



# ***"Urine Cultures"***

## ***Relevance and Best Practices***

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# THIS IS YOUR DAY; THIS IS YOUR FORUM



Interpretation variability/confusion

Role of the urinalysis

Asymptomatic bacteriuria

Method/processing differences

Quality assurance measures

Organism-specific examples

Report commentary

Algorithm examples

LET'S TALK



# iCLICKER ICE BREAKER i



Which reflexive urinalyses are offered by your laboratory?

- A. UA macroscopic to UA microscopic
- B. UA microscopic to urine culture
- C. UA macro to UA micro to urine culture
- D. We offer several permutations of reflexive options that may eventually end up in culture.
- E. We do not offer reflexive culture off of UA.



# iCLICKER ICE BREAKER ii



For laboratories that employ urinalysis reflex to culture...  
how's it working?

- A. Great
- B. We still culture a lot of dirty urines.
- C. Providers still request a culture even when it does not reflex.
- D. Where is choice D?

 <b>ICE BREAKER BINGO</b>				
FIND SOMEONE WHO...				
HAS A BIRTHDAY THIS MONTH	HAS TRAVELED OUTSIDE THE COUNTRY	CAN PLAY AN INSTRUMENT	HAS A TATTOO	CAN SPEAK A FOREIGN LANGUAGE
IS AN ONLY CHILD	IS A LEFTY	ACTUALLY FLOSSES THEIR TEETH EVERYDAY	HAS A FOOD ALLERGY	PLAYED ON A SCHOOL SPORTS TEAM
WATCHES REALITY TELEVISION	RAN A MARATHON	 FREE SPACE	HAD BRACES	HAS BROKEN A BONE
HAS LIVED IN ANOTHER STATE/COUNTRY	HATES MATH	LOVES TO SING KARAOKE	HAS MET A CELEBRITY	HAS NEVER SEEN A STAR WARS FILM
HAS A PET	CAN TOUCH THEIR TOES	HAS A FACEBOOK ACCOUNT	DISLIKES CHOCOLATE	MADE A NEW YEAR'S RESOLUTION AND KEPT IT



# iCLICKER ICE BREAKER iii



Do you have access to EHR (beyond what is given on LIS “workcard”) when working up urine cultures?

- A. No
- B. No; instead, I utilize the LIS to check urinalysis results.
- C. Yes, but I do not refer to it.
- D. Yes, I utilize it when “making my decisions”.
- E. I’m confused; it’s gonna be a long day.



# Case One



65-year-old male seen in ED for fall;  
midstream urine



# iCLICKER FOR REAL 1



What would you do with this culture?

- A. Identification and susceptibility
- B. Identification only
- C. Report out as contamination
- D. I need additional information (i.e., urinalysis result).
- E. Ask the boss



# Case Two

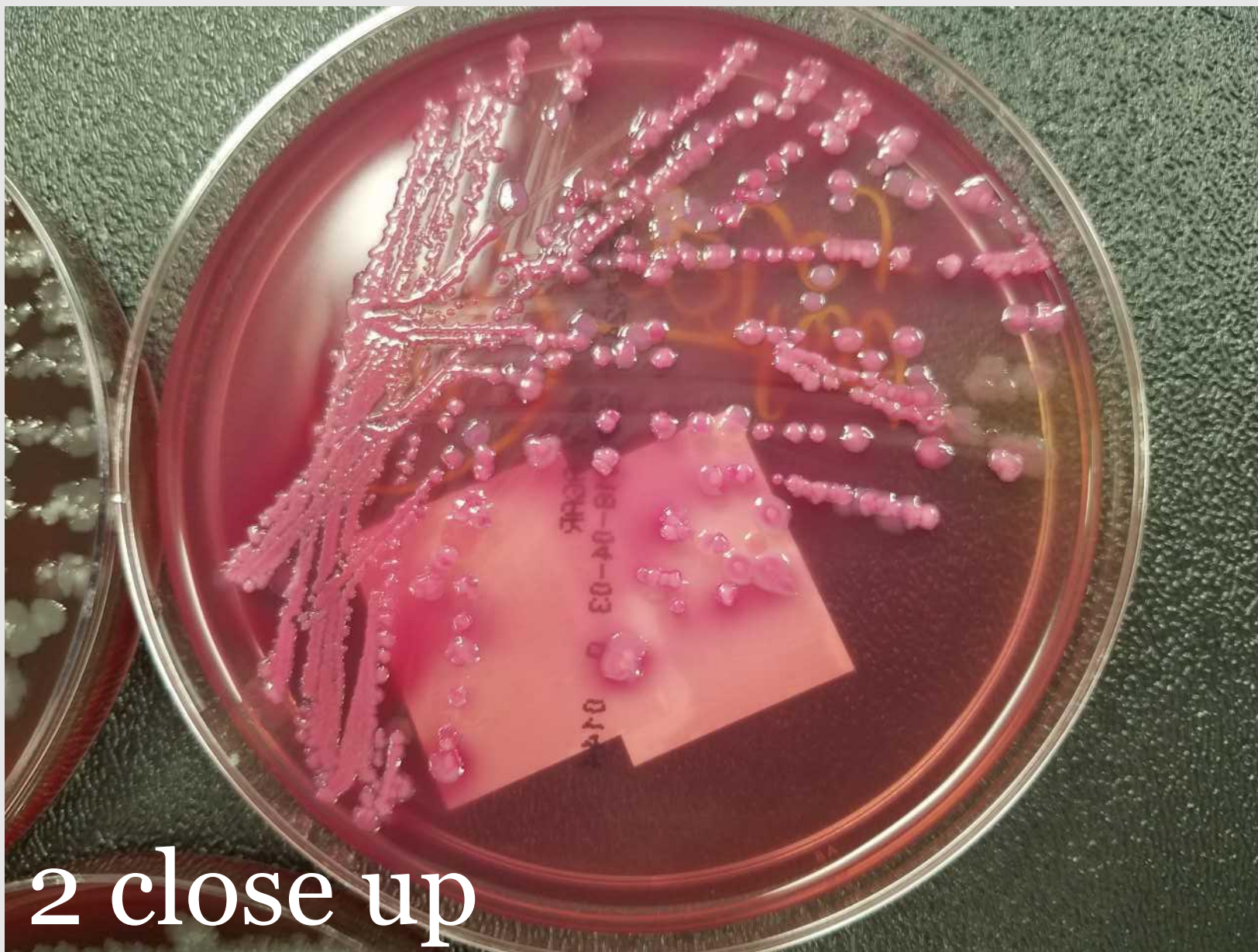


51-year-old male seen in urology for incontinence;  
urine from indwelling catheter



2





2 close up

# iCLICKER FOR REAL 2



What would you do with this culture?

- A. Identification and susceptibility
- B. Identification only
- C. Report out as contamination
- D. I need additional information (i.e., urinalysis result).
- E. Ask the boss



# One laboratory reported...



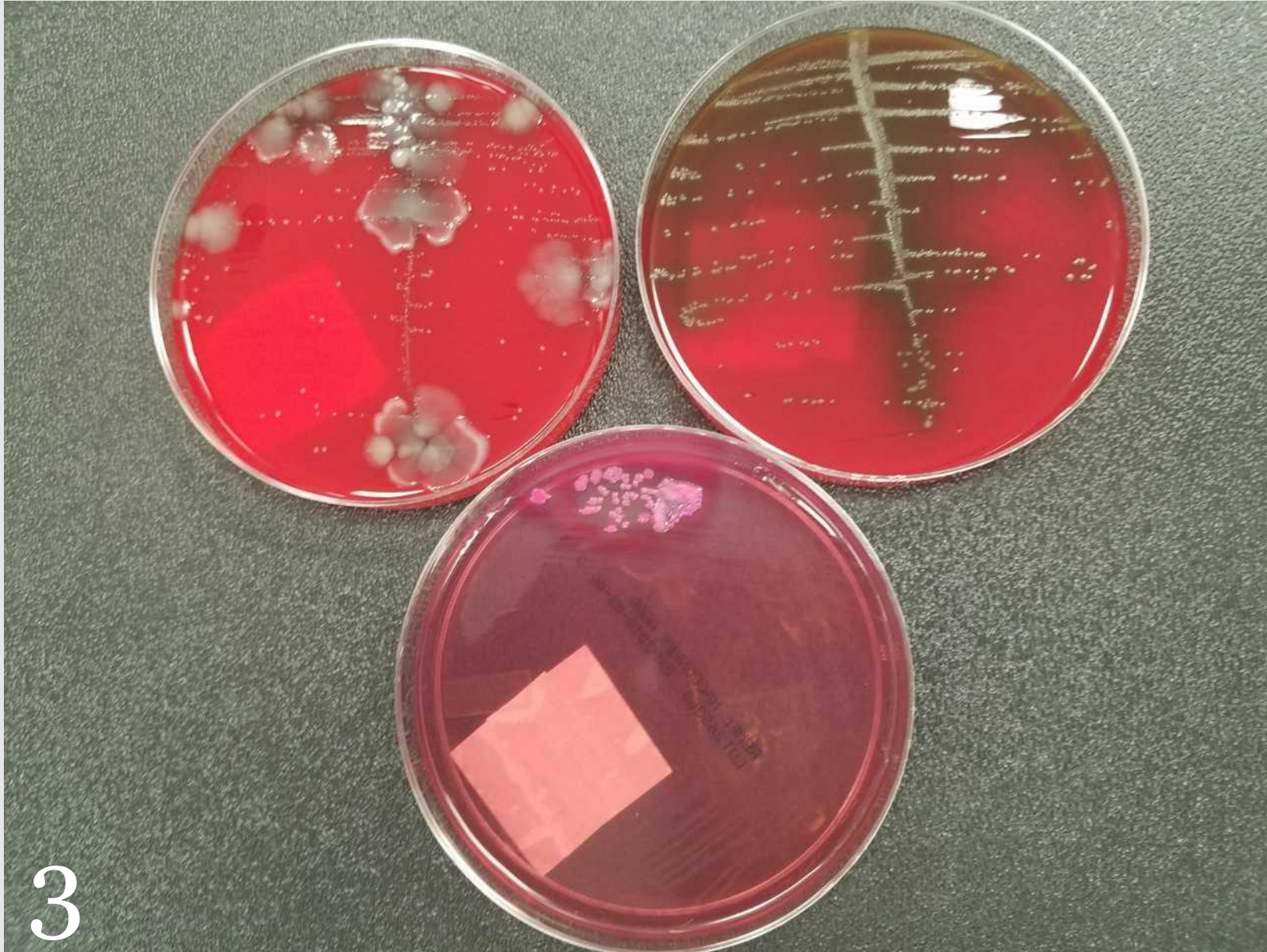
>100,000 org/mL mixed types Gram-negative rods  
No further workup performed. Foley cath specimen has >3 organisms. Suspect possible colonization. Recommend changing Foley prior to recollection.

>100,000 org/mL mixed contaminants

# Case Three

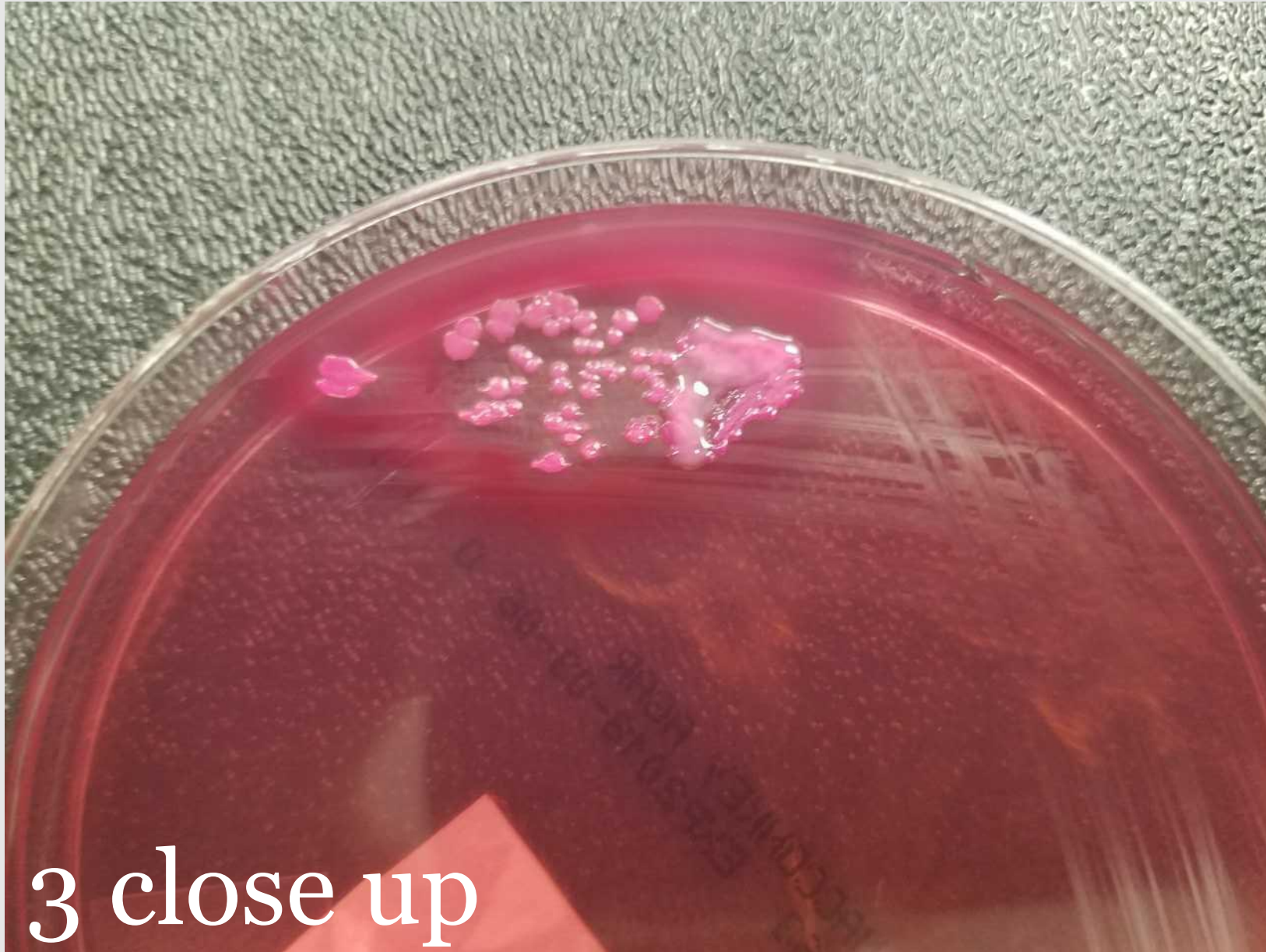


65-year-old male seen in clinic for confusion;  
midstream urine



3





3 close up



# iCLICKER FOR REAL 3a



What would you do with this culture?

- A. Identification and susceptibility for all isolates
- B. Identification and susceptibility for GNRs
- C. Identification of GNRs
- D. Report out as contamination
- E. Ask the boss



# *What if we gave you this...*



Nitrites	negative
Leukocyte esterase	moderate
Epithelial cells/HPF	6-10
Leukocytes/HPF	too numerous to count
Bacteria	3+

# iCLICKER FOR REAL 3b



Now...what would you do with this culture?

- A. Identification and susceptibility for all isolates
- B. Identification and susceptibility for GNRs
- C. Identification of GNRs
- D. Report out as contamination
- E. Ask the boss

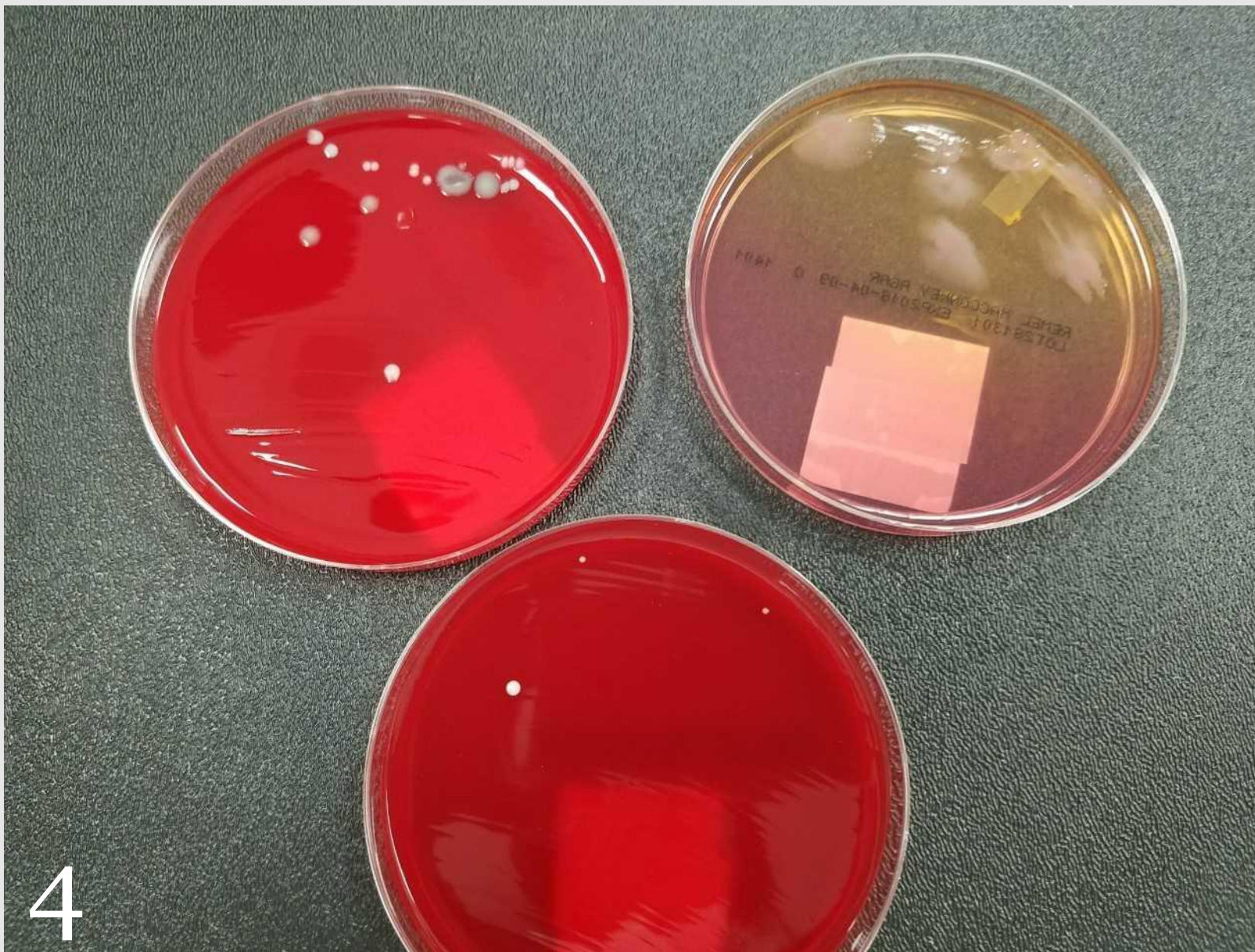


# Case Four



65-year-old female seen in clinic for dysuria;  
midstream urine





4

# iCLICKER FOR REAL 4a



What would you do with this culture?

- A. Identification and susceptibility for all isolates
- B. Identification of GNRs
- C. Nothing major due to low colony count
- D. Report out as contamination
- E. Ask the boss

# *What if we gave you this...*



Nitrites	negative
Leukocyte esterase	moderate
Epithelial cells/HPF	none
Leukocytes/HPF	11-20
Bacteria	1+

# iCLICKER FOR REAL 4b



Now...what would you do with this culture?

- A. Identification and susceptibility for all isolates
- B. Identification of GNRs
- C. Nothing major due to low colony count
- D. Report out as contamination
- E. Ask the boss



*Oh, by the way...*



Nitrites	negative
Leukocyte esterase	moderate
Epithelial cells/HPF	none
Leukocytes/HPF	11-20
Bacteria	1+

**PATIENT WAS TREATED WITH CIPROFLOXACIN**

# ROLE OF URINALYSIS



- Urinalysis results can, among other things, help determine if there is indication of urinary tract infection
- Providers interested in nitrites, leukocyte esterase, blood
- ...a positive urinalysis indicates presence of a bacterial infection, right?

**EXCEPT WHEN IT DOESN'T**

# POSITIVE PREDICTIVE VALUE



- Positive predictive value for pyuria ranges from 4-32%

*J Clin Microbiol.* 54:254-258; 2016

- Positive predictive value for urinalysis ranges from 31-46%

*Clin Biochem.* 46:1285-1289; 2013

*Open Forum Infect Dis.* 1:ofu219; 2014

*Am J Emerg Med.* 27:930-932; 2009

# INTERNAL AUDIT



- Standardization of urine culture interpretation guidelines per *Clinical Microbiology Procedures Handbook*
- Retrospective assessment of 3628 urine cultures emanating from urinalysis reflex
- Arbitrary microbiology (culture) scoring system
  1. Pure culture pathogen
  2. Predominant pathogen (minimal contaminants)
  3. Pathogen = contaminants



# INTERNAL AUDIT



- Standardization of urine culture interpretation guidelines per *Clinical Microbiology Procedures Handbook*
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- Arbitrary microbiology (culture) scoring system
  - 1. Pure culture pathogen
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  - 3. Pathogen = contaminants

**STRINGENT**  
criteria

# INTERNAL AUDIT



- Standardization of urine culture interpretation guidelines per *Clinical Microbiology Procedures Handbook*
- Retrospective assessment of 3628 urine cultures emanating from urinalysis reflex
- Arbitrary microbiology (culture) scoring system
  1. Pure culture pathogen
  2. Predominant pathogen (minimal contaminants)
  3. Pathogen = contaminants

Less-stringent  
criteria

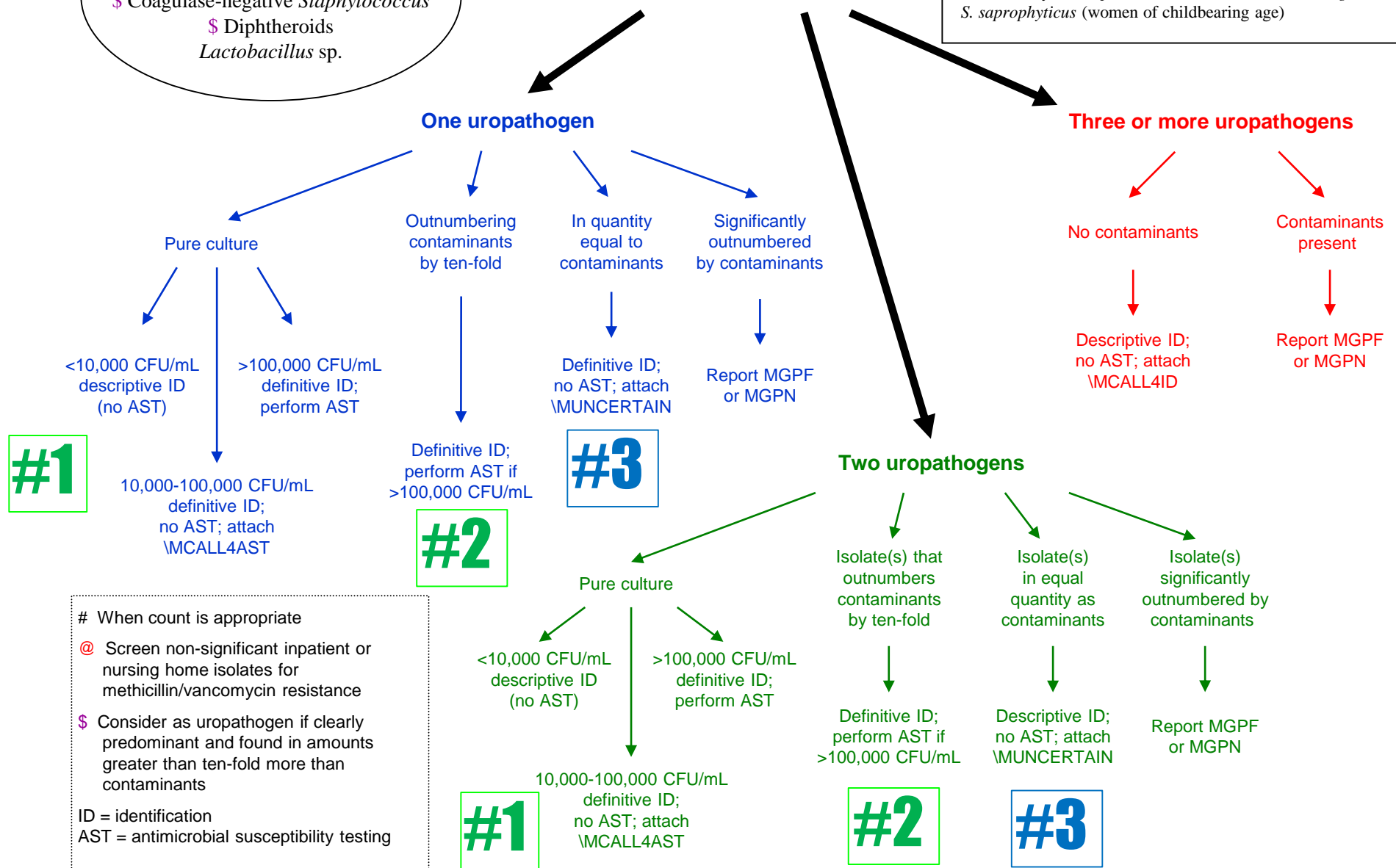


**Contaminants**  
 Viridans group *Streptococcus*  
*Neisseria* sp.  
 \$ Coagulase-negative *Staphylococcus*  
 \$ Diphtheroids  
*Lactobacillus* sp.

**Potential pathogens#**

Gram negative bacilli	\$ <i>Gardnerella vaginalis</i>
@ <i>Staphylococcus aureus</i>	\$ <i>Aerococcus urinae</i>
@ <i>Enterococcus</i> species	<i>Candida albicans</i>
Beta-hemolytic <i>Streptococcus</i>	<i>Candida glabrata</i>
<i>S. saprophyticus</i> (women of childbearing age)	

**Midstream urine**



**#1**

**#2**

**#3**

**#1**

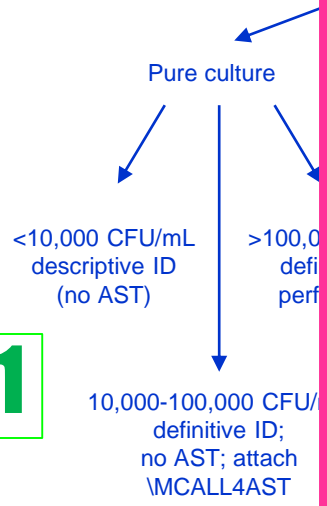
**#2**

**#3**

# When count is appropriate  
 @ Screen non-significant inpatient or nursing home isolates for methicillin/vancomycin resistance  
 \$ Consider as uropathogen if clearly predominant and found in amounts greater than ten-fold more than contaminants  
 ID = identification  
 AST = antimicrobial susceptibility testing



**Contaminants**  
 Viridans group S.  
*Neisseria*  
 \$ Coagulase-negative  
 \$ Diphtheroids  
*Lactobacillus*



#1

# When count is appropriate  
 @ Screen non-significant isolates from nursing home isolates for methicillin/vancomycin resistance  
 \$ Consider as uropathogen if predominant and found in greater than ten-fold more than contaminants  
 ID = identification  
 AST = antimicrobial susceptibility

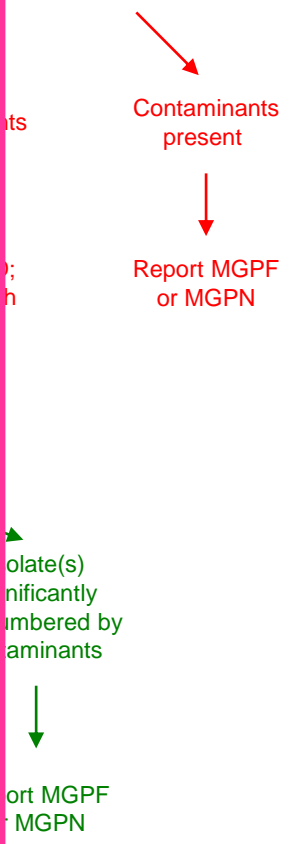
**Table 3.12-1 Urinary microbiota<sup>a</sup>**

Microbiota	Organism	Extent of workup if count is appropriate per Table 3.12-5
Urogenital	Viridans group streptococci, <i>Neisseria</i> spp., diphtheroids, <i>Lactobacillus</i> spp., anaerobes	Report as urogenital microbiota.
Skin	Diphtheroids, <i>Staphylococcus</i> spp.	Report as skin or with urogenital microbiota unless present in amounts >10-fold more than other microbiota. Then treat as below.
Uropathogens	Gram-negative bacilli <i>Staphylococcus</i>	ID to species level and AST ID and AST of <i>S. aureus</i> ; ID of <i>S. saprophyticus</i> with novobiocin disk for females of childbearing age; AST generally not needed for <i>S. saprophyticus</i> or other coagulase-negative staphylococci.
	Yeasts	ID of <i>C. albicans</i> and <i>Candida glabrata</i> ; ID of others to species level only on request
	Beta-hemolytic <i>Streptococcus</i> <i>Enterococcus</i> spp.	ID, especially of group B in women in childbearing years Check for VRE on inpatients; ID to species level and AST only if VRE and on request
	<i>Gardnerella vaginalis</i>	ID only if number is 10 times greater than that of all other microbiota
	<i>Aerococcus urinae</i>	ID only if number is 10 times greater than that of all other microbiota (41) (see Table 3.18.1-4b for tests to identify)
	<i>Corynebacterium</i> (urease positive)	ID and AST, if number is 10 times greater than that of all other microbiota and $\geq 10^5$ CFU/ml.
Bacteremia	All pathogens	Full identification and AST

<sup>a</sup> Abbreviations: AST, antimicrobial susceptibility testing; ID, identification; VRE, vancomycin-resistant enterococcus.

**Uropathogens<sup>#</sup>**  
 \$ *Gardnerella vaginalis*  
 \$ *Aerococcus urinae*  
*Candida albicans*  
*Candida glabrata*  
 (childbearing age)

**Urogenital uropathogens**





# NITRITES



<b>Result</b>	<b>n</b>	<b>Stringent</b>	<b>Less-stringent</b>
Negative	371	26.6%	28.6%
<b>Positive</b>	<b>641</b>	<b>70.8%</b>	<b>82.8%</b>

Percentages reflect “significant” urine culture findings, as previously defined.

# LEUKOCYTE ESTERASE



<b>Result</b>	<b>n</b>	<b>Stringent</b>	<b>Less-stringent</b>
Negative	1245	12.9%	13.7%
Trace	371	33.4%	35.6%
Small	619	25.2%	39.7%
Moderate	672	47.6%	53.4%
Large	715	58.0%	66.6%

Percentages reflect “significant” urine culture findings, as previously defined.

# LEUKOCYTES



<b>Result</b>	<b>n</b>	<b>Stringent</b>	<b>Less-stringent</b>
None seen	157	5.7%	5.7%
0-2/HPF	704	10.8%	11.9%
3-5/HPF	365	18.1%	19.2%
5-10/HPF	598	22.4%	24.2%
10-25/HPF	535	36.6%	40.2%
25-50/HPF	345	51.9%	57.1%
50-100/HPF	312	59.0%	66.0%
<b>&gt;100/HPF</b>	<b>612</b>	<b>66.5%</b>	<b>75.0%</b>

Percentages reflect “significant” urine culture findings, as previously defined.

# PREVIOUS REFLEX



- Positive nitrite

Result	n	Stringent	Less-stringent
Negative	2975	26.6%	28.6%
Positive	641	70.8%	82.8%

- Any leukocyte esterase plus  $\geq 5$  WBC/HPF

Result	n	Stringent	Less-stringent
Meets criteria	2151	47.7%	53.2%

- Observation of bacteria (catheterized urine)

Percentages reflect “significant” urine culture findings, as previously defined.



# REVISED REFLEX



- Positive nitrite

Result	n	Stringent	Less-stringent
Negative	2975	26.6%	28.6%
Positive	641	70.8%	82.8%

- Moderate to large leukocyte esterase

Result	n	Stringent	Less-stringent
Meets criteria	1387	53.0%	60.2%

- ≥ 25 WBC/HPF

Result	n	Stringent	Less-stringent
Meets criteria	1269	60.7%	67.9%

- Observation of bacteria (catheterized urine)

Percentages reflect “significant” urine culture findings, as previously defined.

# NEGATIVE PREDICTIVE VALUE



- Leukocyte esterase, nitrite, bacteria, >5 WBC/HPF each >98% in a low-prevalence ER setting

Clin Biochem. 46:1285-1289; 2013

- Higher-prevalence ER setting

Pyuria (>10 WBC/HPF)	92%
Bacteria	96%
Leukocyte esterase	93%
Nitrite	86%

J Emerg Med. 46:71-76; 2014

# iCLICKER FOR REAL



What is your threshold on IRIS for reporting “abnormal” on bacteria?

A. Trace

B. 1+

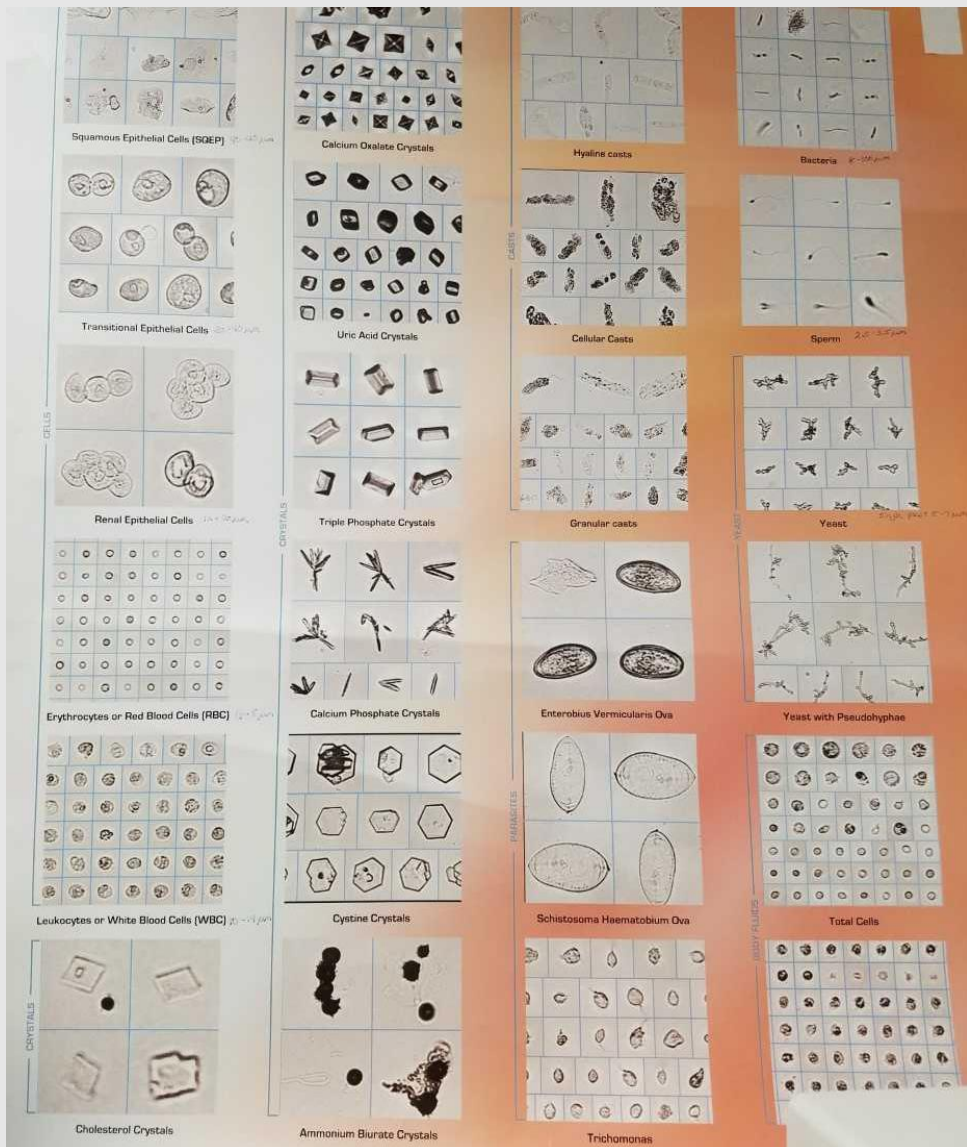
C. 2+

D. 3+

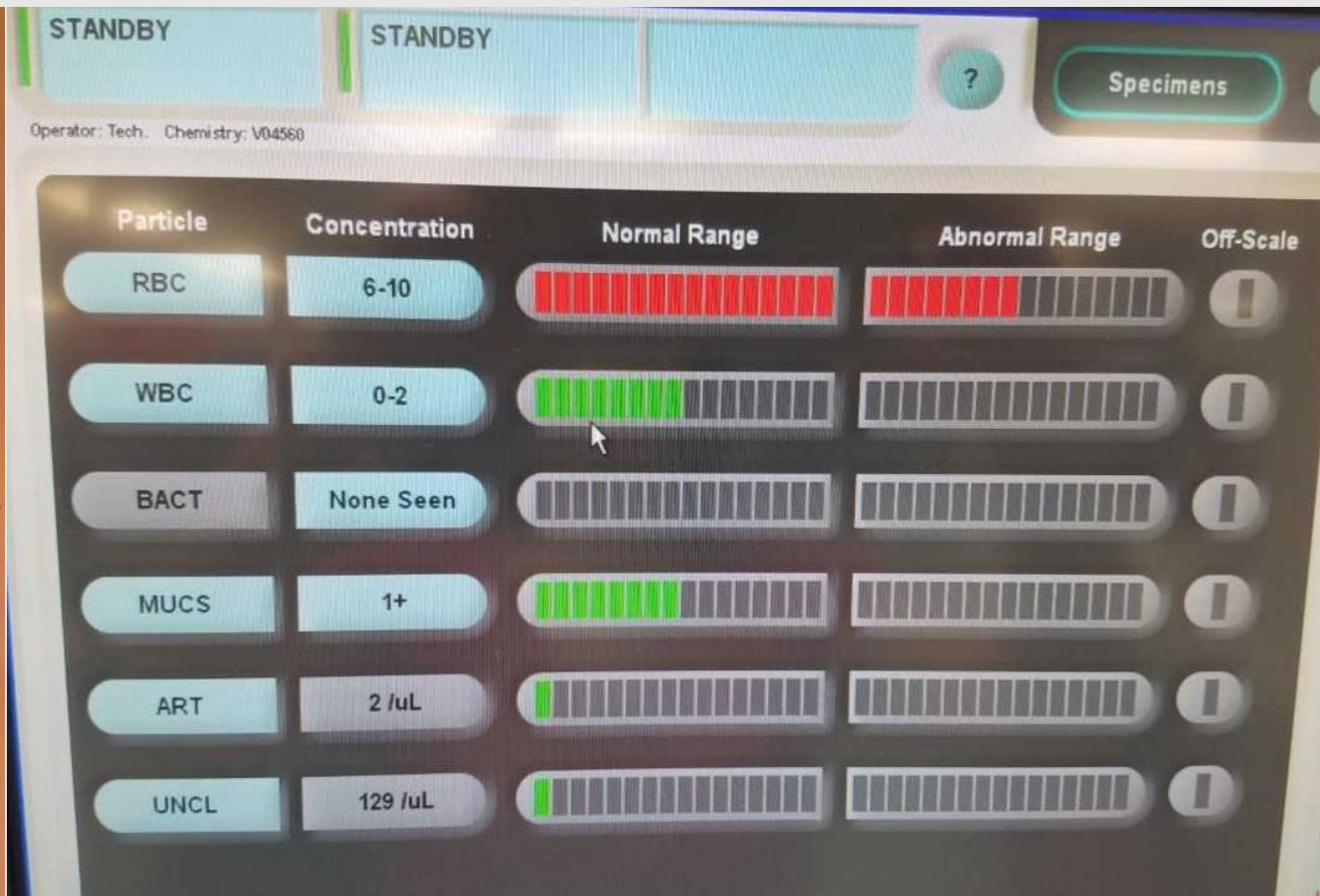
E. Isn't IRIS a member of Kingdom Plantae?







Iris Diagnostics iRICELL® images—the key to Gold Stand



iQ200 Series Urine Microscopy Analyzer

Move your urine microscopy forward with digital images



## Detection of Significant Bacteriuria by Use of the iQ200 Automated Urine Microscope

Enno Stürenburg,<sup>a</sup> Jan Kramer,<sup>a</sup> Gerhard Schön,<sup>b</sup> Georg Cachovan,<sup>c</sup> Ingo Sobottka<sup>a</sup>

TABLE 3 Optimized cutoff values for the iQ200 automated urine microscope

Scenario a (in the presence of bacteria)		Scenario b (in the absence of bacteria)	
All small particles (no. of pcls/ $\mu$ l) <sup>a</sup>	Leukocytes (no. of cells/ $\mu$ l)	All small particles (no. of pcls/ $\mu$ l)	Leukocytes (no. of cells/ $\mu$ l)
>2,000	>15	>8,000	>10
>1,700	>20	>6,500	>30
>1,400	>50	>5,000	>75
>1,200	>100	>4,000	>150
>1,000	>150	>3,000	>600
		>2,500	>1,000
		>2,000	>2,500

<sup>a</sup> pcls, particles.

# MODELING 95% SENSITIVITY...



Parameter	Specificity	No Further Culture
Leukocyte esterase	26.3%	16.3%
Nitrite	9.5%	7.4%
LE + nitrite	35.7%	21.3%
All small particles	44.2%	25.8%
Bacteria	18.5%	12.2%
Leukocytes	18.1%	12.0%
ASP + bacti + WBC	61.0%	34.8%
<b>Chem + Scope</b>	<b>60.6%</b>	<b>34.5%</b>

ASP, bacteria, and leukocyte combination was best predictor  
Could eliminate ~35% of culture set-ups

# LOCAL URINALYSIS REFLEX DATA (IRIS)



Parameter	IRIS User	Non-IRIS Users
UA reflex orders	585	2258
Reflexes (%)	140 (23.9)	679 (30.1) <sup>a</sup>
% pathogen	47.9	51.3 <sup>b</sup>
% contaminants	35.7	28.9 <sup>b</sup>
% no growth	16.4	19.9 <sup>b</sup>

<sup>a</sup> $P = 0.004$  versus percentage reflex from IRIS

<sup>b</sup>Remaining comparisons  $P \geq 0.11$

Eliminated ~20% of culture set-ups

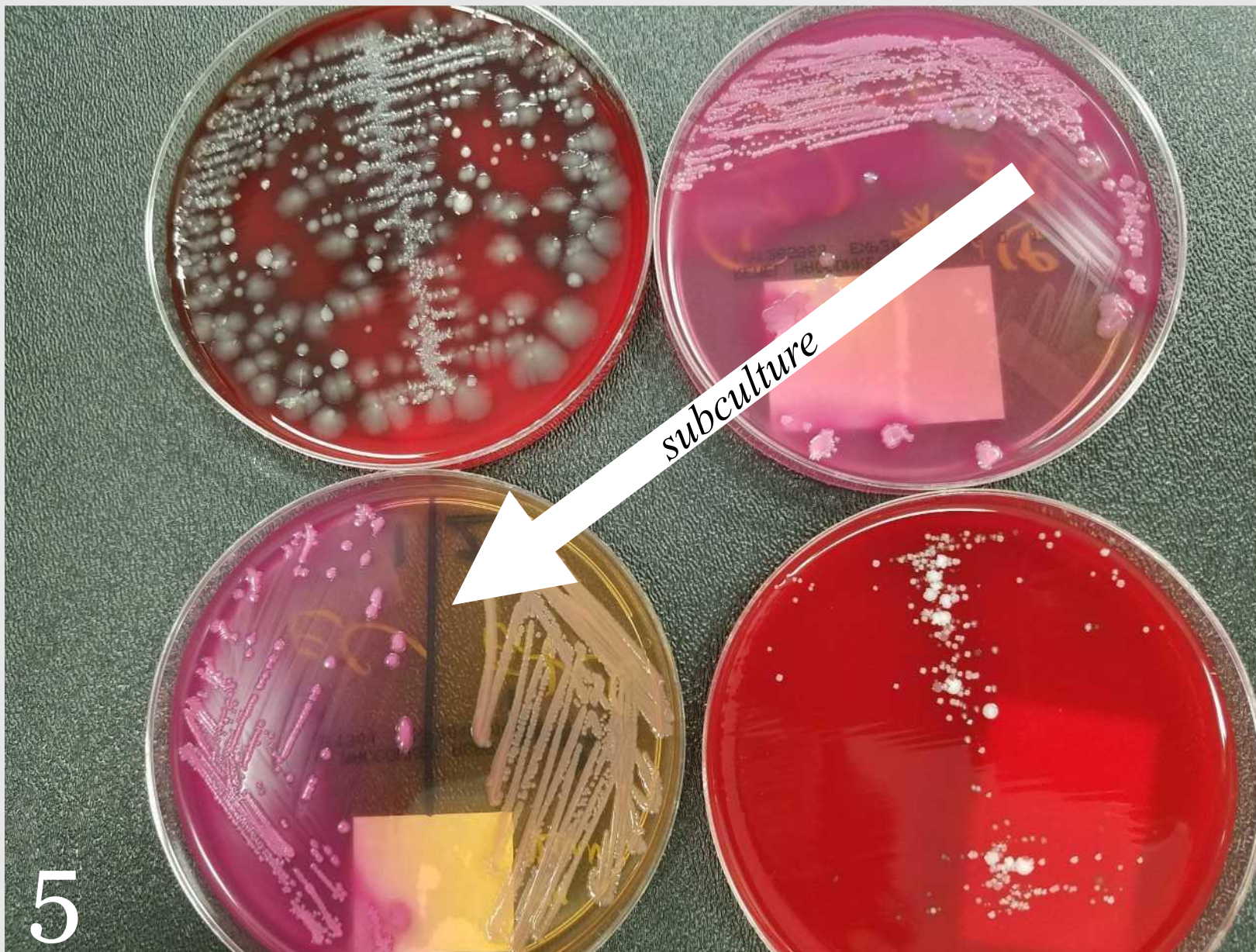
Courtesy Megan Selle



# Case Five



81-year-old female seen in ER for SOB and CHF;  
midstream urine



5

# iCLICKER FOR REAL 5



What would you do with this culture?

- A. Identification and susceptibility for all isolates
- B. Identification and susceptibility for GNRs
- C. Identification of GNRs
- D. Report out as contamination
- E. Ask the boss

# Oh, BTW...



Nitrites	negative
Leukocyte esterase	small
Epithelial cells/HPF	6-10
Leukocytes/HPF	too numerous to count
Bacteria	3+

**PATIENT WAS TREATED WITH CIPROFLOXACIN**

# Case Six



90-year-old female seen in ER for seizure;  
midstream urine





6

# iCLICKER FOR REAL 6



What would you do with this culture?

- A. Identification and susceptibility for all isolates
- B. Identification and susceptibility for GNR
- C. Identification of GNR
- D. Report out as >100,000 mixed contaminants
- E. Ask the boss

# Oh, BTW...



Nitrites	negative
Leukocyte esterase	small
Epithelial cells/HPF	0-2
Leukocytes/HPF	3-5
Bacteria	1+

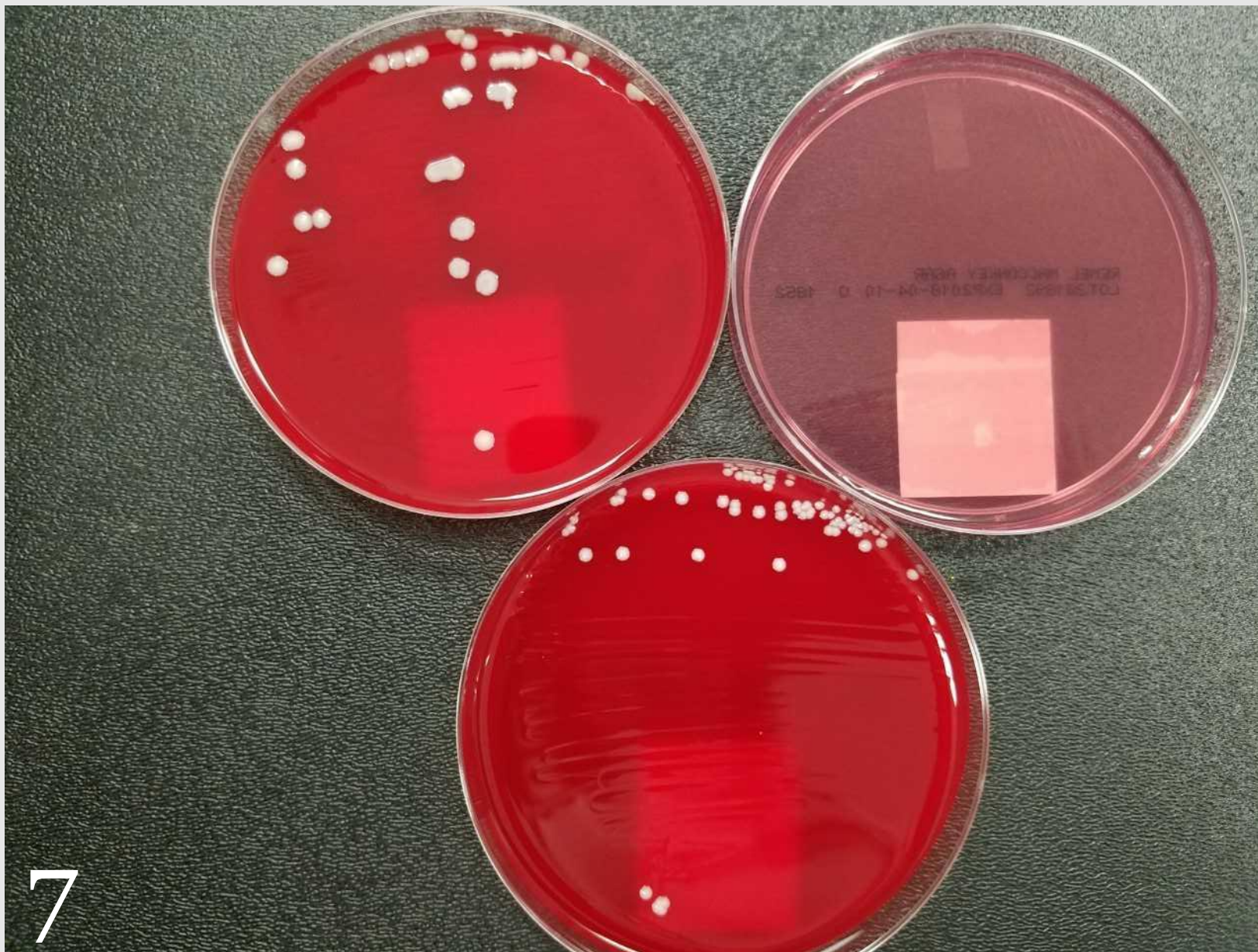
**PATIENT WAS TREATED WITH CIPROFLOXACIN**

# Case Seven



77-year-old female seen in ER for weakness, fatigue;  
midstream urine





7



# iCLICKER FOR REAL 7a



What would you do with this culture?

- A. Identification and susceptibility for GPC
- B. Identification of GPC
- C. Just generically report out low colony count
- D. Ask the boss
- E. I feel as if I am having my performance evaluation.

# *What if we gave you this...*



Nitrites	negative
Leukocyte esterase	trace
Epithelial cells/HPF	0-2
Leukocytes/HPF	21-50
Bacteria	trace

# iCLICKER FOR REAL 7b



Now...what would you do with this culture?

- A. Identification and susceptibility for GPC
- B. Identification of GPC
- C. Just generically report out low colony count
- D. Ask the boss
- E. I feel that I am still having my performance evaluation.

# iCLICKER FOR REAL 7b



Now...what would you do with this culture?

A. Identification and susceptibility for GPC

B. Identification of GPC

C. Just generically report out low colony count

D. Ask the boss

E. I feel that I am still having my performance evaluation.

**PATIENT WAS TREATED WITH CIPROFLOXACIN**

# ASYMPTOMATIC BACTERIURIA



- Common with advanced age or certain underlying conditions
- Poor predictor of urinary tract infection

Clin Infect Dis. 68:e83-75; 2019

**Table 1. Prevalence of Asymptomatic Bacteriuria Reported for Different Populations**

Population	Prevalence, %	Reference
<b>Children</b>		
Boys	<1	[7]
Girls	1–2	[8–10]
<b>Healthy women</b>		
Premenopausal	1.0–5.0	[11]
Pregnant	1.9–9.5	[11]
Postmenopausal (age 50–70 y)	2.8–8.6	[11]
<b>Persons with diabetes</b>		
Women	10.8–16	[12]
Men	0.7–11	[12]
<b>Elderly persons in the community (age ≥70 y)</b>		
Women	10.8–16	[13]
Men	3.6–19	[13]
<b>Elderly persons in a long-term care facility</b>		
Women	25–50	[13]
Men	15–50	[13]
<b>Persons with spinal cord injury</b>		
Intermittent catheter use	23–69	[14]
Sphincterotomy/condom catheter	57	[15]
<b>Persons with kidney transplant</b>		
First month posttransplant	23–24	[16, 17]
1 mo–1 y post-transplant	10–17	[16]
>1 y post-transplant	2–9	[16]
<b>Persons with indwelling catheter use</b>		
Short-term catheter	3%–5%/day	[18]
Long-term	100	[19]



# ASYMPTOMATIC BACTERIURIA



- Pyuria (positive leukocyte esterase or presence of WBC) is not diagnostic of asymptomatic bacteriuria

Present with ASB in 32% of young women

Present with ASB in 90% of elderly in long-term care facilities

Present with ASB in 90% of hemodialysis patients

- Bacteriuria (positive nitrite test, microscopic detection of bacteria) does not rule out contamination or asymptomatic bacteriuria

# Current Pyuria Cutoffs Promote Inappropriate Urinary Tract Infection Diagnosis in Older Women

Manu P. Bilsen,<sup>1,✉</sup> Margaretha J. Aantjes,<sup>1</sup> Esther van Andel,<sup>2</sup> Janneke E. Stalenhoef,<sup>3</sup> Cees van Nieuwkoop,<sup>4,5</sup> Eliane M. S. Leyten,<sup>6</sup> Nathalie M. Delfos,<sup>7</sup> Martijn Sibjom,<sup>5</sup> Mattijs E. Numans,<sup>5</sup> Wilco P. Achterberg,<sup>5</sup> Simon P. Mooijaart,<sup>8</sup> Martha T. van der Beek,<sup>9</sup> Christa M. Cobbaert,<sup>2</sup> Simon P. Conroy,<sup>10</sup> Leo G. Visser,<sup>1</sup> and Merel M. C. Lambregts<sup>1</sup>

Pyuria cutoff 10 leukocytes/ $\mu$ L

## UTI group

women  $\geq$  65 years  
 $\geq$  2 lower urinary tract symptoms  
1 pathogen  $\geq$   $10^4$ /mL (n = 63)

## Control group

women  $\geq$  65 years  
asymptomatic  
1 pathogen  $\geq$   $10^5$ /mL (n = 18)  
negative culture (n = 25)  
no growth (n = 58)



**Table 2. Median Urine Leukocyte Values of Patients With Urinary Tract Infection and Controls (With Subgroups), Measured by Automated Microscopy and Urine Flowcytometry**

	UTI Group	Control Group		
		ASB	Negative Culture	Mixed Flora
<b>Automated microscopy</b>				
n	56	18	24	57
Automated microscopy in cells/ $\mu$ L, median (IQR)	900 (430–900)	296 (49–773)	4 (1–30)	18 (5–57)
<b>Urine flowcytometry</b>				
n	35	17	24	58
Urine flowcytometry in cells/ $\mu$ L, median (IQR)	1575 (581–4673)	197 (43–1368)	6 (1–35)	20 (4–88)

“Degree of pyuria can help distinguish UTI in older women from asymptomatic controls, including those with asymptomatic bacteriuria.”

**Table 3. Sensitivity, Specificity, and Positive and Negative Likelihood Ratios for the Current and Theoretical Pyuria Thresholds for Diagnosing Urinary Tract Infection in Older Women**

	10 cells/ $\mu$ L	50 cells/ $\mu$ L	100 cells/ $\mu$ L	200 cells/ $\mu$ L	300 cells/ $\mu$ L	400 cells/ $\mu$ L
Sensitivity, % (95% CI)	100 (94–100)	98 (92–100)	93 (84–98)	89 (80–96)	84 (73–92)	77 (65–87)
Specificity, % (95% CI)	36 (28–48)	66 (56–75)	71 (61–79)	86 (78–92)	88 (81–93)	92 (86–96)
LR <sub>pos</sub> (95% CI)	1.6 (1.4–1.9)	2.9 (2.2–3.8)	3.2 (2.3–4.3)	6.3 (3.9–10.3)	6.9 (4.0–11.9)	9.5 (4.8–18.7)
LR <sub>neg</sub> (95% CI)	0.0 (0.0–0.1)	0.03 (0.004–0.2)	0.1 (0.04–0.3)	0.1 (0.06–0.3)	0.2 (0.1–0.3)	0.3 (0.2–0.4)

“Currently used cutoff for pyuria has a very low specificity for UTI in older women.”

# ASYMPTOMATIC BACTERIURIA



- “The diagnosis of a UTI requires both significant bacteriuria and symptoms consistent with infection, such as dysuria or urgency. In the absence of symptoms, positive urine cultures represent asymptomatic bacteriuria.”

Clinical Microbiology Procedures Handbook

- Screening/treatment not indicated for patients with asymptomatic bacteriuria EXCEPT:

Pregnant women

Individuals undergoing urologic procedures

Clin Infect Dis. 40:643-654; 2005



## Clinical Practice Guideline for the Management of Asymptomatic Bacteriuria: 2019 Update by the Infectious Diseases Society of America<sup>a</sup>

Lindsay E. Nicolle,<sup>1</sup> Kalpana Gupta,<sup>2</sup> Suzanne F. Bradley,<sup>3</sup> Richard Colgan,<sup>4</sup> Gregory P. DeMuri,<sup>5</sup> Dimitri Drekonja,<sup>6</sup> Linda O. Eckert,<sup>7</sup> Suzanne E. Geerlings,<sup>8</sup> Béla Köves,<sup>9</sup> Thomas M. Hooton,<sup>10</sup> Manisha Juthani-Mehta,<sup>11</sup> Shandra L. Knight,<sup>12</sup> Sanjay Saint,<sup>13</sup> Anthony J. Schaeffer,<sup>14</sup> Barbara Trautner,<sup>15</sup> Bjorn Wullt,<sup>16</sup> and Reed Siemieniuk<sup>17</sup>

### **AGAINST**

pediatric patients

healthy, non-pregnant women

older, community dwellers--functionally impaired

older long-term care facility dwellers

diabetics

renal transplant (> 1 month)

non-renal solid organ transplant

impaired voiding following spinal cord injury

indwelling catheter

elective non-urologic surgery

implantation or living with urologic devices

No Recommendation  
high-risk neutropenia  
time of indwelling catheter removal



# PRE-ANALYTICAL I



- Urine culture should be done **ONLY** in context of symptoms compatible with urinary tract infection

Fever

Urgency

Suprapubic tenderness

Frequency

Dysuria

Altered mental status

Hypotension

*JAMA Intern Med. 175:171-1713; 2015*

- Up to 50% of urine cultures ordered in ER or internal medicine are from patients without symptoms

Potential misdiagnosis

High burden of testing for laboratory

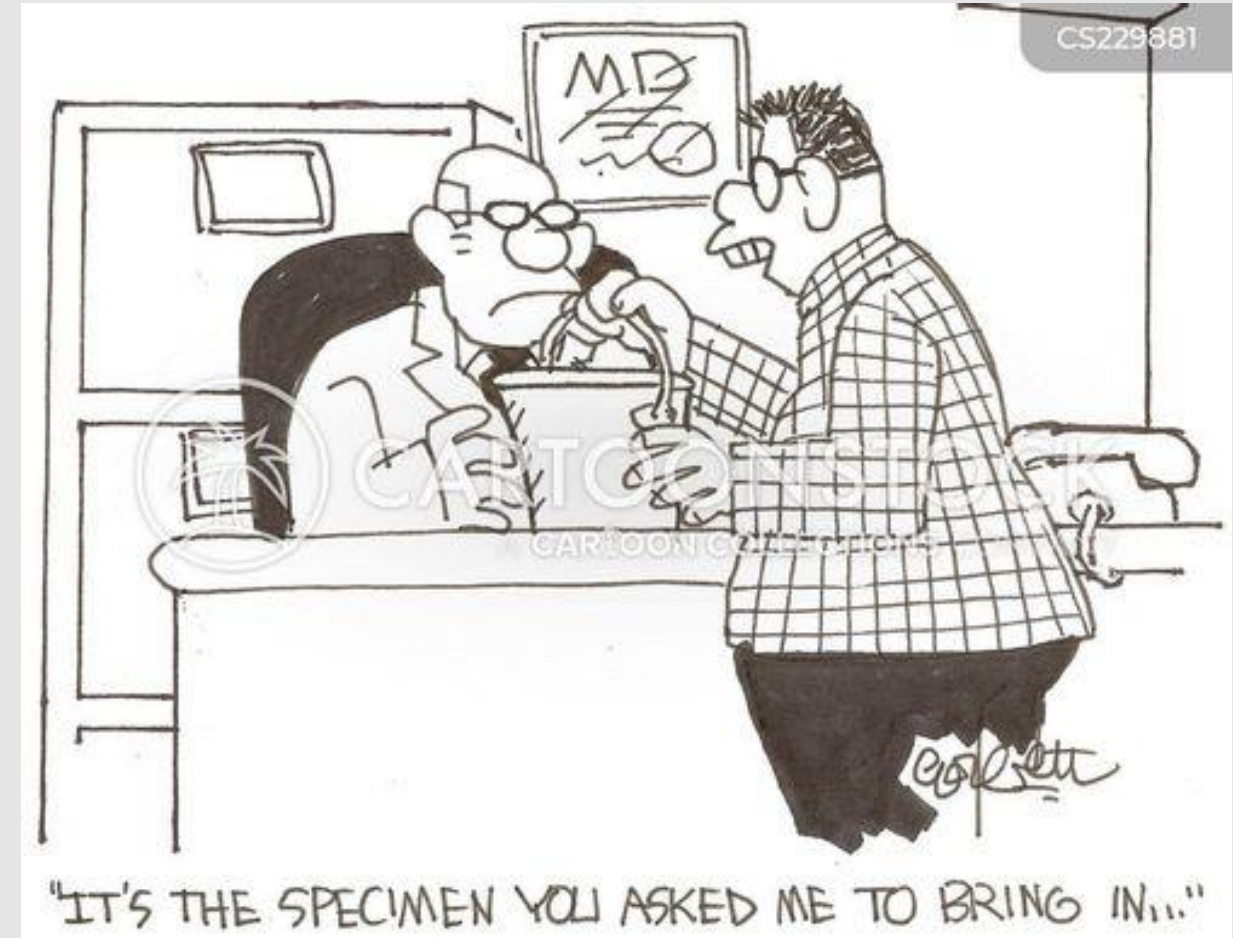
Potential overutilization of antimicrobial agents

*Clin Infect Dis. 40:643-654; 2005*

# PRE-ANALYTICAL II



- Acceptable specimens
  - Midstream (clean catch)  
*.....are we sure?*
  - Catheter collection  
*.....are we sure?*
  - Suprapubic aspiration
- Reject
  - Foley tips
  - Urine from catheter bag
- Work-up caveats (later)



# PRE-ANALYTICAL III



- Valid at room temperature up to 20 minutes

Biochemia Medica. 24:89-104; 2014

- Fridge up to 24 hours; 48 hours in some literature

BMC Vet Res. 17:379; 2021

- Boric acid

Equivalent to fridge in preventing bacterial overgrowth

Can affect urinalysis and chemistry data

May not be compatible for molecular aliquoting

J Clin Microbiol. 10:42-45; 1979

# iCLICKER FOR REAL



Does your laboratory perform quality assurance monitoring of urine culture contamination/no growth rates?

- A. We track urine culture contamination rates.
- B. We track no growth urine culture rates.
- C. We somehow have the time to track both.
- D. Why do you keep asking me these questions?
- E. What is quality assurance?

# iCLICKER FOR REAL



What cutoff do you use for (significant) colony counts in pediatrics?

- A. Kids are people too; 100,000 CFU/mL
- B. Kids are special; 50,000 CFU/mL
- C. Kids are very special; we report anything on pediatrics.
- D. I would love to know what a childrens hospital laboratory does.
- E. I have had it up to here with my own kids.



# Support for the Use of a New Cutoff to Define a Positive Urine Culture in Young Children

Nader Shaikh, MD, MPH,<sup>a</sup> Sojin Lee, PhD,<sup>a</sup> Janina A. Krumbek, PhD,<sup>b</sup> Marcia Kurs-Lasky, MS<sup>a</sup>

341 kids with fever

(age range <2 mos to 35 mos;  
mean 12.5 mos)

Conventional culture (cath urine)

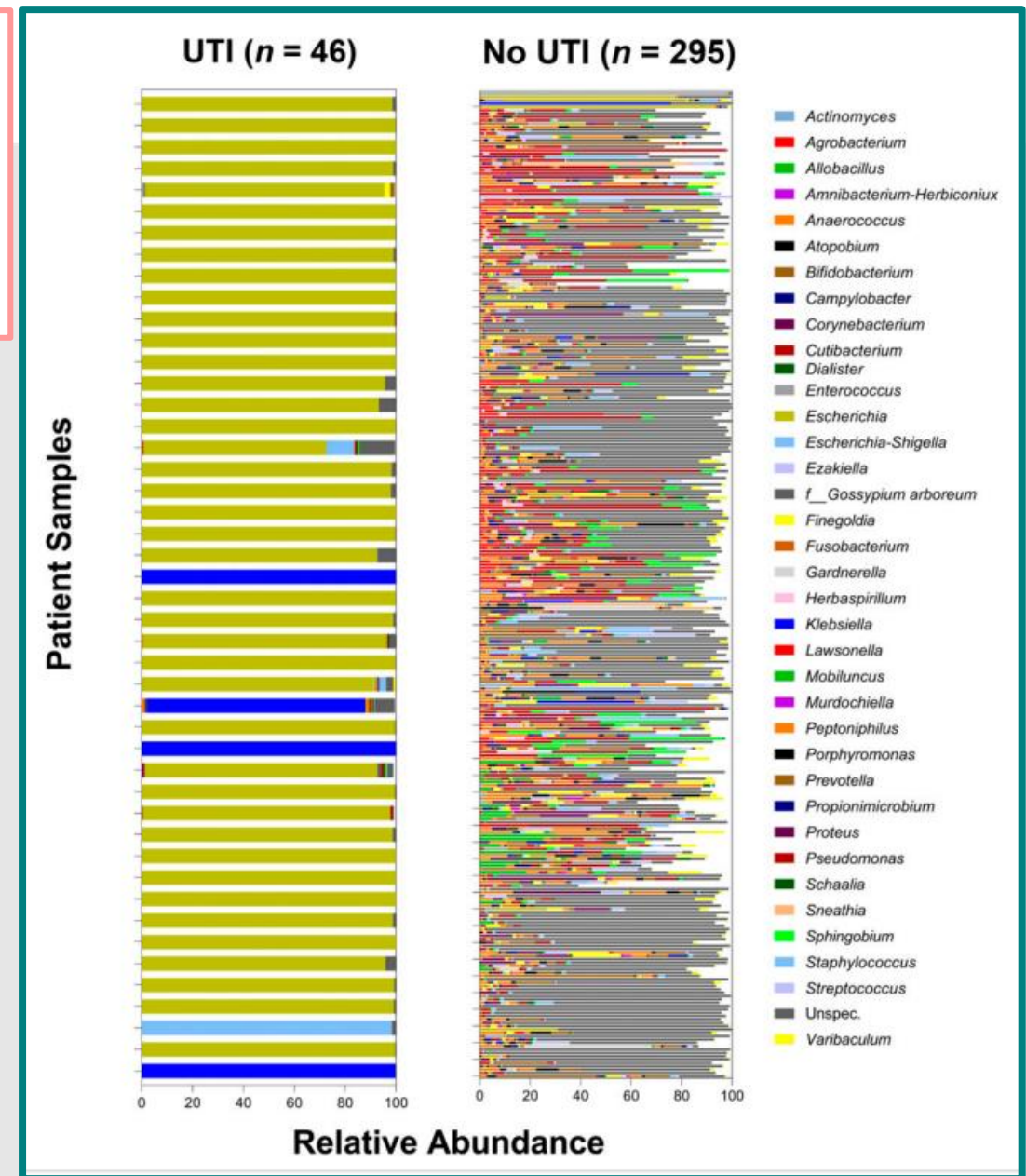
16S rRNA sequencing (cath urine)

reference method

80% relative abundance

Inflammatory markers in urine

10 WBC, trace esterase, lipocalin



# RESULTS



**TABLE 2** Accuracy of Conventional Urine Culture at Different Cutoffs Compared With 16S rRNA Gene Amplicon Sequencing

	Number Correctly Identified as Having UTI	Number Correctly Identified as Not Having UTI	Sensitivity (95% confidence interval)	Specificity (95% confidence interval)
Primary analysis <sup>a</sup>				
Cutoff of 10 000	45/46	291/295	98 (93–100)	99 (97–100)
Cutoff of 50 000	37/46	293/295	80 (68–93)	99 (98–100)
Cutoff of 100 000	32/46	293/295	70 (55–84)	99 (98–100)



**TABLE 3** Characteristics of Children in Whom Urinary Tract Infection Would Have Been Missed When Using a Cutoff of 50 000 CFU/mL (instead of 10 000 CFU/mL).

Age (months)	Elevated WBC Count or Leukocyte Esterase <sup>a</sup>	Elevated NGAL <sup>b</sup>	Most Abundant Organism on 16S (relative abundance)	Conventional Culture Result: Organism(s) and Colony Count per mL
12	No	Yes	<i>Klebsiella</i> (0.86)	<i>Klebsiella</i> , 10 000–49 000
27	Yes	Yes	<i>Escherichia coli</i> (0.91)	<i>E. coli</i> , 10 000–49 000
16	Yes	No	<i>Escherichia coli</i> (0.92)	<i>E. coli</i> , 10 000–49 000
28	Yes	Yes	<i>Escherichia coli</i> (>0.99)	<i>E. coli</i> , 10 000–49 000
13	Yes	Yes	<i>Escherichia coli</i> (0.98)	<i>E. coli</i> , 10 000–49 000
9	No	Yes	<i>Escherichia coli</i> (0.83)	<i>E. coli</i> , 10 000–49 000
7	Yes	Yes	<i>Escherichia coli</i> (>0.99)	<i>E. coli</i> , 10 000–49 000
10	Yes	Yes	<i>Escherichia coli</i> (0.99)	<i>E. coli</i> , 10 000–49 000

<sup>a</sup>  $\geq 10$  WBC per cubic millimeter,  $\geq 5$  WBC per Hpf, or  $\geq$  trace leukocyte esterase.

<sup>b</sup> NGAL level 39.9 ng/mL and above.

# Case Eight



85-year-old female seen in ER for altered mental status;  
(straight) catheterized urine





8

# iCLICKER FOR REAL 8



Have you ever heard of *Aerococcus urinae*?

- A. Yes.
- B. Yes...and I would love to share our experiences.
- C. No, but I would love to know more.
- D. No. Speaking of urine, I am ready for a bathroom break.
- E. You actually meant *Aeromonas*, correct?





M35-A2  
Vol. 28 No. 29  
Replaces M35-A  
Vol. 22 No. 18

# Abbreviated Identification of Bacteria and Yeast; Approved Guideline—Second Edition

This document provides the minimum identification criteria that can be used to rapidly identify organisms commonly isolated from clinical specimens.

A guideline for global application developed through the Clinical and Laboratory Standards Institute consensus process.



# *Aerococcus viridans* (“official line item”)



- Presumptive identification
  - GPC (tetrads, clusters)
  - Catalase-negative
  - $\alpha$ -hemolytic
- Additional tests for definitive identification
  - PYR-positive
  - LAP-negative

# Viridans group *Streptococcus*



- Presumptive identification

GPC (pairs, chains)      Catalase-negative  
Non-hemolytic or  $\alpha$ -hemolysis

- Additional tests for definitive identification

PYR-negative      LAP-positive  
Bile solubility-negative if  $\alpha$ -hemolytic

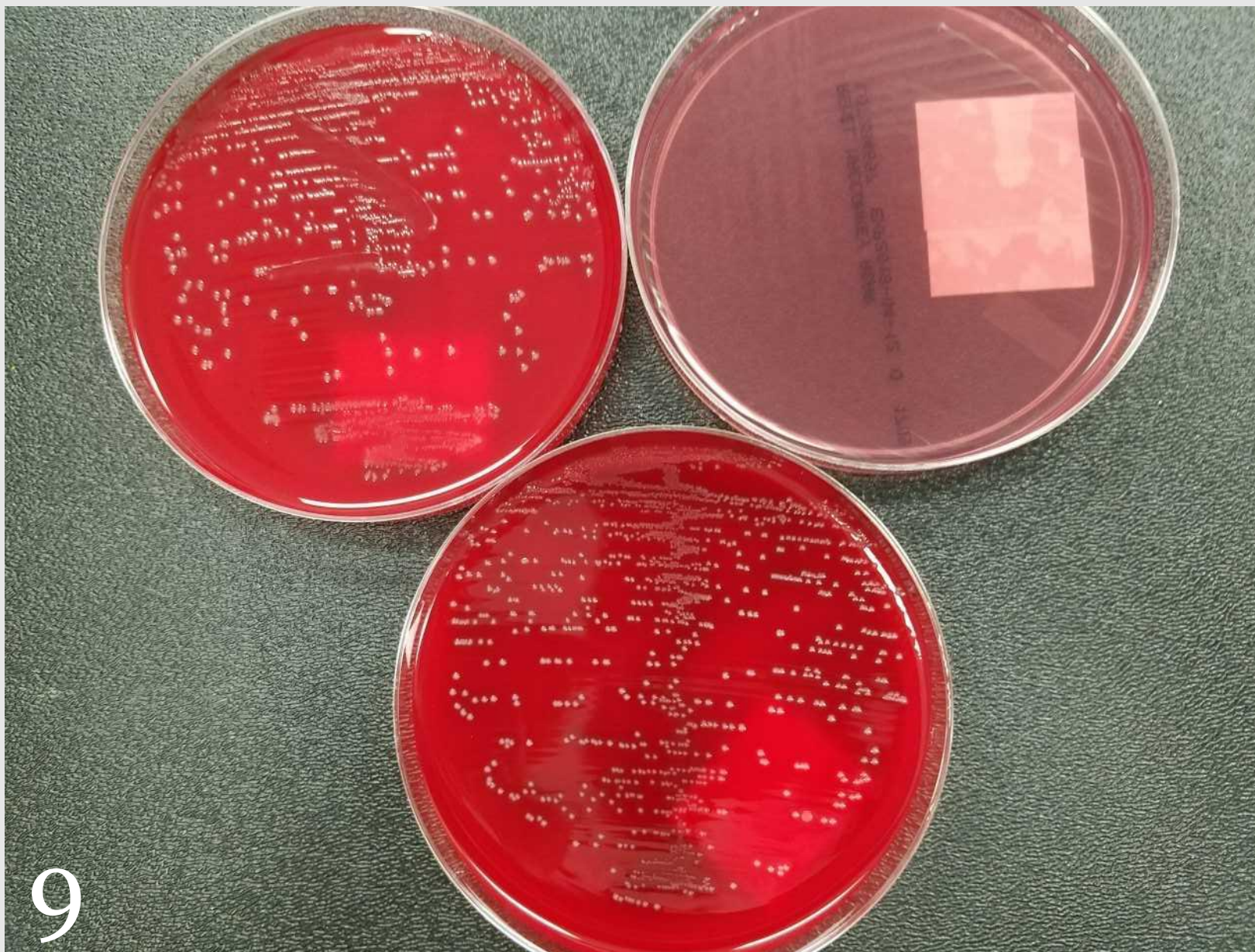
- IF NOT IN CHAINS

*Pediococcus* spp. resistant to vancomycin  
*Aerococcus urinae* is urinary pathogen in tetrads

# Case Nine

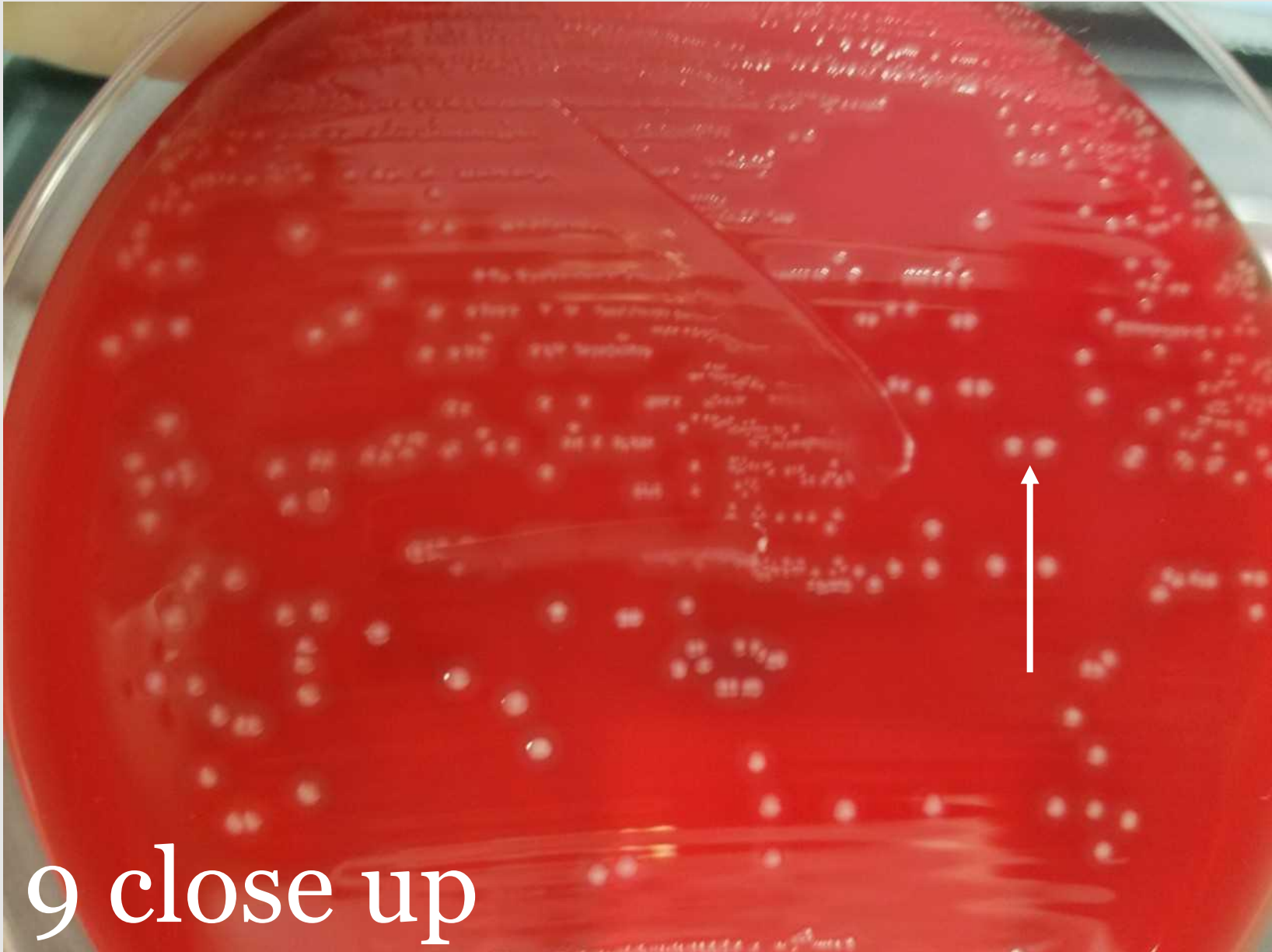


26-year-old female seen in clinic;  
midstream urine



9





9 close up

# iCLICKER FOR REAL 9



Disk diffusion testing performed on *Streptococcus agalactiae*; what do you do next?

- A. Report erythromycin after D-testing
- B. Report clindamycin after D-testing
- C. Report neither clindamycin nor erythromycin
- D. Report both clindamycin and erythromycin
- E. Place a phone call to OB/GYN office

# NEW OWNERSHIP



AMERICAN  
SOCIETY FOR  
MICROBIOLOGY

## Guidelines for the Detection and Identification of Group B *Streptococcus*

Initially posted: March 10, 2020

Updated: July 23, 2021

Laura Filkins, PhD, D(ABMM), Jocelyn Hauser PhD, MLS(ASCP)<sup>CM</sup>,

Barbara Robinson-Dunn, PhD, D(ABMM), FAAM, Robert Tibbetts, PhD, D(ABMM), F(CCM),

Bobby Boyanton, MD, Paula Revell PhD, D(ABMM)

*on behalf of the American Society for Microbiology Clinical and Public Health Microbiology  
Committee, Subcommittee on Laboratory Practices*

- 36- to 37-week screening
- Prophylaxis recommendations

Penicillin/ampicillin

Cefazolin (non-severe allergy)

Clindamycin (severe allergy)



The American College of  
Obstetricians and Gynecologists  
WOMEN'S HEALTH CARE PHYSICIANS

**INTERIM UPDATE**

## ACOG COMMITTEE OPINION

Number 797

*(Replaces Committee Opinion No. 782, June 2019)*

### Committee on Obstetric Practice

*The American Academy of Pediatrics, the American College of Nurse-Midwives, the Association of Women's Health, Obstetric and Neonatal Nurses, and the Society for Maternal-Fetal Medicine endorse this document. Although the American Society for Microbiology cannot endorse this document because the content is outside the organization's scope, they have reviewed the document. This Committee Opinion was developed by the American College of Obstetricians and Gynecologists' (ACOG) Committee on Obstetric Practice in collaboration with the American College of Nurse-Midwives liaison member Tekoa L. King, CNM, MPH; ACOG Committee on Obstetric Practice committee member Neil S. Silverman, MD; and ACOG Committee on Practice Bulletins-Obstetrics committee member Mark Turrentino, MD.*

**INTERIM UPDATE:** The content in this Committee Opinion has been updated as highlighted (or removed as necessary) to reflect a limited, focused change in the language regarding penicillin allergy testing, categories for penicillin (ie, low-risk and high-risk of anaphylaxis or severe reaction) (Table 2), and penicillin dose (Figure 3).

### Prevention of Group B Streptococcal Early-Onset Disease in Newborns

Obstet Gynecol. 134:e19-e40; 2019

# *Streptococcus agalactiae* IN URINE



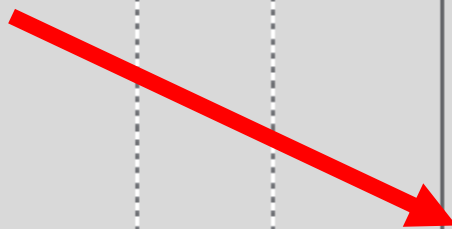
- Report *S. agalactiae* in any quantity from urine cultures from pregnant women during any trimester
  - High CC in symptomatic → adverse pregnancy outcomes
  - Low CC in asymptomatic → risk for early-onset neonatal disease
- Any amount is indication for intrapartum prophylaxis
- Susceptibility testing for all isolates from pregnant women with severe penicillin allergy
  - Clindamycin (erythromycin)
  - Vancomycin

# CAVEAT I



Table 2H-1. *Streptococcus* spp.  $\beta$ -Hemolytic Group (Continued)

Antimicrobial Agent	Disk Content	Interpretive Categories and Zone Diameter Breakpoints, nearest whole mm			Interpretive Categories and MIC Breakpoints, $\mu\text{g}/\text{mL}$			Comments
		S	I	R	S	I	R	
<b>MACROLIDES</b>								
(14) Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin.								
(15) Not routinely reported on <b>organisms isolated</b> from the urinary tract.								
Erythromycin	15 $\mu\text{g}$	$\geq 21$	16-20	$\leq 15$	$\leq 0.25$	0.5	$\geq 1$	(16) Rx: Recommendations for intrapartum prophylaxis for group B streptococci are penicillin or ampicillin. Although cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin, but may be resistant to erythromycin and clindamycin. When a group B <i>Streptococcus</i> is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis), erythromycin and clindamycin (including ICR) should be tested, and only clindamycin should be reported. Erythromycin should be tested for ICR determination only and should not be reported. See Table 3I.
Azithromycin*	15 $\mu\text{g}$	$\geq 18$	14-17	$\leq 13$	$\leq 0.5$	1	$\geq 2$	
Clarithromycin*	15 $\mu\text{g}$	$\geq 21$	17-20	$\leq 16$	$\leq 0.25$	0.5	$\geq 1$	
Dirithromycin*	15 $\mu\text{g}$	$\geq 18$	14-17	$\leq 13$	$\leq 0.5$	1	$\geq 2$	





# CAVEAT II



Table 1M  
*Streptococcus* spp.  $\beta$ -Hemolytic Group  
 M02 and M07

Table 1M. *Streptococcus* spp.  $\beta$ -Hemolytic Group

Tier 1: Antimicrobial agents that are appropriate for routine, primary testing and reporting	Tier 2: Antimicrobial agents that are appropriate for routine, primary testing but may be reported following cascade reporting rules established at each institution	Tier 3: Antimicrobial agents that are appropriate for routine, primary testing in institutions that serve patients at high risk for MDROs but should only be reported following cascade reporting rules established at each institution	Tier 4: Antimicrobial agents that may warrant testing and reporting by clinician request if antimicrobial agents in other tiers are not optimal because of various factors
Clindamycin <sup>a,b</sup>			
Erythromycin <sup>a,b,c</sup>			
Penicillin <sup>d</sup> or ampicillin <sup>d</sup>		Cefotaxime or ceftriaxone	Cefepime Ceftaroline
	Tetracycline <sup>e</sup>		
		Vancomycin	
			Linezolid Tedizolid <sup>f</sup>
			Daptomycin <sup>f,g,h</sup>
			Levofloxacin
			Dalbavancin <sup>h,i</sup>
			Oritavancin <sup>h</sup>
			Telavancin <sup>h</sup>

Abbreviations: ICR, inducible clindamycin resistance; MDRO, multidrug-resistant organism.

### Footnotes

a. Not routinely reported for organisms isolated from urinary tract.

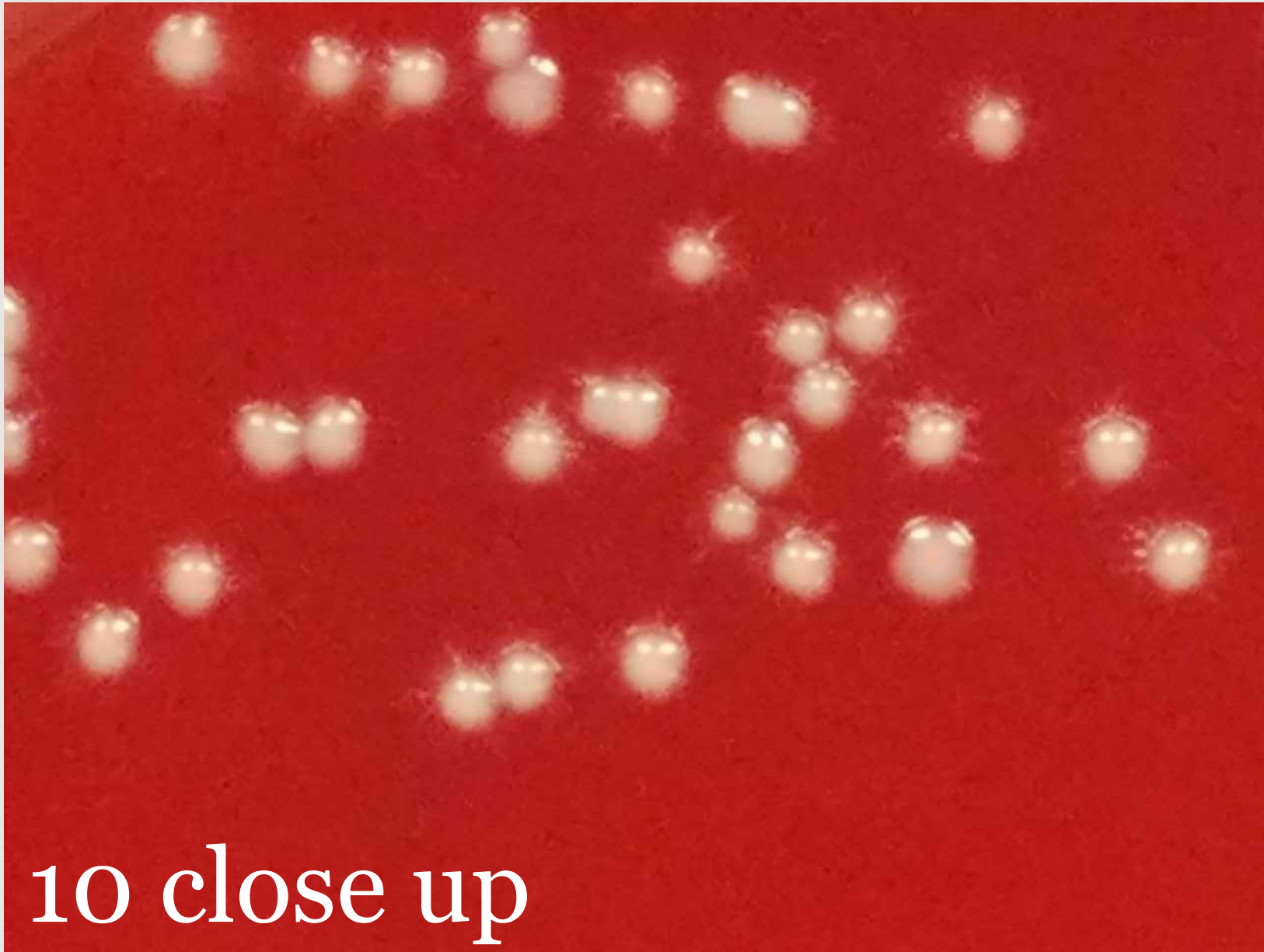
# Case Ten



64-year-old female on internal medicine unit;  
catheterized urine



10



10 close up

# iCLICKER FOR REAL 10



Do you identify yeast from urine cultures?

- A. We ignore it.
- B. We just call it yeast.
- C. We only identify *Candida albicans*.
- D. We only identify *Candida glabrata*.
- E. We identify *Candida albicans* and *Candida glabrata*.



# *Candida albicans*



- Presumptive identification

  - Budding yeast in smear

- Additional tests for definitive identification

  - “Feet” in less than 48 hours OR  
Germ tube-positive

- Notes

  - Not easily separated from *Candida dubliniensis*



# *Candida glabrata*

- Presumptive identification

Small yeast in smear with no hyphae

Better growth on chocolate agar than blood agar

- Additional tests for definitive identification

Better growth on EMB agar than blood agar

Rapid trehalose-positive at 42°C

CLSI M35-A2

Diagn Microbiol Infect Dis. 28:65-67; 1997

TABLE 1 Growth Characteristics on Primary Culture Plates

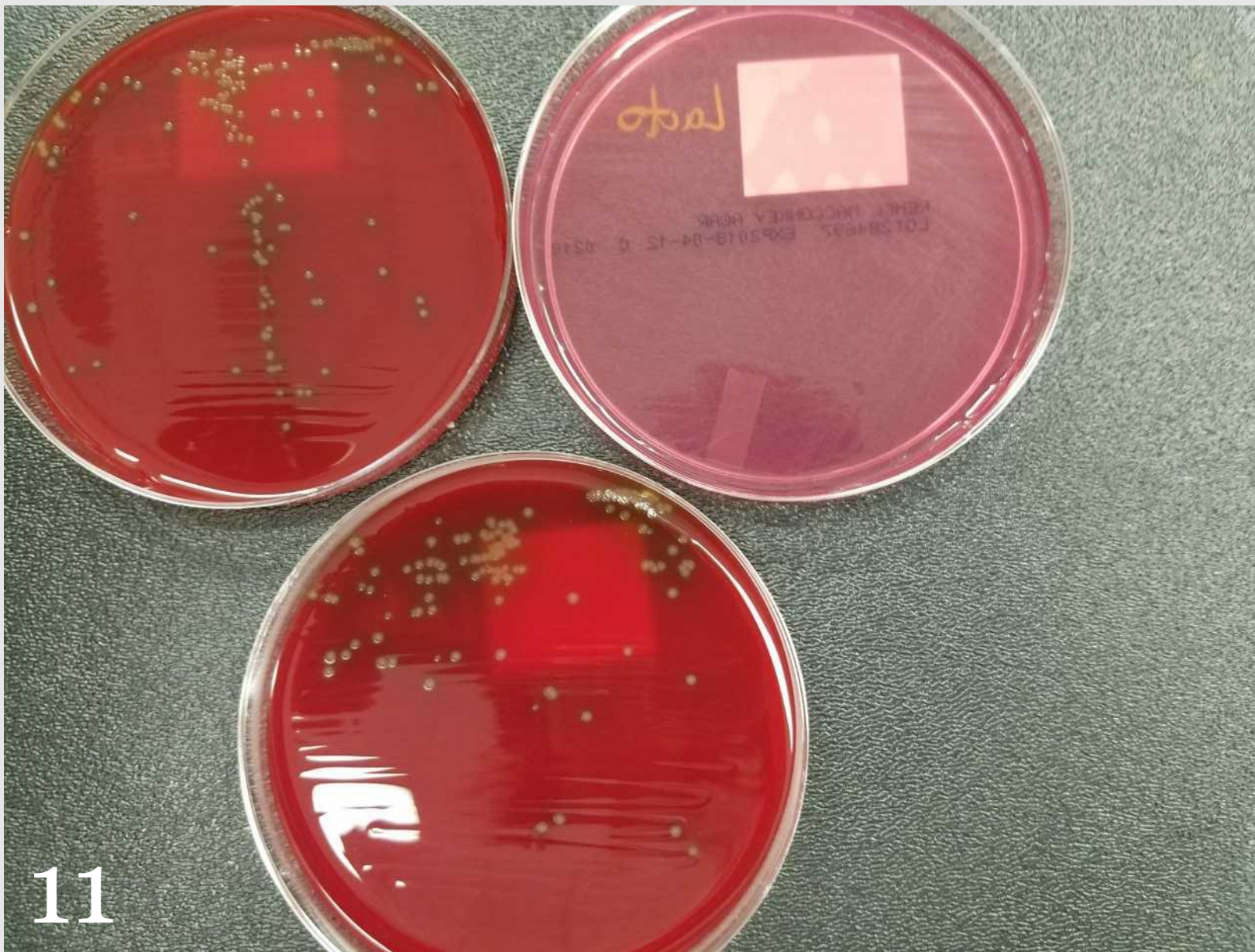
	<i>C. glabrata</i>	Other Species
EMB growth > BAP <sup>a</sup>	92	0
EMB = or < BAP	10	267
Total	102	267

<sup>a</sup> Colonies twice the size, or no growth on BAP.

# Case Eleven



35-year-old female seen in clinic;  
midstream urine



11





11 close up



# iCLICKER FOR REAL 11a



Pure culture > 100,000 CFU/mL; your report?

- A. >100,000 CFU/mL contaminant
- B. >100,000 CFU/mL *Lactobacillus* spp.
- C. >100,000 CFU/mL *Lactobacillus* spp. with comment that susceptibility testing not available in your laboratory
- D. I need to check the UA.
- E. I need some more coffee (maybe with a shot).

# iCLICKER FOR REAL 11b



Pure culture > 100,000 CFU/mL; your report?

- A. >100,000 CFU/mL contaminant
- B. >100,000 CFU/mL *Lactobacillus* spp.
- C. >100,000 CFU/mL *Lactobacillus* spp.; be sure to hang on to isolate for send-out susceptibility testing
- D. I really, really want to check the UA.
- E. Just bring the entire flask.

# Case Twelve



46-year-old female seen in clinic;  
midstream urine



12



# iCLICKER FOR REAL 12



Do you perform susceptibility testing on urinary isolates of *Enterococcus* spp.?

- A. Yes
- B. Yes, but we report a limited panel.
- C. No; we never see this in urine.
- D. We see this in urine, but don't do susceptibility testing.
- E. Didn't we talk about *Aerococcus* spp. already?



# COMMENTS (AST)



“Ampicillin is the drug of choice for treating enterococcal (including vancomycin-resistant enterococci) infections restricted to the urinary tract. Alternative drugs are nitrofurantoin or a fluoroquinolone.”

# COMMENTS (AST)



## Yeast

“Clinical significance not determined. It isn’t necessary to treat all yeast found in urine. Antifungal treatment recommended for very low birth weight infants, patients undergoing invasive genitourinary procedures, neutropenic patients, renal transplant patients, and symptomatic patients.”

## *Staphylococcus saprophyticus*

“Routine susceptibility testing of urine isolates of *S. saprophyticus* is not advised per recommended guidelines. Infections respond to common urinary microbial agents (e.g. nitrofurantoin, trimethoprim/sulfamethoxazole, or a fluoroquinolone).”

# COMMENTS (AST)



## *Aerococcus urinae*

“Validated susceptibility method not available. Usually susceptible to penicillins, rifampin, cefepime, and vancomycin. Effectiveness of cephalosporins and aminoglycosides is uncertain.”

## *Aerococcus viridans*

“Validated susceptibility method not available. Usually susceptible to penicillin, macrolides, sulfonamides and trimethoprim.”

## *Streptococcus agalactiae*

“If either clindamycin or erythromycin is being considered for intrapartum chemoprophylaxis, the physician should contact the microbiology department to request susceptibility tests.”

# COMMENTS (WORK UP)



## UNCERTAIN

“Clinical significance of isolate(s), in context of significant contaminant urogenital and/or skin flora, is uncertain. Suggest appropriate recollection with timely delivery to the laboratory, if clinically indicated.”

## COLONIZED FOLEY

“The presence of multiple potential pathogens in a urine specimen obtained from an indwelling catheter may be indicative of catheter device contamination.”

# COMMENTS (WORK UP)



## COLONIZED FOLEY???

“No further workup performed. Foley catheter specimen has >3 organisms. Suspect possible colonization. Recommend changing Foley prior to recollection.”

## CONTAMINATED FOLEY

“Culture results indicate probable urogenital and/or skin flora contamination. Suggest appropriate recollection (e.g., straight catheterization) with timely delivery to the laboratory, if clinically indicated.”



# iCLICKER FOR REAL



Do you know if the catheterized urine that you are receiving is from a straight catheter or an indwelling catheter?

- A. Yes, we have separate test codes for these two.
- B. Yes, one test code--must indicate specific source.
- C. No, we do not.
- D. We only get Foleys.
- E. Is it time for the taco bar?

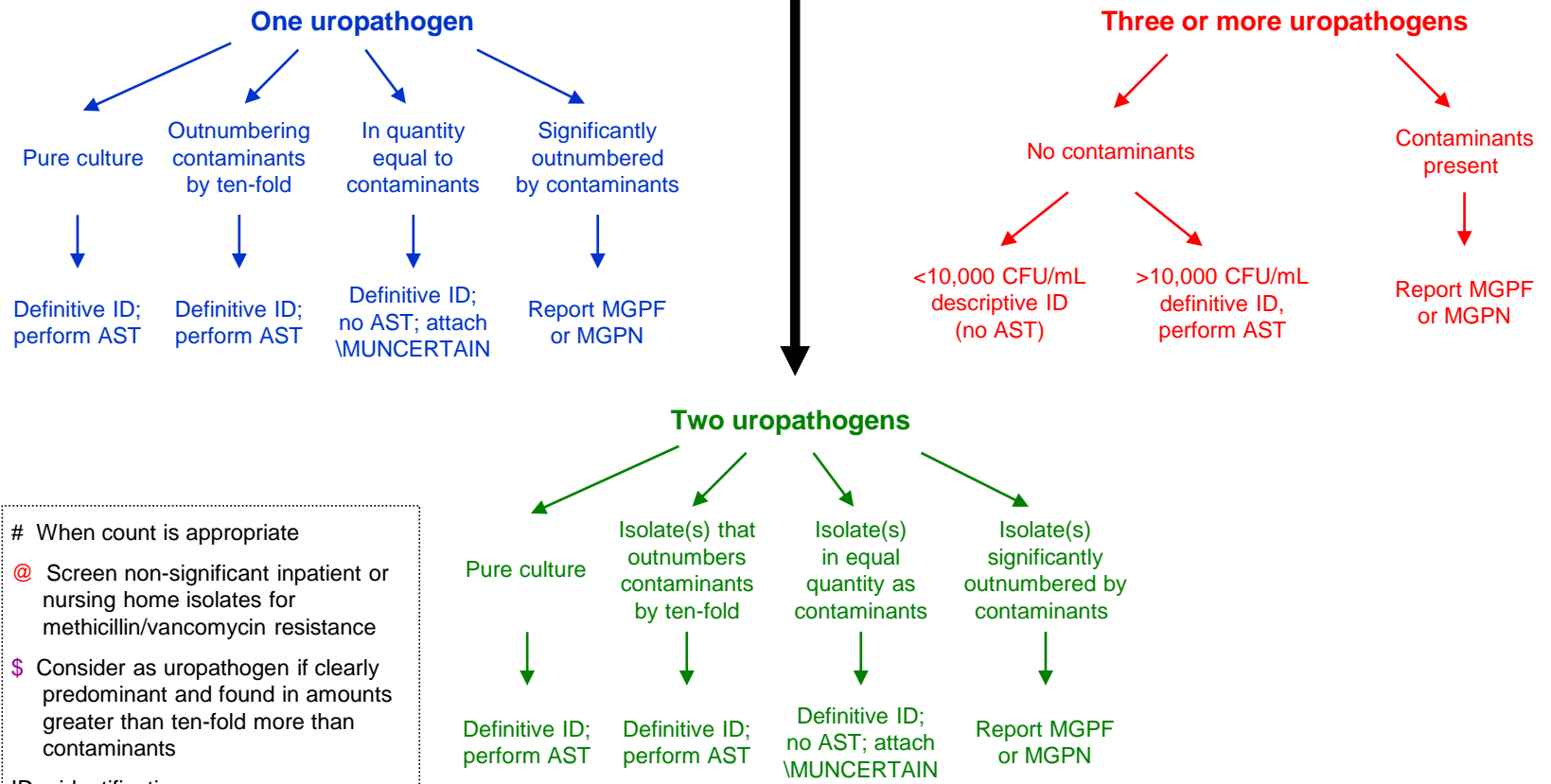
# SAMPLE ALGORITHM 1



**Contaminants**  
 Viridans group *Streptococcus*  
*Neisseria* sp.  
 § Coagulase-negative *Staphylococcus*  
 § Diphtheroids  
*Lactobacillus* sp.

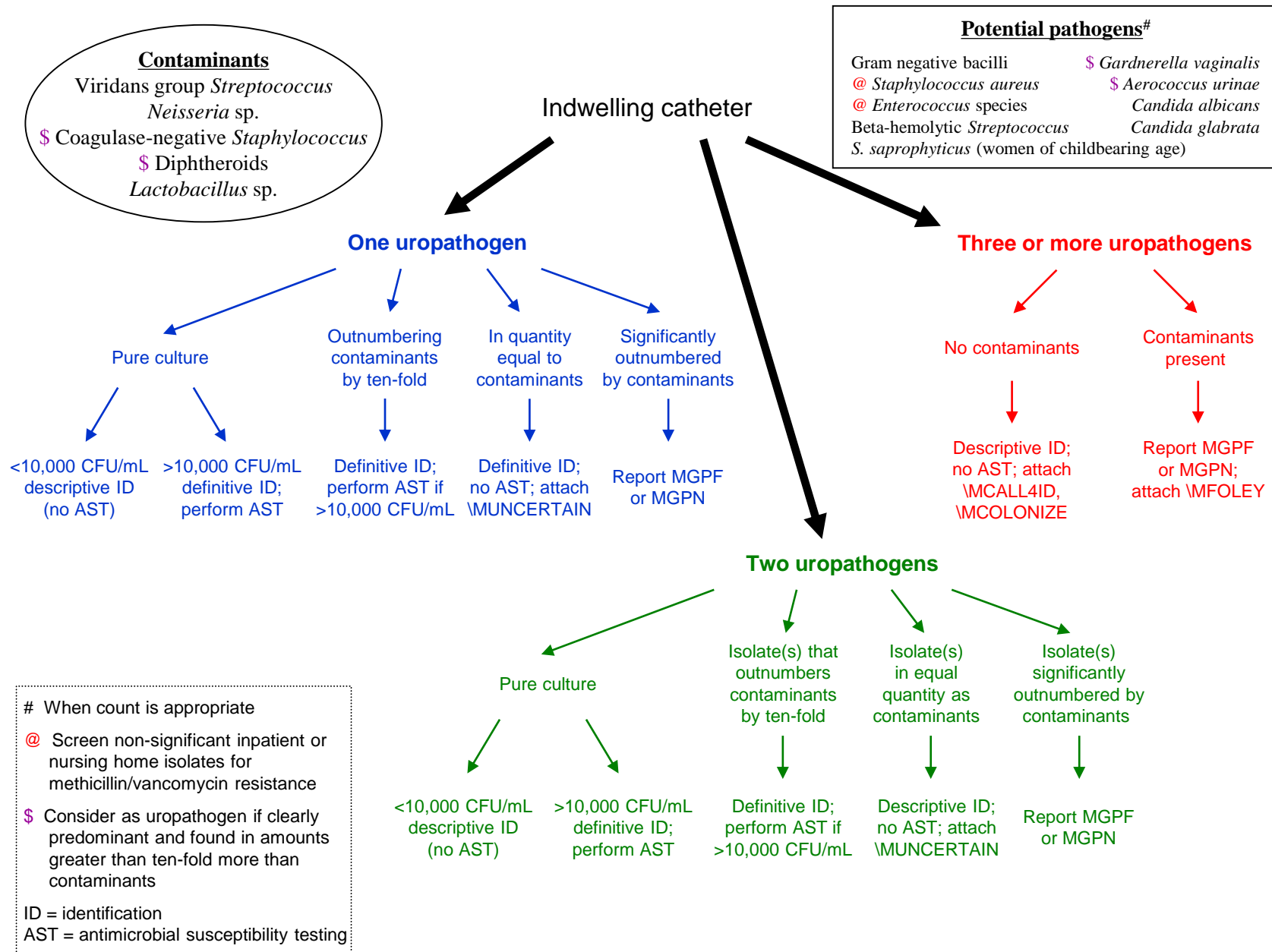
**Potential pathogens#**  
 Gram negative bacilli § *Gardnerella vaginalis*  
 @ *Staphylococcus aureus* § *Aerococcus urinae*  
 @ *Enterococcus* species *Candida albicans*  
 Beta-hemolytic *Streptococcus* *Candida glabrata*  
*S. saprophyticus* (women of childbearing age)

Suprapubic aspiration  
 Straight catheterization  
 Cystoscopy



# When count is appropriate  
 @ Screen non-significant inpatient or nursing home isolates for methicillin/vancomycin resistance  
 § Consider as uropathogen if clearly predominant and found in amounts greater than ten-fold more than contaminants  
 ID = identification  
 AST = antimicrobial susceptibility testing

# SAMPLE ALGORITHM 2



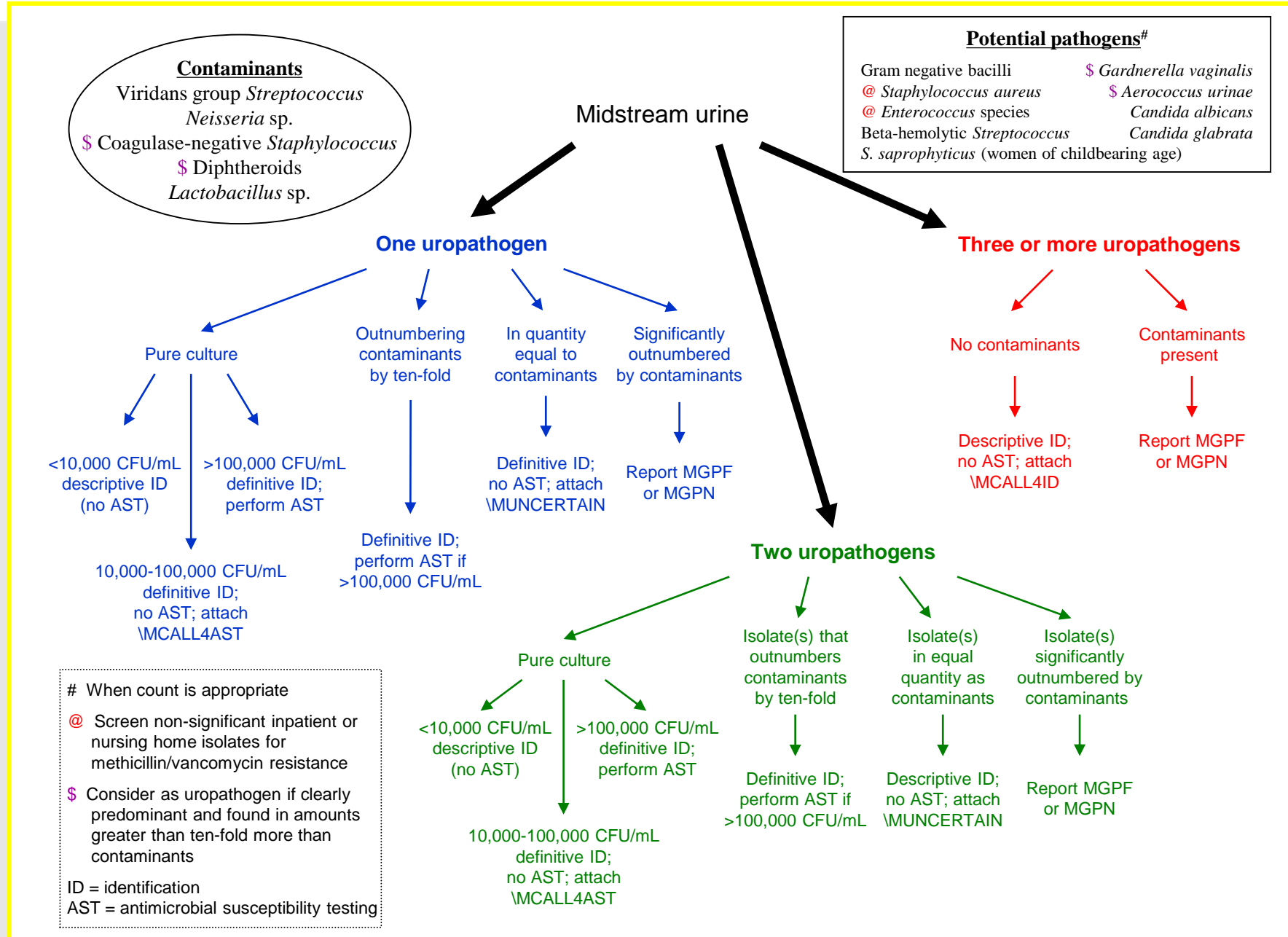
# When count is appropriate

@ Screen non-significant inpatient or nursing home isolates for methicillin/vancomycin resistance

§ Consider as uropathogen if clearly predominant and found in amounts greater than ten-fold more than contaminants

ID = identification  
AST = antimicrobial susceptibility testing

# SAMPLE ALGORITHM 3



# COMING SOON: URINE PCR?



## Pathnostics Guidance UTI

- 30 organisms
- 32 antibiotic resistance genes

## SolarisDX UTI ID

- 16 pathogens
- Resistance information
- AST
- Reflex testing for UA
- Results next day (including AST)

## Genetworx UTI

- 20 pathogens
- 22 resistance genes
- Results within 2 days (including AST)



Urology Times Journal 2023



# WHAT DOES RESEARCH SHOW?



Comparative Study > Urology. 2020 Feb;136:119-126. doi: 10.1016/j.urology.2019.10.018.

Epub 2019 Nov 9.

## Multiplex PCR Based Urinary Tract Infection (UTI) Analysis Compared to Traditional Urine Culture in Identifying Significant Pathogens in Symptomatic Patients

Kirk J Wojno<sup>1</sup>, David Baunoch<sup>2</sup>, Natalie Luke<sup>3</sup>, Michael Opel<sup>3</sup>, Howard Korman<sup>4</sup>, Colleen Kelly<sup>5</sup>, S. Mohammad A. Jafri<sup>4</sup>, Patrick Keating<sup>4</sup>, Dylan Hazelton<sup>4</sup>, Stephany Hindu<sup>4</sup>, Bridget Makhloof<sup>4</sup>, David Wenzler<sup>4</sup>, Mansour Sabry<sup>4</sup>, Frank Burks<sup>4</sup>, Miguel Penaranda<sup>3</sup>, David E Smith<sup>3</sup>, Andrew Korman<sup>4</sup>, Larry Sirls<sup>4</sup>

- Retrospective record review
- 582 patients with parallel testing

	# Positive
PCR	326 (56%)
Culture	217 (37%)

	Culture Positive	Culture Negative
PCR Positive	196 (34%)	130 (22%)
PCR Negative	21 (4%)	235 (40%)

**Conclusion:** Multiplex PCR is noninferior to urine culture for detection and identification of bacteria. Further investigation may show that the accuracy and speed of PCR to diagnose UTI can significantly improve patient outcomes.

# REIMBURSEMENT



According to the the Medicare MoIDx program, molecular UTI panel testing is indicated for a “patient being symptomatic and at higher risk for UTI complications (ie, the elderly, patients with recurrent symptomatic UTIs and/or complicated urinary tract anatomy) and/or is seen in urogynecology or urology specialty care settings.”<sup>24</sup>

# WHAT DO THE CRITICS SAY?



- It cannot reliably discern between pathogenic and colonizing agents. Collection techniques that involve swabbing the briefs may further contaminate the sample.
- It has a higher sensitivity rate than a standard urine culture, but is more likely to generate a positive result for organisms that are not considered clinically significant (e.g., organisms found as a part of normal skin flora).
- It detects DNA of organisms that are no longer viable, unlike standard urine culture technique. Results from PCR are displayed as cells/mL or copies/ $\mu$ L, which counts all alive and dead cells in a sample. The standard colony-forming units/mL (CFUs/mL) measure takes into account only the cells that can actively divide under specified conditions.
- There is a lack of data to provide guidance on the interpretation of organism-specific cell counts. The current treatment threshold for  $\geq 100,000$  CFUs/mL in a symptomatic resident is not equivalent to the copies/ $\mu$ L or cells/mL result that is reported from PCR testing.
- Reports that are generated recommending antibiotic therapies based upon the PCR test result may encourage the clinician to select overly-broad antibiotics to cover organisms that are colonizers.

