Urinary Tract Infection Series
APHL Training Webinars

I - Processing and Work up of Urine Specimens in the Clinical Lab – Susan Novak Ph.D.
II - AST of Bacteria that Cause Urinary Tract Infections – Janet Hindler M.S.
III - Management of Patients with Urinary Tract Infections – Jared Spotkov M.D.
Processing and Work up of Urine Specimens in the Clinical Lab

APHL – October 14, 2014

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The only comprehensive online resource for clinical microbiologists.

- **Q & A** allows users to submit their microbiology questions for an expert’s response, as well as the opportunity to search a database of more than 1,000 questions that have already been answered.
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- **What's New** keeps you up-to-date on upcoming clinical events & Portal announcements.
- **ASM Programs** can be found on one site that houses all of ASM’s clinical content.
- **Lab Management** links users to a variety of tools that help facilitate and optimize the work of the laboratory manager.

http://clinmicro.asm.org
Research Studies

- Roche Molecular
- Pocared
- Nanosphere
- Bruker

- No personal disclosures
Kaiser Permanente

- Kaiser Southern California
  - >3.8 Million Members So Cal
  - 14 Hospitals
    - Each with Medical Center Lab
  - ~200 Medical Office Buildings
  - ~6000 physicians
  - ~200,000 Admissions Per Year
  - 1 Centralized Regional Reference Laboratory
    - Microbiology (Bacti, AFB, Mycology, Parasit, Serology – ID & AI, Virology, Molecular)
    - Bacteriology - ~2200 urine cultures/day, 55,000 urine cultures/month
    - 4 Million tests annually

Kaiser Permanente
Overview/Objectives

- Challenges with Urine Cultures!!?? *Old topic, anything new??*
- The Specimen – Collection/Preservation, Transport and Processing
- Protocols/media for working up urine cultures
- Newer approaches / technology
Urinary Cultures

- Urinary Tract Infection (UTI) is one of the most commonly encountered infectious diseases
- Accounts for the majority of workload in the clinical laboratory
- Accounts for >8 million visits per year in the OP setting. Data is historic and most likely underestimates impact to healthcare setting
- Asymptomatic bacteriuria is generally not considered clinically significant but can be in some patient populations
- Given the accuracy of a diagnosis based on patient symptoms in select patient groups the infection (uncomplicated UTI) can be managed without an in-person medical assessment
- Complicated UTI’s must be managed differently and the distinction remains important

Challenges with Urine Cultures

- Reflex from Urinalysis
  - Urinalysis – Ranges exist for sens/spec in literature\(^1\)
  - Patient population dependent

- High volume – many are negative

- Culture is the Gold Standard
  - Integrity of sample/Processing – issue for offsite and/or higher volume labs
  - Clinical cutoffs?
    - relates to newer technologies as well
    - Confusing for the laboratory
  - Contamination
  - 24 vs 48 incubation
  - Use of Chromagar

\(^1\) S. Bent, 2002 JAMA
Challenges with Urine Cultures

- Newer technologies/Varied approaches other than culture
  - Mass spectrometry
  - Urine Screening Analyzers
  - Can they be used reliably??
    - Mixed data
    - They can improve TAT for negative cultures
    - Way to help manage labor shortages – not plating or working up presumed negatives
    - Free up resources – divert elsewhere

- No need for appointment or laboratory testing in uUTI cases
Reflex from Urinalysis

- Recent survey of clinical microbiologists indicate about 50% of labs automatically reflex urine cultures based on urinalysis results.

- Institutions have varied cutoffs for reflexing culture from urinalysis.

- One recent study looked at the outcome of urine culture cancellation based on urinalysis results.
  - Retrospective study showed it would eliminate 39% of urine cultures; 3.5% of the positive cultures would have been missed.
  - Discussion
    - Could eliminate a number of unnecessary cultures.
    - Some patient populations should perhaps be excluded/Education necessary.
    - Many UTIs can be treated without any testing.

C. Jones et al, Clinical Laboratory in Emergency Medicine, 2013 vol 46
Urine Collection and Transport

- Good medicine, impact of CMS

- Collected urine should include
  - Patient name
  - Source
  - Time of collection

- **Urine specimens should be processed immediately or refrigerated but generally accepted that specimen should reach the lab within 30 minutes and processed**

- Longer transport times consider preservative, ie. Boric Acid.
  - Volume critical – at least 3 ml
  - <3ml boric acid can have a detrimental affect on bacteria
  - Stabilize urine for 48 hours
Urine Collection and Transport

- American Society for Microbiology Laboratory Practices Committee – Dr. Mark LaRocco
  - Performing a systematic review for urine pre-analytics
  - Collection, preservation and storage
  - Should be available in 2015
EVIDENCE-BASED LABORATORY PRACTICE GUIDELINES

ASM develops Evidence-based Laboratory Practice Guidelines (EBLPG) that address laboratory quality issues, pre- or post-analytic, that need improvement. ASM adheres to the CDC's A-6 methodology. This methodology is transparent, objective, and rigorous to provide evidence-based information to healthcare stakeholders about the effectiveness of quality improvement practices.

Currently, three guidelines are under development:

1. "What practices are effective at increasing timeliness for providing targeted therapy for those patients who are admitted for or are found to have bloodstream infections (e.g., positive blood cultures to) to improve clinical outcomes (LOS, antibiotic costs, morbidity, mortality)?"

2. "Does optimizing the collection, preservation and transport of urine for microbiological culture improve the diagnosis and management of patients with urinary tract infections?"
Processing

- Newer automation can assist in processing not only urine specimens but other liquid samples such as eSwabs.
- Ability of newer technology can save on FTEs related to processing, improve quality of plating and impact ergonomic injuries of those performing tasks with repetitive motion.
Kaiser Southern California History with Automation

Isoplater 2002, inocuLAB 2004, Innova 2010
From 2004-2012 KP membership has grown ~15%
Urine Culture - Incubation

- Variation in incubation times exist between laboratories
- Literature exists to support the practice of 1 day incubation
- Some literature shows extended incubation time will pick up select pathogens
- Varied practices exist within laboratories in regards to overall incubation times
- Laboratory Diagnosis of Urinary Tract Infections
  - ASM Cumitech 2C
<table>
<thead>
<tr>
<th>Organism(s) (no. of isolates)</th>
<th>Blood agar</th>
<th>CLED agar</th>
<th>McConkey agar</th>
<th>CPS ID2</th>
<th>CHROMagar Orientation from BBL</th>
<th>CHROMagar Orientation from The CHROMagar Company</th>
<th>Chromogenic UTI Medium</th>
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<td></td>
<td>Day 1</td>
<td>Day 2</td>
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<td>Klebsiella pneumoniae (30)</td>
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<td>Klebsiella-Enterobacter (1)</td>
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<td>Proteus mirabilis (14)</td>
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<td>Proteus vulgaris (1)</td>
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<td>Serratia marcescens (1)</td>
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<tr>
<td>Gram-negative nonfermentative rod (1)</td>
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<td>1</td>
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<td>Pseudomonas aeruginosa (15)</td>
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<td>Alpha-hemolytic streptococci (1)</td>
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<td>13</td>
<td>13</td>
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<td>7</td>
<td>11</td>
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<td>Group G streptococci (1)</td>
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<td>0</td>
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<td>Coagulase-negative staphylococci (14)</td>
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<td>14</td>
<td>14</td>
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<td>Staphylococcus aureus (2)</td>
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<tr>
<td>Staphylococcus saprophyticus (1)</td>
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<td>1</td>
<td>1</td>
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<tr>
<td>Yeasts (14)</td>
<td>12</td>
<td>13</td>
<td>12</td>
<td>13</td>
<td>7</td>
<td>8</td>
<td>7</td>
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<tr>
<td>Total (420)</td>
<td>399</td>
<td>405</td>
<td>398</td>
<td>404</td>
<td>277</td>
<td>278</td>
<td>376</td>
</tr>
</tbody>
</table>
Urine Culture – Work up

- Bacteriuria is considered by most clinicians to be the definitive marker for UTI
- Early studies found that $10^5$ were indicative of UTI
- More recent studies indicate this cutoff can miss a significant group of patients and support lower levels ($10^2 - 10^4$) be considered positive \(^1\)
- Since most laboratories do not report below $10^4$ in voided urine specimens these culture reports should be interpreted with caution \(^2\)
- Lower levels of bacteriuria have been shown to predict UTI in many settings. Levels $>10^2$ have shown sensitivities and specificities of 95/85% respectively \(^3\)

\(^1\) S. Fihn, NEJM 2003; M. Wilson, CID 2004
\(^2\) T. Hooton, NEJM 2012
\(^3\) ASM Cumitech 2C, W. Stamm, NEJM 1982
Urine Culture – Work up

- Inconsistency of the guidelines causes confusion for clinical laboratorians

- Following tables extracted from Clinical Microbiology Newsletter, Vol 36, June 15, 2014 – Marie Pezzlo, MA

- Combine ASM Cumitech 2C and IDSA guidelines on CAUTIs

- Grp B Strep – CDC 2010 Guideline now states that GBS should be identified in pure culture or when mixed with a second organism in numbers of $\geq 10^4$ CFU/ml
### Urine Culture – Work up

Work up of voided urine specimens

<table>
<thead>
<tr>
<th>No. of isolates</th>
<th>Colony count CFU/ml</th>
<th>Definitive ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥10⁴</td>
<td>Yes if PU</td>
</tr>
<tr>
<td></td>
<td>&lt;10⁴</td>
<td>No Desc ID only</td>
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<tr>
<td>2</td>
<td>Both ≥10⁴</td>
<td>Yes if PU</td>
</tr>
<tr>
<td></td>
<td>Both &lt;10⁴</td>
<td>No Desc ID only</td>
</tr>
<tr>
<td></td>
<td>1 ≥10⁴ / 1 &lt;10⁴</td>
<td>Yes only for ≥10⁴ PU</td>
</tr>
<tr>
<td>3</td>
<td>1 ≥10⁵</td>
<td>Yes if PU</td>
</tr>
<tr>
<td></td>
<td>Any other combo</td>
<td>No Desc ID only</td>
</tr>
</tbody>
</table>

PU = Possible Uropathogen
### Urine Cultures – Work up

Workup of urine specimens collected by invasive methods

<table>
<thead>
<tr>
<th>No. of isolates</th>
<th>Colony count CFU/ml</th>
<th>Definitive ID</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\geq 1000 \ (10^3)$</td>
<td>Yes if PU</td>
</tr>
<tr>
<td></td>
<td>$&lt;10^3$</td>
<td>No Desc ID only</td>
</tr>
<tr>
<td>2</td>
<td>Both $\geq 10^3$</td>
<td>Yes if PU</td>
</tr>
<tr>
<td></td>
<td>Both $&lt;10^3$</td>
<td>No Desc ID only</td>
</tr>
<tr>
<td></td>
<td>$1 \geq 10^3 / 1 &lt;10^3$</td>
<td>Yes only for $\geq 10^3$ PU</td>
</tr>
<tr>
<td>3</td>
<td>$1 \geq 10^4$</td>
<td>Yes if PU</td>
</tr>
<tr>
<td></td>
<td>Any other combo</td>
<td>No Desc ID only</td>
</tr>
</tbody>
</table>

Indwelling and non-indwelling catheters, suprapubic aspirate, cystoscopy, nephrostomy
Urinary Pathogens

- E. coli is responsible for 70-90% of uncomplicated cystitis
  - ~50% for complicated cystitis
- In recent years select unusual organisms have been associated with UTI’s
- Less common isolates
  - Aerococcus, C. ureolyticum, Acinetobacter spp., Actinobaculum schaalii, Lactobacillus delbrueckii
  - Other possible uropathogens – could these be associated with sterile pyuria\(^1\)?
    - Mycobacteria spp., Mycoplasma hominis, U. urealyticum, C. trachomatis, T. vaginalis

\(^1\) Urine is Not Sterile... Hilt et al. March 2014, JCM
Urinary Pathogens

- Awareness of unusual pathogens is important
  - Risk associated with infection with *Aerococcus urinae*
    - Elderly, prostatic hypertrophy
    - Risk assessment cannot be done in the laboratory working up specimens
    - Colonies may be mistaken for streptococci, alpha hemolytic
    - Gram staining of alpha-hemolytic, cat -, cocci should be performed
  - *A. viridans*
  - *C. urealyticum*
    - Renal transplant patients/post transplant UTI
  - Other coryne
  - Role for MALDI-TOF
Urine Culture – Work up

- IDSA

Diagnosis, Prevention, and Treatment of Catheter-Associated Urinary Tract Infection in Adults: 2009 International Clinical Practice Guidelines from the Infectious Diseases Society of America

Thomas M. Hooton,1 Suzanne F. Bradley,2 Diana D. Cardenas,2 Richard Colgan,4 Suzanne E. Geerlings,7 James C. Rice,9 Sanjay Saint,6 Anthony J. Schaeffer,9 Paul A. Tambay,7 Peter Tenke,9 and Lindsay E. Nicolle10,11

Departments of 1Medicine and 2Rehabilitation Medicine, University of Miami, Miami, Florida; 3Department of Internal Medicine, Ann Arbor Veterans Affairs Medical Center and the University of Michigan, Ann Arbor, Michigan; 4Department of Family and Community Medicine, University of Maryland, Baltimore; 5Department of Medicine, University of Texas, Galveston; 6Department of Urology, Northwestern University, Chicago, Illinois; 7Department of Infectious Diseases, Tropical Medicine, and AIDS, University of Amsterdam, Amsterdam, The Netherlands; 8Department of Medicine, National University of Singapore, Singapore; 9Department of Urology, Jahn Ference Del-Pesti Korhaz, Budapest, Hungary; and Departments of 10Internal Medicine and 11Medical Microbiology, University of Manitoba, Winnipeg, Canada
Urine Culture and Catheter Replacement before Treatment

45. A urine specimen for culture should be obtained prior to initiating antimicrobial therapy for presumed CA-UTI because of the wide spectrum of potential infecting organisms and the increased likelihood of antimicrobial resistance (A-III).

46. If an indwelling catheter has been in place for >2 weeks at the onset of CA-UTI and is still indicated, the catheter should be replaced to hasten resolution of symptoms and to reduce the risk of subsequent CA-bacteriuria and CA-UTI (A-I).

   i. The urine culture should be obtained from the freshly placed catheter prior to the initiation of antimicrobial therapy to help guide treatment (A-II).

   ii. If use of the catheter can be discontinued, a culture of a voided midstream urine specimen should be obtained prior to the initiation of antimicrobial therapy to help guide treatment (A-III).
Urine Culture - Chromagar

- Chromogenic media – substrates in media that target specific classes of enzymes produced by certain bacteria or yeast
- Target enzyme hydrolyze chromogenic substrates – colored products allow for easy ID of specific organisms – *E. coli/Enterococcus*

- Workflow studies - limited
  - D’Souza et al, JCM, 2004 - >50% reduction in inoculation time and >20% reduction in workup time
  - Ohkusu, JCM, 2000 – 70% cost savings compared to their conventional work up
  - Manickam et al, JCM, 2013 – 28% reduction in workload for number of procedures mostly related to ID set up

- Cost implications / Impact of Mass Spec??
- Future role of automation – digital imaging??
Escherichia coli (ATCC® 25922)

BluEcoli™
Novel Approaches other than Culture

- Kaiser Permanente – Southern California
  - Physician – HealthConnect, Educational Material, Symposia
  - Created **Call Center**
    - Women with uncomplicated UTI can call in and over the phone
    - Talk with nurse – questionnaire
    - Get a prescription
    - Outcomes
      - No physician appointment
      - Ease to patient
      - Impacts access in our clinics in a positive way
      - Decrease urine culture volume in clinical laboratory

Recurrent DYSURIA/UTI in women 18-65 screening history and management plan

Patient Name:

PF#:________________________

DOB:____________________(E)

Phone: (D)____________________

Confirm: Patient prefers home treatment  o Yes  o No

1. Treated for UTI before?
   o Yes  o No

2. Confirm UTI symptoms:
   o Yes  o No Burning
   o Yes  o No Urgency
   o Yes  o No Frequency
   o Yes  o No Bladder Pressure

When did these symptoms start?

3. Exclusion Criteria: if Yes, book appointment today
   o Yes  o No Fever > 100.5
   o Yes  o No Vomiting
   o Yes  o No Vag. itching or abs. discharge
   o Yes  o No Pregnant or might be
   o Yes  o No Diabetic
   o Yes  o No Immunocompromised (e.g., active cancer,
     Chemotherapy, corticosteroids, immunosuppressive
     meds, etc)

4. Three or more UTIs in the past year?
   o Yes  o No

If YES, order urine culture, treat now and book routine
appointment to discuss future management and/or estrogen status
evaluation if post-menopausal

5. Medication History: List specific medications
   Current medications

Primary MD Name________________loc________________
Treating MD Name________________loc________________
LVN/RN Name________________loc________________
NP/PA Name________________loc________________

7. ORDER A URINE CULTURE, if YES to any of
   the following:
   o Yes  o No 3 or more UTIs in the past year
   o Yes  o No treated for UTI in past 2 weeks
   o Yes  o No persistent symptoms after treatment
     (failed treatment course)
   o Yes  o No hx of kidney stone

8. Ask if breastfeeding:
   o Yes  o No

9. Prescription: Selection by MD or NP/PA.
   Recommended in the following order:
   o *Trimethoprim Sulfa–DS 160/800 mg BID x 3
     days (#6)
   *Avoid if on anticonvulsants or coumadin or if
   allergic to sulfa
   *Avoid when breastfeeding an infant under 2
   months of age
   o Nitrofurantoin (Macro-Bid) 100 mg BID x 7 days
     (#14)
   o Cephalexin 500 mg BID x 7 days (#28-40)
   o *Ciprofloxacin 250 mg BID x 3 days (#6)
   *Do not use in breastfeeding women

10. Pharmacy
    Location:
    Telephone #
KP On-Call UTI Protocol
URINE TESTS -- NOT ALWAYS NEEDED!

It has been well documented that women in the outpatient setting with an uncomplicated cystitis/lower urinary tract infection (no serious comorbidities, no frequent recurrence, no renal involvement, not pregnant) between the ages of 18-64 can be treated empirically with antibiotics and do not require a culture. In fact if a patient calls on the phone with symptoms consistent with an uncomplicated UTI and there are no risk factors it has been shown that the patient can be treated empirically over the phone.

The Regional Laboratory Utilization Action Team (ReLUAT) in conjunction with Regional Infectious Diseases Specialists recommends:

For uncomplicated Cystitis (Lower Urinary Tract Infection in Low Risk Women age 18-64) with clear signs and symptoms of a UTI:

- NO URINE CULTURE is needed for an uncomplicated UTI (in a female patient with no serious comorbidities, not pregnant, no frequent recurrence, no renal infection suspected)
- No Urinalysis, in fact, is needed if the diagnosis is a clear-cut uncomplicated UTI
- Empiric treatment with (please note varying durations of treatment)
  - Nitrofurantoin monohydrate/macrocrystals 100 mg twice daily for 7 days or
  - Trimethoprim-sulfamethoxazole DS twice daily for 3 days or
  - Cephalexin 500 mg twice daily for 7 days or
  - Ciprofloxacin 250 mg twice daily for 3 days

Please note that for complicated urinary tract infection (recurrent infections, failure of treatment, suspected renal infection/pyelonephritis, serious comorbid conditions or pregnancy), urine analysis and urine cultures are indicated.
Tracking our Success

- Laboratory Utilization Action Team – LUAT
- Each Medical Center responsible for initiatives set forth by regional group
  - Slide set for education to be used at each area
- Analytical Support for data
- Manage outcomes
- Education still needed within OP setting
UC Resulted Orders Per 1000 Members
Female Members Ages 18–64
2013Q2–2014Q2

Orders Per 1000 Members

WLA  WH  SD  SB  RIV  PC  OC  LA  KC  FON  DNY  BPK  AV  SCAL
30.8  39.0  47.3  35.0  42.2  44.4  35.9  38.9  50.4  34.3  33.0  34.8  40.1  39.9

Source: Clarity, MIA
Urine Culture SCAL Orders per 1000 Members
Female Members Ages 18–64
2011Q2–2014Q2

Source: Clarity, MIA
Non-Culture Approaches

- Instrumentation to screen out negative urine specimens
  - UF-1000i – Sysmex
  - iQ200 – Iris
  - sediMAX – Menarini Diagnostics

- Instrumentation – ID / quantitation directly from sample
  - POCARED Diagnostics

- Instrumentation – ID from sample (screened by other method)
  - Mass Spectrometry – bioMerieux, Bruker Daltonics
UF-1000i Technology

Automatic Classification

The UF-1000i utilizes laser-based fluorescent flow cytometry for precise particle counts unachievable by visual methods. Identification is based on the scatter produced as each cell passes through the laser. Fluorescence from highly specific stains helps accurately classify the particles through adaptive cluster analysis.

- Fluorescence
  - Stainability & Length
- Side Scatter
  - Internal complexity
- Forward Scatter
  - Size & Length
UF-1000i Technology: Every Cell has a “Fingerprint”

<table>
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<tr>
<th></th>
<th>Forward scattered light waveform</th>
<th>Lateral fluorescent light waveform</th>
<th>Lateral scattered light waveform</th>
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<tr>
<td>WBC</td>
<td><img src="image4.png" alt="Waveform" /></td>
<td><img src="image5.png" alt="Waveform" /></td>
<td><img src="image6.png" alt="Waveform" /></td>
</tr>
<tr>
<td>Bacteria</td>
<td><img src="image7.png" alt="Waveform" /></td>
<td><img src="image8.png" alt="Waveform" /></td>
<td><img src="image9.png" alt="Waveform" /></td>
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<tr>
<td>Epithelial Cells</td>
<td><img src="image10.png" alt="Waveform" /></td>
<td><img src="image11.png" alt="Waveform" /></td>
<td><img src="image12.png" alt="Waveform" /></td>
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UF-1000i Technology: Adaptive Cluster Analysis
## References

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Journal/Details</th>
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<tbody>
<tr>
<td>Pieretti et al</td>
<td>JCM 2010</td>
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<tr>
<td>DeRosa et al</td>
<td>Clin Chim Acta 2010</td>
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<tr>
<td>Breoeren et al</td>
<td>JCM 2011</td>
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<tr>
<td>Manoni et al</td>
<td>Diag Micro Inf Dis</td>
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<tr>
<td>Wang et al</td>
<td>Microbiol and Inf Dis 2010</td>
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</tbody>
</table>
iQ200

- Urine analyzer that detects leukocytes, bacteria, and a new sediment indicator, the “all small particles” (ASP) coupled with an automated strip reader (iChem Velocity) (Iris Diagnostics)
- Urine content is analyzed by assessment of digital images of the particles passing in front of a microscope objective
- Sturenburg et al, JCM, August 2014, vol 52
  - Using cutoff of $\geq 10^4$ (and settings to achieve 95% sensitivity) they reduced their cultures by 30-35%
sedIMAX

- Automated urine sediment analysis
- Provides whole field images for the screening of urine samples
- Falbo et al. JCM, 2012

| TABLE 1 Performance of urine sediment analysis compared to dipstick analysis when urine culture positivity is established at $10^4$ CFU/ml |
|---|---|---|---|---|---|---|
| Test | Characteristics | Sensitivity | Specificity | PPV | NPV | FNR | FPR |
| Urine sediment | WBC > 4 cells/HPF, bacteria > 10 elements/HPF | 98.3 | 59.0 | 34.9 | 99.4 | 1.7 | 41.0 |
| Dipstick | Leukocyte esterase > 25 leu/μl, nitrites positive, blood > 0.03 erythrocytes/μl | 33.1 | 98.6 | 82.4 | 88.2 | 66.9 | 1.4 |
POCARED's P-1000™ is an automated rapid system that employs intrinsic fluorescence, optical data analysis and specific algorithms to analyze multi-dimensional optical characteristics of microorganisms. The instrument captures the emitted light from the interaction between photons and molecules to detect the pathogens' unique optical properties and subsequently an algorithm determines identification and quantitation.
2 Independent Platforms

- Optical Cup
- P-1000™ Disposable
- SP Disposable
- P-1000™ Analyzer
- Carousel Docking Station
- SP: Sample Processor
**Workflow processing**

Specimen screening (Pos/Neg), Organisms identification and enumeration

The entire process including sample preparation, analysis and results reporting, takes approximately 20 minutes for a single sample and 2 hours for a full batch of 42 samples.

Both the SP and P-1000™ analyzer can be operated by a lab assistant versus lab technician.

Flexible P-1000™ user interface provides several reporting options catering to the lab technician's needs and is fully compatible with existing lab information systems.

- The POCARED sample preparation system is based on mechanical filtration and a proprietary wet foam elution.
- Target cells are re-suspended into a user selected buffer/matrix with adjustable output volume (down to 100µl), providing purified and concentrated sample.
- Each microorganism can be identified through its unique optical properties in response to UV wavelengths.
- Eliminates the need for culture.
- “Gold standard” accuracy.

Analytical data includes the organism's enumeration and species identification.

Additional information includes any errors occurred while processing the sample.

KAISER PERMANENTE
CULTURE-FREE Microbiology®

- Time to actionable results: Sample preparation, analysis and report generation
  - Single sample: 20 minutes
  - A batch of 42 samples: 2 Hours

- Preservative and/or Non-preservative tubes/containers are supported

- SP and P-1000™ Platforms are designed for laboratory assistant operation

- P-1000™ will have interfacing capabilities

- The SP and P-1000™ are in clinical evaluation as part of a multi-center study

¹ Assumes a 42 sample batch
### Initial evaluation of 1073 seeded & clinical specimens

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>Sensitivity %</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>220</td>
<td>96</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>110</td>
<td>94</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>135</td>
<td>96</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>112</td>
<td>93</td>
</tr>
<tr>
<td>E. cloacae</td>
<td>132</td>
<td>92</td>
</tr>
<tr>
<td>S. saprophyticus</td>
<td>109</td>
<td>100</td>
</tr>
<tr>
<td>P. mirabilis</td>
<td>81</td>
<td>93</td>
</tr>
<tr>
<td>Candida albicans</td>
<td>93</td>
<td>91</td>
</tr>
</tbody>
</table>

Pezzlo, 2007 ASM General Meeting
Mass Spectrometry

- MALDI-TOF – *Matrix-assisted laser desorption ionization-time of flight* mass spectrometry
- Reliable method for culture ID
- Ferreira et al. JCM 2010
  - 4 ml urine centrifuged (2000xg – remove WBC) and (15,000xg – collect bacteria)
  - Pellet washed and applied to mass spec template
- Sanchez-Juanes et al. JCM 2014
  - Improve mass spec ID with urine pretreatment with SDS
### Ferreira et al. JCM 2010

<table>
<thead>
<tr>
<th>Process</th>
<th>n</th>
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<tbody>
<tr>
<td>Screened by u1000i and processed for culture and MALDI</td>
<td>260</td>
</tr>
<tr>
<td>Positive by u1000i/negative culture/negative MALDI</td>
<td>20</td>
</tr>
<tr>
<td>Significant growth single org</td>
<td>235</td>
</tr>
<tr>
<td>Significant &gt;10^5 growth by culture (1 organism)</td>
<td>220</td>
</tr>
<tr>
<td>Maldi ID @ genus level</td>
<td>202(92.7%)</td>
</tr>
<tr>
<td>Maldi ID @ species level</td>
<td>163(91.8%)</td>
</tr>
</tbody>
</table>
In Summary

- There are many facets to managing urine specimen integrity
  - New guidelines will be forthcoming next year from ASM

- Guidelines for working up urine cultures available through IDSA and other entities
  - Institutional preferences may prevail

- Many options are available for specimen work up – each laboratory should look at specific parameters for culture setup to meet individual needs

- Automation may have a role in providing valuable feedback to clinicians that might obviate the need for a urine culture

- Newer automation could provide identification/quantification without culture

- Depending on the patient population uncomplicated urinary tract infections can be treated empirically which can have a significant impact not only on urine cultures volumes but care access
Thank you

Becton Dickinson
Sysmex
POCARED