Fluids and Electrolytes: Clinical Problems and Their Solutions

Patricia A. Gabow, M.D.

Fluids and Electrolytes

Clinical Problems and Their Solutions

Patricia A. Gabow, M.D. *Associate Professor of Medicine, University of Colorado Health Sciences Center, Denver, Colorado; Director, Department of Medicine, Denver General Hospital*

Little, Brown and Company, Boston/Toronto

First Edition

Library of Congress Catalog Card No. 82-83348
ISBN 0-316-30114-0
Printed in the United States of America
SEM

Fluids and Electrolytes
Clinical Problems and Their Solutions

To the patients who provided the clinical problems for this book, and to my husband, for his loving support in all things

Preface

In these times of routine chemistry determinations, virtually all hospitalized patients undergo these tests. Therefore, every physician, regardless of his or her subspecialty, should be able to interpret correctly the data obtained from these routine determinations and to make appropriate therapeutic decisions from them.

This book grew out of an effort to communicate to medical students the essential concepts of fluid and electrolyte management that are used in understanding the results obtained from routine serum chemistry measurements and arterial blood gas analysis. Although originally planned for medical students, it seemed to fulfill a need to accomplish this goal for interns, residents, fellows, and practicing physicians as well.

The chapters in the book are divided into two main sections. The first section deals with factual materials on a given subject. The questions posed in this first section are best answered by reading the references suggested at the end of the chapter. The second section of each chapter centers on clinical problems. The questions posed in the second section are ones that arise in day-to-day patient management. They will serve to test how completely the factual material has been understood. Thus, if one cannot effectively manage the patient(s) presented in the second section of each chapter, more time should be spent in understanding the material presented in the first section, for the physician's knowledge is meaningful only if it can be applied to treating patients correctly and effectively.

P. A. G.

Contents

1. Urinalysis

A few months careful study in the wards of a hospital and in the deadhouse will serve to convince any unprejudiced person that the nature of renal disease may be diagnosed in many cases by the microscopial character of the urinary deposit.

Dr. Lionel S. Beale, 1852

Questions

1. What colors can a urine sample be, and what do these colors indicate pathologically?
2. How is specific gravity helpful in the clinical evaluation of a patient? What is the correlation between specific gravity and osmolality? In a hospital setting, what is the most common cause for a high specific gravity with a markedly lower osmolality?
3. What is the pH of an essentially bicarbonate-free urine; of a maximally acidified urine? What clinical information can be obtained from a dipstick test for urine pH?
4. a. What proteins are detected by the urine dipstick test for protein?
   b. A 50-year-old woman was admitted with anemia and hypercalcemia. Urinalysis by the medical student revealed no protein. The laboratory, however, using sulfosalicylic acid, reported 3+ protein in the same urine sample. How do you interpret these findings? What gives you a false positive test for albumin?
   c. A diabetic patient was referred for evaluation of proteinuria. In reviewing the old chart to determine the probable onset of proteinuria, one needs to correlate what other variable on the urinalysis with the protein?
5. What does the urine dipstick test for blood detect? How can these possible causes be differentiated?
6. What substances are detected by the urine dipstick test for ketones? In what clinical situations do urine ketones underestimate the degree of ketoacidosis? Why? In what clinical settings can positive serum ketones overestimate the amount of ketoacids?
7. What is measured by the glucose dipstick test? In what clinical settings does glucosuria occur?
8. What cellular elements can be identified in a urinalysis? How many of each type can be seen in a normal urinalysis? How does one interpret an abnormal number?
9. How should one obtain, save, and prepare a urine specimen to look for casts? What casts can be found in a urine specimen, and how should they be interpreted?
10. What urinary crystals can be seen that help in establishing a clinical diagnosis?

Solutions to Questions

1. The following colors of a urine sample reflect the causes listed below:

Color	*Abnormality or Cause*
Red	Hematuria Hemoglobin Myoglobin (muscle pigment) Beets Rifampin
Orange	Bilirubin Pyridium (urinary analgesic used in treating cystitis)
Brown	Hemoglobin (in acid urine) Myoglobin Bilirubin
Magenta	Porphyria (on exposure to air)
Black	Alcaptonuria (on exposure to air) Metastatic malignant melanoma (on exposure to air, due to melanin pigment) Blackwater fever (hemoglobinuria from malaria)
White (milk-colored)	Chyluria; most common cause in the world is filariasis; in the U.S., pulmonary tuberculosis or a pulmonary tumor obstructing the thoracic duct

2. Since specific gravity gives a rough estimate of the concentration of the urine, this measurement should be used to assess appropriate water handling by a patient. The most accurate measurement of urinary concentration, however, is measured osmolality. The lack of correlation of specific gravity and osmolality is due to the fact that specific gravity reflects not only numbers but also density of particles, whereas osmolality is a colligative property and reflects only the number of particles.

   In a hospital setting, intravenous contrast material is probably the most frequent cause of a marked dissociation of specific gravity and osmolality. This cause should certainly be considered when specific gravity exceeds what is normally seen physiologically, that is, 1.030.

3. The pH of a bicarbonate-free urine is 6.0 or less; a maximally acidified urine is 4.5 to 5.0.

   The following clinical information can be obtained from urine pH:

   a. To evaluate appropriate acidification: It is important to recognize that the urine dipstick test for pH is not very accurate; if measurement of pH is indicated to verify appropriate renal acidification, pH by meter should be obtained of a freshly voided urine specimen. The patient who has hyperchloremic acidosis without a history of diarrhea (see Chap. 3) should always have urine pH measured to ascertain if the urine is appropriately acidified, that is, less than 5.5. Urine pH greater than 5.5 in the presence of metabolic acidosis and acidemia supports a diagnosis of distal renal tubular acidosis (see Chap. 3). This focuses attention, then, on the kidney rather than the gastrointestinal tract as the site of HCO_3 loss.

b. To follow therapy: For example, in the treatment of a sodium chloride–responsive metabolic alkalosis, HCO_3 should start to be excreted. Thus, when urine pH exceeds 6.1, euvolemia is being approached and the excess HCO_3 is being excreted.

In certain clinical situations such as salicylate and phenobarbital intoxication, alkalization promotes excretion of these substances. As HCO_3 is administered, urine pH should be checked and should be greater than 7.0 in this setting.

c. To assess urinary tract disease: Urine pH of 8.0 in a patient should raise the question of an infection with urea-splitting organisms such as *Proteus* organisms. A consistently acid pH in a patient with uric acid stones may promote the stone formation. Similarly, in a patient with multiple myeloma, acid urine may contribute to the development of myeloma kidney.

4. a. The urine dipstick test for protein detects albumin only. It does not detect amino acids, globulins, tubular protein (Tamm-Horsfall protein), or myeloma protein (Bence Jones protein). The last is of particular clinical importance in that a negative dipstick test in a patient with multiple myeloma does not exclude the possibility of substantial Bence Jones proteinuria.

b. This patient probably has multiple myeloma. If the patient has Bence Jones proteinuria, the medical student would get a negative test for protein using the dipstick, and the laboratory, using sulfosalicylic acid precipitation, would get a positive test, since this method detects all proteins. A very alkaline urine will give a false positive test on albumin. The color change on the dipstick is dependent on the electrical charges on the albumin molecule, and a high pH affects this charge and results in some color change. However, this should never be the reason for 3+ and 4+ protein on urinalysis.

c. In assessing the significance of "dipstick proteinuria," it must be emphasized that this reflects protein concentration and not the absolute amount of protein in the urine. A dipstick value for protein needs to be interpreted in relation to urine specific gravity. For example, a trace or 1+ protein determination in a urine specimen with high specific gravity may represent insignificant proteinuria, whereas 1+ in a urine sample with specific gravity of 1.005 may reflect significant proteinuria.

5. The urine dipstick test for hemoglobin detects hemoglobin and myoglobulin. Myoglobulin is a heme pigment and is measured by the orthotolidine reaction on the dipstick.

If a patient has dipstick-positive urine with no red blood cells (RBCs) seen on microscopic examination, either the patient has hemoglobinuria or myoglobinuria. These two can generally be differentiated by looking at serum. With hemoglobinuria the serum is pigmented, and with myoglobinuria the serum is clear. This occurs because hemoglobin is only filtered after the haptoglobin has been saturated and free hemoglobin appears; myoglobulin is less protein-bound, is a significantly smaller molecule (one-fourth the size of hemoglobin), and is therefore filtered. Thus, looking at the serum for pigmentation is very helpful.

6. The urine dipsticks, "ketosticks," and Acetest tablets all measure acetoacetic acid, 3-hydroxybutyric (3-OH butyric) acid, and acetone. However, the sensitivity for acetoacetic acid is many times that for 3-OH butyric acid and acetone. Therefore, even high levels of the latter compounds may not be reflected in determinations by Acetest reactions. This is important in three clinical situations:
   a. Alcoholic ketoacidosis (AKA)
   b. Combined diabetic ketoacidosis (DKA) and lactic acidosis
   c. Recovery from ketoacidosis

   Alcoholic ketoacidosis occurs in alcoholic patients. The usual history is that of a recent "binge" followed by several days of nausea, vomiting, and no food intake. The patient presents with an anion gap metabolic acidosis and may have no or barely detectable ketones by dipstick or Acetest and high levels of 3-OH butyric acid (see Chap. 3). The state in which the ketoacids exist is determined by the redox state of the mitochondria, that is, the NADH/NAD ratio.

$$\text{Acetoacetic acid} \xrightleftharpoons{\text{NADH/NAD}} \text{3-OH butyric acid}$$

With glucose and phosphorus administration, recovery begins, the anion gap decreases, the serum bicarbonate concentration increases, and the measured serum ketones may rise. With recovery, the NADH/NAD ratio is reduced, and 3-OH butyric acid is shifted to acetoacetic acid. Therefore, one can actually see increasing ketonemia as measured by Acetest while the anion gap is decreasing and the serum bicarbonate concentration is increasing. For example:

	Initial	*6 Hours*
Sodium	135 mEq/L	137 mEq/L
Potassium	4.0 mEq/L	3.5 mEq/L
Bicarbonate	7 mEq/L	12 mEq/L
Chloride	100 mEq/L	102 mEq/L
Anion gap	28 mEq/L	23 mEq/L
Acetone	Trace at 1 : 1	1 : 4

Therefore, to make the diagnosis of AKA one must realize that measured ketones do not reflect 3-OH butyric acid levels. One must also be careful not to interpret the apparent increase in serum ketones as a worsening clinical condition, rather than as recovery and ketoacid conversion.

Diabetic patients are prone not only to DKA but also to lactic acidosis. In those patients where both occur, the NADH/NAD ratio is increased in both the cytoplasm (shifting pyruvate to lactate) and the mitochondria (shifting acetoacetic acid to 3-OH butyric acid). Therefore, they will have decreased Acetest measurements for the level of ketonemia; the Acetest dilution may well increase with recovery. Acetest may remain positive in DKA after the anion gap has normalized because acetone is present for 48 to 72 hours.

7. The glucose dipstick test measures only glucose, since it is impregnated with glucose oxidase. The Clinitest tablets measure all reducing sugars. Glucose is handled by the kidney by filtration and reabsorption; therefore, glucose could appear in the urine either because filtered load is increased, exceeding a normal tubular reabsorptive capacity, or because the tubular capacity to reabsorb glucose has been reduced. The increased filtered load results from hyperglycemia and from increased glomerular filtration rate; the latter occurs in pregnancy. The reduced tubular capacity to reabsorb glucose occurs with renal glucosuria of the decreased threshold or increased splay type, proximal renal tubular acidosis, and some parenchymal renal diseases.

   It is important to recognize these nonhyperglycemic causes of glucosuria, since in the absence of hyperglycemia, no insulin or oral hypoglycemic agents should be given for treatment of the glucosuria.

8. Epithelial cells of several types can be seen in a urinalysis. A few transitional epithelial cells can be seen in any normal urinalysis. These cells are two to four times the size of white blood cells (WBCs) and are usually pear-shaped or spindle-shaped. Large numbers suggest abnormal cell desquamation as may occur with inflammation or a tumor.

   Squamous epithelial cells are large, flat cells, originating from the urethra and vagina. A large number of these cells in a urine specimen obtained from a female suggests vaginal contamination of the specimen, and in that circumstance correct interpretation of RBCs, WBCs, bacteria, and culture is not possible.

   Renal tubular epithelial cells (RTCs) are large cells, one-third larger than WBCs, with clear, eccentric nuclei. Like all epithelial surfaces, the renal epithelial surface does have cell turnover, and therefore, an occasional RTC in a urinalysis is not abnormal. If one sees sheets or casts of these cells, the diagnosis of acute renal failure should be entertained.

Red blood cells can be seen in the urine. One to two RBCs per high-power field are within normal limits. More than this number are pathologic. RBCs in the urine can represent bleeding from any point in the urinary tract, from the urethral meatus to the renal parenchyma. In addition, systemic coagulation abnormalities can result in hematuria. Therefore, a patient with isolated hematuria requires investigation of the coagulation system and the entire urinary tract.

One to five WBCs per high-power field are within normal limits. Numbers in excess of this amount are pathologic. WBCs in the urine represent inflammation anywhere in the urinary tract, from the urethra to the parenchyma. It is important to note that this reflects inflammation, not infection. For example, pyuria could occur from chemical cystitis (bubble bath cystitis in young girls), acute interstitial nephritis from drugs, and acute exudative glomerulonephritis like poststreptococcal glomerulonephritis.

9. Cast: "A urinary cast is a readable message from the nephrons. Formed elements in casts are labelled as coming from the parenchyma of the kidney with a certitude that is rare in other laboratory tests" [1]. Urine to be examined for casts should be a freshly voided morning specimen. It should be spun in a conical test tube at medium speed for 3 minutes. The supernatant should be gently drained off and the button of material carefully withdrawn with a pipette and placed on a slide. Casts are best preserved in a cold, acid urine.

   One can see casts of all the cellular elements listed above in #8 except for transitional and squamous epithelial cells. Casts localize the pathologic process to the kidney. An RTC cast raises questions of acute renal failure; RBC casts mean glomerulonephritis. WBC casts indicate inflammation in the kidney. A number of noncellular casts can also be seen.

   Hyaline casts are difficult to see under a microscope, being essentially the same refractile index as the glass. They are composed of serum proteins. Four to five in a urinalysis can be normal. Numbers in excess of this are seen in states such as dehydration with low urine flow rates and in heavy proteinuria.

   Granular casts, as the name implies, are composed of granules in a matrix, Tamm-Horsfall (tubular) protein; the granules are composed of a wide variety of serum proteins. In general, these do not connote a specific pathologic process, but rather a low urine flow rate.

   Waxy casts look like slices of paraffin. They are yellowish in color and are highly refractile. Their exact origin is unclear, but they are seen in chronic renal failure.

   Broad casts are formed in collecting tubules and can be any type, that is, hyaline, granular, and so forth. They occur when there is decreased function, and therefore decreased flow, in a collecting tubule draining many nephrons and hence are compatible with severe renal failure.

10. The crystals to recognize for diagnostic purposes are calcium oxalate, cystine, uric acid, and hippuric acid.

    Many calcium oxalate crystals or hippuric acid crystals in the urine of a patient with severe anion gap metabolic acidosis should suggest ethylene glycol intoxication (see Chap. 3). Many calcium oxalate crystals in other patients suggest disorders of calcium and/or oxalate metabolism.

    Cystine crystals in a patient with stones would suggest cystinuria.

    Uric acid crystals, of course, occur normally, but in patients with stone diathesis or acute renal failure, hyperuricosuria should be considered.

Reference

1. Schreiner, G. E. *Urinary Sediments*. New York: Med Com, 1969.

2. Acute Renal Failure

General Questions

1. Define *acute renal failure* (ARF).
2. In what clinical setting(s) does the question of ARF most commonly arise?
3. In this setting(s), there are three other major pathophysiologic events that must be considered in addition to ARF. What are they?
4. List the most common causes for the renal dysfunction in each of the four major categories.
5. What data from the history, symptoms, and signs may be helpful in distinguishing among prerenal azotemia (PRA), obstructive uropathy (OU), chronic renal failure (CRF), and ARF? What laboratory data may be helpful in identifying the specific ongoing disease processes involved? Construct a table.
6. What findings from urinalysis may be helpful in distinguishing among the four major categories? Construct a table.
7. What serum chemistries may be helpful in distinguishing among PRA, OU, CRF, and ARF? Comment specifically on hematocrit, serum electrolytes, calcium, and phosphorus.
8. Make a table of urinary chemistries and their characteristic values in ARF and PRA.
9. Are any radiographic examinations helpful in distinguishing among any of the four diagnostic possibilities?
10. Are there any instances in which a patient can have ARF and not be oliguric? What diagnosis should be considered in the patient who is totally anuric?
11. What is the natural history of ARF?
12. What are the complications of ARF and the mechanisms of these complications?
13. What are the aims and therapeutic modalities utilized in conservative management of ARF?
14. What are the indications for dialysis therapy in a patient with ARF?
15. What is meant by *prophylactic dialysis?*

Solutions to General Questions

1. Acute renal failure (ARF) is the rapid deterioration of renal function associated with the accumulation of nitrogenous wastes that is not due to extrarenal factors.
2. Acute oliguria is usually the clinical setting that calls attention to the possibility of ARF. An elevated or rising blood urea nitrogen (BUN) or serum creatinine also raises the question of ARF.
3. Prerenal azotemia (PRA) in which renal perfusion is markedly decreased; postrenal azotemia, or obstructive uropathy (OU); chronic renal failure (CRF); and acute presentation of chronic disease need to be considered when a patient with diminished renal function is first seen. The last situation frequently occurs in patients who do not receive regular health care.

4. The most common causes for the renal dysfunction in each major category are as follows:
   a. Prerenal azotemia
      (1) Intravascular volume depletion
      (2) Impaired cardiac function
      (3) Peripheral vasodilation
      (4) Increased renal vascular resistance
      (5) Bilateral renal artery obstruction
   b. Obstructive uropathy
      (1) Uretheral obstruction
      (2) Bladder neck obstruction
      (3) Bilateral ureteral obstruction
   c. Chronic renal failure
      (1) Glomerular disease
      (2) Interstitial disease
      (3) Vascular disease
   d. Acute renal failure
      (1) Ischemic disorders
      (2) Nephrotoxins
      (3) Glomerulonephritis
      (4) Vascular disorders
5. The interviewer's questions should be directed toward finding a cause for one of the major categories of renal dysfunction and accompanying manifestations.

Disorder	*History*	*Symptoms*	*Signs*	*Laboratory Data*
Prerenal azotemia	Losses 1. Vomiting	Dizziness	Orthostatic hypotension and tachycardia (if this is not found with the patient in a sitting position, it should be assessed with the patient in an upright position)	Hypokalemia, hyperbicarbonatemia, increased BUN/creatinine ratio[a]
	2. Diarrhea	Dizziness		Hypokalemia, hypobicarbonatemia