Chapter 4

RENAL FUNCTION

Urine Composition

Normal ranges are wide as urine volume and solute composition can vary greatly depending on:

- Diet
- Physical activity
- Health

Kidneys are principal organ for regulating body fluid composition

Renal excretion is primary elimination route of soluble metabolic wastes

Wastes exclusively excreted by kidneys can be used to assess kidney function (creatinine, urea)

Measures of Concentration

Osmolality

- Osmoles per kilogram (Os/kg) (milliosmoles used for convenience)
- Affected by solute number, not size or weight
- Final osmolality determined in distal and collecting tubules when antidiuretic hormone (ADH) is present
- Normally urine osmolality is 1 to 3 times that of plasma

Specific gravity

- Comparison of density of urine to that of water
- Normally ranges from 1.002 to 1.035
- Depends on number of particles and mass

Urine Volume

Polyuria—greater than 3 L/day

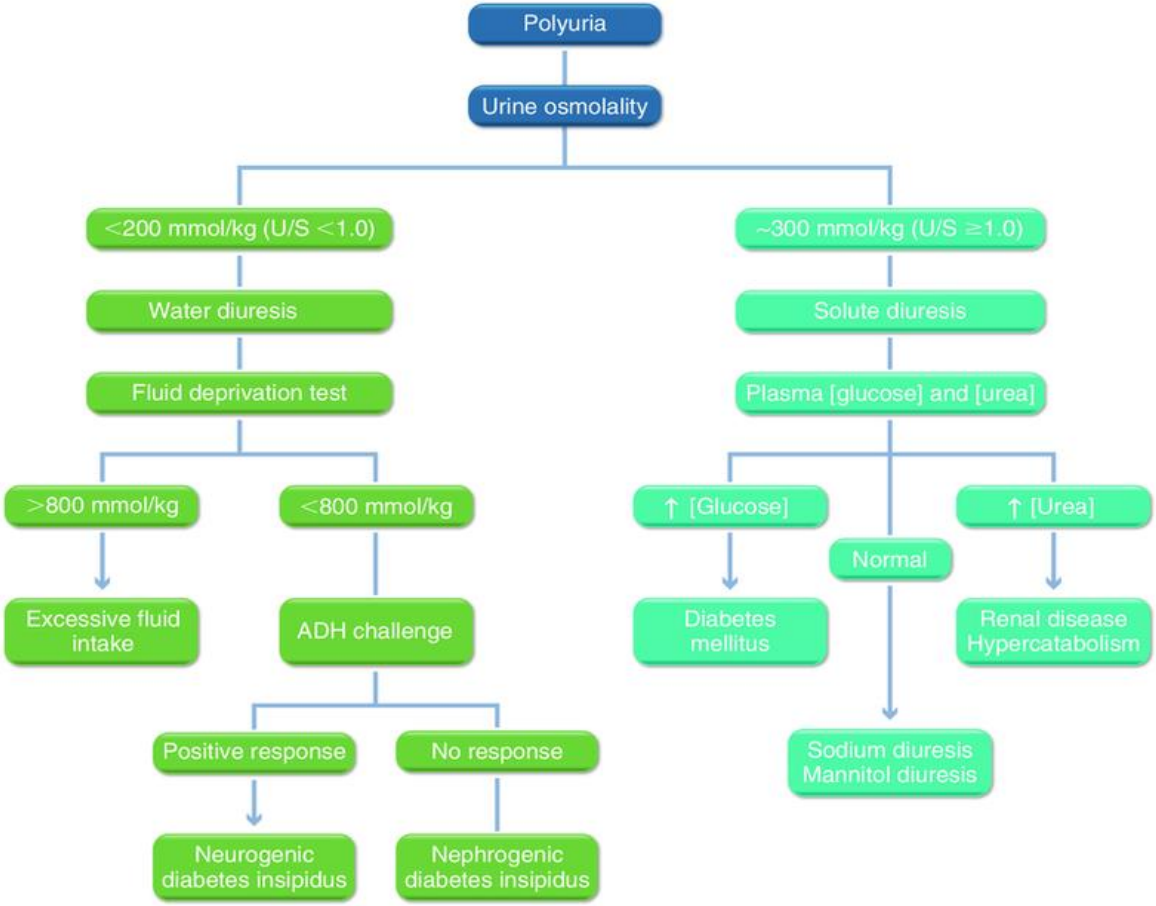
- Conditions with water diuresis (osmolality <200 mOsm/kg)
  - ADH secretion inadequate or receptors ineffective
- Conditions with solute diuresis (osmolality ≥300 mOsm/kg)
  - No common feature, but involve glucose, urea, or sodium

Oliguria—less than 400 mL/day

- Urinary obstruction, tubular dysfunction, fluid loss

Anuria—absence or cessation of urine excretion

- Progressive renal disease or renal failure



A flowchart for the evaluation of polyuria. *ADH*, Antidiuretic hormone; *U/S*, urine-to-serum osmolality ratio. (Redrawn from Walmsley RN, White GH: *A guide to diagnostic clinical chemistry*, Melbourne, 1983, Blackwell Science.)

Testing Renal Concentrating Ability

Assess tubular reabsorptive function by demonstrating tubules can produce concentrated urine specimen (osmolality >800 mOsm or specific gravity >1.025)

Osmolality preferred

- More accurate reflection of kidney's concentrating ability, since only solute number affects it

Three most prevalent solutes:

- Urea
- Chloride
- Sodium

Fixation of Solute Concentration

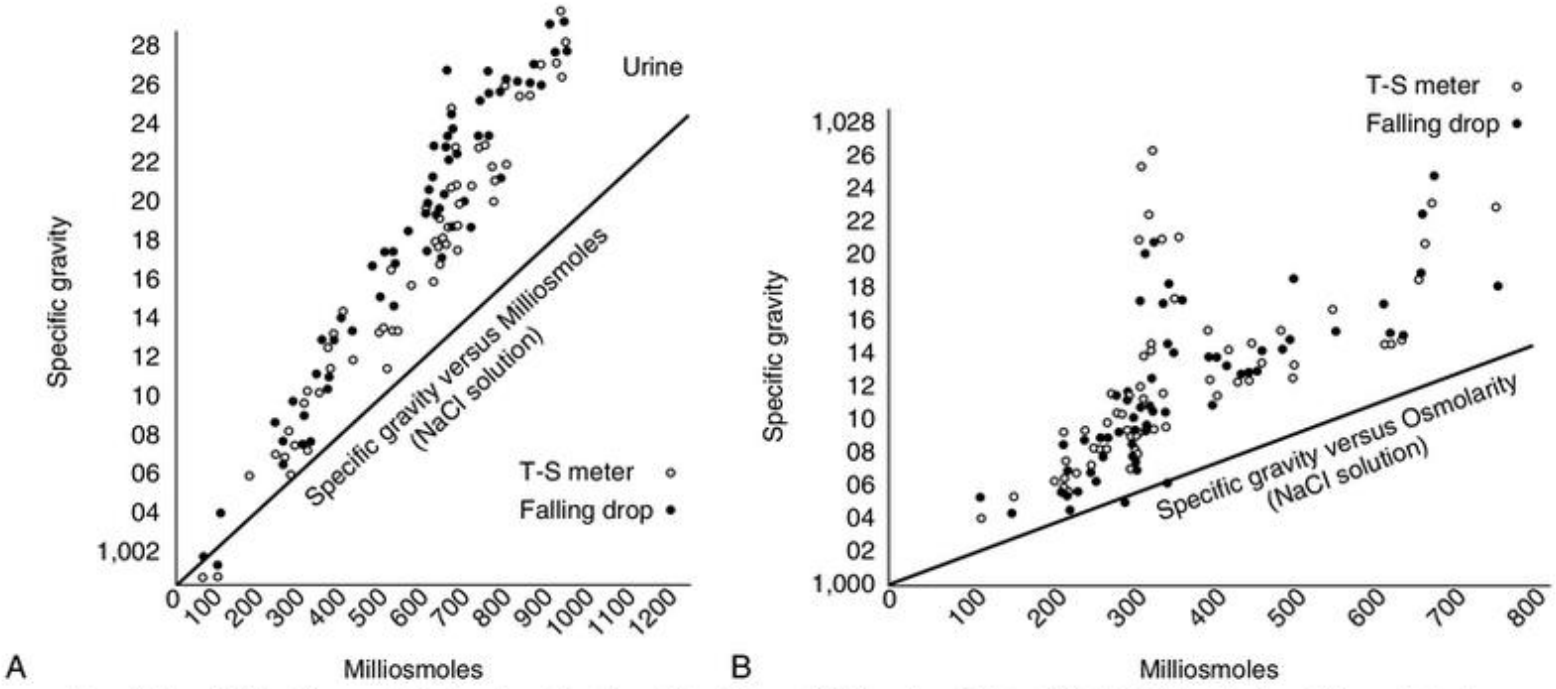
In some chronic renal diseases, concentrating ability slowly diminishes until specific gravity or osmolality are unchanging

Urine concentration same as ultrafiltrate

Specific gravity of 1.010 or approximately 300 mOsm/kg

Causes polyuria and nocturia

Figure 4-4. A comparison of urine specific gravity and urine osmolality. Specific gravity measurements were determined by a direct method (falling drop) and an indirect method (refractometry). The straight lines represent the specific gravity and osmolality results obtained with solutions of varying sodium chloride concentrations. (A) A comparison of urines obtained from healthy medical students. (B) A comparison of urines obtained from patients on renal service. (From Holmes JH: *Workshop on urinalysis and renal function studies*, Chicago, 1962, American Society of Clinical Pathologists. Used with permission.)



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Fluid Deprivation Tests

Used to differentiate causes of polyuria due to water diuresis

- "Neurogenic" diabetes insipidus
  - ADH decreased
- "Nephrogenic" diabetes insipidus
  - Lack of renal response to ADH

Water consumption restricted

Urine specimen checked about 12 hours later

If concentrated, test is ended. If not, test continues.

Can compare with plasma concentration or administer ADH to see if that helps

Renal Clearance Tests to Assess Glomerular Filtration Rate (GFR)

Volume of plasma in milliliters that is completely cleared of a substance per unit of time

Volume of plasma filtered directly affects volume and composition of urine excreted

Calculate renal clearance (C) using plasma concentration of substance (P), urine concentration (U), and volume of urine (V)

$$C(mL/min) = \frac{U(mg/dL) \times V(mL/min)}{P(mg/dL)}$$

Clearance Tests

Tests for GFR use substances removed solely by glomerular filtration (inulin)

Tests for tubular secretion use substances removed solely by tubular secretion (phenolsulfonphthalein [PSP] or *p*-aminohippurate)

Can use endogenous or exogenous substances

Inulin is reference method for GFR testing, although rarely used

Creatinine clearance is most commonly used

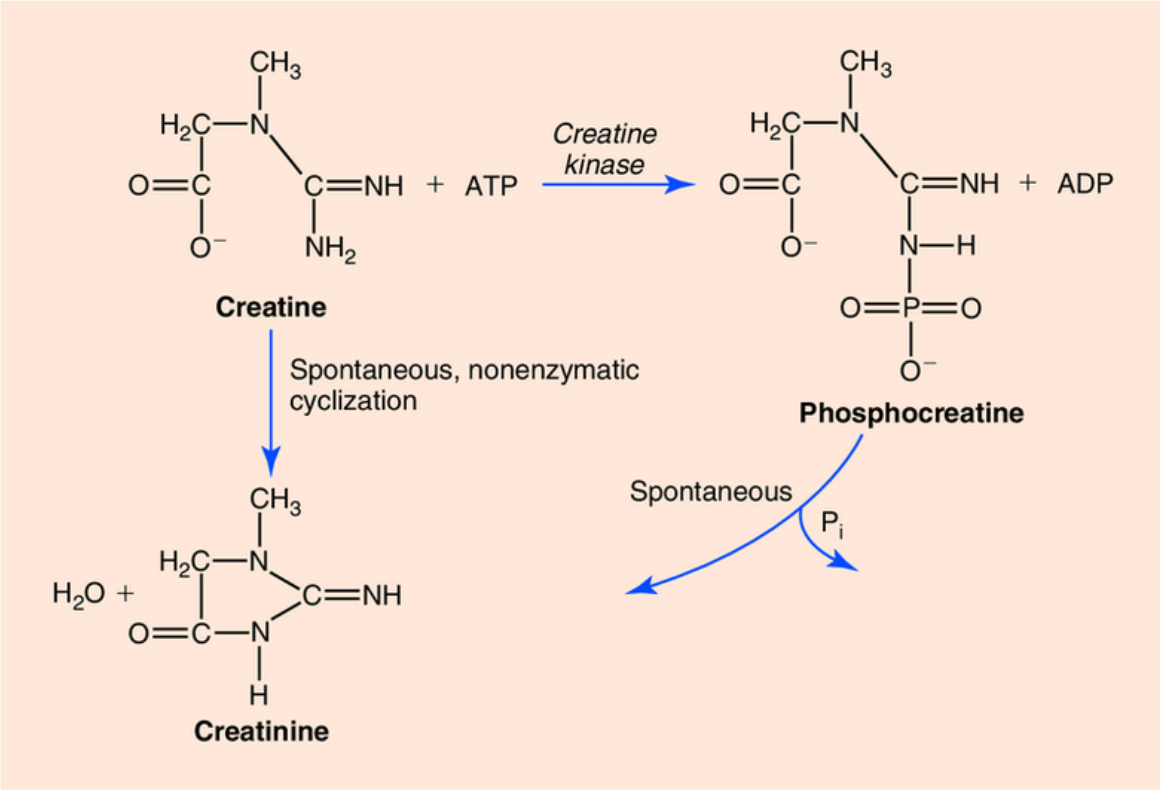
Creatinine Clearance

Creatinine is a waste product of creatine in muscles, produced at a relatively constant rate and excreted by kidneys

Requires a 24-hour urine creatinine (U) and serum creatinine (P) drawn sometime during urine collection period, urine volume (V), and an estimate of body surface area (from height and weight using a nomogram)

$$C(\text{mL/min}) = \frac{U \times V}{P} \times \frac{1.73\text{m}^2}{SA}$$

Figure 4-5. The formation of creatinine from creatine and phosphocreatine. *ADP*, Adenosine diphosphate; *ATP*, adenosine triphosphate.



Advantages/Disadvantages of Creatinine Clearance

Plasma and urine creatinine tests easily performed

Accuracy and precision of methods well studied

Small amount of creatinine secreted by tubules (7% to 10%), resulting in an increased urine concentration of creatinine

If nonspecific Jaffe method is used to measure, P creatinine will be overestimated, offsetting increased U value, giving values close to inulin clearance results

Estimated Glomerular Filtration Rate (eGFR)

Simple, effective tool that helps to detect chronic kidney disease

Used for high-risk individuals with diabetes, hypertension, heart disease, or family history of kidney disease

Calculation based on serum creatinine level and patient's age, gender, and ethnicity

Most accurate values are less than or equal to 60 mL/min, so values greater than 60 are reported simply as greater than 60. Numerical values are reported for values less than or equal to 60 mL/min.

$Beta_2$-Microglobulin

A low-molecular-weight protein found on surface of nucleated cells and shed into plasma

Readily passes through glomeruli and is 99.9% reabsorbed by proximal tubules

Marker of reduced tubular function when it increases in urine

Used clinically to:

- Identify early kidney transplant rejection
- Differentiate tubular and glomerular diseases

Cystatin C

Low-molecular-weight protein that has potential as a marker for long-term monitoring of renal function

Produced by nucleated cells and filtered by glomerulus and is catabolized by tubular cells

Increased plasma levels reflect decreased glomerular function

Not yet used routinely

Screening for Albuminuria

Albuminuria appears early in diabetic nephropathy

Early detection of low levels of albumin in urine (microalbuminuria) signals need for additional testing and aggressive intervention

Presence of albumin is caused by increased glomerular permeability due to changes in glomerular filtration barrier

Single most important factor associated with glomerular proteinuria is hyperglycemia

Other Tests

p-Aminohippurate clearance

- Exogenous nontoxic weak acid secreted almost exclusively by proximal tubules, used as indicator of renal tubular secretory function

Measurement of titratable acid versus urinary ammonia

- Assess tubular function for removing acids

Oral ammonium chloride test

- Give ammonium chloride, and measure series of urine pH and plasma bicarbonate. Used to diagnose renal tubular acidosis

Most Commonly Used Tests for Evaluating Renal Function

Creatinine clearance for assessment of GFR

Urine osmolality for tubular concentrating ability

Urine protein electrophoresis to evaluate glomerular permeability to plasma proteins

Plasma creatinine

eGFR calculation