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HENRY FORD HEALTH + MICHIGAN STATE UNIVERSITY Health Sciences

International Vaccine Institute

Integrated Activity and Tools for Antimicrobial Stewardship, Infection Prevention & diagnostic Stewardship

Microbiology Basics for the Steward

CAPTURA
Capturing data on Antimicrobial resistance Patterns and Trends in Use in Regions of Asia

TACE ASIA
Technical Assistance for Clinical Engagement

MOTT MACDONALD

UKaid
from the British people

The Fleming Fund
Regional Grants

Overview

1. Introduction to microbiology lab role in antimicrobial stewardship
2. Specimen collection and strategies for sampling
3. Laboratory processing
4. Creating and interpreting an antibiogram

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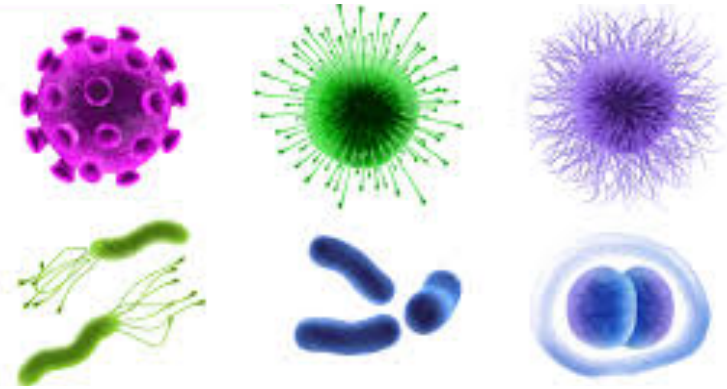
Introduction to AMS and Microbiology



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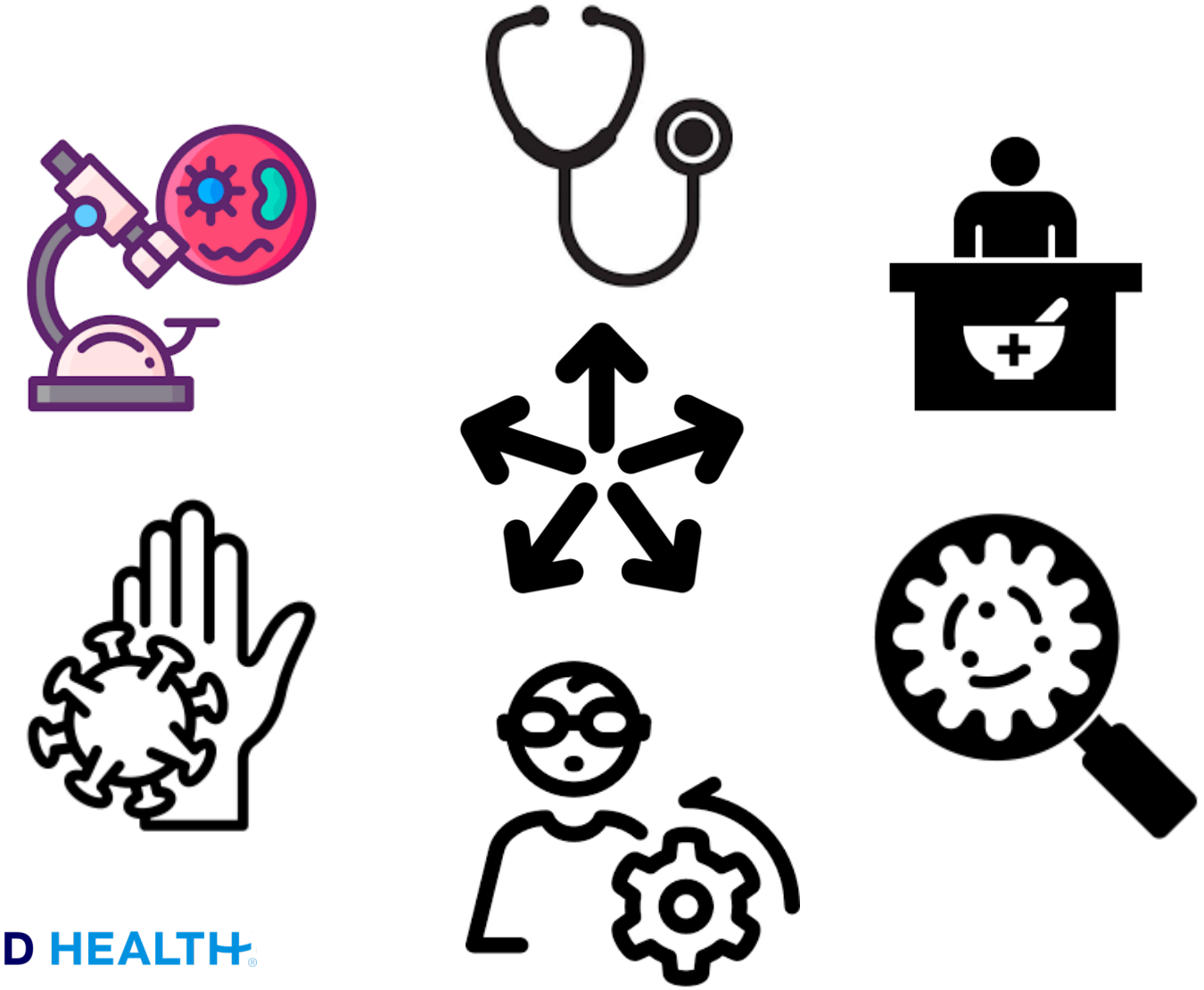
AMS and Microbiology

- Suboptimal antimicrobial use often stems from inappropriate interpretation OR use of microbiological test results:
  - lack of a microbiologically confirmed diagnosis
  - lab test errors
  - failure to submit appropriate specimens for culture
  - misuse of microbiology resources
  - overreliance on empirical antimicrobial therapy with disregard of microbiological results

Key Players in a Stewardship Team



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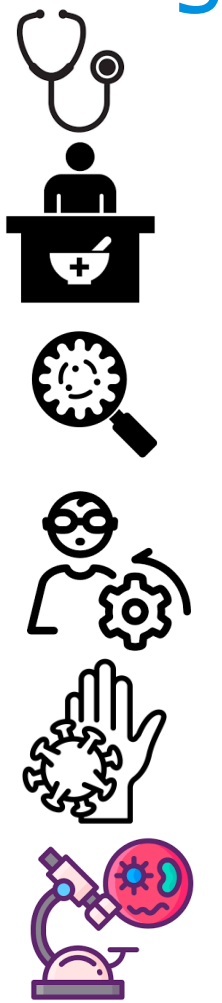
Hi-lighting Key Players in a Stewardship Team



- **Clinical Microbiologist**
  - Rapid diagnosis of infections
  - Notifying clinicians when critical infections detected
  - Surveillance for resistance
  - Antimicrobial susceptibility testing
  - Cumulative antimicrobial susceptibility reports
  - Infection control

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Morency-Potvin, P., Schwartz, D. N., & Weinstein, R. A. (2016). Antimicrobial Stewardship: How the Microbiology Laboratory Can Right the Ship. Clinical microbiology reviews, 30(1), 381–407. https://doi.org/10.1128/CMR.00066-16

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Specimen Collection & Strategies for Sampling

1. Is the illness caused by a microbe?
2. Which one?
3. Susceptibility profile?

Blood Culture Collection

- For the great majority of etiologic agents of blood stream infections, **conventional** blood culture methods provide positive results **within 48 hours**
- Incubation for >5 days seldom is required when modern automated continuous monitoring blood culture systems and media are used
- Some less common etiologic agents cannot be detected with current blood culture methods:
  - E.g. *Bartonella, Coxiella burnetii, Tropheryma whipplei, Barontella* spp.

Reducing Blood Culture Contamination

1. Diagnostic stewardship
2. Proper skin antisepsis
3. Bottle disinfection
4. Appropriate culture collection site
5. Hand hygiene
6. Phlebotomy teams/education on technique
7. Surveillance and feedback*
8. Diversion devices*

Appropriate Collection of Blood Cultures

- High risk false positive results when blood cultures are obtained from an indwelling line
  - **Not** to be obtained from an existing line or port **except** for when patient is rapidly deteriorating **or** if unable to obtain culture peripherally
  - Blood Cultures are **not** to be obtained **during the process of inserting** a **new peripheral IV, central line, midline or port except** for the rare occasion when the patient is rapidly deteriorating or if unable to obtain culture peripherally
- Rationale for drawing cultures from IV lines or ports should be documented in the chart
- Blood culture **volume is essential**
  - **3% increase in sensitivity for every extra mL collected**
  - Blood culture bottles **require 5 mL of blood if using glass culture bottles, and 10 mL of blood if plastic culture bottles**

Wiggers JB, Xiong W, Daneman N. Sending repeat cultures: is there a role in the management of bacteremic episodes? (SCRIBE study). BMC infectious diseases. 2016 Dec; 16(1):286.

When do you consider blood cultures to be "negative?"

slido

Please download and install the Slido app on all computers you use

When do you consider blood cultures to be "negative?"

ⓘ Start presenting to display the poll results on this slide.

Indications for Obtaining Urine Culture (NON kidney transplant patients)

- Urine culture is indicated in symptomatic patients meeting one of below 4 criteria:

1. Acute dysuria (burning with urination) **OR**
2. Fever or leukocytosis **PLUS**
   - Flank or costovertebral angle pain or tenderness, suprapubic pain, acute macroscopic/gross hematuria, new onset or marked increase in incontinence, new or marked increase in frequency OR
3. 2 or more of the following criteria:
   - Suprapubic pain, acute macroscopic/gross hematuria, new onset or marked increase in incontinence, new or marked increase in urgency, new or marked increase in frequency OR
4. New onset mental status changes without alternative explanation PLUS leukocytosis or hypotension or >/= 2 SIRS

When NOT to Obtain Urine Cultures

- Bacteriuria or pyuria is NOT an indication for urine culture or antimicrobial therapy
- Change in urine color, odor, or turbidity are NOT indications for urine culture
- Test of cure is not indicated for patients after urinary tract infection
- Catheter-associated Asymptomatic Bacteriuria is presence of bacteria in urine sample due to bacterial colonization of urinary tract / indwelling urinary catheter – this alone does NOT cause symptoms and does not indicate an infection that needs antibiotics (unless pregnant or undergoing certain invasive urologic procedures)
- A randomized controlled trial suggests no benefit to surveillance urine cultures and treatment of asymptomatic bacteriuria in kidney transplant patients
- In general, it is not recommended to obtain a urine culture in patients without urinary specific or otherwise unexplained systemic signs and symptoms of infection

Urine Specimen Collection

- Obtain urine samples **aseptically**
  - If require a small volume for exam (e.g. urinalysis), aspirate the urine from the needleless sampling port with a sterile syringe/cannula adapter after cleansing the port with a disinfectant
- Urine cultures should **not** be taken from external urinary catheter devices or from the indwelling urinary catheter collection bag
- As a reminder, remove indwelling catheter as soon as possible if NOT needed to reduce risk of catheter-associated urinary tract infection (CAUTI)

Wound Cultures

- Treating a superficial wound colonized by commensal bacteria and no inflammation with antibiotics has no evidence supporting that it aids wound healing or prevents infections
- To reduce the likelihood of identification of non-pathogenic colonizers, all infected wounds should be cultured by obtaining tissue through either curettage or biopsy to be most accurate
- Samples should be collected after wound cleansing and debridement
- If possible, specimens should be collected before antibiotic therapy has begun, to avoid false-negative culture results

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Laboratory Processing

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Culture Techniques

- **Solid media cultures**
  - **Agar** plates (blood, MacConkey) and incubated under appropriate conditions
- **Liquid media cultures**
  - Blood cx and sterile body fluids onto **broth** media to enhance detection of low level bacteremia or fungemia
- **Specialized media**
  - For **fastidious** organisms, specialized media and conditions
    - E.g. Lowenstein Jensen media for Mycobacterium tuberculosis
- **Automated systems**
  - For culture incubation and monitoring -> reduce turnaround time -> **improve detection rates**
- **Identification and susceptibility testing…**

Identification Methods

- **Traditional**: biochemical tests, cultures
- **Rapid methods**: Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS), Molecular Assays
  - MALDI-TOF – analyze unique protein signatures of microorganisms -> rapidly identify fungi and bacteria
  - Molecular assays (including PCR-based) – detect specific pathogens and resistance genes directly from clinical specimens

Susceptibility Testing

- **Phenotypic Methods**
  - Broth microdilution, disk diffusion, gradient diffusion
  - Determine MIC
  - Use of automated systems to increase speed and accuracy of above
- **Genotypic Methods**
  - Molecular assays: detect resistance genes ; LESS accurate in detecting polymicrobial infections
  - Can be discrepancy* between genotype and phenotype
- **Advanced Techniques**
  - MALDI-TOF MS based methods emerging: Minimal Profile Change Concentrations (MPCC) and Direct-on-Target Microdroplet Growth Assay (DOT-MGA) to increase speed and accuracy of testing

Yee, R., Dien Bard, J., & Simner, P. J. (2021). The Genotype-to-Phenotype Dilemma: How Should Laboratories Approach Discordant Susceptibility Results?. *Journal of clinical microbiology*, *59*(6), e00138-20. https://doi.org/10.1128/JCM.00138-20

Biomarkers

- NO single biomarker identified with high diagnostic accuracy

Biomarkers for diagnosis and prognosis of sepsis, identified by literature search, with select references

Biomarker	Commercially Available Assay	Biomarker Evaluated for Diagnostic Usefulness by Disease Category			Prognostic Usefulness	Patient Population		Health Care Setting		Study Design		
		Sepsis	Severe Sepsis	Septic Shock		Adult	Pediatric	ED	Hospital (ICU)	Clinical, Observational	Clinical, Randomized-Controlled, Interventional	Experimental
CRP	Yes	✓	✓	✓	(✓)	X	X	X	X	X	X	—
PCT	Yes	✓	✓	✓	(✓)	X	X	X	X	X	X	X
IL-6, IL-8	Yes	✓	✓	✓	✓	✓	✓	X	X	X	X	X
ADM	Yes [a]	(✓)	✓	✓	✓	✓	—	—	X	X	—	X
LBP	Yes [a]	✓	(✓)	(✓)	—	✓	—	—	X	X	—	—
PTX3	No	—	(✓)	(✓)	(✓)	✓	—	X	X	X	—	—
EAA	No	(✓)	(✓)	(✓)	(✓)	✓	—	—	X	X	—	X

✓, the test is useful; (✓), limited usefulness or insufficient data for evaluation; X, studies met specific patient care settings and study design characteristics as specified in the table; —, the studies had no usefuln setting.

Abbreviations: ADM, adrenomedullin; CRP, C-reactive protein; EAA, endotoxin activity assay; IL, interleukin; LBP, lipopolysaccharide-binding protein; PCT, procalcitonin; PTX3, pentraxin 3.

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Riedel, S., & Carroll, K. C. (2013). Laboratory detection of sepsis: biomarkers and molecular approaches. *Clinics in laboratory medicine*, *33*(3), 413–437. https://doi.org/10.1016/j.cll.2013.03.006

Procalcitonin Use

- Upregulated in epithelial cells encountering bacterial pathogens and down-regulated in viral infections
  - May avert unnecessary antibiotic use in viral infections
- Timeline:
  - Rises 3-6 hours and peaks at 12-24 hours after bacterial infection
  - Declines up to 50% per day with appropriate treatment
- Applications:
  - Supports decision making on duration of antibacterial treatment
  - Limited evidence for treatment initiation
  - Nonspecific*

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Antibiograms

Creation & Interpretation

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Role of Antibiograms (AKA CASRs)

- **Clinical tools** to report + track antibiotic susceptibility + guide empiric antimicrobial therapy
- Can be tailored to **various settings**: general inpatient, outpatient, ICU
- Many uses:
  - Assisting prescribers select effective therapy when culture results are pending
  - Informing and updating local guidelines for empirical treatment of common infection syndromes
  - Updating periprocedural or perioperative prophylaxis recommendations
  - Providing a rationale for antimicrobial formulary selection
  - Surveying local resistance and benchmarking
  - Identifying targets for stewardship interventions and best practices
  - Providing the context for new drug susceptibility testing results

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Creating Antibiogram

- Multidisciplinary approach
- Clinical and Laboratory of Standards Institute (CLSI) publishes the M39 Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data, which is a commonly referenced guideline on how to create antibiograms
- Steps to take:
  1. Data collection
  2. Data analysis
  3. Stratification
  4. Compilation
  5. Review and Validation
  6. Dissemination

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Barlam, T. F., Cosgrove, S. E., Abbo, L. M., MacDougall, C., Schuetz, A. N., Septimus, E. J., Srinivasan, A., Dellit, T. H., Falck-Ytter, Y. T., Fishman, N. O., Hamilton, C. W., Jenkins, T. C., Lipsett, P. A., Malani, P. N., May, L. S., Moran, G. J., Neuhauser, M. M., Newland, J. G., Ohl, C. A., Samore, M. H., … Trivedi, K. K. (2016). Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, *62*(10), e51–e77. https://doi.org/10.1093/cid/ciw118

Krishnamoorthy, S. G., Raj, V., Viswanathan, B., Dhanasekaran, G. P., Palaniappan, D., & Borra, S. S. (2022). Enhancing the empiric antibiotic selection by introducing an antibiogram toolkit in a tertiary care hospital in Southern India - A prospective study. Journal of clinical pharmacy and therapeutics, 47(4), 507–516. https://doi.org/10.1111/jcpt.13571

Developing an Antibiogram

- A cumulative report of bacterial susceptibility to antibiotics
  - Minimum **1 year** interval
  - Reports % of isolates that are **susceptible**
- Must be reported per organism
  - Should have at least **30 isolates***
  - Must be from clinical isolates (not screening cultures)
  - First isolate per patient per interval
- Created to reflect specific populations
  - Specific hospital units (ICU vs General Medical Unit)
  - Inpatient vs Outpatient

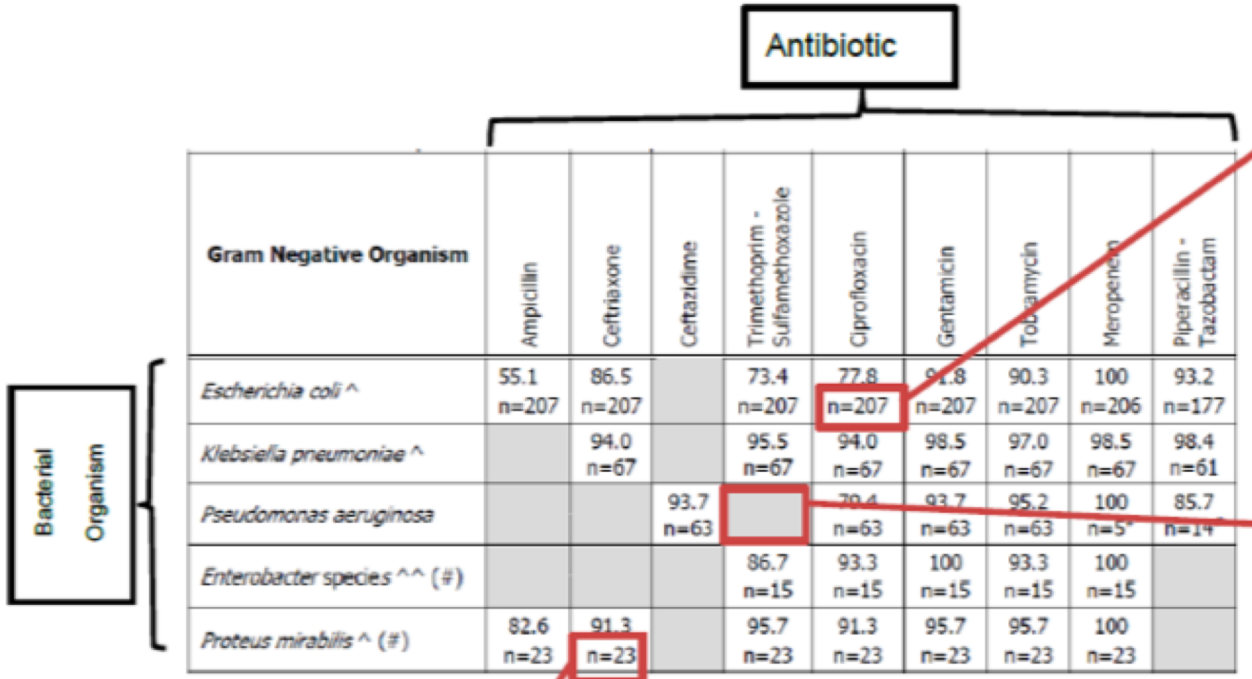
Steps to Creating an Antibiogram

1) Request the following data from your lab for the last one year:
    1) Culture date, culture source, culture results (organism), antibiotic susceptibility
    2) Or review charts by hand if not available
    3) Use the first isolate for the patient if patient-specific cultures are repeated
2) Add the information into a spreadsheet format
    1) Create a table like on the next slide
    2) Remove antibiotics that would never be used for that infection to avoid confusion
3) Decide how you will disseminate the results
4) Decide how regularly you will update the antibiogram

Using Antibiogram for Stewardship

- **Formulary considerations:**
  - Consider formulary changes using the antibiogram as a guide (change agents within the same class)
  - Could add $$$ to specify which antibiotics are most costly for the hospital
- **Antibiotic restriction:**
  - Use of specific agents or classes of agents may be restricted or controlled based on antibiogram susceptibility trends
- **Order set:**
  - Incorporating antibiogram data and trends into hospital-specific order sets, guidelines, and clinical pathways in order to increase or decrease use of specific agents based on susceptibility

Three quick tips to using the antibiogram



Gram Negative Organism	Ampicillin	Ceftriaxone	Ceftazidime	Trimethoprim - Sulfamethoxazole	Ciprofloxacin	Gentamicin	Tobramycin	Meropenem	Piperacillin - Tazobactam
Escherichia coli ^	55.1 n=207	86.5 n=207		73.4 n=207	77.8 n=207	91.8 n=207	90.3 n=207	100 n=206	93.2 n=177
Klebsiella pneumoniae ^		94.0 n=67		95.5 n=67	94.0 n=67	98.5 n=67	97.0 n=67	98.5 n=67	98.4 n=61
Pseudomonas aeruginosa			93.7 n=63		79.4 n=63	93.7 n=63	95.2 n=63	100 n=5*	85.7 n=14
Enterobacter species ^^ (#)				86.7 n=15	93.3 n=15	100 n=15	93.3 n=15	100 n=15	
Proteus mirabilis ^ (#)	82.6 n=23	91.3 n=23		95.7 n=23	91.3 n=23	95.7 n=23	95.7 n=23	100 n=23	

1. The number of isolates (n= #) reflects the number of bacterial isolates tested. The higher the number, the more accurate the sensitivity results

2. Grey boxes indicate that no data is available for the organism against the antibiotic

3. If the number of isolates is less than 30, the results are considered unreliable in guiding empiric treatment decisions

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Case #1

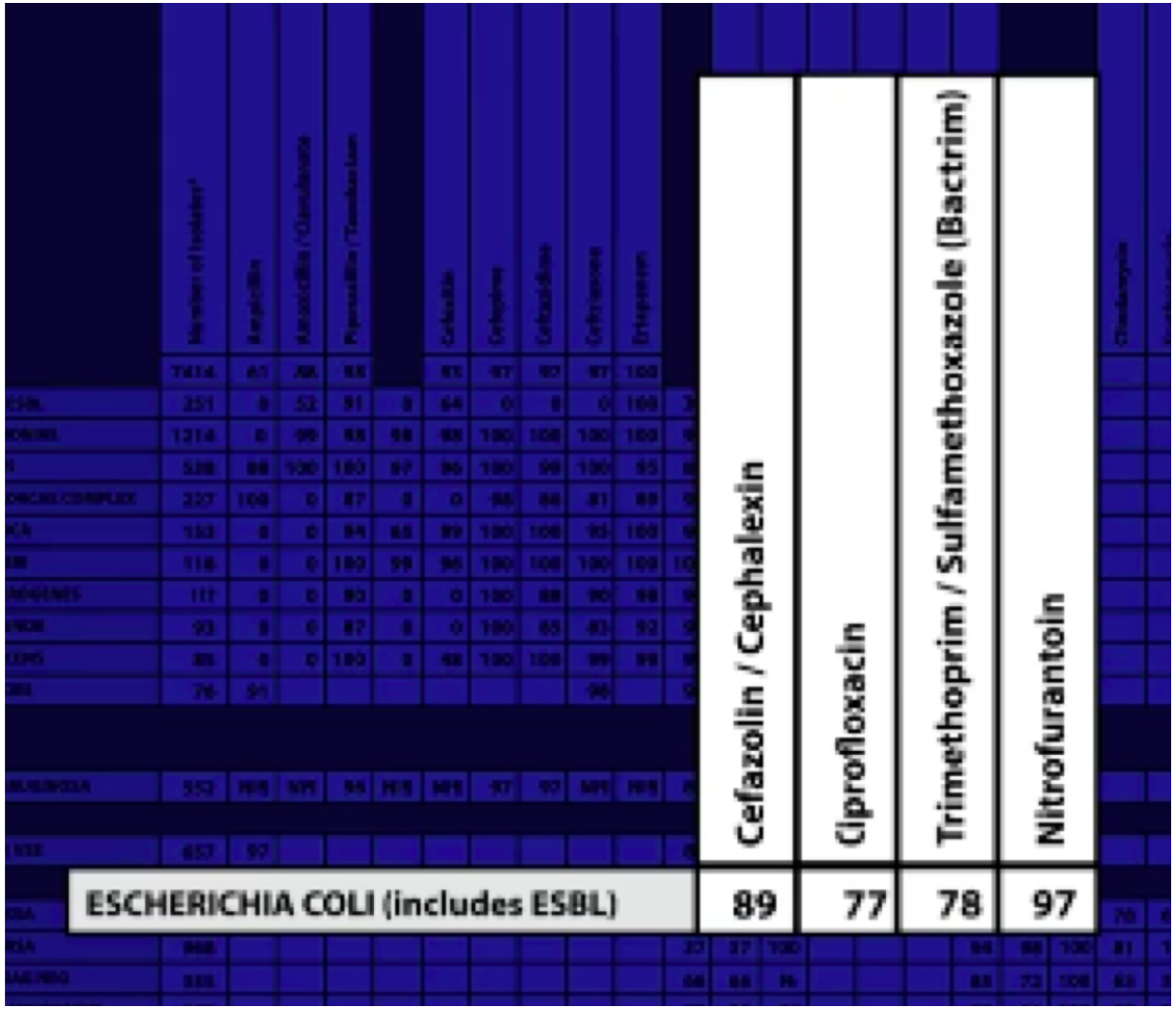
- 36 year old female presents to your office with classic signs of UTI, including dysuria and increased frequency. She rarely gets UTI, but when she does, she takes ciprofloxacin. She is otherwise healthy and has no drug allergies. The urine dipstick is positive for leukocyte esterase and bacteria.

  –What is the most likely organism causing her UTI?

Case #1

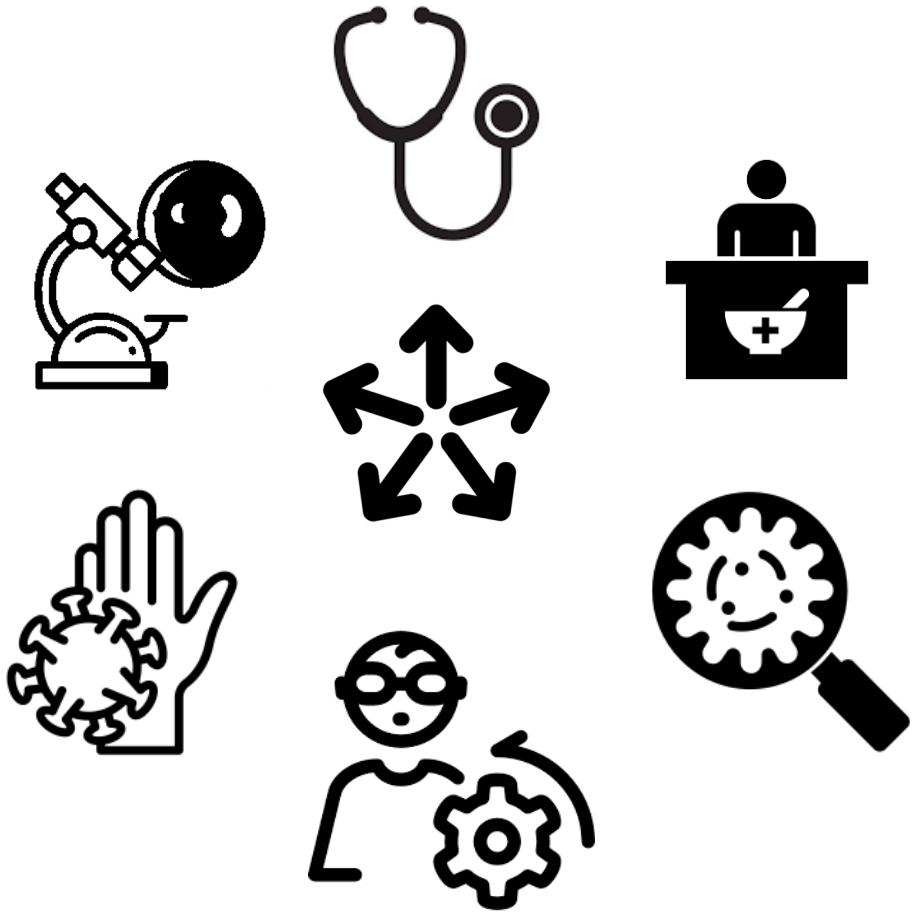
What antibiotic would you choose based on the antibiogram?

A. Cefazolin
B. Ciprofloxacin
C. Trimethoprim/sulfa
D. Nitrofurantoin



Summary

- The hospital microbiology lab plays a critical role in infection control and AMS programs
- Collaboration for surveillance and reporting of results
- Creation of antibiograms



Thank-you!

Questions?