in cm; S.Cr: serum creatinine.

Ref: Clinical chemistry: a laboratory perspective. By Wendy Arneson & Jean Brickell, ©2007. Publisher: F.A. Davies. Chap6 /Page 205

Estimated GFR (eGFR)

- Cr clearance is measured using a 24-hour urine collection, but this does introduce potential errors in terms of completion of the collection.
- An alternative and convenient method is to employ various formulae devised to calculate Cr clearance using parameters such as serum creatinine level, sex, age, and weight of the subject
- Cockroft-Gault formula
  - Depends on Serum Cr only
  - It predicts Cr clearance and is not corrected for Body surface area (BSA)
  - It assumes women have a 15% lower Cr Clearance than men

$$\text{CrCl (mL/min)} = \frac{(140\text{-age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \ (\times\ 0.85 \text{ if female})$$

- Limitations of eGFR calculated using Cockroft-Gault formula
- It should not be used if
  - Serum creatinine is changing rapidly
  - the diet is unusual, e.g., strict vegetarian
  - Low muscle mass, e.g., muscle wasting
  - Obesity

Serum Cr vs. Cr clearance

- Serum Cr is a better KFT than Cr clearance because
  - Serum creatinine is more accurate.
  - Serum creatinine level is constant throughout adult life
- Cr clearance is recommended in the following conditions
  - Patients with early (minor) renal disease.
  - Assessment of possible kidney donors.
  - Detection of renal toxicity of some nephrotoxic drugs

Adult Reference ranges

- Urinary excretion of creatinine is 0.5 - 2.0 g per 24 hours in a normal adult, varying according to muscular weight.
  - Serum creatinine: 55 – 120 μmol/l
  - Creatinine clearance: (males) 90 – 140 ml/min
  - (females) 80 – 125 ml/min

- A raised serum creatinine is
  - A good indicator of impaired renal function
- But normal serum creatinine
  - Does not necessarily indicate normal renal function as serum creatinine may not be elevated until GFR has fallen by as much as 50%

Final Product of kidney: Urine

- **Healthy urine:**
- 0.4-2 L/day
- Clear, amber colored
- pH 5.0-6.0
- Osmolality: 50-1400 mOsms/kg
- Protein: 50-80 mg/day
  - Albumin: <30 mg/day
- Glucose: <0.5 g/day

Analytic Procedures (cont'd)

- Urine Electrophoresis
  - Distinguishes between acute glomerular nephropathy & tubular proteinuria
  - Screens for abnormal monoclonal or polyclonal globulins
- β2-Microglobulin
  - Used clinically to assess renal tubular function in renal transplant patients, with elevated levels indicating organ rejection
- Myoglobin
  - Myoglobin clearance has been proposed as an effective early indicator of myoglobin-induced acute renal failure.
  - Blood levels of myoglobin can rise very quickly with severe muscle injury. In rhabdomyolysis, myoglobin release from skeletal muscle is sufficient to overload the proximal tubules and cause acute renal failure

Analytic Procedures (cont'd)

- Microalbumin
  - **Microalbuminuria:** small amounts of albumin in urine
  - Urine microalbumin measurement is important in management of patients with diabetes mellitus, who are at risk for nephropathy.
  - Type 1 diabetes: 30–45% risk; type 2 diabetes: 30% risk
  - In later phase of nephropathy, increased glomerular capillary permeability allows small amounts of albumin to pass into urine.
  - If detected in early phase by microalbumin measurement, progression to end-stage renal disease can be prevented.
  - Urinary albumin concentrations of 30-300 mg/24 hours are predictive of diabetic nephropathy.

Urinary Albumin

- Test for microablbuminuria must be sensitive to low conc. Urinalysis dipstick is not sensitive to low conc of albumin.
- Quantitative albumin-specific immunoassays, usually using nephelometry or immunoturbidimetry,
- Reaction: dye binding methods
- Calculations: [U. albumin mg/dL] X [U. volume dL] /day
- Ref range: 30-300 mg/day on 2 of 3 collections is indicative of microalbuminuria

Urinary protein

- The conc of protein in urine is less than the concentration in blood, thus a more sensitive methodology must be performed to measure the concentration of urine proteins
- Reaction principle:
- Turbidometric: proteins are ppt using sulfosalicylic acid or TCA. Ppt protein is measured photometrically using dye binding methods
- Calculations: [U. protein mg/dL] X [U. volume dL] /day
- Specimen: 12 or 24-hr urine sample, 24hr sample is preferred
- Ref range: < 100 mg/day

Serum Urea

- Since historic assays for urea were based on the measurement of nitrogen, the term blood urea nitrogen (BUN) has been used to refer to urea determination.
- Urea nitrogen (urea N) is a more appropriate term.

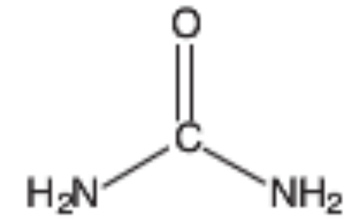


FIGURE 12-1 Structure of urea.

Serum Urea

- It is a gross indicator of renal function
- As a kidney function test, serum urea is inferior to serum creatinine because:
  - High protein diet increases urea formation
  - Any condition that ↑ protein catabolism *(Cushing syndrome, diabetes mellitus, starvation, thyrotoxicosis)* →↑ urea formation.
  - 50 % or more of urea filtered at the glomerulus is passively reabsorbed by the renal tubules

Clinical Applications

- Used to evaluate renal function
- To assess hydration status
- Determine nitrogen balance to aid in diagnosis of renal diseases
- To verify adequate of dialysis

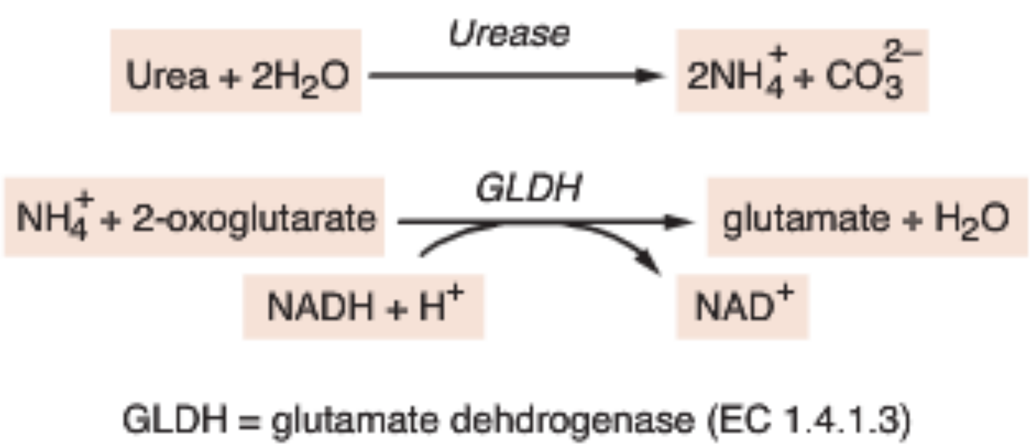


FIGURE 12-2 Enzymatic assay for urea.

Reference Intervals

UREA NITROGEN[8]			
Adult			
	Plasma or serum	6–20 mg/dL	2.1–7.1 mmol/L
	Urine, 24 h	12–20 g/d	0.43–0.71 mol urea/d

Pathophysiology

- Azotemia: an elevated concentration of urea in the blood is called azotemia.
- Uremia: very high plasma urea concentration accompanied by renal failure is called uremia or the uremic syndrome.
- Uremia is fatal if not treated by dialysis or transplantation.

TABLE 12-3 CAUSES OF ABNORMAL PLASMA UREA CONCENTRATION

INCREASED CONCENTRATION	
Prerenal	Congestive heart failure
	Shock, hemorrhage
	Dehydration
	Increased protein catabolism
	High-protein diet
Renal	Acute and chronic renal failure
	Renal disease, including glomerular nephritis and tubular necrosis
Postrenal	Urinary tract obstruction
DECREASED CONCENTRATION	
	Low protein intake
	Severe vomiting and diarrhea
	Liver disease
	Pregnancy

Analytic Procedures (cont'd)

- Neutrophil Gelatinase-Associated Lipocalin
  - NGAL is a 25-kDa protein expressed by neutrophils and epithelial cells; including of the proximal tubule
  - Elevated within 2-6 hours of AKI
  - Measured in plasma and urine
  - Urinary NGAL excretion may not be specific to AKI

Analytic Procedures (cont'd)

- Urinalysis
  - Permits a detailed, in-depth assessment of renal status with an easily obtained specimen
  - Serves as a quick indicator of glucose status & hepatic-biliary function
  - Routine urinalysis includes assessment of:
    - Physical characteristics
    - Chemical analyses
    - Microscopic examination of sediment from a urine sample

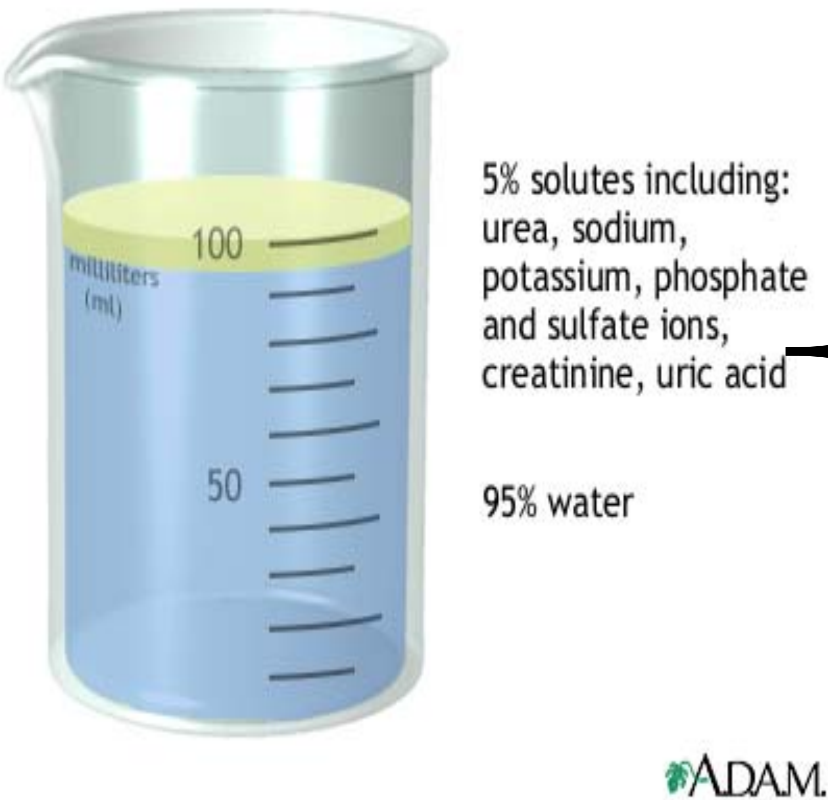
Analytic Procedures (cont'd)

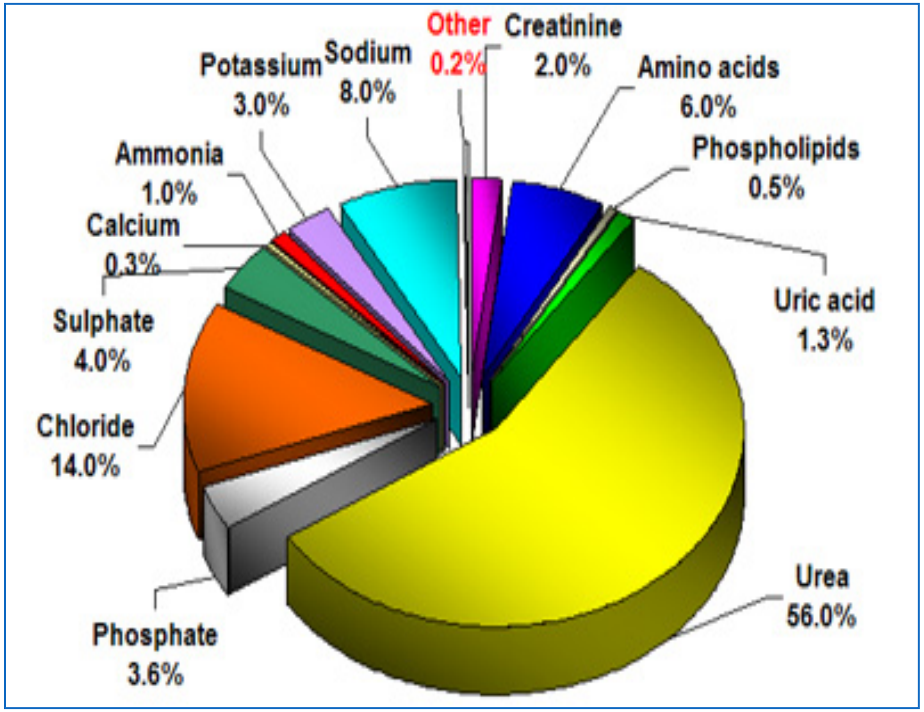
- Urinalysis
  - Physical characteristics
    - Specimen collection
    - Visual appearance
    - Odor
    - Turbidity
    - Volume
    - Specific gravity
    - Lab methods
    - Disease correlation
    - pH
  - Chemical analyses
    - Glucose & ketones
    - Protein
    - Nitrite
    - Leukocyte esterase
    - Bilirubin/urobilinogen
    - Hemoglobin/blood

Analytic Procedures (cont'd)

- Urinalysis
  - Sediment examination
    - Red blood cells
    - White blood cells
    - Epithelial cells
    - Miscellaneous elements
    - Bacteria
    - Hyaline casts
    - Granular casts
    - Cellular casts
  - Crystals
    - Acid environment
    - Alkaline environment
    - Other

Components of urine





Urinalysis (UA)

- UA includes routine (1-3) and special (4-5) testing:
  1. Assessment of physical characteristics/macroscopic,
  2. Chemical analyses (Urine dipstick),
  3. Microscopic examination of the sediment from a (random) urine specimen
  4. Culture
  5. Cytological examination

Physical examination of urine

- Done with the naked eye, a very important part of the test. Findings should be documented.

- Visual appearance / Color (affected by drugs, food, general condition).
- Turbidity (clear; cloudy, particles).
- Volume.
- Odor (affected by infection, diet)

- **Color**

– Colorless	Diluted urine
– Yellow-amber	Urochromes (urobilin)
– Deep Yellow	Conc. urine, Riboflavin
– Yellow-brown to green	Bilirubin / Biliverdin
– Red-brown (fresh)	Blood / Hemoglobin
– Red-brown (standing)	Porphyrins
– Brownish-black	Alkaptonuria (Homogentisic acid), Melanin (melanoma)
– Drugs, foods (like beets)	May alter color

- **Odor**

– Ammonia-like	(Urea-splitting bacteria)
– Foul, offensive	Old specimen, pus or inflammation
– Sweet	Glucose
– Fruity	Ketones
– Maple syrup-like	Maple Syrup Urine Disease

- **Turbidity**
  - It depends on pH and dissolved solids
  - Typically cells or crystals.
  - Turbid: gross bacteriuria
  - Smoky: hematuria
  - Thread-like: full of mucus
  - Alkaline urine: ppt of amorphous phosphates & carbonates
  - Acidic urine: ppt of amorphous urates
  - Cellular elements and bacteria will clear by centrifugation.
  - Microscopic examination will determine which is present.

- **Volume**
  - Adults produce 750-2000 ml/day (Average 1500ml)
  - Polyuria: diabetes mellitus & insipidus, chronic renal disease
  - Anuria & oliguria (<200 ml/d): in nephritis, urinary tract obstruction, AKI & kidney failure

- **Specific gravity (SG)**
- SG = wt of 1ml of urine/wt of 1ml water
- Ref. range: 1.003- 1.035 g/ml
- Low SG: diabetes insipidus, pyelonephritis, glomerulonephritis
- High SG: diabetes meillitus, congestive heart failure, dehydration

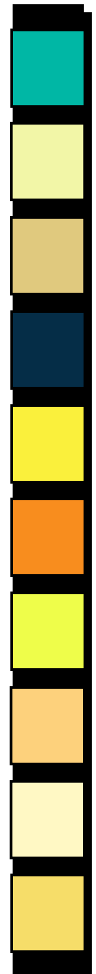
- **pH**
- Ref. range: 4.7 – 7.8
- Acidic urine: phosphates conjugated to Na^+, K^+, Ca^{2+} & NH_4^+, excretion of metabolic acids pyruvate, lactate & citrate; diabetes mellitus, renal tubular acidosis
- Alkaline urine: postprandial, ingestion of alkaline food/drugs, UTI, bacterial contamination

Chemical testing of urine

- Usually done with reagent strips.
- Used to determine body processes such as carbohydrate metabolism, liver or kidney function.
- Used to determine infection.
- Can be used to determine presence of drug or toxic environmental substances.

Chemical analysis

Urine Dipstick



Glucose
Bilirubin
Ketones
Specific Gravity
Blood
pH
Protein
Urobilinogen
Nitrite
Leukocyte Esterase

Case 1

Glucose		++
Bilirubin		Negative
Ketones		Trace
S.G.		1.015
Blood		Negative
pH		6.0
Protein		Negative
Urobilinogen		1.0 mg/dL
Nitrite		Negative
L.E.		Negative

A 27-year old woman presents with severe abdominal pain.

Physical characteristics: clear-yellow.

Microscopic: Not performed.

Questions:

1. What is the most likely diagnosis?
2. What do you make of the ketone result?
3. What do you expect to happen to the ketone measurement when treatment begins?

CASE STUDY 27-1

A 52-year-old man with a history of AIDS, hypertension, diabetes mellitus, and alcohol abuse was found unconscious in his home by his roommate. In the emergency department, he was hypotensive (103/60 mm Hg), febrile (temperature 101°F), and unresponsive. Computed tomography scan of the abdomen showed cholecystitis and gallstones. Laboratory data are listed.

The patient was diagnosed with acute renal failure. He was administered intravenous fluids; BUN fell to 68 mg/dL and creatinine fell to 2.2 mg/dL. The patient's blood culture report was positive for *E. coli*. He was treated with tobramycin and cefepime. The patient continued to deteriorate and died 5 days after admission. Cause of death was multiorgan failure secondary to AIDS, sepsis, and alcoholic cirrhosis.

Questions

1. What is the significance of the patient's elevated CK? Explain why the physician ordered a CK-MB and troponin level. What can you conclude about the patient's cardiac status?
2. What is the cause of his acute renal failure?
3. What is the significance of the patient's large urine hemoglobin?
4. How would you interpret this patient's liver function tests considering his clinical history?

Drugs of Abuse	Negative	Urinalysis	
Serum ethanol	84 mg/dL	Hemoglobin	Positive
		WBC	4 HPF (0–4)
		RBC	2 HPF (0–4)
CK	3,308 U/L (24–204)	BUN	71 mg/dL (8–21)
CK-MB	1.5 ng/mL (0–7.5)	Creatinine	4.1 mg/dL (0.9–1.5)
Troponin T	<0.01 ng/mL (0–0.4)	Alkaline phosphatase	443 U/L (45–122)
pH	7.50	Aspartate aminotransferase	305 U/L (9–45)
pCO_2	27 mm Hg	Alanine aminotransferase	78 U/L (8–63)
Total CO_2	15 mmol/L	Gamma glutamyl transpeptidase	724 U/L (11–50)
		Total bilirubin	2.7 mg/dL (0.2–1.0)
		Direct bilirubin	2.4 mg/dL (0–0.2)

CASE STUDY 27-3

A 78-year-old woman with a history of hypertension, aortic thoracic graft, and esophageal reflux disease complained of fever (100°F) and weakness. She had been treated 3 weeks before at the hospital for a urinary tract infection. She was admitted to the hospital for a diagnostic workup and transfusion. Her laboratory results are as follows:

Na^+	129 mmol/L	Hct	25.6%
K^+	3.7 mmol/L	Hgb	8.5 g/dL
Cl^-	97 mmol/L	WBC	9,700
CO_2	19 mmol/L		
BUN	52 mg/dL		
Creatinine	3.2 mg/dL		

Urine culture was positive for *Citrobacter*. Urinalysis results are listed:

Color	Hazy/yellow
Specific gravity	1.015
pH	5
Blood	Large
Protein	2
Glucose	Negative
Ketones	Negative
Nitrates	Negative
RBC	>25
WBC	1–4
Casts	Granular, 1–4

The patient's renal function continued to decline, and she was put on hemodialysis. A renal biopsy was performed that showed end-stage crescentic glomerulonephritis. Two days later, the patient sustained a perforated duodenal ulcer, which required surgery and blood transfusion. Subsequently, she developed coagulopathy and liver failure. Her condition continued to deteriorate in the next few days, and she died following removal of life support.

Questions

1. Looking at the urinalysis, what is the significance of the results of 2+ protein and >25 RBCs?
2. What is the most likely cause of glomerulonephritis?
3. Why was the patient put on hemodialysis?