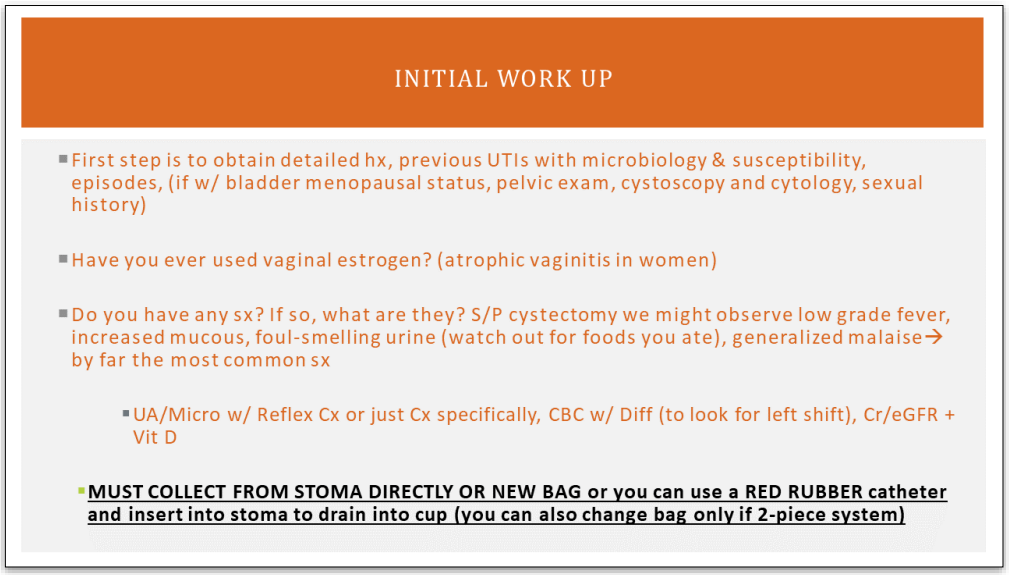
Krisztina Emodi:



Okay, perfect. Again, when I meet my patients we like to go from here, and what our workup should look like, and how do we think about this from a systemic standpoint. People with a bladder, generally we want to have a very detailed history of any previous infections. I want the microbiology of those infections, the susceptibilities from your physician, whether or not you are post-menopausal, this is very, very important, and I think oftentimes overlooked, because women responds to vaginal estrogen very nicely. Generally, there is atrophic vaginitis as we age, especially postmenopausal women. Once we withdraw estrogen there is a significant decrease in volume of the muscular structure and the wall of the vagina. There is some pelvic floor instability. There's increased, basically the connective tissue and this looseness in the ligaments in the pelvic floor. Estrogen stimulates the proliferation of lactobacillus, which is your kind of, sort of your best friend. It allows for vaginal pH to drop, and really allows ... and prevents colonization of different pathogenic bacteria. Again, these are folks with having a bladder.

Men with bladders are slightly different, because if you have a man with a bladder, with an infection, it's automatically considered to be a complex infection, which I think it's a different topic. The questions I have for my patient's status post cystectomy, again, "What are your symptoms?" Because you're not going to have the regular, "I have maybe a lower abdominal pain. It burst when pee, I pee every hour," because you either have a neobladder or you basically have urostomy on your abdomen. So status post cystectomy, we might observe the low grade fever, increased mucus, foul-smelling urine. I think again, the biggest observation over the years from my practice is having generalized fatigue, and by far this is the most common symptom, and overlooked. Personally, I will always get, depending on where we are,

if I'm not a 100% sure what we are doing, I will get a UA and microscopy with what we call a reflex culture. Important to be reflex culture because this way, if there's enough abnormality or enough white cells or bacteria picked up on this, the lab is automatically culturing the specimen so nothing gets lost.

Krisztina Emodi:

Oftentimes when I deal with bladder cancer status post cystectomy, I don't need the dip, a UA microscopy, in real life, is not very helpful because we are not dealing with sterile urine. Your UA and microscopy was developed for people with bladders, and we are looking at very particular values, whether you have hemoglobin in your urine, whether you have bacteria in your urine, so none of these things are applicable. I always tell my folks living, especially further from us, "Anytime your clinician orders a UA/microscopy, just ask what are they looking for." If they're ordering it for your annual visit, because they want to be sure if you have diabetes, you're not spilling sugar, you're not spilling protein, you're not in ketosis, those are very valid reasons to order a UA/microscopy. However, if you're just looking for an infection, we need to go straight to culture.

Unfortunately, what ends up happening oftentimes, asymptomatic post cystectomy bladder cancer patients end up getting a UA and microscopy, goes to culture, comes back positive, and guess what? You are put on cycles and cycles of antibiotics and treatment, which is at this point really unnecessary. This clearly would foster potentially antibiotic resistance and overtreatment, to a point where we might be knocking out an entire class of antibiotics in a clinical scenario when you actually are asymptomatic.

I also look for any kind of shifts in your blood work. I will get blood work. Usually I want my CBC to have what we call a differential, the differential is this little tiny information, breaking up the different cells in your blood. Even if before your white count gets high, I can see from the differential if something is brewing up. To me, it gives enough information, especially if it's a Friday afternoon and I need to have someone on treatment over the weekend. I want to see your creatinine. I want to see your filtration, again, this can indicate dehydration if you're not feeling well. If your creatinine is significantly different from your baseline, let's say your baseline is 1.1, now your creatine comes back 1.9, you've hydrated, then I would be getting a renal ultrasound to be absolutely a 100% sure that I'm not dealing with a stricture, or something mechanical that needs to be addressed.

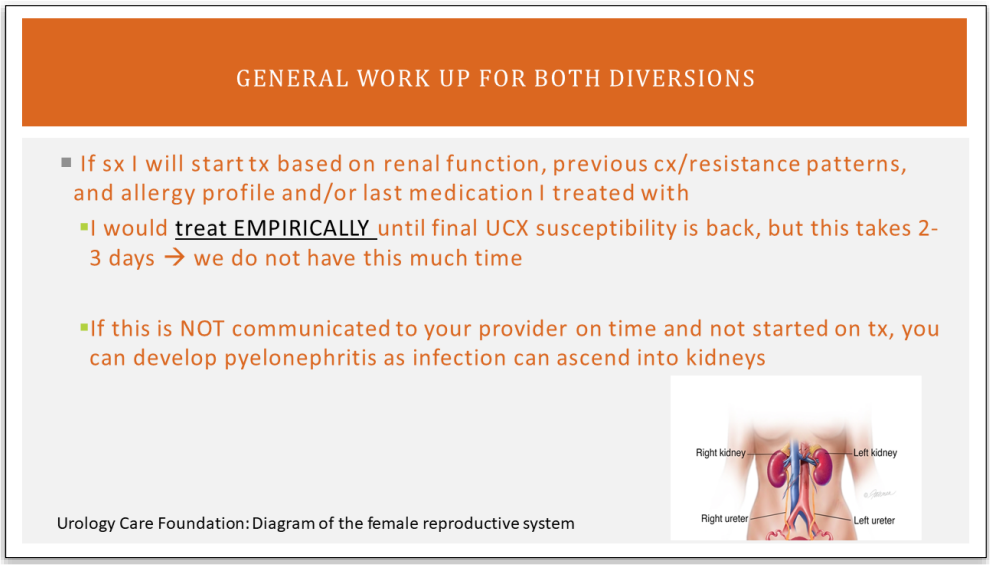
Krisztina Emodi:

I got lots of questions about collection. Collecting from the stoma directly is a must, or from a brand new bag. So, if you have a two-piece system, you can detach the bag, leave the flange on if you just changed it the day before, and your bag must be brand new. Anytime you have hours of urine in that bag there is bacterial overgrowth, and whatever else I'm going to get is not going to be accurate. If this is not possible, if you have a one piece bag, obviously you have to take the bag off and change it to collect the stoma directly, or if you have stenosis or unable to collect for some reason from the bag, or I really want the "cleanest catch of urine," which I will do it in clinic if I need to.

There is a very tiny red rubber catheter that people can use for self catheterizing. I will insert a red rubber catheter without any lubrication. I don't want anything disrupting my sample. You can insert this directly into the stoma, and just have the end of that red rubber to drip into a urinary collection cup. The red rubber is not going to hurt your stoma, if you push it in too far it's literally going to hit the back wall of that conduit, and turn around and come back at you on the other end.

Krisztina Emodi:

I generally also check Vitamin D levels in all my patients, although this is not necessarily UTI-related, partly because so many people are deficient, but vitamin D also enhances some antimicrobial peptides that are produced in the urinary tract. The theory goes that this potentially helps protecting from microbial invasion, basically helping the bladder epithelium. I absolutely want all my patients to have high normal D levels, and I would say when I check D levels, maybe 60% of my patients are actually deficient, thinking they get enough D from the sun, which is not the case.



General workup for both diversions. If you're asymptomatic I will start your treatment based on your renal function, based on any previous culture-resistant patterns that I'm able to identify on your reports, your allergy profile, and what medication have you treated with last potentially. This is called treating empirically, which means it's a Friday afternoon, you don't feel great, I am suspicious that you are coming down with an actual infection by tomorrow, but it's a Saturday. As long as you collect your urine, which takes two to three days to finalize with your culture and susceptibility, I'm able to start you on treatment. Generally, I will send in whatever the best medication I think, it is generally Septra, or Augmentin, Macrobid. I try to stay away from Fluoroquinolones, this is your Ciprofloxacin, Levaquin, these are the medications with the black box warning, and can actually be very harmful even in therapeutic doses.

I feel like the further we get from major hospitals, smaller clinics, very often treat patients with Ciprofloxacin. Important to know when to use Ciprofloxacin or Levaquin, and predominantly we want these medications to be brought on board, but I'm suspicious of pyelonephritis. I have had questions about pyelonephritis. Basically the difference between having a "urinary tract infection risk of pyelonephritis," is now this bacteria that is colonizing your neobladder or your conduit is ascending through those ureters, ascending into the kidney and causing a massive potentially infection. Pyelonephritis presents usually with tenderness in your back and mid back, that's called a CV tenderness. You will have a higher grade fever, so if your fever, 102 chugging towards 103, that is definitely pyelonephritis versus just a standard UTI. Adults do not spike high fevers like that. The differentiation, again, I'm trying to avoid an admission to the hospital here. I will start somebody on Fluoroquinolone, because those are the only medications actually that can treat pyelonephritis outside.

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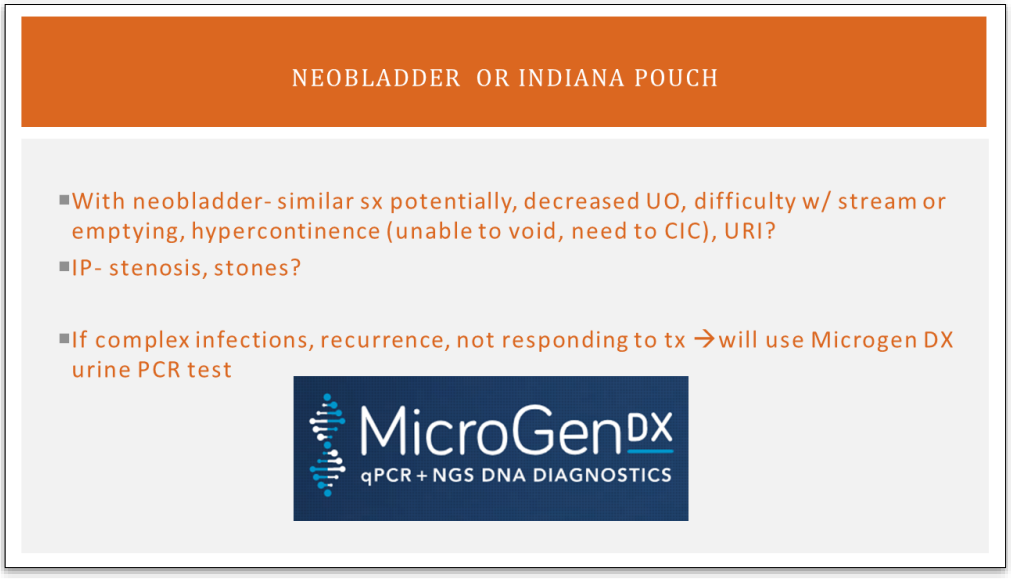
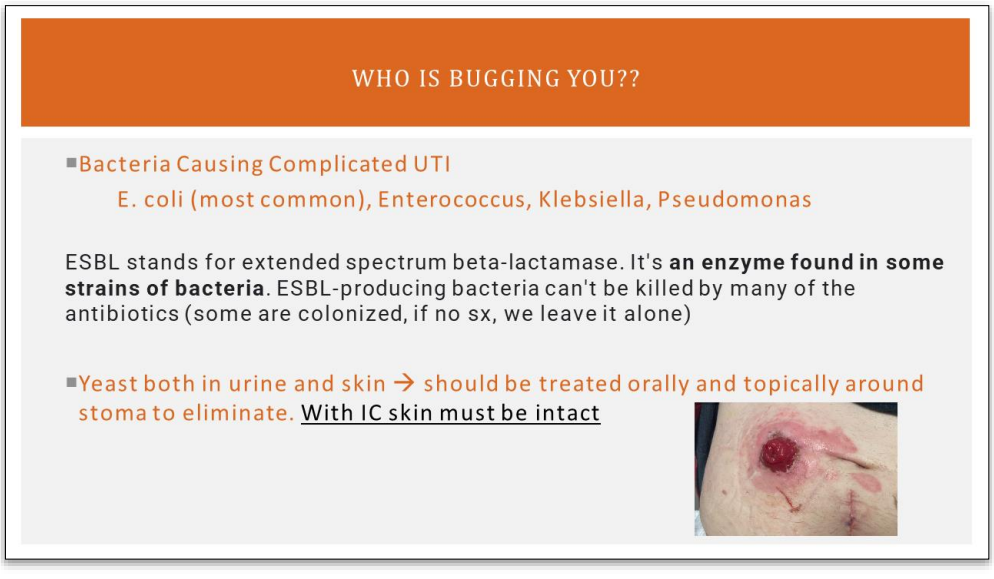
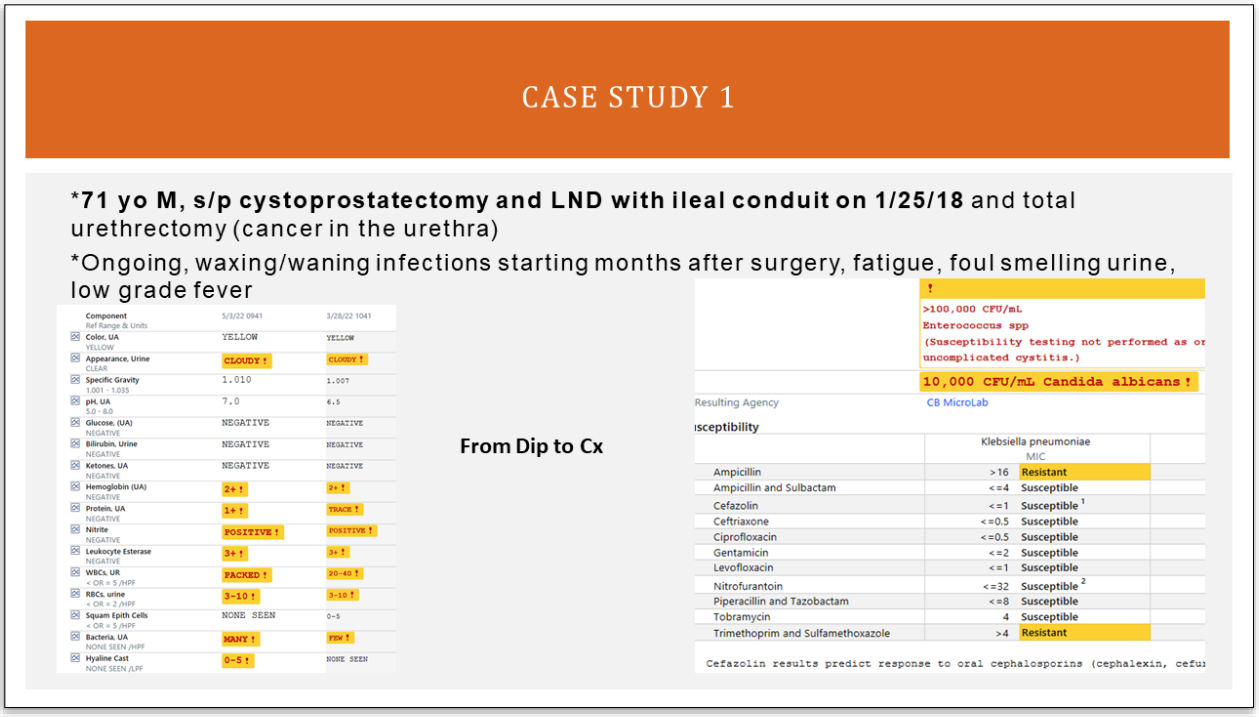


If a neobladder, similar situation, you might have decreased urine output, difficulty with stream, difficulty emptying, there is a clinical situation which is called hypercontinence, simply you're unable to avoid, and you have to self-catheterize. Sometimes people developing upper respiratory infections, because histologically some of these cells develop similarly from long tissue versus urinary tract. Oftentimes, I will see people with the neobladder having upper respiratory issues, and their neobladder can go haywire literally. We want to be mindful of respiratory infections. Again, any stenosis, any stones, this is predominantly important for the Indiana pouch.

If I have had multiple workups, complex infections, nothing's working, I'm working with a company called MicroGenDX, and this is ... I'm not part of any of these companies, it's just I'm using their urine PCR. It's a very cool test in a way that when you look on the left side I see all the bacteria, all the colonic counts and everything, whether you're resistant to oral and IV compatibilities, when I'm really hitting the end of my road trying to figure out what is happening to someone.



The most common bacteria we find are gram-negative, so this is again your E.coli, Enterococcus, Klebsiella, Pseudomonas. Again, if your skin is not intact, like my most recent patient here, if I'm needing to treat yeast on the skin, this yeast can crawl through back into the stoma, and potentially we have a yeast UTI along this. Your skin absolutely must be a 100% intact, along with not having infections.



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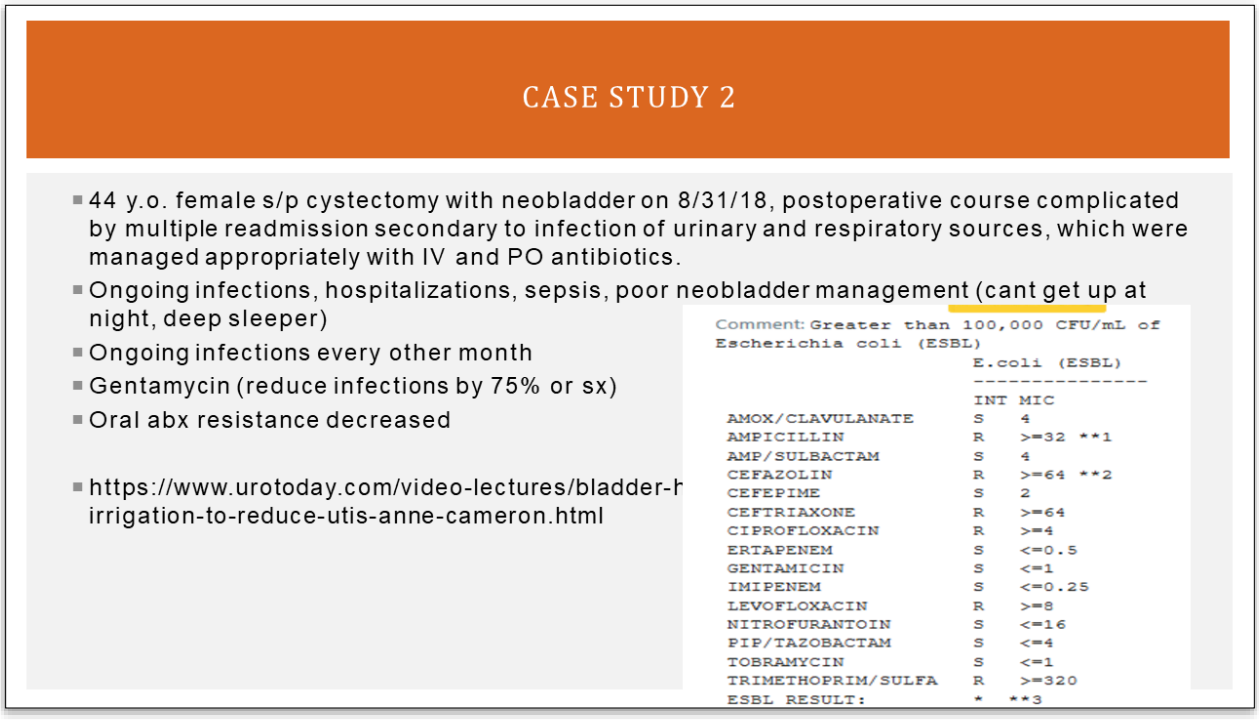
I wanted to present a few cases. These are all my patients who I've treated over the years. I have a 71-year old university professor, status was cystoprostatectomy node dissection, January of 2018. Later, we all said to remove the urethra because of cancer, and just in the side notes, if there's any discharge from the urethra, especially for men, that has to be addressed with your clinician to be sure that there is no cancer recurrence in the urothelium. In men, generally the urethra is left behind after your surgery. This patient had ongoing infections, all symptomatic, started about a month after his surgery, ongoing fatigue, foul-smelling urine, low grade fevers between January of 2018 to October of 2018. We had eight different infections that I had to treat.

When you're looking at a dip from an ileal conduit, and this is from a new bag or from the stoma directly, it is very inconclusive. I'm expecting a positive nitrate. None of this is really making or breaking what I'm doing, but again, some labs require the dip before we culture. When you're looking on the right side, there is three different pathogen growing along with yeast. This person actually had probably fairly intact skin along with Enterococcus, and I think ... here it is, Klebsiella. So, susceptibility for your clinical team is really important so I can actually look at this, and determine what medication you need to be on, and for how long.



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Second person is a 44-year old female with a neobladder, August of 2018. Her postoperative course was very complicated, multiple readmissions, multiple infections, IV antibiotics, oral antibiotics, nothing really worked. Over time we figured out that she had fairly poor neobladder management, not getting up at night. She was a very deep sleeper, slept through three alarm clocks, but at the end of the day, these infections were ongoing, leading to hospitalizations every time. So I sort of run off the clinical pathway here, and I started what we call Gentamicin instillations into her neobladder.

There is clinical evidence that in high-risk situations you can reduce ongoing infections that are not systemic, meaning your Gentamicin is instilled into the bladder, so she's using basically a catheter. Using a syringe you're putting in this Gentamicin mixed with normal saline. We clamped the catheter, she sleeps with it for four hours then she drains it. She still has some infections, however, every time, I guess, susceptibility, she's still responding to Augmentin, which is the first medication. She will have Augmentin on hand just because, I've known her for so many years, she still will have some fevers over time. Thank God this regimen actually has worked for us. If anybody has some of these complex infections, Gentamicin and how to use this is in the link that I have sourced here.