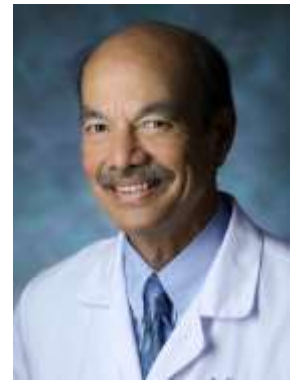




Heath

“UTI”:An Old Diagnosis in a New World

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As currently construed, urinary tract infection, or “UTI”, is diagnosed in a variety of clinical situations ranging from the trivial to the fatal (Table 1). Harmful overtreatment is commonplace. “Significant bacteriuria,” on which most diagnoses are based, refers to findings on agar-based cultures (we will call this standard bacteriuria), first used in the 1880s. It is defined as the occurrence of $>10^5$ /ml bacteria on a blood agar plate. “Significant bacteriuria” has no significance in identifying patients who will benefit from antibiotic treatment. Genetic techniques, expanded culture and other modern diagnostic methods show that the healthy urinary tract hosts a complex, generally beneficial microbiome and a virome. Current management strategies, deeply flawed on their own terms, now also require a conviction that only bacteria detected by standard cultures can be pathogenic and that organisms that do not grow on standard cultures may be safely ignored.

Representative problems in common practice

Two presentations of “UTI” are particularly troubling. The first is acute dysuria, considered synonymous with “UTI” by many patients and some clinicians. One strategy is simply to treat such patients. Perhaps more commonly, laboratory evaluation is ordered and if the patient has standard bacteriuria, antibiotic treatment is given. About half of symptomatic patients will have “significant bacteriuria.”¹ This standard-of-

care approach to treating acute uncomplicated cystitis ignores two important facts. First, both standard bacteriuria and urinary symptoms frequently resolve and recur spontaneously.²⁻⁴ Second, subsequent pyelonephritis is rare and the incidence does not seem to be reduced by antibiotic treatment.⁵ “Acute uncomplicated cystitis rarely progresses to severe disease, even if untreated; thus, the primary goal of treatment is to ameliorate symptoms”⁶. For eons, and at present in under-resourced settings, acute uncomplicated cystitis has not been treated with antibiotics, and severe illness or lasting ill-effects are very rare.

Pain resolves more quickly with antibiotics; however, a safe effective analgesic would reduce much antibiotic overuse with little or no risk.

“Significant bacteriuria” has no significance in identifying patients who will benefit from antibiotic treatment.

The second lamentable use of the diagnosis of “UTI” is seen when frail older patients with altered mental status or altered color or odor of urine are found to have bacteriuria.⁷ In patients who are otherwise well, no evidence shows that delirium outcomes are improved by antibiotic treatment and patients may certainly be harmed. Guidelines and consensus statements recommend against such practice (Table 2).⁸ Treatment to improve the odor or appearance of urine is mentioned only to condemn the practice. Ceftriaxone should rarely be used to deodorize urine. Because the term “UTI” can be applied, however, treatment commonly follows.⁹ In older women living in institutions, the prevalence of standard

asymptomatic bacteriuria (ASB) can approach 50%, so the likelihood of finding incidental bacteriuria is high.¹⁰ In a prospective cohort study of 343 delirious patients with ASB, those treated with antibiotics had no difference in functional recovery but had a higher rate of *C. difficile* disease.¹¹

The era of the microbiome
Overtreatment of “UTI” based on a finding of standard bacteriuria is widespread. With new evidence about the urinary microbiome, antibiotic treatment is ever more indefensible. Gene-sequencing and sophisticated culture techniques show that “asymptomatic bacteriuria” is not a diagnosis but the normal state of a healthy urinary tract.¹² The discovery of this urinary microbiome suggests clinicians have been focusing on a small part of a much larger picture and assuming that bacteriuria is an unusual and harmful event.¹³ Demonstration of the microbiome has 2 direct implications. First, attributing dysuria, delirium, falls, reduced functionality, odoriferous or discolored urine, etc. to standard bacteriuria can only be justified if all bacteria that are possibly pathogenic can be identified using agar-based cultures, and that any bacteria that cannot be seen easily should be ignored. Second, stable microbiomes seem to provide benefit to patients and antibiotic disruption may cause important harm. In the gut, *C. difficile* disease is a notorious example.

Cai et al studied a group of women who had recurrent “symptomatic UTI” and were later found on screening to have ASB. Half were randomized to receive antibiotic treatment and this group had higher rates of symptomatic recurrence over the next year than those randomized to receive no treatment. The authors concluded that asymptomatic bacteriuria “may play a protective role in preventing symptomatic recurrence.”¹⁴ Unmentioned was the stable but uncultivable microbial com-

Table 1. Clinical situations sometimes diagnosed as “UTI”

- ◆ **Presence of “significant bacteriuria”***
 - by itself
 - with dysuria
 - with change in mental or functional status
 - with change in odor or color of urine
 - with bacteremia and same organism in blood and urine
 - with “flank pain” and signs of invasive infection
 - with nonspecific symptoms such as dizziness, fatigue, falls, seizure
- ◆ Presence of dysuria (or sometimes other urinary tract symptoms) regardless of bacteriuria

*“Bacteriuria” refers to findings on conventional cultures, defined as >10⁵ cfu/ml.

munity that surely contributed.

Conclusion

Antibiotic treatment of “UTI” generally provides little or no benefit to patients who are not systemically ill. Treatment shortens duration of dysuria in patients with acute uncomplicated cystitis and benefits patients with asymptomatic bacteriuria who are pregnant or soon to undergo urologic procedures. Patients with incident confusion who are found to have bacteriuria have not been shown to benefit from treatment, and expert advice opposes defining, diagnosing or treating this syndrome as a “UTI.” The harm, without benefit, of treating ASB, with the exceptions noted above, has long been known, but the practice continues unabated. Recognition that the natural state of the healthy urinary tract is ASB should have some impact on this dismal practice.

The willingness to blame acute symptoms on bacteriuria should be tempered by the knowledge that everyone is bacteriuric all the time and that stable microbial communities are generally beneficial. Antibiotic treatment based on agar-based culture results is an obsolete and harmful practice. As Costello and colleagues note, “transitioning clinical practice from the Body-as-Battleground to the Human-as-Habitat perspective will require rethinking how one manages the human body”.¹⁵ Patient safety and public health can be improved immediately

Table 2. Expert advice on definition, need for testing and need for treatment of "UTI" in patients with incident delirium who are in long-term care and are not catheterized⁸

Advice	Source
<i>A patient with delirium and bacteriuria does not meet the definition of "UTI."</i>	Surveillance Definitions of Infections in Long-Term Care Facilities: Revisiting the McGeer Criteria. ¹⁶
<i>Evaluation for "UTI" is not recommended for patients with delirium, bacteriuria and fever.</i>	Clinical Practice Guideline for the Evaluation of Fever and Infection in Older Adult Residents of Long-Term Care Facilities: 2008 Update by the IDSA ¹⁷
<i>Antibiotic treatment for UTI is not recommended for a patient with delirium, bacteriuria, and fever. (Elsewhere in the Consensus, however, antibiotic treatment for the combination of fever and delirium is accepted, without reference to urinary tract findings.)</i>	Development of Minimum Criteria for the Initiation of Antibiotics in Residents of Long-Term Care Facilities: Results of a Consensus Conference ¹⁸
<i>Don't use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present.</i>	American Geriatrics Society identifies five things that healthcare providers and patients should question ¹⁹

by acting on what is known about standard bacteriuria. As the science of the microbiome matures, the term "UTI" will join "ague" and "dropsy" in the category of illnesses that time has passed by.

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World Antibiotic Awareness Week : November 13-19



Upcoming Events

November 13, 2017

Educational webinar: The role of point of care C-reactive protein testing in reducing inappropriate antibiotic use; presented by Liz Cross, University of Hertfordshire, UK; produced by Whitehat Communications and sponsored by Alere

November 13-19, 2017

U.S. Antibiotic Awareness Week (formerly *Get Smart About Antibiotics Week*): CDC's annual one-week observance to raise awareness of the threat of antibiotic resistance—an international collaboration with European Antibiotic Awareness Day, Australia's Antibiotic Awareness Week, Canada's Antibiotic Awareness Week, and World Antibiotic Awareness Week

October 29-November 1, 2017

Antimicrobial and Resistance: Opportunities and Challenges (T4), A Keystone Symposia Conference, organizers: Gautam Dantas and Jennifer Leeds, Santa Fe, New Mexico, USA

Jan 19-20, 2018

ICAR 2018: International Congress on Antimicrobial Resistance, Thanajvur, India

February 22-24, 2018

Annual Scientific Meeting Antimicrobials 2018, Brisbane Australia

April 14-15, 2018

15th Annual Global Health & Innovation Conference Yale University, New Haven, Connecticut

April 21-24, 2018

ECCMID 2018: 28th European Congress of Clinical Microbiology and Infectious Diseases, Madrid, Spain,

June 7-11, 2018

ASM Microbe, Atlanta, GA

June 13-15 2018

Association for Professionals in Infection Control and Epidemiology (APIC) Annual Conference, Minneapolis, MN

June 22-25 2018,

5th International One Health Congress, Saskatoon Canada - with special focus on antimicrobial resistance, translational science, and recent advances in the fields of zoonoses and emerging infectious diseases.

July 14-15, 2018

4th World Congress and Exhibition on Antibiotics and Antibiotic Resistance: A New Era in Antibiotics Drug Development. Barcelona, Spain