Laboratory diagnosis of UTI revisited

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Background

• UTI accounts for
  – 3% of GP consultations
  – 12% of antibiotic prescriptions in general practice

• UTI associated bacteraemia is the commonest cause of community acquired bacteraemia in the UK

• In nursing homes, UTI is the 3rd commonest cause for antibiotic prescription
Why revisit diagnosis of UTI?

• Continuing high level of contamination of specimens received in the lab
• Implication of introduction of new technology and automation
  – Digital imaging replacing microscopy
  – Laboratory automation (Kiestra)
• Diminishing laboratory and clinical expertise in interpreting results
• Antibiotic stewardship
Pre-analytical stage

• Clinical Information on Test requests:
  – Reason for test
  – Description of symptoms, esp. frequency
  – Type of specimen and time of collection
  – Prior antibiotic treatment
  – Underlying clinical condition if any
  – Dipstick result
Collection of urine

• Hierarchy of collection methods
  – Suprapubic aspirate
  – Midstream urine or Clean-catch urine
  – In & Out catheter
  – Bag urine (babies and young children)
  – Catheter port
Suprapubic aspirate


Indications for SPA

- Urinary retention (eg, prostate hypertrophy or cancer, gynecologic malignancy, spinal cord injury)
- Urinalysis or urine culture in neonates or children younger than 2 years (Nelson JD, Peters PC. Suprapubic aspiration of urine in premature and term infants. Paediatrics 1965;36:132)
- Phimosis
- Chronic infection of the urethra or periurethral glands
- Urethral stricture
- Urethral Trauma
Clean catch or midstream of urine

• First part of urine contaminated by urethral bacteria. Distal part of urethra colonised in
  – a third of males (Helmholz HE. Determination of bacterial counts of the urethra; a new method, with results of study of 82 men. Journal of Urology 1950;64:158-156)
  But
  – Recent randomized study found that no difference in contamination rates between samples obtained with no technique (not MSU and no cleansing: 29% contaminated; n = 77), samples obtained MSU with perineal cleansing and spreading of the labia and samples obtained MSU with perineal cleansing and a vaginal tampon in place (31% contaminated, n = 81).

• Prospective study obtained a series of urine samples (a new sample was obtained each day for 8 days, using a different set of instructions each day) from 111 healthy young women.

• No significant difference in contamination rates between the following techniques: no precautions (31%), MSU (23.9%), MSU with perineal cleansing (20.4%), MSU and holding labia apart (21.1%). However, holding the labia apart as the sole technique was associated with a lower contamination rate (13%) in this study.

MSU and MSU with prior cleansing were obtained during consecutive urinations in a series of 105 asymptomatic female health care workers. 64% of samples obtained by each method were found to be contaminated.

Conclusions of the Horizon scanning report

• No NICE or SIGN guidelines on sample collection or interpretation of results in the elderly
• No studies on external urine collection devices in elderly females
• No research on urine collection in last decade
• If validated, alternative collection methods are likely to be more cost-effective than SPA, Clean catch and in/out catheters
• Large well designed studies needed to evaluate the alternative methods
• Observational studies needed to see how urines are collected in the elderly
Cleancatch® Midstream collection device (previously Whiz midstream collection device)

• Rationale: Difficult to collect MSU in females without getting hands and external surface wet. (I am told)

• What does the device do:
  – (as stated in Jackson et al) "is not simply a funnel, but incorporates a flow-sensitive channel and diverter that, using urodynamic principles, excludes the initial low-flow portion of the urinary stream, thus discarding the contaminated early stream volume, and automatically collects the midstream volume without interrupting the stream."
Figure 1: The CleanCatch® Midstream device

**Automatic Capture**
The CleanCatch® Midstream™ device automatically captures a midstream urine sample and prevents overfilling of the sample tube.

- Midstream Urine
- Air released from the sample tube as it fills
- Initial Stream Urine
FIG. 1. Diagrammatic representation of the UCD and instructions for use.

Procedure for Use:

1. Remove cap and firmly attach the tube.

2. Use sitting... Urinate normally — no need to pause while passing urine.
   or hovering...
   or standing.

3. Detach the specimen and replace cap.

4. Dispose of device as instructed.

STERILE Do not touch the inside of the device or sample tube.
SINGLE USE ONLY

Table 1: Semi – quantitative culture results for urine specimens from conventional and CleanCatch® Midstream collections

<table>
<thead>
<tr>
<th>Culture result</th>
<th>Number of specimens</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Conventional</td>
<td>CleanCatch® Midstream UCD</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>No significant growth</td>
<td>902</td>
<td>927</td>
<td>1829</td>
<td></td>
</tr>
<tr>
<td>Equivocal single species</td>
<td>17</td>
<td>16</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Equivocal mixed growth</td>
<td>122</td>
<td>89</td>
<td>211</td>
<td></td>
</tr>
<tr>
<td>Heavy mixed growth</td>
<td>33</td>
<td>13</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>UTI</td>
<td>31</td>
<td>32</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1105</td>
<td>1077</td>
<td>2182</td>
<td></td>
</tr>
</tbody>
</table>

Notes: UTI was defined as >100,000 CFU/ mL with 1 or 2 different organisms identified.

Those using the UCD preferred it to the conventional method (67.5%) and experienced significantly less spillage during sample collection (27% vs 46%)
• Midstream Contamination rate 4% (Dryden et al. Improving the quality of midstream urine with a collection device. Poster-D1591. ICCAC, 2007)

• NHS Evidence-based Purchasing Centre 07004, January 2008
  – Acquisition costs: universal- £ 0.09; MSU collection device- £1.12
  – Minimum cost savings of £1.69 when cost of recall, retesting, treatment etc included.
  – Significant potential
  – Available through NHS supplies
Collection of urine in the elderly

• In and out catheter became unpopular because risk of causing UTI (Beeson PB. The case against catheter. American Journal of Medicine. 1958;24:1-3)

• SPA and in-out catheter are now considered as reference methods in the elderly.

• Alternative methods of collection
  – Condom drainage
  – Diapers
CSU

• When to send a sample for culture in people with catheters: expert opinion is that no constellation of symptoms and signs can accurately predict the likelihood of a symptomatic UTI in catheterised people (and therefore, the need to send a sample for culture).

• Elderly people: People with an indwelling catheter: expert consensus is that the minimum criteria for initiating antibiotics for bacteriuria include the presence of at least one of the following: fever, new costovertebral tenderness, rigors, or new onset delirium.

Automation in urine microbiology: Microscopy

- SediMAX

Processes 80 urines/hr

Built-in microscope and image processing software. Able to identify & count range of particles. High quality images on screen
Advantages

• Faster
• More efficient. Can be used to rationalise culture only on urines with WBCs or organisms
• Less inter-operator variation
• Identifies cells more accurately
• Archiving system and Easy to review at bench rounds
• Excellent for teaching and prevention of de-skilling
• Manual over-ride if necessary
Disadvantages

• Occasional inaccuracies, eg misidentifying RBCs and yeasts
• Capital and maintenance costs
• Occasional breakdown
• Lacks versatility of BMS
Total Lab Automation: A conceptual leap

- The BD Kiestra™ TLA (Total Lab Automation) solution provides a flexible, customizable and high performance system.
- The BD Kiestra™ TLA system optimizes workflow as workbenches are connected to the system and will offer integration of a growing family of scalable BD automation modules such as the BD Bruker™ MALDI Biotyper™ automated ID and the BD Phoenix™ automated AST instruments.

Adapted from: BD product website
Are there any disadvantages of Kiestra (personal impressions)

- Capital and maintenance costs
- Complete change in the way of working of the lab – the tail that wags the dog!
- Inoqula module used for liquid specimens (e.g., urine) can be temperamental and needs one plate/urine (Goodbye, Leigh-Williams filter paper method – 8-12 urines/plate)
- Identifying colonial morphology from images of the plates takes some practice
- Can’t smell the plates!
Interpretation of results: Symptomatic bacteriuria

• > $10^5$/ml cfu in most cases but can readily be reduced to $10^4$/ml due to high fluid intake, frequency, recent or current antibiotics, low pH, high urea or osmolality. (Sanderson P. Laboratory methods in Urinary Tract Infections. 1998. Ed: Brumfitt W, Hamilton-Miller J and Bailey R. Chapman & Hall Medical)

• 50% of symptomatic women with coliforms in SPA or in-out catheterisation have counts less than $10^5$/ml cfu (Stamm et al. Diagnosis of coliform infection in acutely dysuric women. NEJM 1982;307:463-468)
European Urology Association guidelines (2013) for microbiological diagnosis of UTI

- $\geq 10^3$/ml cfu of uropathogens in MSU of women with acute uncomplicated cystitis
- $\geq 10^4$/ml cfu of uropathogens in MSU of women with acute uncomplicated pyelonephritis
- $\geq 10^5$/ml cfu of uropathogens in MSU of women or $\geq 10^4$/ml cfu in MSU of men or straight catheter urine in women, in complicated UTI
- Any number of organisms are significant in SPA
- Asymptomatic bacteriuria requires two cultures ($\geq 10^5$/ml cfu) showing same strain/species taken 24 hours apart
European Federation for Urinalysis Guidelines

- **Laboratory decision-limits for significant bacteriuria:** The cut-offs for symptomatic urinary tract infection caused by primary pathogens (E. coli and S. saprophyticus) are set at $\geq 10^3$ CFU/mL in mid-stream urine specimens.

- **For secondary pathogens (such as Enterobacter species, Enterococcus species, Klebsiella species, P. mirabilis, P. aeruginosa etc)** cuts off are set as $\geq 10^4$ cfu/mL for women and $\geq 10^3$ CFU/mL for men.

Interpretation of Mixed Cultures

- Predominant organism should be reported if $\geq 10^4$/ml cfu if pus cells present (reporting bias in favour of GNR?) in symptomatic patients
- More mixed cultures with 10µl as for Inoqula (Kiestra/BD) (Personal observation)
- 11% of mixed cultures from clean catch specimens represent treatable infections
- Higher rates of significant mixed bacteriuria in the elderly common (up to 30%) esp in patients with vesicovaginal fistula, incomplete emptying and catheters
Enterococci: Over-reported?

- Gut carriage: $10^4$/ gram of faeces
- Commonly colonises perineum
- Reports of increasing prevalence of enterococcal UTI, especially in nosocomial infections and secondary to instrumentation
- But frequently associated with epithelial cells and over 50% of urines with significant enterococcal bacteriuria have no pyuria (Personal observation)
- Only 1 in 4 MSUs with enterococcal bacteriuria confirmed by in-out catheterisation
- 50% of patients with significant bacteriuria are asymptomatic and 50% of these patients received antibiotics.

  H.N. Khair et al. Vancomycin resistance has no influence on outcomes of enterococcal bacteriuria. Journal of Hospital Infection 85 (2013) 183e188
Conclusions

• Provision of clinical details on the test request and collection of uncontaminated urine specimen remains a challenge but devices available.
• Lab automation will improve processing of specimens but may present new challenges such as increased reporting of mixed growths.
• Lab/medical staff should be aware of:
  – Lower limits of CFU/ml for symptomatic UTI
  – Mixed growths that can be significant
  – Enterococci that can be frequently contaminants