SECTION E – NEURO & SEPSIS

Chapter 21: A 50-year-old woman with flank pain

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"HONEY, YOU SEEM CONFUSED. I'LL BET IT'S FROM THE PAIN PILLS."

SECTION E / CHAPTER 21

A 50-year-old woman with flank pain

Flank pain in adults is common with 1.3 million ED visits per year;[1] this is not surprising as "kidney stones" occur in up to 8.8% of the population.[2] The differential diagnosis for acute flank pain ranges from benign etiologies such as a muscular strain or zoster to more serious pathology including malignancy or a ruptured abdominal aortic aneurysm (AAA).[3]

The evaluation is easy, right? Just order a CT scan which will "automatically" exclude the bad stuff, including AAA, cancer, small bowel obstruction (SBO), perforated viscus, retrocecal appendix, pancreatitis… and, if we are lucky, it will "rule-in" a ureteral stone, giving us a quick diagnosis and disposition. Well, not so fast! There are a few questions remaining:

1. Can we avoid CT imaging by clinically diagnosing ureteral colic?
2. When imaging for a stone, how often are we surprised by a life-threatening etiology?
3. Does size and location of ureteral stone predict the chance of spontaneous expulsion?
4. Does medical expulsion therapy work?
5. Are labs helpful for uncomplicated ureterolithiasis?
6. The nightmare scenario: How do patients with seemingly uncomplicated ureteral stones go bad… and how are they managed if this occurs?

Buckle your seatbelt as we put *you* in the footsteps of the EM provider at the initial visit and keep you there until the bounceback. Spoiler alert: Our patient returns 2 days later, crashing soon after hitting the emergency department double-bay doors.

INITIAL ED VISIT

HPI: The patient is a 51-year-old woman with no significant past medical history who presents with right flank pain. She reports that she woke up 2½ hours ago, with sudden onset right flank pain. She had some mild nausea but after attempting to drink water she had an episode of vomiting, nonbloody, nonbilious. She denies chest pain or pressure, shortness of breath, abdominal pain, diarrhea or bloody stools, dysuria, increased urinary frequency, or hematuria. She has no history of kidney stones or pyelonephritis.

Allergies: PCN
Social history: No smoking or alcohol
Family history: See HPI
ROS: All other systems reviewed and are negative except as noted. Nursing triage notes were reviewed

PMH: Migraine headaches
PSH: Knee, breast biopsy

PE:

Vitals:						
Temp (F)	**Pulse**	**Resp**	**Syst**	**Diast**	**Sat**	**Pain**
98.2	**70**	**16**	**132**	**86**	**99% (RA)**	**9/10**

GA: A&OX3, appears very uncomfortable
EYES: PERRL
CV: RRR without m/r/g. Normal heart sounds. Good capillary refill. No peripheral edema
RESP: CTAB, no wheezes, rales, rhonchi. Good chest excursion
ABD: Soft and NT throughout, Murphy's sign negative, without r/r/g [rigidity/rebound/guarding]
BACK: No CVAT
SKIN: Normal without petechiae, vesicles, erythema

Urinalysis:
Appearance: Cloudy
Specific gravity 1.011
pH: 7.0
Glucose: Neg
Ketones: 5mg/dl
Blood: 100/ul
Leukocyte esterase: 100/ul
Nitrite: Neg
Protein: 15mg/dl
WBC: 0–5
RBC: 25–50
Squam epi: Occasional
Bacteria: Few

TESTING: Noncontrast helical CT scan abdomen/pelvis: 6mm obstructing right ureteral stone at the mid aspect of the ureter.

MDM: She received morphine and ondansetron. Her records have been reviewed. There is no evidence of associated urinary infection with only 0–5 white blood cells, however I have sent urine for culture since she has leukocyte esterase. I suspect this is related to inflammation from the stone. Will discharge to home with Flomax, Naprosyn, Norco, Phenergan, and MiraLAX. Repeat exam benign, she is much more comfortable after morphine, but still having some discomfort, so will order Norco PO prior to discharge.

IMPRESSION: Ureteral calculus, left

PLAN: Urine strainer, f/u with urology in 3–4 days

Seems straightforward. The management is seemingly open and shut and quite well done—most of us would correctly also send this patient right home. But there is a "game changer" question which was not asked… a question that if answered in the affirmative, would have completely changed the disposition and likely the outcome.

Documentation and patient safety issues:

1. It may seem nit-picky, but how do you wake up with a "sudden onset" of flank pain? Did the pain wake her from sleep or did the pain start suddenly after she woke up, as is typical with a ureteral stone? When deciding whether a patient has pyelonephritis, a ureteral stone, or another etiology, a well-defined onset may be helpful.
2. Medical decision-making (MDM): Part 1 – The provider did a nice job of addressing an abnormality in the lab results: the WBCs found in the urine. This is an important risk management/patient safety technique; specifically addressing unexpected findings discovered during the evaluation. The explanation (ureteral inflammation) sounds reasonable (though may have been a guess and not literature-based), but the provider was left with some concern, so a urine culture was ordered.
3. Medical decision-making (MDM): Part 2 – When deciding on a disposition, we employ an age-old technique; risk stratification. Are we comfortable sending home a patient where we are 95% certain of the diagnosis, or do we strive for 99%? Much of this depends on the diagnosis we are considering. We may be comfortable with a 1% risk of missing an Achilles tendon rupture, but not a 1% risk of missing a ruptured AAA or a subarachnoid hemorrhage. When life-threatening entities are possible, we need to have a fail-safe strategy to catch the atypical presentation; the patient must know when and why to return. It is clear this provider considered infection, and while it may have been reasonable to discharge the patient without antibiotics, why not engage the patient/family with a discussion of unlikely but possible diagnoses remaining… and document the discussion in the "medical decision making" section? This is better for patient safety and more legally protective than simply printing the pre-scripted "aftercare instructions."[4,5]
4. The "game changer" question: "Have you had a fever?" Arguably the most important question in a patient with a confirmed ureteral stone; if this question had been answered in the affirmative, without other explanation for the increased temperature, the possibility of an "infected stone"would have been increased and the management would have likely been different. There was a notation made that the few urine WBCs seen could have been from ureteral irritation due to the stone, indicating the provider considered the possibility of infection. There was good documentation as to other symptoms including a detailed review of symptoms (ROS) stating: "She denies chest pain or pressure, shortness of breath, abdominal pain, diarrhea or bloody stools, dysuria, increased urinary frequency, or hematuria." Infection was considered, but the provider did not inquire about an age-old hallmark of infection—fever.

Section editor comments (Osborn):

Agree that this is a good question to ask. There are various possible responses from "no" to "I felt hot" to "it was 102 degrees at home" [and I took acetaminophen just prior to arrival]. Though our patient was afebrile in the ED, with concern for infection, would a second set of vital signs have been helpful?

What about the work-up? Seems routine and reasonable. We evaluate patients with back pain, flank pain, and “kidney stone” every day; the following is a review of the evaluation and management of flank pain and ureteral stones. More on ultrasound with the bounceback visit...

1. Is it possible to avoid CT imaging by clinically diagnosing ureteral colic?

The classic teaching is that a ureteral stone presents with a sudden onset of sharp and severe, "colicky" pain radiating to the unilateral groin/testicle (in a patient doing a “kidney stone dance”). Pyelonephritis, conversely, presents as a gradual onset of dull and constant flank/back pain with infectious urinary symptoms including dysuria, urinary frequency, and/or urgency.

But allow us to throw a wrench in this "classic" thinking. Consider a patient with a radiographically diagnosed stone who is leaving the ED after their hydromorphone and ondansetron; the only "dance" they are doing is one of joy because their pain is controlled. They still have a stone, but they no longer are exhibiting the "classic" symptoms—why? The severe pain which brought them to the ED was likely from a stone that was *moving* down the ureter. A stationary stone is more difficult to differentiate from pyelo, as there may be no pain or constant and mild pain.

Moore, et al. derived a clinical decision rule, the STONE score, by using a retrospective derivation of 1,040 patients who had a "flank pain protocol" CT to predict the presence of uncomplicated ureteral stones. They then used a prospective validation of 491 patients in whom "the clinician intended to obtain a CT scan for kidney stone." They found the 5 factors most predictive of a ureteral stone included.

1. Male sex
2. Short duration of pain (< 6 hours)
3. Non-black race
4. Presence of nausea or vomiting
5. Microscopic hematuria[3]

They used pilot data and previous studies to estimate that about 50% of CT scans for flank pain would have a ureteral stone. If all 5 findings were present, then a ureteral stone was identified 88.6% (validation set) to 89.6% (derivation set) of the time. But more importantly, the group most likely to have a stone was least likely (< 2%) to have an alternative important cause of their symptoms.[3] So how good is a clinical diagnosis of a stone? Pretty good if the patient presents classically, but in an elderly patient or with an atypical presentation… not good enough. The most interesting findings of the study were the rate of alternative diagnoses.

2. When imaging for a stone, how often are we surprised by a life-threatening etiology?

In many ways, the best utility of a CT scan in patients with flank pain is not to *rule-in* ureteral stones, but to *rule-out* serious alternative diagnoses. Balancing perceived patient expectations of imaging with the potential harm of radiation is difficult, but a conversation using a "shared-decision making" (SDM)[6] model may decrease the use of CT scans. The SDM conversation needs to be between two *reasonable alternative* approaches; for example, a 70-year-old with severe flank pain and no history of stones is not the time to improve your "through-put" numbers!

Combining the derivation and validation set performed by Moore, et al. (above) yielded 1,531 total patients; there was a serious diagnosis in a small, but significant number of patients:

Diverticulitis	10 (0.65%)
Appendicitis	9 (0.59%)
Malignancy	5 (0.32%)
Cholecystitis	3 (0.19%)
Bowel obstruction	2 (0.13%)
Perforated viscus	1 (0.065%)
Abdominal aortic aneurysm (AAA)	1 (0.07%)
Pancreatitis	1 (0.07%)
Total serious alternative diagnoses (note that there were other diagnoses in the total including ovarian pathology, colitis, pneumonia, etc) = 48 (3.1%)[3]	

Adapted from Moore CL, Bomann S, Daniels B. Derivation and validation of a clinical prediction rule for uncomplicated ureteral stone--the STONE score: retrospective and prospective observational cohort studies. BMJ. 2014 Mar 26. 348:g2191.

These findings are similar to an examination of 950 patients by Luchs, et al. who had a CT performed for renal colic, identifying 7% alternative diagnoses (which decreased to 5.6% if ovarian cysts were excluded).[7]

Rapp, et al. examined 613 patients undergoing non-contrast CT scan for flank pain and found if there was presence of all four "Vstone" criteria (flank pain, hematuria, nausea/vomiting, and prior stone) a ureteral stone was present 59% of the time, but the presence of flank pain alone, only yielded 6% ureteral stone disease.[8]

Bottom line: Whereas the different studies describe ureteral stone findings (flank pain, hematuria, short-duration pain), the most interesting findings are the rate of alternative diagnoses such as malignancy or AAA, which range between 3–7%.

3. Does size and location of ureteral calculi predict the probability of spontaneous passage?

Coll, et al. looked at 850 patients and found that 115/172 ureteral stones passed spontaneously and 57 required a urologic intervention.

- Stones 1mm in diameter passed spontaneously 87% of the time.
- Stones 2–4mm passed 76% of the time.
- Stones 5–7mm passed 60% of the time.
- Stones larger than 9mm passed 25% of the time.

Location mattered too, with spontaneous passage of 79% of stones at the ureterovesical junction, 60% of mid-ureteral stones, and 48% in the proximal ureter.[9]

Bottom line: Even for large, proximal stones, if the pain is controlled, it is worth waiting for spontaneous explusion.

4. What about medical expulsion therapy (MET)?

Pickard, et al. performed a meta-analysis of previous randomized controlled trials randomly assigning 1136 participants to tamsulosin (378), nifedipine (304), or placebo (379). They found no difference in stone expulsion between the 3 groups but there were more adverse events reported in the nifedipine group (3 patients with symptoms of diarrhea, vomiting, headache, chest pain, difficulty breathing) and the placebo group (1 patient with headache, dizziness and chronic abdominal pain).[10]

Just when this large meta-analysis would seem to put this issue to rest, along comes another systematic review and meta-analysis of 8 randomized, double-blind, controlled trials including 1,384 patients by Wang, et al. in Annals of Emergency Medicine. This study stratified stones by size and found that for stones measuring 5–10mm, there was an increased rate of stone passage with tamsulosin with a number needed to treat (NNT) of 5, but with the group < 4–5mm, there was no benefit. There were no significant adverse effects of dizziness or hypotension in either group.[11]

Similar results were reported with 403 patients in a double-blind, placebo-controlled, randomized, multicenter trial by Furyk, et al. finding a NNT of 4.5 in a prespecified group for stones 5–10mm.[12] A 2018 *Cochrane Review* had similar results.[13]

Bottom line: There was an NNT of 5 for MET in patients whose stone was 5–10mm in size.

5. Should labs have been obtained? Does the absence of hematuria exclude the possibility of ureterolithiasis?

WBC count:

An elevated WBC count may be deceptive due to stress demargination of circulating leukocytes and is generally unhelpful. Tintinalli recommends against obtaining a WBC count with uncomplicated ureteral colic.[14]

Renal function:

One older study suggested that patients who are stone formers have decreased renal function, but this was not in patients currently with a ureteral stone.[15] A more recent study of 384 stone formers vs. 457 controls found that the rise in serum creatinine is transient and minimal, with a baseline creatinine of 0.84mg/dL before the stone event compared to 0.97mg/dL at the stone event, returning to baseline at the first visit post-stone.[16] This data argues against obtaining serum labs for uncomplicated stones.

Urinalysis:

Blood:

The urinalysis (UA) is arguably the most useful test, although the absence of hematuria does not exclude ureterolithiasis. One retrospective study of 140 patients presenting with ureteral stones found 14.5% to have no hematuria on their UA.[17] Bove, et al. examined 267 consecutive patients with flank pain and found that 11% of patients with stones did not have the presence of blood or RBCs.[18] Luchs, et al. had similar findings after examining 950 patients with CT done for renal colic, of which 587 (62%) had a ureteral stone. Of these patients, only 84% had hematuria.[7]

So, blood is sometimes helpful, but lack of blood cannot exclude the presence of a stone, leading us to arguably the most important laboratory finding…presence of a concurrent infection.

Infection:
Our patient had a urinalysis notable for positive leukocyte esterase activity in the absence of leukocytes on urine microscopy (0–5 WBCs/HPF) and negative urinary nitrite testing. Is this predictive of an infection? Positive leukocyte esterase activity is 77–86% sensitive, but only 54% specific for culture-positive urinary infection.[19,20] Is the specificity high enough that our patient should have been managed with antibiotics and drainage or more investigation including serum labs, lactate, and repeat exam and vital sign assessment?

Our patient's nitrite was negative, seemingly reassuring, until we realize that the sensitivity is low at 45–60%, but if present, the specificity is high at 85–98%.[20] Although not suitable for our patient, it is helpful to use both tests together as the predictive value of combined nitrite and leukocyte esterase for a negative urine culture is 95%.[19]

Without clinical signs of infection, we are not alleging that antibiotics were indicated at the initial visit, but (broken record alert), it would have been nice to know about fever…

6. The nightmare scenario: How do patients with seemingly uncomplicated ureteral stones go bad…and how are they managed if this occurs?
An "infected stone" is treated with respect by experienced emergency providers as these patients can deteriorate quickly. Acute urinary obstruction complicated by septic shock is associated with mortality approximating 30%.[21]

Putting it all together:
This case would have been handled in a similar way by most emergency providers; a routine stone, a routine discharge… but there was an unexpected lab abnormality (leukocyte esterase and a few WBCs) that should prompt consideration and explanation within the medical decision-making documentation. How confident was the provider that "ureteral irritation" caused the abnormality? They were comprehensive in ordering a urine culture, which may be interpreted as at least some degree of clinical concern. Did the patient understand that there was possible infection and that a culture was ordered? If so, it would have been nice to see the conversation documented and aftercare instructions personalized to recommend returning for signs of infection including fever, chills, dizziness, weakness, increased pain, or confusion?

Look, it's not that big of a deal, right? Leukocyte esterase is sensitive, but not specific. Still… wouldn't you feel more comfortable with this additional data, documentation and discharge instructions in place?

ED BOUNCEBACK

Though the patient is straining her urine, she does not catch a stone. A urology appointment is scheduled for Tuesday morning, 2 days after ED discharge. But on the morning of the appointment, her husband notices that she is not acting "exactly right." Her symptoms are nonspecific, so he

does not bring her back to the ED. Her urine has turned into a dark brown color. The urology appointment is scheduled for 10 a.m., but just before they leave home for the appointment, the patient begins to vomit.

ED VIST #2 (2 days after the initial ED visit)

CC (15:27): Confusion

HPI (15:42): The patient is a 51-year-old female with no past medical history presents from her urologist office where she was being seen for known left ureteral stone. Patient began having pain approximately 2 days ago and was seen in the ED at that time. She was found to have a 6mm obstructing left ureteral stone. Since that time urine culture have been sent and has been growing Enterobacter aerogens and Klebsiella. Patient is accompanied by her husband who provides most of the history as the patient is very confused at this time. He states that she began having confusion last night with slurred speech and difficulty walking. He called the ED this morning and was asked to bring her back in, but since they had the urology appointment a few hours later, he chose to take her there. Upon presenting to the urologist office given her confusion she was sent to the ER. Husband reports that she has had decreased oral input, decreased urinary output as well as nausea and vomiting. Patient has been very fatigued and husband initially contributed this to her pain medication, however she has not taken that in 2 days. Patient has had chills but no documented fevers.

Vitals:

Time	Temp (F)	Rt	Pulse	Resp	Syst	Diast	O_2 sat (RA)
15:31	70	Oral	112	22	81	55	92

Pain	Weight
10/10	72kg

CONSTITUTIONAL: She is lethargic, moderate distress, oriented to person only, Speech is slurred and difficult to understand when she tries to speak
HEENT: Mouth and pharynx are clear, but membranes are tacky
NECK: Supple; no adenopathy or JVD
LUNGS: CTAB
CHEST: She is tender over the anterior chest wall
CARDIO: Tachy but regular rate and rhythm, nl. S1 S2
ABD: Soft but there is tenderness in the LLQ
SKIN: Mottling of the hands and fingertips

MDM (15:45): 50-year-old female with known 6 centimeters obstructing stone in left ureteral stone presents with confusion and lethargy since last night. Urine culture from 2/27 growing Enterobacter aerogens and Klebsiella.

ED course (16:02): Soon after completing the orders the nurse finds you, "Doctor, can you please reassess the patient in room 4?" You understand the concern; the patient's blood pressure has dropped to 72/51. Checking back in on the patient, she is more confused, and combative. Her husband is at the bedside, doing his best to keep her under control.
We are at:

DECISION POINT A – YOU ARE FACED WITH 4 QUESTIONS:

1. **What's the diagnosis? She is hypotensive and altered. Are we able to diagnosis septic shock and just send her up to the ICU?**
2. **Is a cephalosporin or a quinolone enough, or are broader spectrum antibiotics indicated?**
3. **You have ordered a 2L bolus; how long should you wait to see if the pressure improves?**
4. **Should she leave the department to get another CT scan to confirm the presence and location of the ureteral obstruction?**

What does the literature say?

Q#1: What's the diagnosis? She is hypotensive and altered. Are we able to diagnose septic shock and just send her up to the ICU?

In 2016, the Sepsis-3 investigators revised the definition of sepsis, stating that sepsis should be defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection." Septic shock is a subset of sepsis, which occurs when "underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality." The task force believed that these new definitions were improvements compared to the former approach using 2 or more SIRS criteria to identify infected patients at high risk of adverse outcome.

Patients with a qSOFA (Quick sequential organ failure assessment) score of 2 or greater have a significantly increased risk of an ICU stay of 3 days or longer and an in-hospital mortality > 10%. This tool should be used to assess patients at risk for organ dysfunction.

qSOFA criteria:
1. Respiratory rate > 22/min
2. Altered mentation
3. Systolic blood pressure < 100mmHg

Sepsis-3 defines septic shock based on:
1. Vasopressor requirement to maintain mean arterial pressure (MAP) of 65mmHg after adequate fluid resuscitation -and-
2. Serum lactate greater than 2mmol/L (> 18mg/dL)

Patients defined by these criteria have mortality rate > 40%.[22] But caution with only using the Sepsis 3 definition. A study of 470 patients by Sterling, et al. found that of patients who met the old definition (but not the Sepsis 3 definition), there was still a 14% mortality in this group, and when a quantitative resuscitation protocol was used, there was significant mortality benefit.[23]

So, does our patient have septic shock? She is febrile with altered level of consciousness and hypotension—even before the lactate level returns, and without "getting in the weeds" with the definitions, the answer is an unequivocal yes! Additionally, she has all 3 of the qSOFA criteria, indicating her risk of mortality is high. Preparing for admission to the ICU at this point will depend on your hospital protocol, but several important treatments need to be started immediately.

Section editor comments (Osborn):

Do not give hospitals or intensivists an out while awaiting additional testing; a patient with BPs of 70's/30's does not need to wait for a lactate to get a definition of septic shock prior to initiating ICU admission. A note of caution on using Sepsis-3 definitions:

1. Across the globe, only one EM medical professional organization signed onto the Sepsis-3 definitions—it was rejected by all other EM organizations to which it was sent.
2. The Centers for Medicare and Medicaid Services (CMS) does not recognize Sepsis-3.
3. Quality organizations (Vizient, etc.) do not recognize the Sepsis-3 definitions

If you use Sepsis-3 to categorize sepsis, no matter how good your care is, it will be seen as worse based on the mortality index. The definitions right now are a mess and likely to continue to evolve.

Consulting editor comments (Weingart):

This question shouldn't have to be coming up; why do we even need these definitions of sepsis? The main reason is so that we can bill and so that government can regulate clinical care and pretend that we can lump everything into algorithmic approaches. That is opposed to treating each patient individually and deciding based on their unique presentation whether or not they're septic. So, by even asking the question, we are failing ourselves as physicians.

If we are forced to use definitions, which ones are good? Sepsis 3.0 was an attempt, at least, to justify a really sick cohort. If you look at their definition of septic shock, it required both resistant hypotension and resistant lactate elevation. That might not catch every single septic shock patient, but what it will do is to confirm that when we do identify septic shock, it is clearly septic shock!

I did like it for that reason; if we're going to compare ourselves, it was a group that everyone could agree was really sick. The problem with most of these definitions is that if you want to make your hospital look good, what you do is you take patients that aren't that ill and lump them into these groups of sick patients because then your mortality looks great; and that always upset me.

The sepsis-3.0 definition at least meant any hospital comparing their patients to another hospital had a pretty fair comparison.

I wish this entire thing would just go away and we could go back to actually being doctors and treating our patients.

Section editor comments (Osborn):

Six hours is the national average ED length of stay for critically ill patients.

The provider should recognize that this patient is severely ill and should have a 30mL/kg IVF bolus, blood cultures, appropriate antibiotics and definitive therapy/source control pursued as quickly as possible. This should be balanced against keeping a patient in the ED too long, as there is a higher in-hospital and ICU mortality in patients boarding for greater than 6 hours.[24]

Q#2: Is a cephalosporin or a quinolone enough, or are broader spectrum antibiotics indicated?

Per the Surviving Sepsis Campaign (SSC) updated response to new bundles, the following should occur within 3 hours of presentation (time of triage in the ED):

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30mL/kg crystalloid[25]

Recommended antibiotic administration initiation is as fast as possible and within 1 hour of septic shock recognition. Antimicrobial selections should provide activity against the likely pathogens based on the patient's source of infection.[26] For community-acquired urinary tract infection, coverage against *E. coli*, other gram negative pathogens and *Enterococcus* are important, but in this case we have cultures results, making a streamlined approach to antibiotics easier. Absent the prior cultures or other data pinpointing the infection source or anticipated pathogens, a broad-spectrum approach with piperacillin-tazobactam or cefepime PLUS vancomycin is a reasonable combination for many patients with severe infection, as inappropriate initial antibiotics are associated with higher mortality. One additional point to consider is the order of antimicrobials when IV access limits initiation of both agents simultaneously. Beta-lactam agents are generally recommended to be started first based on broad antimicrobial activity and brief administration times, compared to vancomycin.

Even with appropriate antimicrobial support, urinary obstruction represents a critical target to achieve source infection control (see Decision Point B, below).

Section editor comments (Osborn):

There are frequent misconceptions that vancomycin is a broad-spectrum antibiotic, and that it should be given first or that one cannot administer 2 IV antibiotics at the same time. Vancomycin generally takes about 1–1.5 hours to administer, so administering that first could constitue a delay in administering the antibiotic most likely to cover the offending bacteria in the setting of shock, in this case the piperacillin-tazobactam.

Q#3: You have ordered a 2L bolus; how long should you wait to see if the pressure improves?

An initial bolus of 30mL/kg crystalloid IVF is recommended, with the understanding that more fluids may be required in some patients. The fluids should be administered rapidly via straight intravenous tubing and pressure bags rather than an IV pump rate of 999mL/hour. Without an adequate response to IVF, consideration should be given to pressors.[26]

Q#4: Should she leave the department to get another CT scan to confirm the presence and location of the ureteral obstruction?

The clinician should be cautious in sending such a critically ill patient to the radiology suite for a CT scan without some stabilization, unless the information will dictate an immediate new intervention. In the interim, bedside exam should exclude other sources of infection and management should be initiated for the likely etiology of septic shock; a urinary infection complicated by ureteral obstruction.

Bedside ultrasound can be used to confirm the presence of unilateral hydronephrosis and may identify focal abscess. A study by Riddell, et al. showed 82% sensitivity of a positive ED ultrasound finding of either hydronephrosis or visualized stones.[27] Another study in over 300 patients comparing EP performance of ultrasound to CT found that hydronephrosis had a positive predictive value (PPV) of 88% for ureteral stone on CT, and lack of hydronephrosis made a stone > 5mm less likely.[28]

DECISION POINT A – ***What did the actual provider do?***

ED course (15:50): Upon recognizing clinical sepsis, the provider orders labs including a CBC, BMP, urine, lactate level and an IVF bolus totaling 30mL/kg, per a sepsis treatment order set. As diagnostic studies are ordered, the provider places a STAT order for Ceftriaxone 1gm IV.

The story continues:
(16:29): Initial labs results:

WBC count = 15.1 (H)
Hb = 12.4 gm/dL
Plt = 118 thou/mcl (L)
Sodium = 126 mmol/L (L)
Bicarbonate = 18
Creatinine = 5.5 mg/dL (H)
Lactate = 5.8 (H)

Looking up, you see the nurse.

"Do we have urine yet?"

"We have asked twice, but she is not cooperating. Also, we have a bit of a problem. She is crawling out of bed. We have a tech and her husband trying to keep her from falling. I need something to calm her down."

"OK," you respond confidently, "Please give Ativan 2mg IV. I'll put the order in right now."

Hearing silence, you look up to see her staring back at you. After an awkward pause, she asks, "Won't that make her pressure worse?" The 2 liters we gave did nothing. Her BP is still in the low 70s.

(16:32): You order another 2L (for a total of 4L) of IVF. It is infused quickly and a recheck shows no change in the BP.

(17:08): You ask the nurse to set up materials for a central line so pressors can be started. You "glove and gown" and set up all the materials. Despite receiving 50mcg of Fentanyl, and 4 staff holding the patient down, you are not able to keep her under adequate control to safely place a femoral central line. With sweat leaching through your gown, you abandon the attempt and return to the drawing board.

Author note: You are back in the shoes of the emergency provider… at decision point B.

DECISION POINT B – YOU ARE FACED WITH 4 QUESTIONS:

1. **What is the best approach for sedation in a hypotensive patient?**
2. **If the patient cannot be sedated, is intubation indicated?**
3. **Is it time for pressors? Can they be started through a peripheral line?**
4. **Who should be called first, urology for stent placement or interventional radiology for a nephrostomy tube?**

What does the literature say?

Q#1: What is the best approach for sedation in a hypotensive patient?

While a wide range of options is available for sedating combative ED patients, selecting a safe and effective agent can be challenging in the presence of hemodynamic compromise. The ideal sedative has a rapid onset of action, minimal cardiovascular compromise, is easily titratable, short-acting, with minimal interaction with other drugs.[29] Sounds simple right? Consider this approach:

1. Choose medications that have a low chance of decreasing blood pressure such as ketamine or etomidate (low dose) or haloperidol.
2. Start with a low dose and see if sedation is adequate and how it affects the blood pressure, maintaining the option to administer more.
3. Be prepared to use a fluid bolus or pressors (consider "push-dose" pressors with phenylephrine or epinephrine) if there is a significant drop in the blood pressure. Bolus dosing of vasopressors, or push-dose pressors, has been successfully used perioperatively and is well described in the anesthesia literature. While there are no ED-specific national guidelines on their use, some have advocated for their implementation given their ease of use and ability to temporize precipitous drops in blood pressure.[30]
4. In patients who are hypotensive before intubation, plan proactively to add norepinephrine before giving the sedative. There may still be a need for temporary push-dose pressors, but there will at least be a baseline vasopressor infusion running already that can be titrated rapidly. In other words, don't rely solely on push-dose pressors in a patient who is already hypotensive and will likely worsen after intubation. Start the vasopressor infusion early.

Section editor comments (Osborn):

Of note, the benefit of haloperidol, ketamine or etomidate in this situation is sedation without respiratory depression. Lorazepam may cause respiratory depression and worsening acidosis.

Consulting editor comments (Weingart):

There are sedation agents that are blood pressure neutral, or blood pressure bolstering. If you have to get immediate control of a situation and the patient is hypotensive, just give them ketamine. And then, while the ketamine dissociation is occurring, you can place a central line, if necessary. Note that droperidol is available again; it has no blood pressure effects, and it will give instantaneous control of the situation. Can we use benzos? Absolutely. But beware, if the patient's agitation is supporting their blood pressure, the benzodiazepine may take away their endogenous catecholamines and things may get much worse. I'd be reluctant to do that without use of a vasopressor. Fix their blood pressure, and then you're more than free to give benzodiazepines.

A word on push-dose pressors. If you are using as a temporizing measure while the nursing staff is getting a vasopressor drip prepared, that is fine, but I would not give continuous rounds of push-dose pressors; I've never supported that. Push-dose is the immediate temporizing measure to allow you the time to get a drip going with a pump.

Author comments (Weinstock):

There are a lot of podcasts detailing an approach to self-mixing meds to then administer by push-dose... but there are pre-mixed syringes available. Like everything in medicine, conditions and procedures which we see and perform commonly allow for expertise, but if we are not doing things frequently, we are prone to error.

Consulting editor comments (Weingart):

If your institution will buy you pre-mixed, then that is a safer way to go. There has been a spate of ED pharmacologist literature showing mixing errors. We have two breeds of emergency physicians; the incredibly detail-oriented resuscitation docs, and the docs who do not do this frequently and leave medication administration to the nurse; these docs shouldn't be mixing.

A note on pushing cardiac epinephrine; it is a peri-code temporizing measure. I don't push one tenth of a cardic epi syringe, I push a half a cc. All of the cardiac epis are graduated at the level of a half cc. That is 50 micrograms; that is a very reasonable dose. You still may overshoot, but you will not overshoot to "bursting blood vessels in the head" levels, and it'll get the job done on a patient who is about to code. So, if the pressure is 40/20, looking like death, by all means take out the cardiac epi and push half a cc. But never push a full amp of cardiac epinephrine on a patient with a pulse.

Q#2: If the patient cannot be sedated, is intubation indicated?

Intubating critically ill patients is rife with risk, as demonstrated by Heffner, et al.; ED emergency intubation carries a peri-procedure cardiac arrest (CA) rate of 3% among normotensive patients, which jumps to 12% among patients with systemic hypotension at the time of induction. Not surprisingly, the mortality was significantly higher in those patients who had a CA (82%) vs. those who did not (24%).[31] These findings are similar to findings from Schwartz, et al. who examined 297 intubations of hypotensive patients, finding a 15% mortality.[32]

OK. Got it. Intubating a hypotensive, septic patient is risky, but do we have a choice? Not only does this agitated patient represent a risk to herself and to staff, but she will emergently need drainage of the obstructed ureter, which will require sedation and perhaps paralysis. If she is not able to be adequately sedated for a central line, certainly she will not sit still for a nephrostomy tube or ureteral stent.

Q#3: Is it time for pressors? Can they be started through a peripheral line?

Per the SCC guidelines, if a patient remains hypotensive after the initial fluid bolus and if they are "fluid responsive," additional fluid boluses may be given. The initial vasopressor of choice is norepinephrine, and this should be titrated to mean arterial pressure (MAP) > 65mmHg.

For our patient, initiating pressor support with norepinephrine would be advisable, especially as the patient remained hypotensive after the 2nd 2L IVF bolus. But we don't have a central line… should we wait? The main concern with administering pressors through a peripheral line is extravasation and tissue ischemia from intense local vasoconstriction. On the other hand, waiting for placement of a central line may delay care in critical patients, as well as expose the patient to the increased risk of placing a central line in the first place.

In 2014 Loubani, et al. attempted to determine the safety of administering pressors through a peripheral intravenous access. In a systematic review of 85 articles they found 270 patients which met inclusion criteria. The mean duration of infusion was 55 hours, and over 85% of the lines were distal to the antecubital vein. They concluded that "short term" administration (< 2 hours) of vasopressor infusions via proximal, well-placed peripheral IVs is unlikely to cause local tissue injury."[33]

In 2015 Cardenas-Garcia, et al. performed an original investigation with almost 3 times the number of patients. They examined 734 patients, ages 72 +/- 15 years who received vasoactive medication 783 times via peripheral IV access including norepinephrine (n=506), dopamine (n=101) and phenylephrine (n=176) for a duration of 49 +/- 22 hours. They found that extravasation occurred 19 times (2%), which was treated in their study with local phentolamine injection and application of local nitroglycerine paste. They found no tissue injury. And to make matters even better, only 13% of patients eventually required central access.[34]

With the patient agitated, confused and hypotensive, she needs additional fluids as well as norepinephrine; we recommend avoiding a delay in care by trying again for a central line, and instead infusing through a large-bore antecubital peripheral line. If her pressure improves, additional sedation may be attempted with ketamine or haloperidol and if unsuccessful intubation can be considered—we have done so much, but there is arguably the most important intervention for sepsis care which has not yet been completed—source control.

Consulting editor comments (Weingart):

If you have a patient exsanguinating, well that's a relatively tough scenario, but in this case, just fix the hypotension. That is the answer. And then you can use whatever you want to sedate them. So, how do you fix the hypotension? Well, you put them on vasopressors. "Oh, well I don't have a central line." I don't care. Even in places that don't have a protocol for peripheral pressors on the floors, put them on peripheral norepinephrine. We have three trials now demonstrating safety. Get them temporized, and then take all the time in the world to put in your central line when you have a sedated, non-hypotensive patient. To wait for a central line in the face of hypotension is maybe the worst thing you can do for these patients. They will deteriorate, you're now under a time pressure to do a procedure that requires meticulous, slow careful attention to detail. And you are limited in how you can sedate the patient; put them on peripheral norepinephrine and then give whatever you want.

Q#4: Who should be called first, urology for stent placement or interventional radiology for a nephrostomy tube?

Let's cut to the chase—this patient has pus under pressure, due to urinary obstruction, and needs it drained as soon as possible. The specific intervention should be individualized by institution and available resources. There is a paucity of data to declare a single best intervention.

Mokhmalji, et al. looked at 40 patients who had stone-induced hydronephrosis and found the success rate of percutaneous nephrostomy drainage was 100% with *decreased* radiation exposure and decreased analgesics compared to a ureteral stent, which had 80% success.[35]

Pearle, et al. randomized 42 patients with concomitant obstruction and urinary tract infection, defined by temperature greater than 38° C and/or WBC count greater than 17,000), to either percutaneous nephrostomy or ureteral stent and found 1 failure in the nephrostomy group, decreased procedural and fluoroscopy time in the stent group, and a similar "time to normal temperature," "time to normal WBC count" and hospital length of stay between groups. They concluded that "neither modality demonstrated superiority in promoting a more rapid recovery after drainage." Ureteral stent placement was more costly.[36]

Cristoph, et al. agreed with Mokhmalji that both interventions had similar clinical efficacy[37] as did the Canadian Urological Association (2015), concluding these recommendations for infected ureteral stones:

1. Obstructing stones with infection require emergent drainage.
2. Nephrostomy tube and stent have equivalent outcomes and choice should be based on availability of resources.
3. Broad-spectrum antibiotics should be started early.
4. Definitive stone management should be delayed until decompression and antibiotics have been administered.[38]

Consulting editor comments (Weingart):

With an obstructing infected stone, the first thing needed is source control; there's no doubt about that. The decision between options is situation and institution-dependent and best arranged in advance so you are not talking to multiple specialists at 3 AM—you need to force it to happen because these patients are sick and can't wait until morning. A delay goes against all our rules of source control and sepsis.

Now, just as a bonus, be aware that your job is not yet over as these patients have a tendency to get super sick after the drainage happens; this is incredibly common. They get their percutaneous nephrostomy tube, and then they acutely decompensate for a couple hours as there's a huge release of inflammatory hormones. I don't know exactly why; I just know it happens. So, if your plan was, well they'll be much better after they get their procedure and "I'll just get them a floor bed," this will fail. They either need an ICU, or to stay in the ED and be watched until better, then they can go up to the floor.

DECISION POINT B – ***What did the actual provider do?***

MDM (16:52): The urine has returned, showing specific gravity of 1.046, blood, leukocyte esterase (75/UL), WBC 3,352. RBC 791, and moderate bacteria. The patient remains hypotensive with a BP of 70s/50s despite 5L IVF.

MDM (17:08): Despite 5 L of normal saline fluid, the patient remains hypotensive. We attempted to get a central line, but patient became delirious and combative. After attempts to restrain her with 50mcg fentanyl she was still confused which seemed to be secondary to encephalopathy from septic shock.

ED course:
(17:54): Norepinephrine at 7mcg/min through a peripheral 18g IV.
(18:33): The decision was made to place a nephrostomy tube in the interventional radiology suite after intubation and "likely placement of a CVC."

The story continues: With the continued IV fluids and the norepinephrine, the patient's blood pressure improves to 100/60. The provider tells the staff that they will proceed with intubation. We are at:

DECISION POINT C – YOU ARE FACED WITH 4 QUESTIONS:

1. **Which medications should be used for rapid sequence intubation (RSI) in a hypotensive septic patient?**
2. **Why do some patients "crash" after intubation?**
3. **Which ventilator setting should be used after intubation of a septic patient?**
4. **My septic patient is intubated, now what?**

What does the literature say?

Q#1: Which medications should be used for rapid sequence intubation (RSI) in a hypotensive septic patient?

Wow, now we have a bear in a hornet's nest. Our goal is to make patients safer without causing harm, but the mortality of intubating a septic patient is high. Which sedatives are optimal in a hypotensive shock patient?

Stollings, et al. reviewed the Medline® database from 1966–2013 and published a comprehensive review of medications used with rapid sequence intubation (RSI).[39] Not surprisingly, they confirmed that most induction agents can cause or exacerbate hypotension. Here is some more detailed information on two medications commonly used for sedation/induction in RSI:

Etomidate:
Class/action: Sedative-hypnotic
Dose: 0.2mg/kg–0.6mg/kg
Recommended dose in patients with hypotension is 0.1–0.2mg/kg, and not the standard 0.3mg/kg
Use of adjusted body weight with morbid obesity is also recommended.
Metabolism: Hepatic
Advantages: Minimal hemodynamic effects, decreases ICP, no histamine release, quick onset of action, short duration of action.
Disadvantages: May induce suppression of cortisol and aldosterone (see Jabre study below).
Note: Myoclonus occurs 22–63% of the time but is typically short-lived and is clinically inconsequential, especially when combined with a neuromuscular blocker.

Ketamine:
Class/action: Causes intense amnesia secondary to dissociative effects and has analgesic properties
Dose: 1–2mg/kg (typically 100mg)
Metabolism: Hepatic
Advantages: Exerts sympathomimetic effects including increases in heart rate, blood pressure, and cardiac output. Contrary to initial reports, does not increase ICP.
Disadvantages: May result in decreased cardiac output in patients with severe heart failure, may rarely increase oral secretions (making intubation more difficult), and can be associated with emergence delirium, nightmares and hallucinations.

What happens when these drugs are compared head-to-head? Jabre, et al. examined etomidate and ketamine for RSI in a multi-center, randomized, single-blind trial. They examined 655 patients requiring sedation for RSI randomized to receive a single dose of etomidate 0.3mg/kg (328 patients) or ketamine 2mg/kg (327 patients). After exclusions, they analyzed 234 patients in the etomidate group and 235 in the ketamine group with a primary study endpoint of the maximum sequential organ failure assessment (SOFA) during the first 3 days of ICU admission. The percentage of patients with a decreased serum cortisol was higher in the etomidate group, but there were no serious adverse events with either drug.[40]

Conclusion: All induction agents can exacerbate hypotension, but both etomidate and ketamine are best choices. Dose reduction to half the typical induction agent dose is also recommended and is often adequate for sedation.

Q#2: Why do some patients "crash" after intubation?

Why is a potentially life-saving intervention, intubation, risky? Rapid sequence intubation (RSI) induces complicated physiologic changes. Sympatholysis from induction agents and conversion to positive pressure breathing negatively impact cardiac venous return. As such, pre-intubation fluid optimization should always be considered prior to RSI, even in patients who are not in shock.

In addition, our septic patient with lactic acidosis is attempting to compensate via increased respiratory rate. They are blowing off CO_2 in an attempt to correct acid/base status. As their disease progresses, despite the interventions of the emergency provider, intubation may become necessary, but respiratory compensation is halted with RSI, which can worsen acidosis. Is there a way to make this critical intervention safer? In addition to the previous comments about RSI hypnotic selection and dosing and preinduction fluid optimization, patients with high minute ventilation requirements prior to intubation often require peri-RSI ventilation and attention to initial ventilator settings to compensate for metabolic acidosis

Weingart, et al. describe a process of "delayed-sequence intubation" where 62 patients at high risk for immediate intubation (primarily because of hypoxemia) were enrolled in a prospective, observational, multi-center trial. The patients received a dissociative dose of ketamine, then either high-flow oxygen with a non-rebreather mask or noninvasive positive pressure ventilation (NIPPV). They found that oxygen saturations increased from a mean of 89.9–98.8% afterward, and there were no complications observed in the patients receiving delayed sequence intubation.[41]

Whereas, their hypoxemic patient population was not the same as our hypotensive septic patient, the goal should be to stabilize the patient prior to intubation with fluid resuscitation, antibiotics, pressors (if needed), and ensuring adequate oxygenation—this is exactly what occurred in our patient… eventually.

Q#3: Which ventilator setting should be used after intubation of a septic patient?

A broad stroke approach utilizes these recommendations:

- Tidal volume: Initial target should be 6mL/kg of predicted body weight,42 though other authors recommend 8mL/kg.[43]
- Don't wait for the ICU staff to do it—what begins in the ED matters. In a 2017 study, Fuller, et al. found that ventilator settings initiated in the emergency department impact clinical outcomes in patients with ARDS.[44]
- Mode: Volume-assist mode.[43]
- Initial respiratory rate: 15–16 breaths/min although a rate of 30–40 breaths/min is acceptable to achieve $PaCO_2$ goals.[43]
- FiO_2 should be rapidly titrated to 30–40%, if tolerated by patient, with a positive end-expiratory pressure (PEEP) of 5cm H_2O. If the patient is hypoxemic, evaluate the patient for ARDS (definition being PaO_2/FiO_2 ratio of < 300 with non cardiogenic pulmonary edema and a PEEP > 5) [ARDSnet].
- Goal plateau pressure < 30cm H_2O.[42,43]

An arterial or venous blood gas should be drawn 20–30 minutes after intubation to allow titration of ventilator settings.[43] Using the VBG in combination with the pulse oximeter is a viable alternative

to obtaining an ABG,[45] understanding that patients in shock with poor perfusion may have a VBG that is not reliably predictive of arterial gas exchange.

Q#4: My septic patient is intubated, now what?

Redux to our problem from above, our patient is now intubated but remains hypotensive. We are still between a rock and a hard place; it is cruel to have a patient intubated without sedation, but we don't want our sedative therapy to make the patient's blood pressure worse.

The Surviving Sepsis Campaign (SSC) 2016 guidelines recommended the following possible approaches for sedation and analgesia of intubated patients:[42]

- Sedation should be targeted to specific titration end-points (as opposed to using continuous or intermittent sedation). This approach should reduce the duration of mechanical ventilation and the ICU stay. Possible approaches to minimizing sedation include:
  - "Nurse-directed" protocols with a sedation scale
  - Intermittent as opposed to continuous sedation
  - Daily sedation interruption[46]
- Midazolam (or benzos) are not recommended by the SCCM sedation guidelines, instead propofol or dexmedetomidine are preferred. Ketamine is another option. If a benzo is required, midazolam q 1hr prn might be a better approach.
- Consider use of opioids alone (without any sedatives) as this may result in decreased duration of mechanical ventilation.

DECISION POINT C – *What did the actual provider do?*

MDM (18:04):

- I have attempted to place a femoral CVC; however, patient was too combative for successful placement. The patient was intubated for septic shock delirium and airway protection and also prior to interventional radiology for nephrostomy tube placement for her obstructing stone.
- The patient was given etomidate 15mg and succinylcholine 100mg and then intubated with a GlideScope with a 7.0 endotracheal tube. The tube was initially placed at 22cm, but CXR showed the tube to be at the level of the carina, so was withdrawn to 20cm and a repeat CXR demonstrated good position. Post-intubation sedation was propofol.
- The patient was initially placed on assist mode ventilation, rate of 14, tidal volume 500cc, PEEP 5 and FiO2 100%, but the FiO2 was quickly decreased to 40%.

ED course (18:56): The patient was transferred to the interventional radiology (IR) suite for placement of a nephrostomy tube. When the tube was placed, it returned a copious amount of purulent material.

What was the patient outcome?
The ICU course was initially rocky, with the patient requiring the addition of vasopressin to maintain a mean arterial pressure (MAP) of 65. She remained in the ICU for 3 days then was moved to the floor and eventually discharged.

Final hospital impression:
- Septic shock and severe sepsis
- Urinary infection
- Obstructing ureteral stone
- Acute kidney injury
- *Enterobacter* bacteremia

Debrief:
Care was well done, but there were some areas for possible improvement:
1. Initial history should have determined presence of infectious symptoms, specifically presence of fever.
2. Discharge instructions from the first visit should detail reasons to return, specifically fever or confusion.
3. At the second visit, the diagnosis was recognized quickly, and appropriate care was initiated, but arrangements for source control (nephrostomy tube or stent) should have been started simultaneously.
4. While the goal of starting a central line was acceptable, it should have been recognized that with her amount of agitation, it was going to be difficult. A surgeon would not take a patient to the OR without adequate anesthesia… in our patient, pressors could have been started through a peripheral line, then sedation administered.
5. Sedative agents which could have been tried before Ativan were ketamine or haloperidol.
6. Kudos to the doctor for adequate resuscitation before intubation, this was well done and decreased her peri-intubation risk significantly

Chapter summary:
- Midstream urine is a poor predictor of infected pelvic urine, especially if there is a completely obstructing stone.
- Nitrite is specific for a UTI, but not sensitive. Leukocyte esterase is sensitive, but not specific.
- Patients with a ureteral stone should be assessed for a possible infection with questions directed for symptoms such as chills, dizziness, confusion, and signs of tachycardia, tachypnea, hypotension, confusion… as well as fever.
- The combination of a ureteral stone and sepsis is a true urologic emergency that requires prompt drainage either with a nephrostomy tube or ureteral stent, whichever is most readily available.
- Hypotensive patients have a high peri-intubation risk. Resuscitate before intubation and use induction agents least likely to exacerbate hypotension.
- Engaging the patient and family with the discharge planning process will increase the chance that they will return if symptoms worsen, change, or don't improve. Inform patients who are being discharged with an uncomplicated ureteral stone to return for any infectious symptoms.

References:

1. Foster G, Stocks C, Borofsky MS. Emergency department visits and hospital admissions for kidney stone disease, 2009: Statistical Brief #139. 2012 Jul. In: Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Available at https://www.hcup-us.ahrq.gov/reports/statbriefs/statbriefs.jsp. Rockville (MD): Agency for Healthcare Research and Quality (US); 2006 Feb. Available at: https://www.ncbi.nlm. nih.gov/books/NBK100827/
2. Assimos D, Krambeck A, Miller NL, et al. Surgical management of stones: American Urological Association/Endourological Society guideline Part 1. J Urol 2016;196(4):1153–60.
3. Moore CL, Bomann S, Daniels B, et al. Derivation and validation of a clinical prediction rule for uncomplicated ureteral stone—the STONE score: Retrospective and prospective observational cohort studies. BMJ 2014. 348:g2191.
4. Engel K, Buckley BA, Forth VE, et al. Patient understanding of emergency department discharge instructions: where are knowledge deficits greatest? Acad Emerg Med 2012;19(9):E1035–44.
5. Lawrence LM, Jenkins CA, Zhou C, et al. The effect of diagnosis-specific computerized discharge instructions on 72-hour return visits to the pediatric emergency department. Pediatr Emerg Care 2009;25(11):733–8.
6. Hess EP, Grudzen CR, Thomson R, et al. Shared decision-making in the emergency department: respecting patient autonomy when seconds count. Acad Emerg Med 2015;22(7):856–64.
7. Luchs JS, Katz DS, Lane MJ, et al. Utility of hematuria testing in patients with suspected renal colic: correlation with unenhanced helical CT results. Urology 2002;59(6):839–42.
8. Rapp DE, Wood NL, Bassignani M, et al. Clinical variables and stone detection in patients with flank pain. Can J Urol 2016;23(5):8441–45.
9. Coll DM, Varanelli MJ, Smith RC. Relationship of spontaneous passage of ureteral calculi to stone size and location as revealed by unenhanced helical CT. AJR Am J Roentgenol 2002;178(1):101–3.
10. Pickard R, Starr K, MacLennan G, et al. Medical expulsive therapy in adults with ureteric colic: A multicentre, randomised, placebo-controlled trial. Lancet 2015;386(9991):341–9.
11. Wang R, Smith-Bindman R, Whitaker E, et al. Effect of tamsulosin on stone passage for uereteral stones: A systematic review and meta-analysis. Ann Emerg Med 2017;69(3):353–61.e3.
12. Furyk JS, Chu K, Banks C, et al. Distal ureteric stones and tamsulosin: A double-blind, placebo-controlled, randomized, multicenter trial. Ann Emerg Med 2016;67(1):86–95.
13. Campschroer T, Zhu X, Vernooij RWM, et al. Alpha-blockers as medical expulsive therapy for ureteral stones. Cochrane Database Syst Rev 2018;4:CD008509.
14. Tintinalli JE, ed. Emergency medicine, a comprehensive study guide. 5th ed. New York, NY: McGraw Hill, 2000.
15. Worcester EM, Parks JH, Evan AP, et al. Renal function in patients with nephrolithiasis. J Urol 2006;176(2):600–3.
16. Haley WE, Enders FT, Vaughan LE, et al. Kidney function after the first kidney stone event. Mayo Clinic Proceed 2016;91(12):1744–52.
17. Press SM, Smith AD, et al. Incidence of negative hematuria in patients with acute urinary lithiasis presenting to the emergency room with flank pain. Urology 1995;45(5):753–7.
18. Bove P, Kaplan D, Dalrymple N, et al. Reexamining the value of hematuria testing in patients with acute flank pain. J Urol 1999;162(3 Pt1):685–7.
19. Rehmani R. Accuracy of urine dipstick to predict urinary tract infections in an emergency

department. J Ayub Med Coll Abbottabad 2004;16(1):4–7.
20. Deville WL, Yzermans JC, van Duijn NP, et al. The urine dipstick test useful to rule out infections. A meta-analysis of the accuracy. BMC Urol 2004;4:4.
21. Reyner K, Heffner AC, Karvetski CH. Urinary obstruction is an important complicating factor in patients with septic shock due to urinary infection. Am J Emerg Med 2016;34(4):694–6.
22. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016;315(8):801–10.
23. Sterling SA, Puskarich MA, Glass AF, et al. The impact of the Sepsis-3 Septic shock definition on previously defined septic shock patients. Crit Care Med 2017;45(9):1436–42.
24. Chaltin DB, Trzeciak S, Likourezos A, et al. Impact of delayed transfer of critically ill patients from the emergency department to the intensive care unit. Crit Care Med 2007;35(6):1477–83.
25. Surviving sepsis campaign: Updated bundles in response to new evidence. https://emcrit.org/wp-content/uploads/2015/04/SSC_Bundle.pdf
26. Riddell J, Case A, Wopat R, et al. Sensitivity of emergency bedside ultrasound to detect hydronephrosis in patients with computed tomography-proven stones. West J Emerg Med 2014;15(1):96–100.
27. Leo MM, Langlois BK, Pare JR, et al. Ultrasound vs. computed tomography for severity of hydronephrosis and its importance in renal colic. West J Emerg Med 2017;18(4):559-68.
28. Brusco L. Choice of sedation for critically ill patients: A rational approach. Adv Stud Med 2002;2(9):343–9.
29. Weingart S. Push-dose pressors for immediate blood pressure control. Clin Exp Emerg Med 2015;2(2):131–32.
30. Heffner AC, Swords DS, Neale MN, et al, Incidence and factors associated with cardiac arrest complicating emergency airway management. Resuscitation 2013;84(11):1500–4.
31. Schwartz DE, Matthay MA, Cohen NH, et al, Death and other complications of emergency airway management in critically ill adults. A prospective investigation of 297 tracheal intubations. Anesthesiology 1995;82(2):367–76.
32. Loubani OM, Green RS. A systematic review of extravasation and local tissue injury from administration of vasopressors through peripheral intravenous catheters and central venous catheters. J Crit Care 2015;30(3)653.e9–17.
33. Cardenas-Garcia J, Schaub KF, Belchikov YG, et al. Safety of peripheral intravenous administration of vasoactive medication. J Hosp Med 2015;10(9):581–5.
34. Mokhmalji H, Braun PM, Martinez Portillo FJ, et al. Percutaneous nephrostomy versus ureteral stents for diversion of hydronephrosis caused by stones: a prospective, randomized clinical trial. J Urol 2001;165(4):1088–92.
35. Pearle MS, Pierce HL, Miller GL, et al. Optimal method of urgent decompression of the collecting system for obstruction and infection due to ureteral calculi. J Urol 1998;160(4):1260–4.
36. Christoph F, Weikert S, Muller M, et al. How sepsic is urosepsis? Clinical course of infected hydronephrosis and therapeutic strategies. World J Urol 2005;23(4):243–7.
37. Ordon M, Andonian S, Blew B, et al. CUA Guideline: Management of ureteral calculi. Can Urol Assoc J 2015;9(11–12):E837.
38. Stollings JL, Diedrich DA, Oyen LJ, et al. Rapid-sequence intubation: a review of the process and considerations when choosing medications. Ann Pharmacother 2014;48(1):62–76.
39. Jabre P, Combes X, Lapostolle F, et al. Etomidate versus ketamine for rapid sequence intubation

in acutely ill patients: A multicentre randomised controlled trial. Lancet 2009;374(9686):293–300.
40. Weingart SD, Trueger NS, Wong N, et al. Delayed sequence intubation: A prospective observational trial. Ann Emerg Med 2015;65(4):349–55.
41. Rhodes A, Evans L, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med 2017;45(3):486–552.
42. Weingart SD. Managing initial mechanical ventilation in the emergency department. Ann Emerg Med 2016;68(5):614–7.
43. Fuller BM, Ferguson IT, Mohr NM, et al. A quasi-experimental, before-after trial examining the impact of an emergency department mechanical ventilator protocol on clinical outcomes and lung-protective ventilation in acute respiratory distress syndrome. Crit Care Med 2017;45(4):645–52.
44. Zeserson E, Goodgame B, Hess JD, et al. Correlation of venous blood gas and pulse oximetry with arterial blood gas in the undifferentiated critically ill patient. 2018;33(3):176–81.
45. Kress JP, Pohlman AS, O'Connor MF, et al. Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. New Engl J Med 2000;342(20):1471–7.