

Supplementary Results: Atypical symptoms in emergency department patients with urosepsis challenge current UTI management guidelines

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Table S1 Subject characteristics

	All uroseptic patients n = 123	Random non-septic patients n = 576
Demographics		
Age, median year (IQR)	70 (61–82)	56 (39–71)
Male, n (%)	66 (54%)	265 (46%)
Race/ethnicity		
White non-Hispanic, n (%)	106 (86%)	425 (74%)
Asian	8 (7%)	21 (4%)
Unknown	4 (3%)	54 (9%)
Hispanic/Latino	3 (2%)	32 (6%)
Black or African American	2 (2%)	44 (8%)
Triage information		
Temperature ≥ 100.4 at triage, n (%)	28 (23%)	8 (1%)
Heart rate, mean (sd)	105 (28)	87 (73-105)
Hypotension at triage (systolic blood pressure < 90 mm Hg), n (%)	27 (22%)	28 (5%)
Initial Glasgow Coma Scale < 15, n (%)	36 (29%)	101 (18%)
Presenting symptoms		
Fever (reported or measured at triage)	79 (64%)	75 (13%)
Genitourinary symptoms	40 (33%)	45 (8%)
Atypical urosepsis presentation*	35 (28%)	460 (80%)
ED course		
Received vasopressors in ED within 24 hours, n (%)	57 (46%)	14 (2%)
Intubated in the ED, n (%)	10 (8%)	14 (2%)
SOFA score, median (IQR)	6 (3–8)	-
Outcomes		
Hospital mortality, n (%)	16 (13%)	28 (5%)

* We define atypical presentation at triage to include patients with no report of fever, no fever measured at triage, and no report of localizing GU symptoms. Of note, four (4) patients with atypical presentations developed fever in the ED after triage.

Table S2 Symptoms of uroseptic patients

Symptom	Uroseptic patients N=123
At least one constitutional symptom, No. (%)	114 (93%)
Fevers/chills/rigors	77 (63%)
Fatigue/malaise/weakness/lightheadedness/lethargy	65 (53%)
Mental status changes	50 (41%)
Body aches or myalgias	6 (5%)
At least one classic genitourinary (GU) symptom	38 (31%)*
Abnormal (cloudy or bloody) urine	12 (10%)
Dysuria	12 (10%)
Back pain	8 (7%)
Flank pain	11 (9%)
GU pain	1 (1%)
At least one nonspecific symptom of major illness	74 (60%)*
Nausea or vomiting	39 (32%)
Abdominal pain*	36 (29%)*
Shortness of breath	18 (15%)
Headache	9 (7%)
Focal neurological symptoms	9 (7%)
Chest pain	6 (5%)
At least one confounding symptom	36 (29%)
Diarrhea	21 (17%)
Dry or unspecified cough	13 (11%)
Productive cough	3 (2%)
Skin abnormalities (redness, swelling, or abscess)	3 (2%)
Upper respiratory viral (sore throat, stuffy nose, or ear pain)	5 (4%)
Extremity pain	2 (2%)

* We did not categorize abdominal pain as a classic GU symptom. Only 6 of the 38 patients with “atypical symptoms” had any documented abdominal pain which was generally non-specific abdominal cramping or bloating. Additional details about symptoms of atypical urosepsis patients with abdominal pain are provided in the last five rows of Table S3 (“Detailed characterization of 35 urosepsis patients with atypical presentations”).

Table S3 Detailed characterization of 35 urosepsis patients with atypical presentations (i.e., no GU localizing symptoms; no report of fever; and no fever at triage).

	Vignette	Malaise	Confusion	WBC (L ⁻¹)	Lactate (mmol/L)	Urine studies	UCx growth
1	84M wheelchair-bound p/w 3d of lethargy, confusion	+	+	↑ 43.7	↑ 4.2	Pyuria on UA, >100 WBCs, BACT 3+, +LE	UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI
2	81M p/w SOB, ?STEMI, tachycardia	+	—	↑ 21.2	Unk	Pyuria on UA, 20-50 WBCs, BACT 1+, +LE	No growth (Abx before UCx*)
3	55M w/ CRI on HD and recent bacteremia 2/2 urosepsis p/w hypoxia, SOB, HoTN	—	—	↑ 28.9	↑ 1.8	Pyuria on UA, >100 WBCs, BACT 3+, +LE	UCx grew moderate (10,000 to <100,000 CFU/ml) PSEUDOMONAS AERUGINOSA
4	67F w/ neurogenic bladder, multiple prior UTIs p/w fatigue, weakness, hypoxia. Later found to have acute on chronic bladder obstruction.	+	+	↑ 16.0	0.9	Pyuria on UA, >100 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI
5	53M w/ quadriplegia in rehab facility p/w acute AMS	—	+	7.6	↑ 4.7	Pyuria on UA, 50-100 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) KLEBSIELLA PNEUMONIAE
6	72M w/ bacteremia, bladder CA (muscle invasive sarcomatoid carcinoma) s/p nephrostomy, HLD, AKI p/w SOB. Later found to have	+	—	↑ 28.1	↑ 9.0	Pyuria on UA, 10-20 WBCs, +LE	(Abx before UCx*)

	complete R upper kidney obstruction						
7	80M w/ artificial urethral sphincter p/w confusion	+	+	↑ 18.7	↑ 5.3	Pyuria on UA, 20-50 WBCs, +LE	(Abx before UCx*) UCx grew 100-1000 few E Coli by foley
8	34F hx anaplastic astrocytoma s/p resection, VP shunt, XRT/chemo, prior long course of dexamethasone p/w inability to tolerate good PO, dizziness and nausea	+	—	6.8	↑ 7.7	Pyuria on UA, >100 WBCs, BACT 1+	(Abx before UCx*) UCx grew rare (100 to <1000 CFU/ml) gram negative rods
9	82M w/ hx of Crohn's, polyarteritis on digoxin found unresponsive w/ asystolic arrest w/ episode of VT requiring ACLS x35 mins	—	+	↑ 15.2	↑ 8.9	Pyuria on UA, >100 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) CANDIDA ALBICANS
10	85F w/ dementia, CVA, p/w hypotension, hypoxia. Later found to have 3mm stone with L hydronephrosis and L ureteral dilation	—	+	↑ 18.6	↑ 5.1	Pyuria on UA, >100 WBCs, BACT 3+, +LE	(Abx before UCx*) UCx grew Rare (100 to <1000 CFU/ml) ENTERIC GRAM NEGATIVE RODS.
11	88M s/p partial pneumonectomy for pulmonary TB, left hemicolectomy w/ Hartmann's for diverticular bleed c/b parastomal hernia, recent surgery, recent UTI (on Bactrim) p/w confusion, fatigue	+	+	↑ 15.4	↑ 16.3	Pyuria on UA, 20-50 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS

12	56F h/o HTN p/w weakness and difficulty walking since last night	+	—	↑ 19.6	↑ 4.6		UCx grew abundant (≥100,000 CFU/ml) ESCHERICHIA COLI
13	81M w/ CAD, CHF, HTN, AFib on coumadin, left hip fracture s/p ORIF p/w elevated creatinine, no complaints	—	—	↑ 31.8	↑ 3.0	Pyuria on UA, >100 WBCs, BACT 1+, +LE	UCx grew moderate (10,000 to <100,000 CFU/ml) KLEBSIELLA PNEUMONIAE
14	48F h/o UTIs with E.coli ESBL and Candida p/w weakness and fatigue.	+	+	↑ 50.6	0.9	Pyuria on UA, >100 WBCs, BACT 2+, +LE	UCx grew abundant (≥100,000 CFU/ml) ESCHERICHIA COLI
15	67M w/ dementia p/w AMS x2 days	+	+	↑ 21.4	↑ 5.2	Pyuria on UA, >100 WBCs, BACT 1+, +LE	UCx grew abundant (≥100,000 CFU/ml) ESCHERICHIA COLI
16	81F PMH of pAF, EtOH use disorder, tachy-brady s/p PPM, HFpEF, HTN, HLD, COPD p/w weakness, n/d	+	—	↑ 18.1	↑ 2.7	Pyuria on UA, 20-50 WBCs, BACT 3+, +LE	UCx grew abundant (≥100,000 CFU/ml) ESCHERICHIA COLI
17	62M w/ seizure disorder, adrenocortical insufficiency with resultant labile sodium, R hemiparesis presents p/w SOB and CP. After initial presentation, developed fever	+	—	↑ 11.1	↑ 2.5	Pyuria on UA, 50-100 WBCs, BACT 3+	(Abx before UCx*) UCx grew few (1000 to <10,000 CFU/ml) MIXED BACTERIA.
18	86F w/ ESRD 2/2 DM p/w tachycardia and hypotension from HD	—	—	↑ 15.7	↑ 4.9	Pyuria on UA, >100 WBCs, BACT	(Abx before UCx*) Abundant (≥100,000 CFU/ml) ESCHERICHIA COLI;

						3+, +LE	
19	76M w/ HTN, prostate CA (on chemo) p/w weakness and diarrhea. Later found to be neutropenic.	+	—	↓ 0.3	↑ 4.1	No pyuria on UA, 5-10 WBCs	UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS
20	50F w/ seizures and recurrent nephrolithiasis and UTIs s/p renal stents p/w unresponsiveness and tonic clonic shaking	+	+	↑ 13.6	↑ 3.3	Pyuria on UA, >100 WBCs, BACT 1+, +LE	No growth (Abx before UCx*)
21	79F w/ ESRD p/w AMS	—	+	↑ 17.0	↑ 6.1	Pyuria on UA, >100 WBCs, BACT 3+, +LE	UCx grew abundant (>=100,000 CFU/ml) YEAST (NOT CANDIDA ALBICANS) Rare (100 to <1000 CFU/ml) PROBABLE ENTEROCOCCUS
22	63F w/ ALS s/p trach, neurogenic bladder s/p suprapubic tube p/w hyperglycemia	—	—	↑ 16.2	↑ 5.8	Pyuria on UA, 20-50 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) SERRATIA MARCESCENS
23	64M w/ MS p/w multiple falls	—	—	9.1	↑ 1.4	Pyuria on UA, 20-50 WBCs, BACT 1+, +LE	(Abx before UCx*) UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS; Rare (100 to <1000 CFU/ml) MIXED BACTERIA.**
24	67M w/ SCI c/b paraplegia, neurogenic bladder s/p indwelling foley p/w unresponsiveness	—	+	↑ 13.7	↑ 2.2	Pyuria on UA, 10-20 WBCs, BACT 2+, +LE	UCx grew abundant (>=100,000 CFU/ml) MORGANELLA MORGANII Abundant (>=100,000 CFU/ml) PROTEUS MIRABILIS
25	86F w/ severe MR, DM, HTN, pulmonary HTN, AFib p/w confusion	+	+	↑ 12.1	↑ 5.5	Pyuria on UA, 20-50 WBCs, BACT 1+, +LE	UCx grew moderate (10,000 to <100,000 CFU/ml) ESCHERICHIA COLI; Abundant (>=100,000 CFU/ml) MIXED BACTERIA.

26	84M w/ HTN, HLD p/w fall. After presentation, developed hypotension in the ED	+	—	↑ 36.5	↑ 1.1	Pyuria on UA, >100 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS; Abundant (>=100,000 CFU/ml) MIXED BACTERIA WITH 1 POTENTIAL PATHOGEN IN RARE AMOUNT
27	97yo man, PMH HTN, BPH and gout, who p/w increased weakness and confusion	+	+	7.5	↑ 1.6	Pyuria on UA, >100 WBCs, BACT 3+, +LE	UCx grew moderate (10,000 to <100,000 CFU/ml) MIXED BACTERIA.
28	75M w/ CKD on HD, CHF (EF 20%), p/w hypotension and AMS	—	+	↑ 17.1	↑ 1.9	Pyuria on UA, 20-50 WBCs, +LE	UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA
29	80M p/w AMS	—	+	↑ 14.8	↑ 1.7	Pyuria on UA, 50-100 WBCs, BACT 3+, +LE	UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI Abundant (>=100,000 CFU/ml) ESCHERICHIA COLI of a second type
The following subjects with atypical presentations reported abdominal pain							
30	83M w/ HTN, HLD, Asthma, s/p recent TURP p/w AMS and hypotension	—	+	↑ 21.7	↑ 3.1	Pyuria on UA, >100 WBCs, BACT 1+, +LE	UCx grew abundant (>=100,000 CFU/ml) ENTEROCOCCUS
31	52F w/ short gut, Crohn's ileostomy, bowel resections, frequent UTIs p/w 2-3 days of worsening diffuse abdominal pain, dry heaves and diffuse body pain.	—	—	↑ 29.1	2.4	Pyuria on UA, >100 WBCs, BACT 1+, +LE	Abundant (>=100,000 CFU/ml) KLEBSIELLA PNEUMONIAE

32	85M w/ CAD, AFib, myasthenia gravis (on IMURAN), HLD, HTN, CKD (baseline Cr 1.48), DVT (on coumadin) p/w LLQ abdominal pain.	—	—	8.1	0.8	Pyuria on UA, >100 WBCs, BACT 2+, +LE	UCx grew abundant (>=100,000 CFU/ml) KLEBSIELLA PNEUMONIAE, Abundant (>=100,000 CFU/ml) PSEUDOMONAS AERUGINOSA, Few (1000 to <10,000 CFU/ml) MIXED BACTERIA
33	83M w/ head and neck cancer p/w coffee-ground emesis	+	—	↑ 15.8	↑ 9.6	Pyuria on UA, >100 WBCs, BACT 3+, +LE	UCx grew abundant (>=100,000 CFU/ml) ESCHERICHIA COLI, Abundant (>=100,000 CFU/ml) ESCHERICHIA COLI of a second type, Abundant (>=100,000 CFU/ml) STAPHYLOCOCCUS AUREUS
34	60M w/ COPD, HTN, Hep C (not currently on meds) p/w watery diarrhea, nonbloody, no fever, mild abd cramping.	+	—	↑ 23.1	↑ 1.8	Pyuria on UA, 50-100 WBCs, BACT 3+, +LE	UCx grew moderate (10,000 to <100,000 CFU/ml) NONHEMOLYTIC STREPTOCOCCUS
35	55M w/ CVA and residual L sided weakness, schizophrenia, HTN, encephalopathy p/w abdominal pain and distention x 1 week	—	—	↑ 21.1	↑ 4.9	Pyuria on UA, 50-100 WBCs, BACT 1+, +LE	Abundant (>=100,000 CFU/ml) PSEUDOMONAS AERUGINOSA, Abundant (>=100,000 CFU/ml) MUCOID PSEUDOMONAS AERUGINOSA

* Documented time of antibiotic administration was earlier than time of urinalysis collection documented in either the ED nursing notes or the lab specimen detail.

Table S4 Triage SBP of 35 urosepsis patients with atypical presentations.

Study ID	Triage SBP
1	77
2	65
3	131
4	141
5	71
6	126
7	76
8	70
9	30
10	90
11	113
12	125
13	88
14	84
15	136
16	95
17	97
18	93
19	158
20	76
21	103
22	158
23	140
24	102
25	126
26	129
27	120
28	80
29	142
30	52
31	111
32	115
33	105

34	136
35	118

Table S5 Post-diagnostic pathologies of random, non-septic patients

Any toxicological pathology	96 (17%)
Drugs of abuse	78 (14%)
Medication effect	9 (2%)
Withdrawal syndrome	9 (2%)
Any cardiac pathology	88 (15%)
Atrial fibrillation/SVT	45 (8%)
Other, including non-specific chest pain	35 (6%)
Any respiratory pathology	72 (13%)
CHF	40 (7%)
COPD/RAD	24 (4%)
Any neurological pathology	68 (12%)
Other neurological pathology	45 (8%)
Intracerebral hemorrhage	12 (2%)
Any gastrointestinal pathology	61 (11%)
Other, with no antibiotics	34 (6%)
GI bleed	18 (3%)
Any trauma pathology	52 (9%)
Fracture	22 (4%)
Other acute injury	21 (4%)
Any non-bacterial infectious disease	26 (5%)
Viral	24 (4%)
Fungal	3 (1%)
Any renal pathology	22 (4%)
Renal failure	22 (4%)
Any vascular pathology	3 (1%)
Aneurysm rupture	3 (1%)
Any other pathology	171 (30%)