Useful Equations

URINE ELECTROLYTE-FREE WATER CLEARANCE
[1-(UNa + UK/PNa)] x V

URINE K:Cr RATIO
Ratio >13 mEq/g Cr = kidney potassum wasting

FREE WATER DEFICIT
[(measured Na - 140)/140] x total body water
*total body water is 50% of body mass in anyone other than young men in which case TBW is 60% of body mass.

BICARBONATE DRIP
Typical preparation is 150 mEq sodium bicarbonate in 1L D5W or sterile water

LOOP DIURETIC CONVERSIONS
1mg bumetanide = 40mg furosemide
10mg torsemide = 20mg furosemide

EFFECT OF IV FLUID ON INTRAVASCULAR VOLUME
NS/LR 100mL = 25mL intravascular volume
D5W 100mL = ~8 mL intravascular volume

SALT

Pocket Guide to Kidney Disorders in the Hospital

Gerren Hobby • Tracy Mullis

Table of Contents

SALT Pocket Guide to Kidney Disorders in the Hospital

Gerren Hobby, MD
NEA Baptist Hospital
Jonesboro, AR

Tracy Mullis, APRN
NEA Baptist Hospital
Jonesboro, AR

Special Thanks to:

Michael Mackey, MD

Adam Woodruff, MD

Emily Allen, APRN

Sara Culbreath, APRN

This work is not a substitute for individual patient assessment based upon a healthcare professional's evaluation of a patient and consideration of all factors relevant to the patient. We do not provide medical advice or guidance and this work is merely a reference tool for educational purposes only. Healthcare professionals, and not the authors or other individuals listed, are solely responsible for the use of this work including all medical judgments and for any resulting diagnosis and treatments. Given the continuous advances in medicine, independent professional verification of medical diagnoses, indications, appropriate pharmaceutical selections dosages, and treatment options should be made based on the healthcare provider's personal evaluation. Healthcare professionals should consult a variety of sources when making medical decisions. When prescribing medication, healthcare professionals are advised to consult the product information sheet (the manufacturer's package insert) accompanying each drug to verify conditions for use, warnings, side effects and identify any changes in dosage schedule or contraindications. This should especially be performed if the medication to be administered is new, infrequently used or has a narrow therapeutic range. To the maximum extent permitted under applicable law, no responsibility is assumed by us for any injury and/or damage to persons or property, as a matter of products liability, negligence law or otherwise, or from any reference to or use by any person of this work.

The information contained in this book represents the views and opinions of the original creators of this book and does not necessarily represent the views or opinions of NEA Baptist Hospital. This book is not endorsed by NEA Baptist Hospital.

Chapter 1: Urine Sediment

One of the most important aspects of AKI evaluation is examination of the urine sediment. When we refer to urine sediment, we are referring to cells, debris, and other particles present in the urine. There are only a handful of urine sediment findings that we look for on a regular basis. These include casts, red blood cells (RBCs), white blood cells (WBCs), renal tubular epithelial cells, crystals, and amorphic debris.

Urine can contain some or all of the above items. In order to increase the chance that we will see some of the aforementioned urinary findings, we concentrate cells and debris in the urine through centrifugation.

HOW TO SPIN URINE

1. Get a 5-10mL of a fresh urine sample— two hours old or less if possible. Casts break apart over time, turning into amorphous debris. The best urine comes from the port in a patient's foley. To obtain urine from this, wipe the port with an alcohol pad and aspirate the urine using a luer lock syringe. The next best source for urine is the 50mL compartment on a foley urometer. After that, any urine is better than no urine. If the patient does not have a foley, get whatever sample you can get.

2. Centrifuge urine at 1500 rpm for 5 minutes. Be sure to appropriately counterweight the urine sample with an equivalent amount of urine to within 0.25mL.

3. Pour out all of the supernatant in a sink. To do this, invert the vial completely and hold it inverted for 5-10 seconds. This should leave 1-2 drops of urine hanging on the brim of the inverted vial. Gently tap the vial to get rid of these. At this point, you should have 2-3 drops of urine left in the bottom of the vial. Of note, you may or may not be able to see a pellet in the tube.

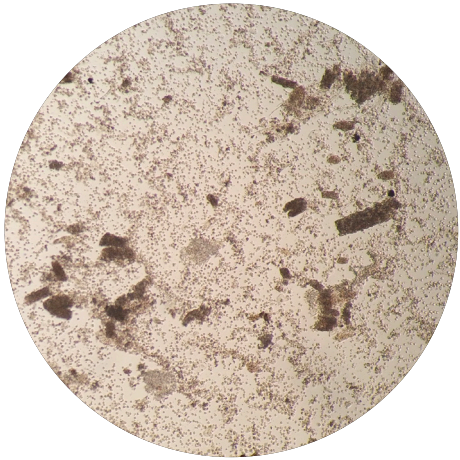
4. Gently tap, shake the tube to resuspend the pellet.

5. Use a pipette to place 1 drop of urine on a glass slide and cover with a slide cover. Use the yellow 10x magnification lens to get an overview of the urine findings. The 10x lens combined with the 10x eyepiece magnifies the specimen 100x. If you would like to look at urine more closely, switch to the 40x lens. As long as the 10x lens is focused on the urine, rotating the lens selector to the 40x lens will not allow the lens to touch the glass slide. To get a better view of cells, utilize phase contrast on the microscope.

5. Lastly, place one drop of Sternheimer-Malbin stain in the vial and gently tap the urine to mix the stain to mix it with the sample. Allow to sit for 3-5 minutes and then view under the microscope. This will allow you to better distinguish certain cell types.

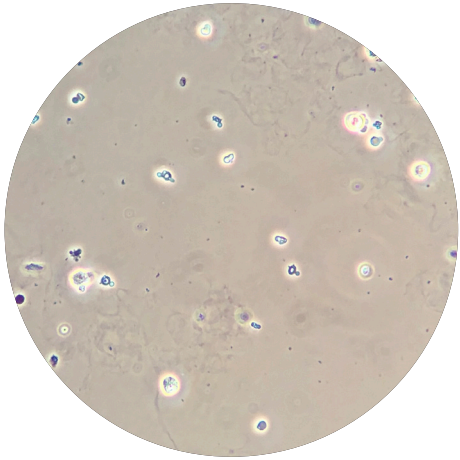
6. Scan the QR code below for a video overview of the process and more images of urine sediment.

Read the sections below for examples and explanations of different urine sediment findings.



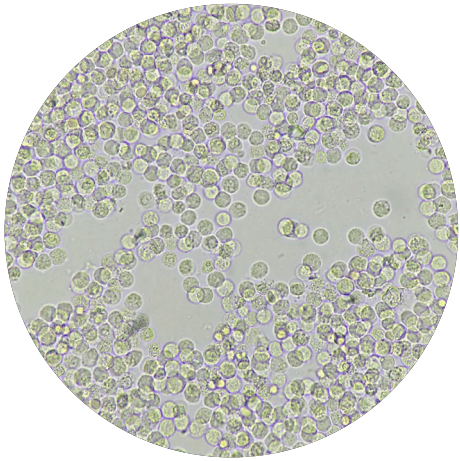
GRANULAR CASTS

These is a urine sediment containing an overall picture of granulasr casts (a.k.a muddy brown casts) in acute tubular necrosis (ATN). When ATN occurs, renal tubular epithelial cells degrade and flow down the nephron to combine with the Tamm-Horsfall protein (a.k.a. uromodulin). Cellular debris gets trapped in this protein to make a cast – a plaster mold of the inside of the nephron. This is what granular casts are made of.



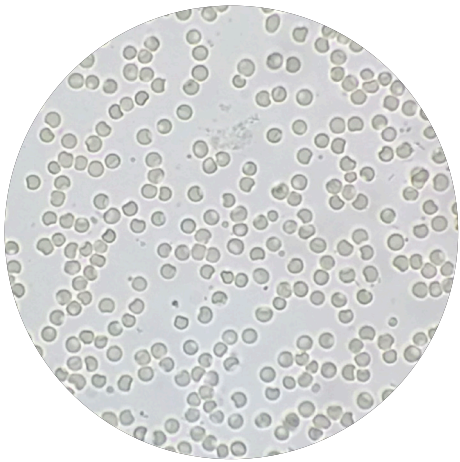
DYSMORPHIC RED BLOOD CELLS

There are several different type of dysmorphic red blood cells (RBCs), but the type specific for glomerulonephritis are acanthocytes. These RBCs are misshapen to resemble doughnuts with blebs. Some say they also resemble turtles, but either way, these dysmorphic RBCs below indicate glomerulonephritis.



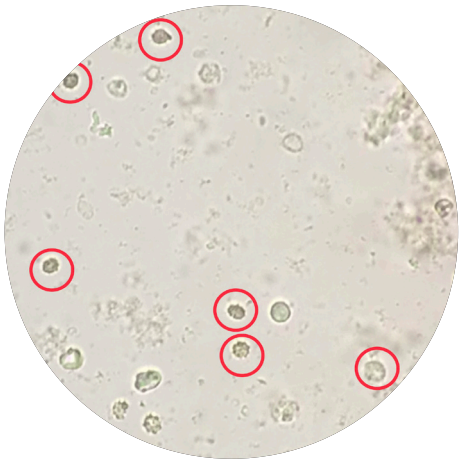
WHITE BLOOD CELLS

White blood cells (WBCs) most often indicate a urinary tract infection. They are also useful in the event that you see a WBC cast in the setting of negative urine cultures — this is a presentation that can indicate acute interstitial nephritis. In the images below, look for cells (that are larger than RBCs) with a notably granular cytoplasm. If you are trying to find a WBC cast, look for cylindrical structures which include WBCs encased within the cast itself.



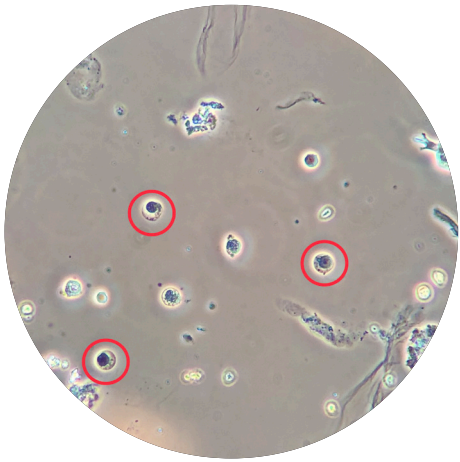
MONOMORPHIC RED BLOOD CELLS

Monomorphic RBCs are simply RBCs which are not misshapen and do not indicate glomerulonephritis. These cells end up in the urine due to trauma in the urinary tract (such as kidney stones, foley placement, ect) and can also increase in quantity due to patient's being on anticoagulants.



CRENATED RED BLOOD CELLS

Crenated RBCs are monomorphic RBCs that have been sitting in urine for a prolonged period of time. The resulting osmotic stress on the RBC membrane causes small spikes to form on the RBC membrane. These spikes are not as pronounced as acanthocyte blebs and importantly, the characteristic doughnut shape of acanthocytes is missing from crenated RBCs. Look at the images below to see crenated RBCs denoted by red circles.



RENAL TUBULAR EPITHELIAL CELLS

As mentioned above, intact renal tubular epithelial (RTE) cells slough off into the urine completely intact during ATN. Look at the images below to see RTE cells denoted by red circles. To distinguish an RTE cells from a WBC, look at the nucleus. An RTE cell will have a large, eccentrically-placed nucleus.

Chapter 2: Evaluation of AKI

AKI EVALUATION

Acute kidney injury is common in hospitals. and leads to increased morbidity, mortality, and increased length of stay. Even a small "bump" in creatinine that meets the minimum criteria for AKI is associated with a 2.2x increased risk of dying (1). This mortality risk increases with the severity of AKI with the most severe forms of AKI being associated with an 8.6-fold increase in mortality (1). Since there are a myriad of ways in which a kidney can break and, we need a systematic method to correctly diagnose the cause of AKI. The following paragraphs describe a fairly simple series of steps that can lead one to the correct diagnosis with apparent deft clinical ability.

DEFINE AKI

To begin, correctly diagnose the presence of AKI. Do not mince your language and be confident about saying that the patient does or does not have AKI. Over the past several decades have been multiple different criteria for AKI including the RIFLE and AKIN criteria, but these are now outdated and we no longer use them. The criteria we currently use are the KDIGO criteria (2) which state that AKI is present if any of the following are present:

- serum Cr rises at least 0.3mg/dL over 48h
- serum Cr rises to 1.5-1.9x baseline over the course of 1 week
- Urine output (UOP) is <0.5mL/kg/hr for 6-12h

Importantly, you did not see the mention of BUN in the criteria. That is because creatinine is the true marker of kidney function and BUN is not. For us, BUN is mostly used to let us know how close we are to needing dialysis. Let's highlight this point with an example. Let's say you have a patient in the hospital who had a Cr of 2.3mg/gL yesterday and the same Cr of 2.3mg/dL today, but the BUN increased from 28mg/dL to 38mg/dL after starting prednisone for a COPD exacerbation. Did their kidney function stay the same or worsen? The correct answer is that their kidney function is absolutely the same as long as their volume status is roughly the same.

Another note is that, although UOP is a criterion for AKI, we don't use this much for medicine patients. Surgeons will look at UOP from hour-to-hour after surgery though. When their patients have an operation with insensible losses, they will look at UOP hourly and give small 250mL fluid boluses for a dropping UOP. In their patients, they have a time-stamped period of volume depletion that they can correct, but in most medicine patients, there are more factors at play such as sepsis, heart failure, etc that make this approach less useful for us. Either way, UOP is a criterion and if the UOP does drop, then a rising Cr often follows.

There is a caveat to the serum Cr criteria as well, and that is volume. It's not uncommon for a sick ICU patient to get round after round of fluid boluses overnight. This dilutes the serum creatinine and can lower the next morning's creatinine, making it look falsely optimistic (3). The easy way to think about this is that if, due to fluid boluses, a patient gained 10% of their total body water, then the

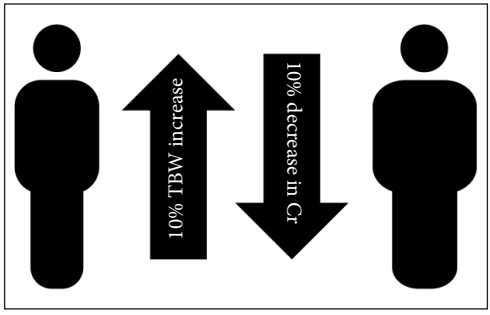


Figure 1: a 10% increase in total body water (TBW) over a short period of time will cause a 10% decrease in the serum creatinine.

Time				
Date	7/15	7/16	7/17	7/18
Sodium	139	138	136	134
Creatinine	0.7	0.6	1.1	1.8
UOP	1500	1100	900	600
BP	129/75	81/42	95/52	97/53
MEDications	ibuprofen	ibuprofen		
Situations		septic shock	septic shock	septic shock
Contrast				
Obstruction				
Prerenal				
Events	sepsis	intubation		

Figure 2: The SCRUB/MEDical SCOPE grid for evaluation of AKI.

creatinine level that came back on the labs is underestimating the creatinine by 10% (as compared to if the patient didn't get all of that fluid). Take this into account when diagnosing AKI initially as well as when you're following creatinine.

FIND THE CAUSE OF AKI

The next step is to find the reason for AKI. If your patient meets criteria for AKI, then you already know that they're at an increased risk of dying. Now is the time to identify the cause of AKI, treat the cause, and be the hero. There are approximately 1001 ways for a kidney to break which means that during the course of a hospital work day you could spend your time meticulously going through hundreds of possibilities. Clearly, this will not work. One option would be to just blindly blame the AKI on "multifactorial causes." We want to be more exact and useful than this though. The following method is a simpler way to go about finding the correct diagnosis. By thinking about the most common causes of AKI as well as having high sensitivity, but low specificity triggers for considering rare diagnoses (i.e. retroperitoneal fibrosis causing obstruction without hydronephrosis), one can move through the causes of renal failure with speed and high accuracy. This is when nephrology becomes fun.

A reduction in cognitive load during this diagnostic process is useful. Focusing on the pertinent data is one thing that separates 3rd year medical students from upper level residents. Too many things on the mind is what makes a developing clinician in a short white coat spend minutes on rounds talking about a potassium of 5.2 mmol/L, but forget to mention the fact that the patient's blood cultures turned positive overnight.

To begin, we need to appreciate that most AKI we see in the hospital is either due to ATN or volume depletion (4). As a general rule, volume depletion should always be in the top 3 considerations (meaning you should always have a rationale for why they most likely do or do not have volume depletion) for patients at the time of hospital admission. It's difficult

to find papers that note the percentage of AKI on hospital admission, but papers utilizing urinary biomarkers are helpful here. It is noted that around 25% of AKI on hospital admission is volume depletion in one paper(4). Another useful paper notes a 50-60% chance(5). Either way, volume depletion is certainly not rare in newly admitted patients with AKI and should be considered. On the other hand, ATN should always be a prime consideration in patients who have been in the hospital for several days and it's always your job to diagnose it (via urine microscopy) or explain why they don't have ATN. In one study, over 70% of ICU patients with AKI had ATN attributable to sepsis or hypotension(6).

Even though volume depletion and ATN are the most common causes of AKI, there are so many more etiologies to consider. Part of the role of a nephrologist is not just to diagnose the common cause of AKI, but also to provide reassurance that more rare etiologies are not present. Numerous causes of AKI exist which begs us to ask if it's even possible to remember every kind of kidney failure in a few words? The answer is a resounding yes. To do so, use the acronyms "SCrUB" and "Medical SCOPE."

Start by SCrUBing the patient's chart for standard numbers that you should know.

S: serum **s**odium
Cr: serum **cr**eatinine
U: **U**OP
B: **b**lood pressure

Trend the numbers on a graph for serum Sodium, serum creatinine, urine output, and blood pressure. These are the mints on the hotel pillow that you should come to expect as standard. The end product will look like figure 2.

The first thing we see is that the serum creatinine increased on 7/13 (arrow) and continued to worsen the next day. Bingo, we have a smaller timeframe of events that could have caused AKI. The first thing to note is that the patient is in the hospital. Is it possible that they developed anti-GBM disease during their stay for acute cholecystitis? Although it would feel pretty cool to make that diagnosis in this setting, it is simply not going to be the cause of AKI. It's more likely that the culprit is something that we did to the patient that harmed him or her. Lining up all these numbers allows us to see important trends. Why look at serum sodium? If it's elevated, consider prerenal azotemia from true volume depletion unless you have another explanation for hypernatremia. Why care about UOP? If the UOP was 1.5L a day until a foley was removed and you observe the UOP falling to zero, then think urinary obstruction. Finally, look at blood pressure. A patient on 3 pressors likely has acute tubular necrosis (ATN). Occasionally though, a patient will have poorly controlled blood pressure at home, come into the hospital at which point, the blood pressure is reduced to 120/80 by an overzealous individual. ATN can actually happen in situations like this and it is not uncommon. In these situations, spin the urine to find granular casts and arrive at a diagnosis of normotensive acute tubular injury. The purpose of "SCRUB" is to align your thinking with the most likely cause of renal failure. It will prevent you from being the one suggesting glomerulonephritis as a top differential in an obvious case of ATN. "SCRUBbing the chart" for these numbers will prevent you from missing the most likely causes.

Before we end the discussion blood pressure, let's talk more about how blood pressure affects kidney function. It can actually do so via four mechanisms:

- Overt hypotension causing ATN
- Normotensive ATN
- Malignant hypertension causing a thrombotic microangiopathy
- Blood pressure slightly below the hemodynamic autoregulatory threshold of kidney function

As mentioned above, ATN is common in the ICU and that patient you have with shock can easily get ATN from hypotension. A similar process can also occur via something called "normotensive ATN." In patients who have had uncontrolled blood pressure for a long duration and live with SBPs of ~180 will eventually come into the hospital for some reason where a SBP of ~210 is found. It's not uncommon for these patients to be placed on a nicardipine drip and their blood pressure lowered to 120 systolic. Because their renal vasculature has become so accustomed to living at higher blood pressures, autoregulation fails at a "normal" blood pressure and they actually develop ATN with the granular casts on urine sediment that you would expect (7). The third mechanism is malignant hypertension. This is actually the kidney form of hypertensive emergency and is a result of increased shear stress on blood vessels which leads to a thrombotic microangiopathy. One thing to keep in mind is that these patients with malignant hypertension may have an underlying complement system mutation associated with atypical hemolytic uremic syndrome (8). Lastly, BPs below the hemodynamic autoregulatory threshold of kidney function can cause a slow decline in kidney function which is only due to hemodynamic causes and not actual tubular injury (9).

The second acronym is MEDical SCOPE which helps us move onto the finer points of AKI diagnosis. This acronym first evaluates MEDications for cause of renal failure. It then goes on to look at situations that are commonly associated with kidney failure such as a heart failure exacerbation. Contrast administration is then examined and is a hot topic these days and a more detailed discussion is noted below. "O" stands for obstruction and includes not only prostate issues, but neurogenic bladders and clots from gross hematuria as well. Prerenal azotemia from true volume depletion is usually easy to spot or diagnose after an improvement in creatinine after a night of IV fluid administration, but more considerations should occur. Look for orthostatic vital signs, decreased skin turgor under the clavicles, and sunken eyes. Lastly, certain events, as shown on the chart, are often associated with AKI. With the combination of these acronyms, you can quickly move through the possibilities for the cause of AKI.

The second acronym is MEDical SCOPE which helps us move onto the finer points of AKI diagnosis.

MEDical: medications
S: situations
O: obstruction
P: prerenal
E: events

MEDICATIONS ASSOCIATED WITH AKI

Below are some quick notes about AKI associated with medications.

NSAIDs: kidney failure from NSAIDs can be caused by all NSAIDs including COX-2 inhibitors and aspirin(10,11). Renal failure due to NSAIDs is most likely to happen in a volume-depleted state.

ACE inhibitor and angiotensin receptor blockers: these can increase the risk for AKI when combined with other factors leading to AKI but do not cause AKI on their own in the hospital setting.

Amphotericin B (liposomal formulation): causes AKI ~15% of the time (12). The onset of AKI typically occurs in 5-9 days after starting treatment (13).

AIN: overall, the diagnostic approach to acute interstitial nephritis (AIN) should be ruling out other causes of AKI which will increase your suspicion for AIN. A kidney biopsy is the gold standard for the diagnosis, but the noninvasive test that strongly suggests AIN is the presence of WBC casts in urine with a culture showing no growth or normal flora. As you will be able to gather from the numbers below, the presence of fever, rash,

and eosinophilia differs among the myriad of drugs that can cause AIN and remembering these percentages is not terribly useful. There are many medications associated with AIN and so almost any are fair game. To dive into the numbers of symptoms of AIN, we only find that only 5-10% of patients present with the classic triad of fever, rash, and eosinophilia. Fever is notably absent in NSAID-induced AIN, but is present in 50-100% of patients with AIN attributed to penicillin derivatives. Across all classes of drugs, fever is present in 30%. Rash is present in 15-50%. Eosinophilia occurs in 80% of cases of AIN from beta-lactams, but is present in no more than one-third of cases caused by other medications. Leukocytes are present in nearly all cases of AIN due to methicillin, but are noted in less than half of cases of AIN due to other medications. Eosinophiluria has a sensitivity of 31% and a specificity of 68% in biopsy-proven acute interstitial nephritis. Put differently, if your pretext probablity of AIN is 16% and you use the commonly used 1% cutoff for urine eosinophils, then the PPV for urine eosinophils for AIN vs ATN is 58%. A negative test for urine eosinophils provides a NPV of 44%. (14). This test is clearly barely nudging the diagnostic probablity of urine esosinophils north or south of a coil flip. Findings of WBC casts in urine sediment without pyelonephritis is highly suggestive of AIN (15). Overall, the diagnostic approach to AIN should be ruling out other causes of AKI which will increase your suspicion for AIN. To clinch the diagnosis, get a kidney biopsy.

Hydralazine: increasingly being recognized as a cause of ANCA vasculitis. Patients will present like ANCA vasculitis, but can have positive serology for both PR3+ and MPO+ as well as ANA. Hypocomplementemia is frequently seen as well (16).

Checkpoint inhibitors: if a patient has been on a checkpoint inhibitor, consider AKI attributable to this. 93% of AKI is due to interstitial nephritis and the median time to onset of AKI is 14 weeks (interquartile range 6-47 weeks). Combination use of both anti-CTLA-4 and anti-PD-1/PD-L1 agents or concomitant proton pump inhibitor use are risk factors for AKI from these agents (17). Glomerular diseases have occurred with these agents, but these are exceedingly rare (18).

SITUATIONS ASSOCIATED WITH AKI

Acute heart failure exacerbation: consider if cardiorenal syndrome is present.

Cholesterol emboli: associated with manipulation of arteries 75% have skin findings. 66% have eosinophilia (defined as >500 eosinophils/uL blood). Most have a subacute presentation with onset of AKI 2-6 weeks after event. 20% have an acute presentation with onset within 1 week after event (16,19) .

Tumor lysis syndrome (TLS): consider in patients recently started on chemotherapy. The Cairo-Bishop laboratory criteria for TLS indicate TLS if at least two of the following are present: phosphorous >4.5mg/dL, uric acid >8.0mg/dL, calcium <7.0mg/dL, or potassium >6.0mmol/L

Decompensated cirrhosis: consider if hepatorenal syndrome is present. Common causes of AKI in cirrhotic patients includes hypovolemia (27% - 50% of all cases), HRS-AKI (15% - 43%), and ATN (14% - 35%) (20). Of note, the old term of HRS-1 as been replaced by "HRS-AKI." The 2021 AASLD defines HRS-AKI if the following criteria are met:

1. Cirrhosis with ascites
2. There is a diagnosis of AKI according to ICA-AKI Criteria (which are the KDIGO AKI criteria without UOP criteria)
3. No response after 2 consecutive days of diuretic withdrawal and plasma volume expansion with albumin 1g/kg body weight per day
4. Absence of shock
5. No current or recent use of nephrotoxic drugs or contrast

6. No signs of structural kidney injury as indicated by proteinuria (defined as absence of >500mg/day proteinuria), microhematuria (absence of >50 RBCs/hpf) and/or abnormal renal ultrasound findings

Thrombocytopenia: if AKI occurs in the setting of thrombocytopenia of unknown etiology, then thrombotic microangiopathy (due to atypical HUS, TTP, HUS, or TMA from another cause) rises on the differential diagnosis. Order urgent workup for microangiopathic hemolytic anemia (MAHA) to see if urgent plasma exchange is needed.

Hemoptysis: if renal failure and hemoptysis are present, then a pulmonary-renal syndrome should be at the top of the differential diagnosis (anti-GBM disease, ANCA vasculitis, lupus nephritis).

Hypernatremia: if AKI is present in the setting of any degree of hypernatremia, then prerenal azotemia from true volume should be considered as a diagnosis.

Hypercalcemia along with unexplained anemia and lytic lesions: if these are present, consider multiple myeloma.

Recent surgery: look at anesthesia notes for intraoperative hypotension

Iodinated contrast: the onset of AKI is typically 24-48h after iodinated contrast exposure, but note that contrast-induced nephropathy (CIN) has traditionally been grossly overdaignosed. The best view on CIN is that IV contrast can cause AKI, but it should be a diagnosis of exclusion. In short, the existence of contrast nephropathy has been based on observational trials. The best trial utilizing propensity matching shows no signal for increased risk for AKI with iodinated contrast (21). Gadolinium doesn't cause AKI, but can cause nephrogenic systemic fibrosis.

OBSTRUCTION

Consider obstruction more strongly in older men, those with recent surgery, AKI in patients with lower midline abdominal pain (from distended bladder), gross hematuria with clots, or a recent foley removal.

PRERENAL CAUSES

Consider in the proper setting. The following physical findings are are associated with the following likelihood ratios for volume depletion being present or absent: dry axilla (LR 3.0/LR 0.6), dry mucous membranes of mouth and nose (LR 3.1/LR 0.4), sunken eyes (LR 3.7LR 3.7), decreased skin turgor in subclavicular area (LR 3.5LR 0.3). Overall, these physical exam findings are only mildly helpful for diagnosing volume depletion. Volume status is not simple to ascertain and requires a combination of history, physical examination, and imaging. Be on the lookout for point-of-care ultrasound as a rising tool for assessing volume status (22).

EVENTS

The following events are all associated with AKI from various causes: cardiac arrest, surgery, hypotension after intubation, rhabdomyolysis (look for seizures, influenza, cocaine, trauma, extreme exertion, malignant hyperthermia, neuroleptic malignant syndrome, amphetamines, other medications), large volume paracentesis. As for rhabdomyolysis, the risk is low when the CK is less than 15-20k, but can happen with CK as low as 5k if other predisposing conditions are present such as volume depletion, ect (23).

TESTING

What testing should be ordered? Get a urinalysis on all patients and spin the urine yourself… on every patient. This will commonly change the diagnosis between prerenal and ATN. In 23% of cases, a pretest diagnosis of prerenal AKI is changed to ATN and in 14% of cases, a pretest diagnosis of ATN is changed to prerenal AKI based on

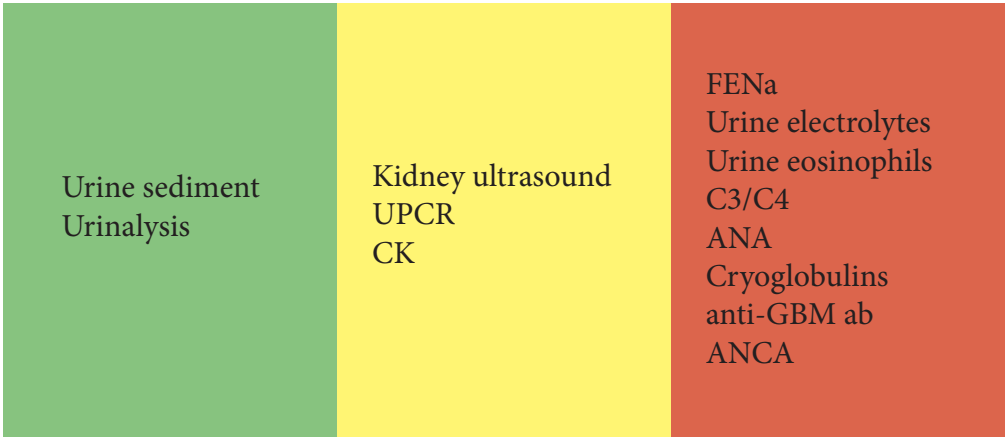


Figure 3: Testing in AKI. Tests in the green box should be routine tests performed in AKI patients. Test in the yellow box are routinely performed, but clinical context may suggest that they are not indicated. Tests in the red box should not be performed unless there is a good reason to do so.

urine sediment examination (24). Also, know that spinning the urine just once on an initial consult misses 25% of ATN (25).

If you know the diagnosis, don't get a renal ultrasound. If you are unsure… get one. A renal ultrasound poses no risk to the patient and it is simply unacceptable to miss a diagnosis of hydronephrosis. As for some numbers, kidney ultrasound is best at ruling out obstruction with a NPV of 98%. Ultrasound does have a high false positive rate of 26% since mild hydronephrosis can be incidentally found in the absence of true obstruction. In those who you think have obstruction, the PPV of a positive ultrasound finding is 70% (26). In those with only mild hydronephrosis as an incidental finding , the PPV is a shockingly low 6% (27). The false negative rate of ultrasound for hydronephrosis is very low at only 2%(26). The sensitivity of ultrasound for moderate to severe hydronephrosis is very high at 98% (26). If you are interested, information on interpretation of IV urography can be found in the lliterature (28). Overall, what this information means is that if you obtain a kidney ultrasound and it is negative for hydronephrosis, then you can feel certain that no obstruction is present. Conversely, hydronephrosis may be seen 26% of the time when no true obstruction is present. Lastly, if a kidney ultrasound is obtained for a non-AKI reason and hydronephrosis is incidentally found, then there is only a 6% chance that they actually have an obstruction.

If there is any suspicion of rhabdo, add a CK onto labs that are already drawn. Almost never worry about getting urinary electrolytes or FENa unless it is obtained before IV fluids are given in the ED. During evaluation of AKI, we infrequently place a large importance on urine electrolytes. Even when considered, they are viewed in the context of the big picture. They are very much less important than history and an overnight response to isotonic crystalloids. Point-of-care ultrasound is increasingly coming into existence as a valuable tool (29). For volume depletion, know that volume is difficult to assess. Physical exam and history can help, but POCUS is the real key to this. Eight zone lung ultrasound is similar to 28 zone ultrasound. POCUS is superior to physical exam for pulmonary edema and is more sensitive than CXR with 88% sensitivity for POCUS vs 73% sensitivity for CXR (30). In the same meta analysis noting the data above, POCUS and CXR were equally specific for pulmonary edema.

Urine protein-to-creatine ratios (UPCR) are becoming less important in our mind and are falling more and more into screening for glomerular disease, which we rarely do for most hospital AKI cases. UPCR is variable even if you control all of the possible factors that skew it's result such as creatinine dietary intake or known dinurinal alterations of UPCR (31). UPCR could be expected to be even more variable in hospitalized AKI patients who are, by definition, excreting less creatinine than they are producing. As such, UPCR in the setting of AKI should always taken with a grain of salt. In addition, if a PCP is reviewing the chart in 3 years and sees a UPCR of 4g/g, then this may trigger unnecessary testing for nephrotic syndrome since they may not do an extensive chart review and know the clinical setting during which the test was ordered. Also, don't bother getting 24h urine collections — we would only consider getting this if we are planning a kidney biopsy or if the patient likely has a nephrotic or nephritic syndrome and we're planning on modifying immunosuppression. Urine eosinophils as mentioned above have limited usefulness. Lastly, don't order glomerular testing unless you are a nephrologist and/or have an incredibly good reason to do so. It takes a reasonably high level of suspicion to order serological testing appropriately. Nephrologists and seasoned clinicians are good at sniffing out glomerular disorders, but if you are in training, it is best to double check these orders with an attending first.

START TREATMENT

If you think true volume depletion is present, start isotonic crystalloids. A good place to start with volume replacement is this — there are only 3 isotonic fluid rates that matter — 50mL/hr, 75mL/hr, and 125mL/hr. A normal rate is 75mL/hr. If you are admitting a patient late at night, you may want to use a rate of 125mL/hr if there is no concern for pulmonary edema. This rate will provide an improvement in the creatinine if volume depletion is present. If you are taking care of a patient and you want to give IV fluids, but they have a poor functional status, or you are worried about causing volume overload, consider a rate of 50mL/hr.

Volume overload is very common in ICU patients and you should know that fluid overload increases mortality in ICU patients (32). In patients with septic shock, appropriate fluid bolus followed by conservative fluid management is associated with the lowest mortality (33). Conservative volume management in patients with respiratory failure in septic shock was not shown to reduce 60 day mortality, but does improve oxygenation and reduces ventilator-free days and ICU stay (34). In that same trial, conservative volume management did not increase rates of shock or dialysis.

As for the choice of isotonic fluids, balanced chloride solutions are generally more physiological, have a mortality benefit in sepsis patients, and don't cause hyperkalemia. Initially, it was found that balanced chloride solutions resulted in less AKI and RRT in an early trial (35). This finding was not reflected in the SPLIT Trial which was done later (36). More recently, we have bigger trials — the SALT-ED, SMART, and BaSICS trials. In the SALT-ED Trial the primary outcome, hospital-free days, was not significantly different. However, major adverse kidney events (composite of all-cause mortality, RRT and persistent renal dysfunction) was lower in the balanced solution group (37). In the SMART Trial the primary outcome, which was major adverse kidney events, was significantly lower in the balanced solution arm and this was driven mostly by in-hospital death and new RRT (37). Again, the primary outcome in the SMART Trial was not different between the two fluid types. The SMART Trial did show a difference in the primary outcome (death from a renal cause, receipt of new renal replacement therapy, or a serum creatinine 2x baseline.

The recent BaSICS Trial was a large, multi-center trial with the primary outcome of 90 day mortality which was not different with fluid type. Some limitations of that study were a lower-than-expected mortality, and the fact that initial fluid resuscitation was not part of the study protocol. Also, half of the patients were elective surgery patients (38). Importantly, in subgroup analysis of the BaSICS Trial, mortality was higher with balanced solutions in the traumatic brain injury group (30% vs 20%). You should not give balanced solutions (which are relatively hypotonic as compared to normal saline) in traumatic brain injury patients for this reason. The PLUS Trial showed no difference between balanced solutions and normal saline (39).

So what is the takehome point from these studies? In the absence of a compelling situation for either normal saline or balanced fluids, it seems reasonable to chose a balanced crystalloid, but use fluids as a medicine and not an afterthought. Apply clinical reasoning to their use and tailor therapy to each patient. In addition to traumatic brain injury patients, there are some other good reasons to choose normal saline. Although balanced chloride solutions prevent a transcellular shift of potassium, oliguric patients depend on distal nephron sodium delivery in order to secrete potassium. These patients may benefit from the higher sodium concentration in normal saline in the setting of hyperkalemia (40). In summary, IV fluids are medicine and should be treated as such. The upcoming PLUS Trial and the BEST-Fluids Trial and will hopefully shed more light on this subject (41).

One last comment on ½ normal saline and bicarbonate drips. Half-normal saline is useful if you want to provide volume repletion for volume depletion, but also want to provide free water to treat hypernatremia. For ½ normal saline, use rates of 75-125mL/hr. Since ½ normal saline is 50% normal saline and 50% water, 100mL/hr of ½ normal saline is equivalent to giving normal saline at 50mL/hr and D5W at 50mL/hr.

Bicarbonate drips are most useful if the pH is <7.1. A standard bicarbonate drip contains 150mEq sodium bicarbonate in 1L of either D5W or sterile water. If the patient is at risk for hypoglycemia (i.e. after they have had IV insulin to treat hyperkalemia), use D5W. Otherwise, sterile water is a good choice. A bicarbonate drip in either D5W or sterile water with 150mEq sodium bicarbonate is considered an isotonic IV fluid. Furthermore, since each 650mg sodium bicarbonate tablet is 7.72 mEq of sodium bicarbonate, each liter of a bicarbonate drip essentially contains 19 sodium bicarbonate tablets. If you run a bicarbonate drip at 75mL/hr, then this is 1.8L over 24h and is providing the equivalent of 35 sodium bicarbonate tablets over the course of a day. This is why bicarbonate drips are more effective at raising the pH than giving bicarb tablets.

Evaluate the patient for obstruction. Get a bladder scan and place a foley if the PVR is >300mL or if the patient has suprapubic pain and cannot void. Alternatively, if the renal ultrasound has already resulted and shows no hydronephrosis, you can forego this. Another option is to use point-of-care ultrasound to assess this at the bedside.

Next, treat volume overload if it is present. Let's start with the most severe scenario for volume overload. If there is severe AKI (Cr >3x baseline), severe fluid overload (as in you are at the bedside placing orders for a STAT CXR, ABG, ECG, troponin), concern for a potential need of dialysis, decreased UOP, and pulmonary edema (requiring ~35-50% venti-mask), don't be shy with lasix. Give a minimum of 80-120mg IV lasix. Place a foley STAT to monitor UOP. If the patient does not make 100-200mL/hr UOP within the first hour, then double the dose. If the second dose does not work, then be thinking that urgent dialysis may be what is needed.

Next, redose medications for reduced kidney function. A few usual suspects for adverse

effects in this setting are opioids, gabapentin, baclofen, and antibiotics. Morphine is probably the worst opioid to use in AKI since it is renally-cleared. Hydrocodone is bad for similar reasons. Opt instead for oxycodone, hydromorphone instead and be cautious with dosing. Fentanyl can also be used, but it's short half-life limits it's ability for proper pain control. Gabapentin frequently causes tremor in the setting of AKI which resolves when gabapentin is reduced or stopped. Baclofen should just be stopped in the setting of AKI since it can cause altered mental status, seizures, respiratory depression, bradycardia, and hypotension (42).

The last question is if dialysis is needed. A simple mnemonic AEIOU is used to remember the reasons for this… acidosis, electrolyte abnormalities, ingestion (poisonings), fluid overload, and uremia. Dialysis utility in poisonings won't be addressed here, but trigger points for thinking about the need for urgent dialysis can be derived from a 2016 NEJM article examining the effectiveness of early vs. late renal replacement therapy initiation (43). These patients had a diagnosis of stage 3 AKI due to acute tubular injury and were on mechanical ventilation, pressors, or both. Indications for renal replacement therapy assigned to the delayed strategy of renal replacement therapy initiation were:

- BUN >112mg/dL
- Serum K+ >6.0mmol/L (or greater than 5.5mmol/L despite medical treatment)
- a pH below 7.15 in the context of either pure metabolic acidosis or mixed acidosis (Paco2 at least 50 mm Hg) without the possibility of increasing alveolar ventilation
- Acute pulmonary edema due to fluid overload responsible for severe hypoxemia requiring an oxygen flow rate >5L/min to maintain SaO2 >95% or those on mechanical ventilation with FiO2 >50% despite diuretic therapy

Every patient is different, but these are solid indications for dialysis that most nephrologists would agree with, other than the fact that you would really need to have a manifestation of uremia to dialyze someone with a high BUN. For timing of dialysis, the relevant trials include AKIKI, ELAIN, IDEAL-ICU, STARRT-AKI, and AKIKI 2 (43–47). In all of these trials except AKIKI-2 (which was more of a late vs very late RRT initiation trial), early initiation of RRT did not improve mortality. In AKIKI 2, the primary outcome of 28 day mortality did not differ between the delayed and very delayed strategy, but in a multivariable analysis of 60 day mortality, there was a HR of 1.65 associated with the very delayed strategy, noting that this may be the more upper limit of delaying RRT. The specific type of patient that AKIKI-2 is most relevant for is such a specific type of patient. The most common reason to start RRT in AKIKI-2 was a BUN >140. This BUN rarely occurs in the absence of other indications for RRT and so AKIKI-2 is not the most-practice changing trial.

As for the specific type of RRT, there is no mortality difference between IHD and CRRT (48–52). If you do choose CRRT, target a total effluent flow of 20-25mL/kg/hr (53,54). If you choose IHD perform it 3x weekly and target a Kt/V of 1.2 per treatment (55,56).

For AKI RRT access, use a non-tunneled HD catheter. The preference for the catheter site is RIJ > femoral > LIJ. This is to prevent slower movement of blood through the catheter. LIJ have higher rates of RRT dysfunction (0.25 vs 0.11) and infection (57). This increased infection rate noted in this trial was attributed to intraluminal blood clots. There is no significant increase in infection for femoral catheters as compared to IJ (58). Use a 24cm catheter for femoral lines. For IJ, use an equation to calculate the correct catheter length, but note that the accuracy of these formulas is questionable (59,60).

You are now armed with the knowledge to

diagnose almost any type of AKI and get them through the night for further evaluation and treatment.

REFERENCES

1. Murugan R, Kellum JA: Acute kidney injury: what's the prognosis? Nat Rev Nephrol 7: 209–217, 2011
2. Kellum JA, Lameire N, KDIGO AKI Guideline Work Group: Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care Lond Engl 17: 204, 2013
3. Macedo E, Bouchard J, Soroko SH, Chertow GM, Himmelfarb J, Ikizler TA, Paganini EP, Mehta RL, Program to Improve Care in Acute Renal Disease Study: Fluid accumulation, recognition and staging of acute kidney injury in critically-ill patients. Crit Care Lond Engl 14: R82, 2010
4. Liaño F, Pascual J: Epidemiology of acute renal failure: a prospective, multicenter, community-based study. Madrid Acute Renal Failure Study Group. Kidney Int 50: 811–818, 1996
5. Soto K, Papoila AL, Coelho S, Bennett M, Ma Q, Rodrigues B, Fidalgo P, Frade F, Devarajan P: Plasma NGAL for the diagnosis of AKI in patients admitted from the emergency department setting. Clin J Am Soc Nephrol CJASN 8: 2053–2063, 2013
6. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, Ikizler TA, Paganini EP, Chertow GM, Program to Improve Care in Acute Renal Disease: Spectrum of acute renal failure in the intensive care unit: the PICARD experience. Kidney Int 66: 1613–1621, 2004
7. Abuelo JG: Normotensive ischemic acute renal failure. N Engl J Med 357: 797–805, 2007
8. Van Laecke S, Van Biesen W: Severe hypertension with renal thrombotic microangiopathy: what happened to the usual suspect? Kidney Int 91: 1271–1274, 2017
9. Palmer BF, Clegg DJ: Renal Considerations in the Treatment of Hypertension. Am J Hypertens 31: 394–401, 2018
10. Berg KJ: Acute effects of acetylsalicylic acid in patients with chronic renal insufficiency. Eur J Clin Pharmacol 11: 111–116, 1977
11. Perazella MA, Tray K: Selective cyclooxygenase-2 inhibitors: a pattern of nephrotoxicity similar to traditional nonsteroidal anti-inflammatory drugs. Am J Med 111: 64–67, 2001
12. Mistro S, Maciel I de M, de Menezes RG, Maia ZP, Schooley RT, Badaró R: Does lipid emulsion reduce amphotericin B nephrotoxicity? A systematic review and meta-analysis. Clin Infect Dis Off Publ Infect Dis Soc Am 54: 1774–1777, 2012
13. Karimzadeh I, Heydari M, Ramzi M, Sagheb MM: Frequency and Associated Factors of Amphotericin B Nephrotoxicity in Hospitalized Patients in Hematology-Oncology Wards in the Southwest of Iran. Nephro-Urol Mon 8: e39581, 2016
14. Muriithi AK, Nasr SH, Leung N: Utility of urine eosinophils in the diagnosis of acute interstitial nephritis. Clin J Am Soc Nephrol CJASN 8: 1857–1862, 2013
15. Perazella MA, Markowitz GS: Drug-induced acute interstitial nephritis. Nat Rev Nephrol 6: 461–470, 2010
16. Santoriello D, Bomback AS, Kudose S, Batal I, Stokes MB, Canetta PA, Radhakrishnan J, Appel GB, D'Agati VD, Markowitz GS: Anti-neutrophil cytoplasmic antibody associated glomerulonephritis complicating treatment with hydralazine. Kidney Int 100: 440–446, 2021
17. Gupta S, Cortazar FB, Riella LV, Leaf DE: Immune Checkpoint Inhibitor Nephrotoxicity: Update 2020. Kidney360 1: 130–140, 2020
18. Kitchlu A, Jhaveri KD, Wadhwani S, Deshpande P, Harel Z, Kishibe T, Henriksen K, Wanchoo R: A Systematic Review of Immune Checkpoint

Inhibitor–Associated Glomerular Disease. Kidney Int Rep 6: 66–77, 2021
19. Kronzon I, Saric M: Cholesterol embolization syndrome. Circulation 122: 631–641, 2010
20. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, Wong F, Kim WR: Diagnosis, Evaluation, and Management of Ascites, Spontaneous Bacterial Peritonitis and Hepatorenal Syndrome: 2021 Practice Guidance by the American Association for the Study of Liver Diseases. Hepatol Baltim Md 74: 1014–1048, 2021
21. Hinson JS, Ehmann MR, Fine DM, Fishman EK, Toerper MF, Rothman RE, Klein EY: Risk of Acute Kidney Injury After Intravenous Contrast Media Administration. Ann Emerg Med 69: 577-586.e4, 2017
22. McGee S: Evidence-based physical diagnosis e-book. 5th ed. Elsevier
23. Bosch X, Poch E, Grau JM: Rhabdomyolysis and acute kidney injury. N Engl J Med 361: 62–72, 2009
24. Perazella MA, Coca SG, Kanbay M, Brewster UC, Parikh CR: Diagnostic value of urine microscopy for differential diagnosis of acute kidney injury in hospitalized patients. Clin J Am Soc Nephrol CJASN 3: 1615–1619, 2008
25. Varghese V, Rivera MS, Alalwan AA, Alghamdi AM, Gonzalez ME, Velez JCQ: Diagnostic Utility of Serial Microscopic Examination of the Urinary Sediment in Acute Kidney Injury. Kidney360 2: 182–191, 2021
26. Ellenbogen PH, Scheible FW, Talner LB, Leopold GR: Sensitivity of gray scale ultrasound in detecting urinary tract obstruction. AJR Am J Roentgenol 130: 731–733, 1978
27. Kamholtz RG, Cronan JJ, Dorfman GS: Obstruction and the minimally dilated renal collecting system: US evaluation. Radiology 170: 51–53, 1989
28. Dyer RB, Chen MY, Zagoria RJ: Intravenous urography: technique and interpretation. Radiogr Rev Publ Radiol Soc N Am Inc 21: 799–821; discussion 822-824, 2001
29. Argaiz ER, Koratala A, Reisinger N: Comprehensive Assessment of Fluid Status by Point-of-Care Ultrasonography. Kidney360 2: 1326–1338, 2021
30. Maw AM, Hassanin A, Ho PM, McInnes MDF, Moss A, Juarez-Colunga E, Soni NJ, Miglioranza MH, Platz E, DeSanto K, Sertich AP, Salame G, Daugherty SL: Diagnostic Accuracy of Point-of-Care Lung Ultrasonography and Chest Radiography in Adults With Symptoms Suggestive of Acute Decompensated Heart Failure: A Systematic Review and Meta-analysis. JAMA Netw Open 2: e190703, 2019
31. Shidham G, Hebert LA: Timed urine collections are not needed to measure urine protein excretion in clinical practice. Am J Kidney Dis Off J Natl Kidney Found 47: 8–14, 2006
32. Bouchard J, Soroko SB, Chertow GM, Himmelfarb J, Ikizler TA, Paganini EP, Mehta RL, Program to Improve Care in Acute Renal Disease (PICARD) Study Group: Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int 76: 422–427, 2009
33. Murphy CV, Schramm GE, Doherty JA, Reichley RM, Gajic O, Afessa B, Micek ST, Kollef MH: The importance of fluid management in acute lung injury secondary to septic shock. Chest 136: 102–109, 2009
34. National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network, Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D, deBoisblanc B, Connors AF, Hite RD, Harabin AL: Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 354: 2564–2575, 2006
35. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M: Association between a chloride-liberal vs chloride-restrictive

intravenous fluid administration strategy and kidney injury in critically ill adults. JAMA 308: 1566–1572, 2012
36. Young P, Bailey M, Beasley R, Henderson S, Mackle D, McArthur C, McGuinness S, Mehrtens J, Myburgh J, Psirides A, Reddy S, Bellomo R, SPLIT Investigators, ANZICS CTG: Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit: The SPLIT Randomized Clinical Trial. JAMA 314: 1701–1710, 2015
37. Self WH, Semler MW, Wanderer JP, Wang L, Byrne DW, Collins SP, Slovis CM, Lindsell CJ, Ehrenfeld JM, Siew ED, Shaw AD, Bernard GR, Rice TW, SALT-ED Investigators: Balanced Crystalloids versus Saline in Noncritically Ill Adults. N Engl J Med 378: 819–828, 2018
38. Zampieri FG, Machado FR, Biondi RS, Freitas FGR, Veiga VC, Figueiredo RC, Lovato WJ, Amêndola CP, Serpa-Neto A, Paranhos JLR, Guedes MAV, Lúcio EA, Oliveira-Júnior LC, Lisboa TC, Lacerda FH, Maia IS, Grion CMC, Assunção MSC, Manoel ALO, Silva-Junior JM, Duarte P, Soares RM, Miranda TA, de Lima LM, Gurgel RM, Paisani DM, Corrêa TD, Azevedo LCP, Kellum JA, Damiani LP, Brandão da Silva N, Cavalcanti AB, BaSICS investigators and the BRICNet members: Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients: The BaSICS Randomized Clinical Trial. JAMA 2021
39. Finfer S, Micallef S, Hammond N, Navarra L, Bellomo R, Billot L, Delaney A, Gallagher M, Gattas D, Li Q, Mackle D, Mysore J, Saxena M, Taylor C, Young P, Myburgh J, PLUS Study Investigators, Australian New Zealand Intensive Care Society Clinical Trials Group: Balanced Multielectrolyte Solution versus Saline in Critically Ill Adults. N Engl J Med 386: 815–826, 2022
40. Mikhael B, Steele DJR, Fenves AZ: In Defense of Normal Saline: Our Perspective. Clin J Am Soc Nephrol 17: 588–590, 2022
41. Collins MG, Fahim MA, Pascoe EM, Dansie KB, Hawley CM, Clayton PA, Howard K, Johnson DW, McArthur CJ, McConnochie RC, Mount PF, Reidlinger D, Robison L, Varghese J, Vergara LA, Weinberg L, Chadban SJ, BEST-Fluids Investigators and the Australasian Kidney Trials Network: Study Protocol for Better Evidence for Selecting Transplant Fluids (BEST-Fluids): a pragmatic, registry-based, multi-center, double-blind, randomized controlled trial evaluating the effect of intravenous fluid therapy with Plasma-Lyte 148 versus 0.9% saline on delayed graft function in deceased donor kidney transplantation. Trials 21: 428, 2020
42. Wolf E, Kothari NR, Roberts JK, Sparks MA: Baclofen Toxicity in Kidney Disease. Am J Kidney Dis 71: 275–280, 2018
43. Gaudry S, Hajage D, Schortgen F, Martin-Lefevre L, Pons B, Boulet E, Boyer A, Chevrel G, Lerolle N, Carpentier D, de Prost N, Lautrette A, Bretagnol A, Mayaux J, Nseir S, Megarbane B, Thirion M, Forel J-M, Maizel J, Yonis H, Markowicz P, Thiery G, Tubach F, Ricard J-D, Dreyfuss D, AKIKI Study Group: Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit. N Engl J Med 375: 122–133, 2016
44. Barbar SD, Clere-Jehl R, Bourredjem A, Hernu R, Montini F, Bruyère R, Lebert C, Bohé J, Badie J, Eraldi J-P, Rigaud J-P, Levy B, Siami S, Louis G, Bouadma L, Constantin J-M, Mercier E, Klouche K, du Cheyron D, Piton G, Annane D, Jaber S, van der Linden T, Blasco G, Mira J-P, Schwebel C, Chimot L, Guiot P, Nay M-A, Meziani F, Helms J, Roger C, Louart B, Trusson R, Dargent A, Binquet C, Quenot J-P, IDEAL-ICU Trial Investigators and the CRICS TRIGGERSEP Network: Timing of Renal-Replacement Therapy in Patients with Acute Kidney Injury and Sepsis. N Engl J Med 379: 1431–1442,

2018
45. Gaudry S, Hajage D, Martin-Lefevre L, Lebbah S, Louis G, Moschietto S, Titeca-Beauport D, Combe BL, Pons B, Prost N de, Besset S, Combes A, Robine A, Beuzelin M, Badie J, Chevrel G, Bohé J, Coupez E, Chudeau N, Barbar S, Vinsonneau C, Forel J-M, Thevenin D, Boulet E, Lakhal K, Aissaoui N, Grange S, Leone M, Lacave G, Nseir S, Poirson F, Mayaux J, Asehnoune K, Geri G, Klouche K, Thiery G, Argaud L, Rozec B, Cadoz C, Andreu P, Reignier J, Ricard J-D, Quenot J-P, Dreyfuss D: Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): a multicentre, open-label, randomised, controlled trial. The Lancet 397: 1293–1300, 2021
46. Timing of Initiation of Renal-Replacement Therapy in Acute Kidney Injury. N Engl J Med 383: 240–251, 2020
47. Zarbock A, Kellum JA, Schmidt C, Van Aken H, Wempe C, Pavenstädt H, Boanta A, Gerß J, Meersch M: Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury: The ELAIN Randomized Clinical Trial. JAMA 315: 2190–2199, 2016
48. Augustine JJ, Sandy D, Seifert TH, Paganini EP: A randomized controlled trial comparing intermittent with continuous dialysis in patients with ARF. Am J Kidney Dis Off J Natl Kidney Found 44: 1000–1007, 2004
49. Mehta RL, McDonald B, Gabbai FB, Pahl M, Pascual MT, Farkas A, Kaplan RM, Collaborative Group for Treatment of ARF in the ICU: A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure. Kidney Int 60: 1154–1163, 2001
50. Schefold JC, von Haehling S, Pschowski R, Bender T, Berkmann C, Briegel S, Hasper D, Jörres A: The effect of continuous versus intermittent renal replacement therapy on the outcome of critically ill patients with acute renal failure (CONVINT): a prospective randomized controlled trial. Crit Care Lond Engl 18: R11, 2014
51. Uehlinger DE, Jakob SM, Ferrari P, Eichelberger M, Huynh-Do U, Marti H-P, Mohaupt MG, Vogt B, Rothen HU, Regli B, Takala J, Frey FJ: Comparison of continuous and intermittent renal replacement therapy for acute renal failure. Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc 20: 1630–1637, 2005
52. Vinsonneau C, Camus C, Combes A, Costa de Beauregard MA, Klouche K, Boulain T, Pallot J-L, Chiche J-D, Taupin P, Landais P, Dhainaut J-F, Hemodiafe Study Group: Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial. Lancet Lond Engl 368: 379–385, 2006
53. RENAL Replacement Therapy Study Investigators, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Lo S, McArthur C, McGuinness S, Myburgh J, Norton R, Scheinkestel C, Su S: Intensity of continuous renal-replacement therapy in critically ill patients. N Engl J Med 361: 1627–1638, 2009
54. VA/NIH Acute Renal Failure Trial Network, Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, Finkel K, Kellum JA, Paganini E, Schein RMH, Smith MW, Swanson KM, Thompson BT, Vijayan A, Watnick S, Star RA, Peduzzi P: Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med 359: 7–20, 2008
55. Paganini EP, Tapolyai M, Goormastic M, Halstenberg W, Kozlowski L, Leblanc M, Lee JC, Moreno L, Sakai K: Establishing a dialysis therapy/patient outcome link in intensive care unit acute dialysis for patients with acute renal failure. Am J Kidney Dis 28: S81–S89, 1996
56. Schiffl H, Lang SM, Fischer R: Daily

hemodialysis and the outcome of acute renal failure. N Engl J Med 346: 305–310, 2002
57. Engstrom BI, Horvath JJ, Stewart JK, Sydnor RH, Miller MJ, Smith TP, Kim CY: Tunneled internal jugular hemodialysis catheters: impact of laterality and tip position on catheter dysfunction and infection rates. J Vasc Interv Radiol JVIR 24: 1295–1302, 2013
58. Parienti J-J, Thirion M, Mégarbane B, Souweine B, Ouchikhe A, Polito A, Forel J-M, Marqué S, Misset B, Airapetian N, Daurel C, Mira J-P, Ramakers M, du Cheyron D, Le Coutour X, Daubin C, Charbonneau P, Members of the Cathedia Study Group: Femoral vs jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement therapy: a randomized controlled trial. JAMA 299: 2413–2422, 2008
59. Czepizak CA, O'Callaghan JM, Venus B: Evaluation of formulas for optimal positioning of central venous catheters. Chest 107: 1662–1664, 1995
60. Struck MF, Schmidt T, Winkler BE, Reinhart K, Schummer W: Formulas for prediction of insertion depths of internal jugular vein catheters adjusted to body height categories. J Vasc Access 17: 191–194, 2016

Chapter 3: Hospital Management of Hypertension

Hypertensive emergency is defined as any condition where elevated blood pressure is accompanied by either target organ damage or some other situation that requires immediate lowering of blood pressure. Hypertensive urgency is defined as systolic pressure >180 mmHg or diastolic pressure >110 mmHg without evidence of target organ damage. Differentiating between these situations and very elevated blood pressure that is circumstantial (i.e., post-op pain) or when reduction is actually hazardous (i.e., post atherosclerotic/embolic stroke) is imperative to ensure proper treatment and patient safety(1). Approximately 1-3% of patients with hypertension will experience a hypertensive emergency in their lifetime (2), making it a rather rare phenomenon. In regards to hospital presentations, hypertensive emergencies account for about 25% of hypertensive associated crises. Whereas, hypertensive urgency makes up roughly 75%.

Symptomology of hypertensive emergencies may include headache, visual disturbance, GI symptoms, encephalopathy, renal impairment, and rarely microangiopathic hemolytic anemia (MAHA). Appropriate history and physical exam findings can often give large clues as to why the blood pressure is elevated. It is important to start appropriate screening for other potential causes such as illicit drug use, medication noncompliance (this is a BIG one), and to consider possible secondary causes - particularly renovascular hypertension - during the initial evaluation.

Type of Hypertensive Emergency	Timeline & Target BP	First-Line Therapy	Second-Line Therapy
Hypertensive crisis with retinopathy, microangiopathy, or AKI	Several hours, MAP -20% to -25%	Labetalol	Nitropruside, nicardipine
Hypertensive encephalopathy	Immediate, MAP -20% to -25%	Labetalol	Nicardipine, nitroprusidde
Acute aortic dissection	Immediate, systolic BP <110mmHg	Nitroprusside and esmolol	Labetalol
Acute pulmonary edema	Immediate, MAP 60-100mmHg	Nitroprusside (w/ loop diuretic)	Nitroglycerine
Myocardial ischemia/infarction	Immediate, MAP 60-100mmHg	Nitroglygerine	Labetalol
Acute ischemic stroke and BP >220/120mmHg	1h, MAP -15%	Labetalol	Nicardipine, nitroprusidde
Cerebral hemorrhage and BP >180mmHg systolic or MAP >130mmHg	1h, systolic BP <180mmHg and MAP <130mmHg	Labetalol	Nicardipine, nitroprusidde
Acute ischemic stroke with indication for thrombotic therapy and BP >185/110mmHg	1h, MAP -15%	Labetalol	Nicardipine, nitroprusidde
Cocane/XTC intoxication	Several hours	Phentolamine (next to benzodiazepines)	Nitroprusside
Adrenergic crisis a/w pheochromocytoma or autonomic hyperreadtivity	Immediate	Phentolamine	Nitroprusside
Peri- and postoperative HTN during/after CABG	Immediate	Nicardipine	Nitroglycerine
Peri- and postoperative HTN during/after craniotomy	Immediate	Nicardipine	Labetalol
Severe preeclampsia/eclampsia	Immediate, BP <160/105mmHg	Labetalol (next to magnesium sulfate and oral HTN meds)	Nicardipine

Figure 1: Types of hypertensive emergencies and their treatment.

Hypertensive emergencies require immediate intervention which includes establishing IV access and initiation of intravenous antihypertensives. Patients should be monitored closely, preferably in the intensive care unit. Which parenteral drug is selected for treatment should be based on clinical findings and patient history (figure 2).

The target blood pressure for patients in a hypertensive emergency is based upon etiology (figure 1). For example, in the event of retinal hemorrhage, microangiopathy, or acute renal failure the mean arterial pressure should be lowered 20-25% over several hours. However, with situations such as aortic dissection or pre-eclampsia, target blood pressure should be achieved as quickly as possible.

After the acute phase is over, evaluation should continue for potential secondary causes if that work up has not been completed and transition from IV to oral therapy should start.. It should be anticipated that most patients with hypertensive emergencies will require multiple oral medications to maintain control. Compelling indications for specific drugs should help guide the decision of treatment (diabetes and heart failure - think ACE/ARB, anxiety - think beta blocker, and so on…). Blood pressure variability is expected in the acute care setting because blood pressure is a constantly changing biometric that is influenced by experiences and emotions. A single isolated reading should neither confirm nor negate effective management. Rather, the overall trend of the blood pressure should be used to determine appropriate medication titration and response. Asymptomatic hypertensive urgency is a problem that is frequently encountered in the acute care setting. The most recent studies show that management of asymptomatic hypertensive urgency is actually better suited for outpatient management than when treated in the emergency room or inpatient setting. Optimization of oral medications, using combination therapies when able, and ensuring that there are no barriers to obtaining medications (financial, lack of access, etc) is the name of the game here. Get them over the acute phase, get them out of the hospital, and understand that close follow up is your best bet at long term blood pressure control.

REFERENCES

1. Kaplan NM. Kaplan's Clinical Hypertension. 11th ed. Wolters Kluwer, 2014.
2. Benken, Scott T. Critical Care Self-Assessent Program 2018: Medical Issues in the ICU. American College of Clinical Pharmacy, 2018.

Drug	Dose	Onset of Action	Duration	Adverse Effects	Special Indications
Nitroprusside	0.25-10.00 µg/kg/min IV	Immediate	1-2min	n/v, muscle twitching, thiocyanate and cyanide toxicity	Not preferred for hypertensive emergencies
Nitroglycerin	5-100 µg/min	2-5min	5-10min	headache, emesis, methemoglobinemia, tolerance with prolonged use	Not preferred, but may be useful for angina
Fenoldopam	0.1-0.6µg/kg/min IV	4-5min	10-15min	tachycardia, increased intraocular pressure	May be indicated for AKI
Nicardipine	5-15mg/h	5-10min	1-4h	headache, nausea, flushing, tachycardia	Most hypertensive urgencies
Clevididipine	1-2mg IV, rapidly increasing dose ot 16mg maximum	2-4min	5-15min		Most hypertensive urgencies
Hydralazine	5-20mg IV	10-20min	1-4h	tachycardia, flushing, headache, vomiting aggravation of angina	Eclampsia, not for aotric dissection
Phentolamine	5-15mg IV	1-2min	3-10min	taachycardia, flusing, headache	Catecholamine excess
Esmolol	250-500µg/kg/min, then 50-300µg/kg/min IV	1-2min	10-20min	hypotension, nausea	Aortic dissection after surgery
Labetalol	20-80mg IV bolue every 10min; 2mg/min IV infusion	5-10min	3-6h	vomiting, scalp tinglng, burning in throat, dizziness, nausea, heart block, ortostatic hypotension	Most hypertensive eergencies except acute heart failure

Figure 2: Medications used in hypertensive emergencies.

Chapter 4: Sodium Disorders

OVERVIEW

Hypernatremia and hyponatremia are common electrolyte abnormalities. In fact hyponatremia is the most common electrolyte abnormality seen in the hospital (1,2). In contrast to potassium levels which can be corrected quickly and easily, sodium tends to move more slowly and brisk movements of this ion are concerning. We'll start our discussion with hypernatremia, the easier of the two topics and then we will dive into hyponatremia.

EVALUATION OF HYPERNATREMIA

In general when you see a patient with hypernatremia in the hospital, our gut level reaction is to give more water to the patient, but the real question we need to ask ourselves is why they would let themselves become hypernatremic in the first place. In general, if someone is alert and has access to water they will essentially not allow themselves to develop hypernatremia under any condition. In the hospital, we are most likely to see hypernatremia in patients who are on mechanical ventilation or frail older patients who do not have the mental capacity or strength to access free water.

The next thing we need to decide is where the water went to. Water loss in someone with active diarrhea or vomiting is easy to spot, but there are multiple ways that water can be lost. Let's start with standard daily water loss in the body. There are three obligatory losses of water in the body and these are (3):

- Obligatory urine water loss: 500mL
- Skin: 500mL
- Respiratory tract: 400mL
- Stool: 200mL
- Total = 600mL

Conversely, obligatory water intake in a normal, healthy human is the following:

- Ingested water: 400mL
- Water content of food: 850mL
- Water of oxidation: 350mL
- Total = 1600mL

Water loss during respiration is tightly linked to the water of oxidation. This metabolic water, derived from oxidation of carbohydrates and fatty acids, evaporates from the respiratory tract in a 1:1 fashion and honestly doesn't play a large role in water balance in the body. This leaves us with essentially just urinary, skin, and stool water loss. As we can see, if an older 70kg patient (TBW 35L) is not eating or drinking anything, then their 1200mL obligatory water loss from urine skin, and stool could cause their sodium to increase each day from 140 mmol/L, 144 mmol/L and then 149 mmol/L.

Like we mentioned, ~99% of the time, hypernatremia in the hospital is due to limited access to water due to frailty or mechanical ventilation +\- GI losses. Typically , we just give free water and move on. As nephrologists though, we need to rule out less likely causes of hypernatremia which bring us to the last point – we need to decide if the patient has pathologic water loss from their kidneys. Other than something obvious like diuretics, the two etiologies for renal water wasting are osmotic diuresis and diabetes insipidus (DI). If the patient has both hypernatremia and polyuria (defined as more than three liters of urine output per day) then a spot urine osmolality will help us find what the cause of the renal water loss is. The following are 3 types of presentations for hypernatremia and polyuria along with a probable diagnosis (3).

- **Hypernatremia + urine osmolality >600mosmol/kg:** a solute diuresis is almost certainly present. This diagnosis is supported even further if water administration does not cause a significant decrease in urine osmolality.

Conversely, if water administration does cause a fall in urine osmolality, then a component of DI could be present as well.

- **Hypernatremia + intermediate urine osmolality of 300-600mosmol/kg:** these patients likely have a component of both DI and a solute diuresis. If the patient has a daily urine osmolar output of >1000 mosmol (calculated by urine osmolality multiplied by the 24h urine volume) then only a solute diuresis is present. If the daily urine osmolar output is <900mosmol, then a component of DI is likely present as well.
- **Hypernatremia + urine osmolality <300mosmol/kg:** these patients have DI.

Solute diuresis is common in the hospital and may be frequently seen in patients who are mechanical ventilation receiving tube feeds. Out of the 3 scenarios above, solute diuresis from tube feeds in an ICU patient will almost always be the right answer.

The only reason why water is reabsorbed in the nephron or secreted into it is through either solute reabsorption or excretion. You are well aware of the concept of osmotic diuresis in diabetics. In this setting, the high osmotic gradient established through glycosuria drags water from the blood side of the nephron into the nephron itself. The same thing can happen when patients get tube feeds. Urea, which is the product of protein catabolism, is produced in higher quantities when patients have high protein intake via tube feeds. Urea is osmotically active in the nephron and when filtered, creates an osmotic gradient just like glucose in diabetics and drags out free water. A patient recovering from AKI and azotemia excretes a fair amount of urea into their urine as they lower their BUN and this process can cause a solute diuresis as well.

And so, this is where our discussion of hypernatremia ends. Again, 99% of the time we see hypernatremia, it's a patient on mechanical ventilation or a frail elderly patient with poor oral intake. In these cases, we just give D5W or increased free water flushes via tube feeding, monitor sodium, and move on. That's it. Just make sure to keep in mind the possibility of a solute diuresis or DI. Diabetes insipidus is so rare to see in the hospital that we won't go more into it at this time, but we'll talk about it on a case-by-case basis if the possibility of it comes up.

TREATMENT OF HYPERNATREMIA

The goal of treatment for hypernatremia is to lower the serum sodium into normal range. Most of what we see is either mild hypernatremia or chronic hypernatremia (present for >48h). As such, we'll focus on the management of chronic hypernatremia. What we can do is we can come up with the free water deficit of a patient shown by the following equation.

[(measured Na - 140)/140] x total body water
*total body water is 50% of body mass in anyone other than young men in which case TBW is 60% of body mass.

The next thing we need to do is give the patient free water. Although, there has never been convincing evidence of cerebral edema or other adverse CNS events due to brisk lowering of serum sodium in adults (4), there's not a good reason to be overly aggressive and a slow lowering of the sodium level is unlikely to cause harm. A good rule-of-thumb is to aim to lower the sodium at a rate of 10mmol/L per day. A fluid repletion rate can be calculated as follows:

Total volume of water replacement in the first day = 3mL/kg body mass x 10

Hourly infusion rate (mL/hr) = total daily water replacement volume ÷ 24

***for a 70kg patient, this would be an hourly rate of 87.5mL/hr (rounded to 75-100mL/hr)**

This calculation will replace the water deficit

that they already have, but does not take into account ongoing water loss. To really fix the water deficit and ongoing water loss, we must replace all of the sources of water loss below:
Water deficit (calculated from the equation above)
Obligatory water loss for skin and stool (respiratory water loss does not count and we will calculate urinary water loss below)
Urinary water loss (see next paragraph)

Urinary water loss is very important as well, especially in polyuric patients. Not all urine volume is electrolyte free water, but the percentage of electrolyte free water increases with increasing UOP and can be estimated by the following (5):

- UOP volume of 0-1L per day: ignore
- UOP volume of 1-3L per day: 50% of this is electrolyte free water
- UOP >3L per day: all of this is free water

Let's give an example to estimate urinary free water loss (figure 1). You have a patient that is making 4L of urine per day. We want to know how much free water he is losing so we can include that into our water replacement strategy. Out of those 4L, we ignore the first liter. UOP liters 2 and 3 are 50% free water which means they indicate 1L free water loss (since 2L divided by 2 is 1). Lastly, the 4th liter is 100% free water which gives us a total of 2L urinary electrolyte free water loss.

EVALUATION OF HYPONATREMIA

When you see a patient with hyponatremia there are five main steps to properly evaluate them:

1. Confirm that the hyponatremia is true hyponatremia (hypoosmolar hyponatremia)
2. Evaluate the severity of hyponatremia
3. Stop medications that can lower the serum sodium further, and lastly go on with your routine hyponatremia evaluation to fully decide why the serum sodium is low.

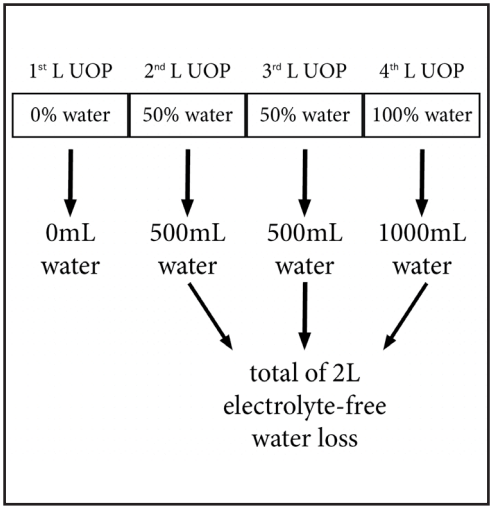


Figure 1: Urinary free water loss

4. Give hypertonic saline if indicated for severe symptoms
5. Decide why the patient has hyponatremia

FIND OUT IF THE PATIENT HAS TRUE HYPONATREMIA

For step 2, we need to decide if the patient has true hyponatremia. If we need to find an answer for this urgently we can always get an ABG with electrolytes and the direct potentiometry of the ABG machine will let us know what the true sodium level is. If there's less urgency as in we don't have to find the serum osmolality within 15 minutes, then we can add a serum osmolality onto the labs that were already drawn. A serum osmolality less than 280 suggests that the patient has true hyponatremia. Needless to say, we also need to make sure that the patient doesn't have hyperglycemia. If the patient does have hyperglycemia then a simple correction factor of adding 2.4mmol/L to the serum sodium for each 100mg/dL the glucose is above 100 can let us know what an estimated true serum sodium level (6). This is higher than the standard correction factor of 1.6 (7). It has been suggested by some that a simplified correction factor of 2.0 is reasonable since we are only gaining a snapshot of an estimate of the true sodium. We tend to use a correction factor of 2.0.

EVALUATE THE SEVERITY OF HYPONATREMIA

For step 1, the following is how we think about the severity of hyponatremia:

- 135-145: normal
- 130-134: CNS symptoms are less likely to occur in this range. A trial that improved sodium levels to >130 observed improvements in mental, social, and physical functioning in those with hyponatremia (8)
- 120-129: at these levels (specifically 124-129), patients can have gait abnormalities that resolve when the sodium level is normalized. Nausea and malaise can be seen with acute hyponatremia with sodium levels of even 125-130mmol/L (9).
- ≥120: the risk of osmotic demyelination is still present but unlikely. It's rare to have osmotic demyelination at presenting sodium levels in this range except in those with cirrhosis or other risk factors (10); it's very possible to have no symptoms in this range if the sodium level has been chronically in this range, but if the sodium level has changed more rapidly, then symptoms may be present.
- <120: severe: all patients are at high risk of osmotic demyelination with overcorrection of serum sodium; it's more likely that symptoms will be present (10).
- <105: very high risk for osmotic demyelination; we would expect to see some type of symptom in these patients (10).

STOP OFFENDING MEDICATIONS

For step 4, stop medications that can make the sodium level worse. This includes thiazide diuretics, thiazide-like diuretics, and any kind of IV fluids. Additionally, look at their medication list and perform a thorough review to see if any of their medications are associated with hyponatremia. Of note, loop diuretics and MRAs do not cause hyponatremia (10). In the first 24 hours of hyponatremia, IV fluids essentially play no role in the management of hyponatremia and can only make things worse. In addition, it's useful to look through the chart and to see if there are any other medications that can potentially be contributing to hyponatremia such as NSAIDs.

STOP OFFENDING MEDICATIONS

For step 4, stop medications that can make the sodium level worse. This includes thiazide diuretics, thiazide-like diuretics, and any kind of IV fluids. Additionally, look at their medication list and perform a thorough review to see if any of their medications are associated with hyponatremia. Of note, loop diuretics and MRAs do not cause hyponatremia (10). In the first 24 hours of hyponatremia, IV fluids essentially play no role in the management of hyponatremia and can only make things worse. In addition, it's useful to look through the chart and to see if there are any other medications that can potentially be contributing to hyponatremia such as NSAIDs.

GIVE HYPERTONIC SALINE IF NEEDED

For step 3, decide if hypertonic saline (3% saline) needs to be given. If the patient is having active seizures or has any symptoms that may be due to increased intracranial pressure (seizures, lethargy, coma, respiratory arrest, headache, nausea, vomiting, tremors, gait abnormality, movement disorders, or confusion), then we should give hypertonic saline in the presence of true hyponatremia (10). A good way to give this is by sequential boluses of 100mL of 3% saline given over 10 minutes. This can be given through a peripheral line (11). This can be repeated up to three times until the severe symptoms resolve. In this setting the goal is to raise the serum sodium by 4-6mmol/L (10). Despite what the serum sodium level is, even if it is severe, a rise in the serum sodium in this range should resolve any severe symptoms from hyponatremia (10). If the patient does not have these severe symptoms then what we do is move on to the next step which is to remove any medications that could potentially worsen the serum sodium. The

treatment of hyponatremia is evolving. In the future, it's likely that we will move towards a DDAVP clamp for treatment of severe hyponatremia which involves the simultaneous administration of hypertonic saline with DDAVP (11).

FIND THE CAUSE OF HYPONATREMIA

For step 5, decipher why the patient has hyponatremia. There are two main ways to do this. The chart below (figure 2) shows the standard algorithm for this. It's simple and intuitive layout helps to organize the process in your mind.

In the standard algorithm (figure 2), the first step is to check the serum osmolality. For hyperosmolar hypernatremia, it should be obvious if the patient has hyperosmolar hyponatremia since the glucose level will give you the correct answer for this. We rarely use mannitol in the hospital and so we typically do not have to worry about this. If the serum osmolality is between 280-295, then this patient probably has pseudohyponatremia. The only caveat to these statements is that if a patient has severe acute kidney injury or they're on dialysis then hyponatremia is due to decreased free water excretion from kidney

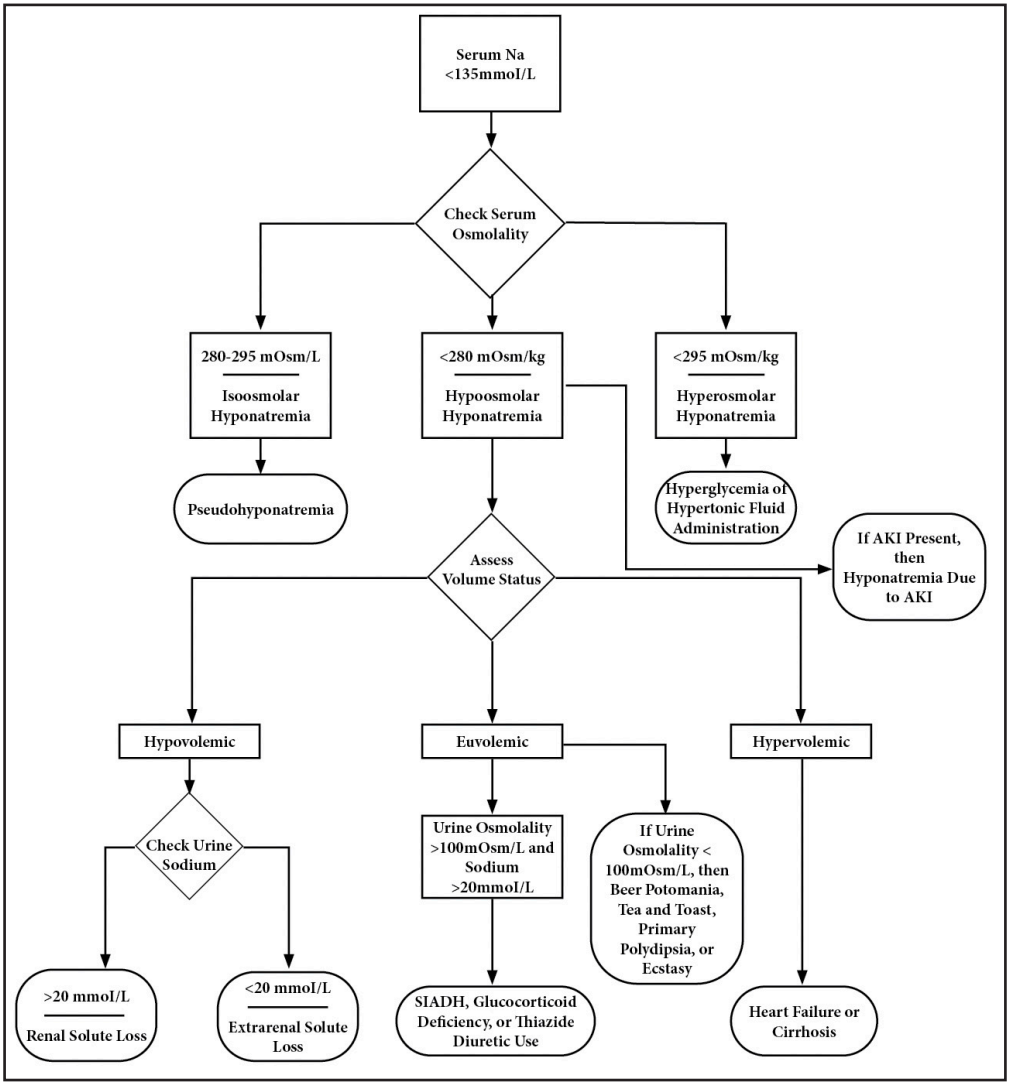


Figure 2: a classic algorithm for evaluation of hyponatremia

failure and your diagnostic evaluation can stop here.

If a patient has a serum osmolality less than 280 (which is going to be most of our consults for hyponatremia) then the next thing we do is assess the volume status. If the patient has typical features of hypervolemia such as lung findings, edema, ascites then the patient has hypervolemia. If the patient has physical exam findings consistent with hypovolemia then we should consider hypovolemic hyponatremia. If the patient does not have findings consistent with hypervolemia or hypovolemia then the patient is euvolemic. Starting with hypervolemia, patients with heart failure or cirrhosis frequently have hyponatremia. If a patient does not have an established history of cirrhosis and is unlikely to have heart failure and only has lower extremity edema, treatment of hyponatremia with diuretics is less likely to treat the hyponatremia. If the patient has euvolemic hyponatremia, then the urine osmolality is helpful. If the patient has urine osmolality less than 100mOsm/L then the patient either has primary polydipsia, or decreased daily osmolar intake. Lastly, it is unlikely that someone has hypovolemic hyponatremia from renal solute loss. This is a rare condition and is not worth going much into right now. A good history of the patient will likely let you know if they have extrarenal solute loss.

An alternative method (figure 3) for diagnosing the cause of hyponatremia can be found in the chart below (12). This of course starts in checking the serum osmolality. This method then goes straight to the urine osmolality which is a very nice approach. The urine osmolality is a surrogate marker for ADH release and gives us a real-time idea of ADH levels.

CORRECT THE SODIUM LEVEL

The next thing to do is make sure that the serum sodium level rises, but in a safe manner. In general, the nephrology community has become more conservative with rises in serum sodium. In any 24 hour period, we should not let the serum sodium rise more than 8 mmol/L per day, but a more conservative threshold of 6-8 mmol/L per day is very reasonable to follow (10). Doing so, prevents the development of osmotic demyelination. As mentioned, in the first

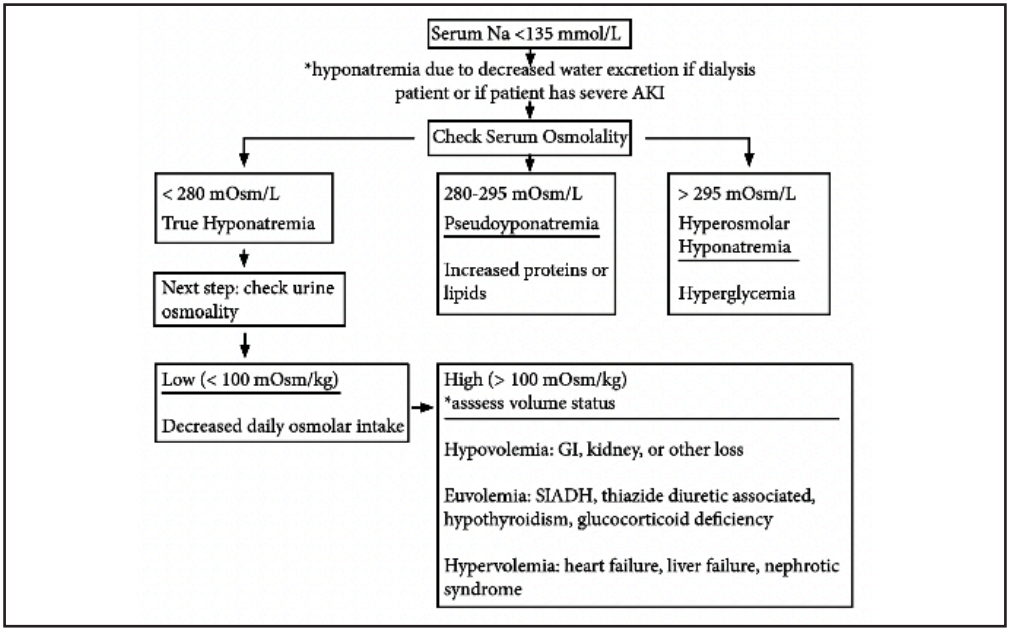


Figure 3: evaluation of hyponatremia utilizing urine osmolality

24 hours the goal is to not let the serum sodium rise more than 8 mmol/L. After that, treatment of the underlying disorder either using salt tablets, vaptans or water restriction is useful. Fluid restriction to less than one liter of fluid intake per day will raise the serum sodium 3 mmol/L in one day and 4 mmol/L over the course of one month (13). Vaptans are infrequently used in the hospital, but may be useful. If these are used at a strength of tolvaptan 7.5 mg daily is a reasonable starting dose with close monitoring of the serum sodium. Vaptan should not be used in liver failure (10). Each patient we see is different and we will have detailed discussions of proper correction strategies that vary on a case-by-case basis.

PREVENT OVERCORRECTION

Evaluate your patient for risk of osmotic demyelination. This includes essentially anyone with cirrhosis, anyone with a sodium level <120 as well as other risk factors known by the acronym SHAAM (10):

S: serum sodium <105
H: hypokalemia
A: alcoholism
A: advanced liver disease
M: malnutrition

Especially in these patients, we should begin to get nervous when the serum sodium rises above 6 or it looks like it will rise more than 6 mmol/L in a day and definitely if it rises more than 8 mmol/L in a day. If this is the case, measures should be taken to prevent overcorrection, which includes administration of free water and potential DDAVP administration..

Overcorrection typically occurs when an offending agent for hyponatremia is removed and we are suddenly left with brisk aquaresis and a subsequent rapid correction of the sodium level. This is a difficult situation and is hard to remedy by water administration alone. In this setting, it is often the correct action to take control of the kidneys and stop free water excretion. This is where desmopressin can be helpful. It can be by giving 2 to 4 mcg intravenously every six to eight hours (14). This will stop free water excretion in the kidneys and allow us to stabilize and relower the serum sodium with free water administration.

OTHER NOTES ON HYPONATREMIA

The cause of hyponatremia in a patient is often multifactorial. Keep looking for inciting factors after you have found the first one. Decreased daily similar intake is often present along with SIADH or thiazide use.

Hypernatremia due to thiazide diuretics generally improves with stopping the thiazide diuretic. These patients will have the tendency to overcorrect and so you need to follow the serum sodium closely in these patients (10).

The patients with SIADH can be difficult to treat. Sometimes, SIADH is acute and due to either nausea, vomiting, lung disease or some other factor like pain (15) A lot of the time, this gets better during the hospitalization and when the patient gets out of the hospital. Fluid restriction is a cornerstone of treatment for these patients. In addition, sodium chloride tablets can be given to increase free water excretion (16). Urea administration is a more effective way of increasing free water excretion, but our hospital does not have urea in its formulary. We should not give normal saline to patients with SIADH because this will make the sodium level worse.

Patients with either a decreased daily osmolar intake or volume depletion will get better with IV fluids and so when you see this pattern happen in the hospital, consider one of these two diagnoses. Importantly, one liter of normal saline has around 300 milliosmoles of solutes in it. If someone does have a decreased daily osmolar intake like tea and toast, if they decrease their urine osmolality to 50 mmol/L then one liter of normal saline will provide enough solids to help them excrete six liters

of free water and so this could be one cause of the rise in serum sodium in patients who get normal saline in the emergency department.

In patients with hypervolemic hyponatremia, which pretty much only includes patients with heart failure or cirrhosis, diuretics are the backbone of treatment in addition to fluid restriction.

There's essentially no difference in the severity of hyponatremia in between patients with heart failure, with a reduced ejection fraction and a preserved ejection fraction (17).

Hyponatremia is a lot more difficult to treat in patients with cirrhosis. In addition, we should not give vaptans to patients with cirrhosis. Tolvaptan is contraindicated in patients with liver disease and conivaptan is a combined V1 receptor, V2 receptor antagonist and may increase support of blood flow and may precipitate variceal bleeding.

REFERENCES

1. Burst V: Etiology and Epidemiology of Hyponatremia. Front Horm Res 52: 24–35, 2019
2. Chawla A, Sterns RH, Nigwekar SU, Cappuccio JD: Mortality and serum sodium: do patients die from or with hyponatremia? Clin J Am Soc Nephrol CJASN 6: 960–965, 2011
3. Rose BD, Post TW: Clinical physiology of acid base and electrolyte disorders. New York, McGraw-Hill
4. Chauhan K, Pattharanitima P, Patel N, Duffy A, Saha A, Chaudhary K, Debnath N, Van Vleck T, Chan L, Nadkarni GN, Coca SG: Rate of Correction of Hypernatremia and Health Outcomes in Critically Ill Patients. Clin J Am Soc Nephrol CJASN 14: 656–663, 2019
5. #170 Hypernatremia is Easy with Joel Topf MD [Internet]. The Curbsiders. 2019 Available from: https://thecurbsiders.com/podcast/170-hypernatremia [cited 2022 Apr 13]
6. Hillier TA, Abbott RD, Barrett EJ: Hyponatremia: evaluating the correction factor for hyperglycemia. Am J Med 106: 399–403, 1999
7. Katz MA: Hyperglycemia-induced hyponatremia--calculation of expected serum sodium depression. N Engl J Med 289: 843–844, 1973
8. Schrier RW, Gross P, Gheorghiade M, Berl T, Verbalis JG, Czerwiec FS, Orlandi C, SALT Investigators: Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. N Engl J Med 355: 2099–2112, 2006
9. Renneboog B, Musch W, Vandemergel X, Manto MU, Decaux G: Mild chronic hyponatremia is associated with falls, unsteadiness, and attention deficits. Am J Med 119: 71.e1–8, 2006
10. Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, Thompson CJ: Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med 126: S1-42, 2013
11. Sood L, Sterns RH, Hix JK, Silver SM, Chen L: Hypertonic saline and desmopressin: a simple strategy for safe correction of severe hyponatremia. Am J Kidney Dis Off J Natl Kidney Found 61: 571–578, 2013
12. Koyner JL, Topf J, Lerma E: Handbook of Critical Care Nephrology. Lippincott Williams & Wilkins
13. Garrahy A, Galloway I, Hannon AM, Dineen R, O'Kelly P, Tormey WP, O'Reilly MW, Williams DJ, Sherlock M, Thompson CJ: Fluid Restriction Therapy for Chronic SIAD; Results of a Prospective Randomized Controlled Trial. J Clin Endocrinol Metab 105: dgaa619, 2020
14. Perianayagam A, Sterns RH, Silver SM, Grieff M, Mayo R, Hix J, Kouides R: DDAVP is effective in preventing and reversing inadvertent overcorrection of hyponatremia. Clin J Am Soc Nephrol CJASN 3: 331–336, 2008
15. Hoorn EJ, Zietse R: Diagnosis and Treatment of Hyponatremia:

Compilation of the Guidelines. J Am Soc Nephrol 28: 1340–1349, 2017
16. Rondon-Berrios H, Berl T: Mild Chronic Hyponatremia in the Ambulatory Setting: Significance and Management. Clin J Am Soc Nephrol 10: 2268–2278, 2015
17. Dunlap ME, Hauptman PJ, Amin AN, Chase SL, Chiodo JA, Chiong JR, Dasta JF: Current Management of Hyponatremia in Acute Heart Failure: A Report From the Hyponatremia Registry for Patients With Euvolemic and Hypervolemic Hyponatremia (HN Registry). J Am Heart Assoc 6: e005261, 2017

Chapter 5: Potassium Disorders

EVALUATION OF HYPERKALEMIA

In Hyperkalemia is one of those disorders you should be able to treat with spinal-level reflexes. Since hyperkalemia will frequently happen in your patients and so it's best to immediately manage it and go forward with addressing all of the other patient issues for the day.

When faced with hyperkalemia, evaluate the severity first.

- 5.1-5.5: mild hyperkalemia
- 5.6-6.0: moderate hyperkalemia
- >6.0: severe hyperkalemia
- >6.5: severe hyperkalemia that needs rapid acting medications regardless of ECG changes (unless pseudohyperkalemia is present)

After this point, decide if the high potassium value is actually real. Pseudohyperkalemia is any high potassium value that is not reflective of the potassium level throughout the patient's circulation. Causes of pseudohyperkalemia are noted in table 1.

Notice that hyperglycemia was not listed in the table. The reason for that is because hyperkalemia due to hyperglycemia is true hyperkalemia. Hyperosmolality increases solvent drag that moves potassium out of the cells. In addition, you have a deficiency of insulin if your glucose level is extremely high. As insulin is one thing that moves potassium into cells, hyperglycemia by default means that insulin-mediated potassium shift into the cells is compromised. The good thing about a potassium level of 6.5 mmol/L in a patient with a blood sugar of 500 mg/dL is that you just give insulin and the potassium level takes care of itself.

If by this time, you have determined that the patient has true hyperkalemia which is not just due to hyperglycemia, the next step

Condition	Mechanism
Thrombocytosis	potassium moves out of platelets after clotting. ABG or iSTAT K+ levels will show a normal K+
Fist clinching	Depolarization of muscle cells during use causes potassium lrelease from cells
Chronic lymphotytic leukemia	Pseudohypokalemia due to K+ release from fragile cells
Hereditary disorders of RBCs	Very rare. RBCs in these individuals willbe permeable to potassium

Table 1: causes of pseudohyperkalemia

in evaluation is to estimate the chronicity of the hyperkalemia. If there is an acute rise in serum potassium (i.e. over the course of hours), then the hyperkalemia is likely due to a trans-cellular shift. If there is persistent hyperkalemia, then it is almost certainly due to a defect in renal excretion.

POTASSIUM SHIFTS

98% of total body potassium stores are intracellular. We have 70 mEq potassium in our extracellular stores and 3500 mEq in our intracellular stores. This means that, in a young 70kg man with a serum potassium level of 5.0 mmol/L, a 0.8% shift of the intracellular potassium stores into extracellular space will cause the serum potassium to rise to 7.0 mmol/L. It's as if our serum potassium levels are standing at the base of the Hoover Dam. Any slight leak in the dam which leaks intracellular potassium can be lethal. We eat potassium and excrete it for the kidneys.

INCREASED POTASSIUM INTAKE OR DECREASED EXCRETION EXCRETION

Although there are two parts to this equation, the rate-limiting step is always due to a defect in renal excretion of potassium. To drive home this point, lets point out what happens if people ingest large amounts of potassium. In one study, healthy adults increased potassium intake from a baseline of 100mEq daily to a very high amount of 400mEq daily for 20 days (1). The baseline K+ was 3.8 mmol/L. At the end of day 2 of the very, very, very, very high potassium diet, the serum potassium was only 4.8 mmol/L. By day 20,

Increased K+ Release From Cells	Reduced Urinary K+ Secretion
Metabolic acidosis	Reduced aldosterone secretion
Hyperglycemia	Reduced response to aldosterone
Increased tissue catabolism	Reduced effective arteriolar blood volume
Beta blockers	AKI or CKD
Exercise	Bactrim
Hyperkalemia periodic paralysis	Cyclosporine
Digtalis Overdose	Tacrolimus
Blood transfusion	NSAIDs
Succinylcholine	Urinary Obstruction
Tacrolimus	Spironolactone
Minoxidil	Potassium-sparing diuretics
Some volatile anesthetics	ACE/ARB
Mannitol	Beta-blockers
	Heparin

Table 2: etiologies of hyperkalemia due to increased K+ release from cells (transcellular shifts) or decreased K+ secretion in the kidney

the serum potassium was only 4.2 mmol/L. Since an increased potassium intake in the setting of normal kidney function doesn't cause hyperkalemia, the differential diagnosis of chronic hyperkalemia is one thing — reduced kidney potassium excretion. In the setting of reduced excretion of potassium, an increase in the intake of potassium, or a shift of potassium from intracellular to extracellular stores will of course raise the potassium. There are multiple medications and conditions that can cause reduced renal excretion. Look at the list below and check your patient for these conditions.

TREATMENT OF HYPERKALEMA

There are two types of true hyperkalemia — hyperkalemia without associated ECG changes or hyperkalemia with ECG changes.
ECG changes that occur in association of hypernatremia include peaked T waves, flattened P waves, prolonged PR interval, a widened QRS, conduction abnormalities, bradycardia, ventricular tachycardia, and asystole. Generally, the order of events is peaked T waves, prolonged PR interval, widening of the QRS complex, then a sine wave pattern, ventricular fibrillation, and asystole(2). There is actually no set potassium level at which these abnormalities occur and an ECG is not a sensitive test for hyperkalemia (3). If any of these changes are present in a patient with hyperkalemia, give the following:

- 1 gram calcium gluconate (4,5). This medication can be given through a peripheral line. Calcium chloride should not be given through a peripheral line as it carries the risk of tissue necrosis(6). It begins immediately through direct chemical antagonism and this effect lasts 60 minutes. Because of this, it should be given again if ECG changes persist and given repeatedly until hyperkalemia is resolved(7).
- Next, give 10 units IV insulin (not subcutaneous) and a 25 gram push of D50 (8,9). Also start a D5W drip a 50-75mL/hr to prevent hypoglycemia if the original glucose level is ~150 or less. If the patient has blood glucose >300mg/dL, don't give any D50 or a D5W drip. Insulin alone lowers potassium by 0.7mmol/L (10).
- 10mg inhaled albuterol can be given, but it's use may be limited due to side effects of tachycardia. Giving albuterol will lower the potassium by 0.7mmol/L itself, but giving it in addition to in addition to insulin/dextrose will lower the potassium by 1.2mmol/L. Remember that this is 4x the normal albuterol dose and so the respiratory therapist may come asking for an explanation before they know why you are giving it.

The next step is to remove potassium out of the body. Sodium zirconium cyclosilicate (SZC) is a cation exchanger that lowers the potassium via GI excretion. A 10g dose three times daily is a reasonable dose. A single 10g dose will lower the potassium level by 0.4mmol/L in 4 hours (11).
Sodium polystyrene sulfonate (SPS); (a.k.a kayexalate) can lower potassium, but carries a risk of colonic necrosis at around 2% (12). Despite the fact that this medication was FDA approved in 1958, there has only been one randomized, double-blind controlled trial (in 2015) which did show that it is superior to placebo for lowering potassium (13). Retrospective data shows that a 15-60g oral dose lowers potassium by 0.4mmol/L and 0.9mmol/L, respectively (14). Other studies showed that a 15-30g dose only lowered the potassium level by 0.14mmol/L (15). Overall, if a patient has an ileus, underlying bowel disease, constipation, or is at risk for constipation (i.e. opioid use), then SPS should not be given since the risk far outweighs the benefits.

EVALAUTION OF HYPOKALEMIMA

In contrast to hypERkalamia, hypOkalemia has a larger differential and nuanced diagnosis. When you encounter hypokalemia,

the step is to decide if you are actually viewing true hypokalemia. Metabolically-active cells such as those seen in acute myeloid leukemia can cause pseudohypokalemia. In this case, once blood is in the test tube, the leukemia cells take up potassium thus making serum potassium look artificially low. You can easily diagnose pseudohypokalemia by getting an iSTAT potassium level or an ABG with electrolytes. The iSTAT or ABG potassium will always be the true potassium.

If there is true hypokalemia, then the following is the next step and involves an evaluation of the differential diagnosis for transcellular shifts. It is honestly pretty rare to see hypokalemia from a transcellular shift. Most of the time, we see hypokalemia due to kidney or GI loss. Keep in mind that transcellular shifts can happen and suspect it if there is an unexplained rapid fall in potassium.

If pseudohypokalemia and transcellular shifts are not the cause, then the other main cause would be an actual loss of potassium from the body. This is either due to renal potassium wasting or GI loss of potassium. Evaluation of renal potassium wasting is useful in this setting. The first thing is to look for obvious causes such as diuretics or hypomagnesemia. If those are not present, then get a spot urine sample for potassium and creatinine. A spot urine creatinine-to-potassium ratio greater than 13mEq/g indicates renal potassium wasting (16).

Again, if kidney potassium wasting is present, first rule out hypomagnesemia and diuretic use. Magnesium acts as a one way valve in the ROMK channel and hypomagnesemia causes a loss of this one way valve with subsequent kidney potassium wasting. If the patient does have renal potassium wasting, consider primary aldosteronism if the patient has hypertension. If this is not likely, consider a wide range of differential diagnosis for kidney potassium wasting. We won't dive into this at this time because it's rare to see in the hospital outside of diuretic use or hypomagnesemia.

TREATMENT OF HYPOKALEMIA

Treatment of hypokalemia is relative simple. If your patient has hypokalemia, check a serum magnesium level and replace if low. Next, you have the option to replace potassium via oral or IV routes. Both routes are equivalent and interchangeable as far as dosing. The most important thing to remember is that the dosing differs based on the potassium level. In short, here is a reasonable dosing strategy:

- If the K+ is 3.0 mmol/L or greater: each 10 mEq PO/IV of KCl will raise the K+ by 0.1 mmol/L.
- If the K+ is <3.0 mmol/L: each 10mEq KCl only raises the K+ by 0.05 mmol/L. Therefore, it will take 20 mEq KCl to raise the K+ by 0.1 mmol/L.
- We target a K+ level of 4.0 mmol/L
- If the patient has AKI, significant CKD, or another condition that raises the risk of hypERkalemia, calculate the dose of KCl needed to reach a K+ level of 4.0 mmol/L, cut the dose in half, and consider a repeat lab later in the day to ensure proper replacement

Let's give a few examples for potassium replacement:

- Patient X, who has normal kidney function and a K+ of 3.2 mmol/L, will need 80 mEq KCl to reach a K+ of 4.0 mmol/L.
- Patient Y, who has normal kidney function and a K+ of 2.9 mmol/L, will need 120 mEq KCl to reach a K+ level of 4.0 mmol/L. They will need 20 mEq KCl to go from 2.9 to 3.0 mmol/L and an additional 100 mEq KCl to go from 3.0 to 4.0 mmol/L.
- If patient X has AKI/CKD/ect, then cut the dose in half and only give 40 mEq KCl
- If patient Y has AKI/CKD, ect, then cut the dose in half and only give 60 mEq KCl. It would be prudent to repeat labs in

the afternoon.

Oral KCl 20 mEq will raise the potassium the same as 20 mEq IV KCl. The main difference is the rate at which you can raise the K+ level. Typically, we only give IV KCl at a rate of 10 mEq per hour. This means it will take 4 hours to give 40 mEq KCl, but actually, it will probably be given slower than this. IV KCl can cause burning at the infusion site when given and so nurses typically have to slow the rate and thus it will take even longer to infuse. KCl given via a central line can be concentrated more than that given via a peripheral line, but it is typically infused at the same rate. Overall, if a patient has severe hypokalemia, a combination of oral and IV KCl is typically best.

There are several formulations of oral KCl:

- **Long-acting KCl tablets:** these are fine for mild hypokalemia, but due to their long-acting nature, they are not the best for raising potassium over a short period of time. To avoid pill esophagitis, avoid in patients who have difficulty swallowing pills.
- **KCl powder:** typically mixed with juice. This is a good method for patinets who are alert (not on mechanical ventilation). It is typically well-tolerated. Additionally, it does not clog NG or OG tubes for patients on mechanical ventilation, but takes an extra step to prepare
- **Premixed KCl liquid:** good for ICU patients with an NG or OG tube since it is ready to use

REFERENCES

1. Rabelink TJ, Koomans HA, Hené RJ, Dorhout Mees EJ: Early and late adjustment to potassium loading in humans. Kidney Int 38: 942–947, 1990
2. Clase CM, Carrero J-J, Ellison DH, Grams ME, Hemmelgarn BR, Jardine MJ, Kovesdy CP, Kline GA, Lindner G, Obrador GT, Palmer BF, Cheung M, Wheeler DC, Winkelmayer WC, Pecoits-Filho R, Conference Participants: Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int 97: 42–61, 2020
3. Montague BT, Ouellette JR, Buller GK: Retrospective review of the frequency of ECG changes in hyperkalemia. Clin J Am Soc Nephrol CJASN 3: 324–330, 2008
4. Palmer BF, Clegg DJ: Renal Considerations in the Treatment of Hypertension. Am J Hypertens 31: 394–401, 2018
5. Kovesdy CP: Management of hyperkalaemia in chronic kidney disease. Nat Rev Nephrol 10: 653–662, 2014
6. Long B, Warix JR, Koyfman A: Controversies in Management of Hyperkalemia. J Emerg Med 55: 192–205, 2018
7. Chamberlain MJ: EMERGENCY TREATMENT OF HYPERKALAEMIA. Lancet Lond Engl 1: 464–467, 1964
8. Harel Z, Kamel KS: Optimal Dose and Method of Administration of Intravenous Insulin in the Management of Emergency Hyperkalemia: A Systematic Review. PloS One 11: e0154963, 2016
9. Sterns RH, Grieff M, Bernstein PL: Treatment of hyperkalemia: something old, something new. Kidney Int 89: 546–554, 2016
10. Allon M, Copkney C: Albuterol and insulin for treatment of hyperkalemia in hemodialysis patients. Kidney Int 38: 869–872, 1990
11. Packham DK, Rasmussen HS, Lavin PT, El-Shahawy MA, Roger SD, Block G, Qunibi W, Pergola P, Singh B: Sodium zirconium cyclosilicate in hyperkalemia. N Engl J Med 372: 222–231, 2015
12. Gerstman BB, Kirkman R, Platt R: Intestinal necrosis associated with postoperative orally administered sodium polystyrene sulfonate in sorbitol. Am J Kidney Dis Off J Natl Kidney Found 20: 159–161, 1992

13. Lepage L, Dufour A-C, Doiron J, Handfield K, Desforges K, Bell R, Vallée M, Savoie M, Perreault S, Laurin L-P, Pichette V, Lafrance J-P: Randomized Clinical Trial of Sodium Polystyrene Sulfonate for the Treatment of Mild Hyperkalemia in CKD. Clin J Am Soc Nephrol CJASN 10: 2136–2142, 2015
14. Mistry M, Shea A, Giguère P, Nguyen M-L: Evaluation of Sodium Polystyrene Sulfonate Dosing Strategies in the Inpatient Management of Hyperkalemia. Ann Pharmacother 50: 455–462, 2016
15. Batterink J, Lin J, Au-Yeung SHM, Cessford T: Effectiveness of Sodium Polystyrene Sulfonate for Short-Term Treatment of Hyperkalemia. Can J Hosp Pharm 68: 296–303, 2015
16. Lin S-H, Lin Y-F, Chen D-T, Chu P, Hsu C-W, Halperin ML: Laboratory tests to determine the cause of hypokalemia and paralysis. Arch Intern Med 164: 1561–1566, 2004

Chapter 6: Acid-Base

Proper acid-base interpretation is important to function well in a hospital setting. Throuhout your training, you have probably heard several approaches to acid-base interpretation. This is initially frustrating for such a standard topic, but the reason for this is that there are multiple ways to interpret acid-base abnormalities. The three main approaches to interpreting acid-base disorders. The first method is what we typically used for acid base interpretation and it is referred to as the Boston approach. The second type of method for interpreting acid base disorders is called the base excess, or Copenhagen approach. The last method for interpreting acid base disorders is called the Stuart approach and it is probably the most obscure out of all the methods.

What we will use for acid base interpretation is the Boston approach. Because it is the most widely used clinically. Specifically, the method we present works well for both clinical situations and for board exams and avoids cumbersome calculations.

Before we begin, there are a few terms we need to know. Acidemia refers only to a pH which is <7.35. Alkalemia only refers to a pH that is >7.45. Acidosis, on the other hand, is a physiological process which tends to lower the pH. For instance, a patient may have a metabolic acidosis which is producing acidemia. Alkalosis, in the same way, is any process that tends to raise the pH. The reason that this is important is that in mixed acid-base disorders, it is possible to have a combined metabolic acidosis and respiratory alkalosis which resulted in a pH of 7.28. In this example, yes a person does have an alkalotic disorder which is present in someone with acidemia, but only because the metabolic acidosis is overpowering the respiratory alkalosis. The terminology is important and will make you look smarter when talking to acid-base buffs like the pulmonologists.

STEPS

1. The most useful first step to interpreting acid-base disorders in our opinion, is to calculate the anion gap first. A normal anion gap is 10mmol/L. If you are calculating the anion gap, you must correct the anion gap for albumin. For each g/dL albumin is below 4.0, add 2.5 millimoles per liter to the anion gap. For instance, if an albumin level is 3.0, then you would add 2.5 to whatever anion gap you calculate based on Na-(CO2+Cl)

2. If the anion gap is elevated, then the next step is to perform the Winters' formula to calculate the expected PCO2 and progress to step number 5.

3. If the anion gap is normal, then what you want to do is determine whether the patient has acidemia or alkalemia. Acidemia is defined by any pH less than 7.35. Alkalemia is defined by any pH greater than 7.45.

    a. If the patient has acidemia, look at the bicarbonate level. If the bicarbonate level is low, then a metabolic acidosis is present. If the PCO2 is high, then respiratory acidosis is present. If the bicarbonate level is low and the pco2 level is high, then a mixed metabolic acidosis and respiratory acidosis is present.

    b. If the patient has alkalemia, look at the bicarbonate level. If the serum bicarbonate level is high, then a metabolic alkalosis is present. If the PCO2 is low, then a respiratory alkalosis is present. If the serum bicarbonate level is high and the PCO2 level is low, then both a metabolic alkalosis and respiratory alkalosis are present.

4. The next thing you need to do is evaluate the patient for the level of compensation.

    a. If the patient has a metabolic acidosis: use the winters equation which is: PCO2 = [1.5 x(HCO3-) +8] +/- 2. If a patient's

PCO2 is higher than expected, then the patient has a concomitant respiratory acidosis. It's a patient's pco2 is lower than expected, then the patient has a concomitant respiratory alkalosis.

b. If the patient has a metabolic alkalosis: PCO2 increases 0.7 mmHg for each 1mmol/L increase in (HCO3-) +/-5. If a patient's PCO2 is higher than expected, then the patient has a concomitant respiratory acidosis. If a patient's PCO2 is lower than expected, then the patient has a concomitant respiratory alkalosis.

c. For respiratory disorders, use the figure 1 to calculate the expected serum bicarbonate level for any change in PCO2. Acute respiratory acidosis will increase the bicarbonate level by 1mmol/L for every 10mmHg change in PCO2. Chronic respiratory acidosis will increase the bicarbonate level 4mmol/L for a 10mmHg increase in PCO2. Conversely, a decrease in PCO2 of 10mmHg will cause a decrease in serum bicarbonate of 2mmol/L and 5mmol/L for acute and chronic respiratory alkalosis, respectively. If the patient's bicarbonate level is lower than expected based on these rules, then the patient has a concomitant metabolic acidosis. If a patient's bicarbonate level is higher than expected, then the patient has a concomitant metabolic alkalosis.

5. If a patient has an anion gap metabolic acidosis, then the next thing to do is to calculate the Delta Gap. The Delta cap is essentially the absolute difference of the anion gap as compared to a normal anion gap of 10 divided by the absolute difference of the measured serum bicarbonate level as compared to a normal serum bicarbonate level of 24. The equation looks like this: [(AG-10)/(24 - measured bicarb)]. the rationale for this is that because 1 mmoL of lactic acid will require 1 mmoL bicarbonate for buffering, thus dropping the serum bicarbonate level in a 1:1 fashion. If the delta gap is <1, then it means that a NAGMA is also present. If the delta gap is >2, then a concominant metabolic alkalosis is present. in this last situation of a concominant metabolic alkalosis, it makes reasonable sense that if someone has an anion gap of 15, but a serum bicarbonate level of 23, then there must be some type of metabolic alkalosis present as well.

Now, quiz yourself. Scan the QR code below and scroll to the bottom of the page to find acid-base practice questions.

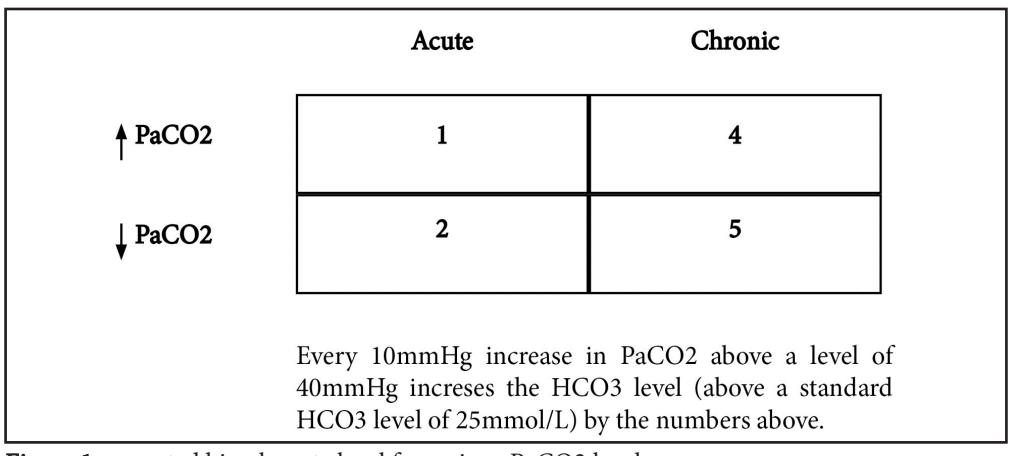


Figure 1: expected bicarbonate level for a given PaCO2 level