Diagnostic Stewardship

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Overview

- Definition
- Objectives
- Pre-analytic
- Analytic
- Post-analytic
- Culture report interpretation
- Impact

Definition

- “Coordinated guidance and interventions to improve appropriate use of microbiological diagnostics to guide therapeutic decisions. It should promote appropriate, timely diagnostic testing, including specimen collection, and pathogen identification and accurate, timely reporting of results to guide patient treatment” -WHO (GLASS manual)

Objectives

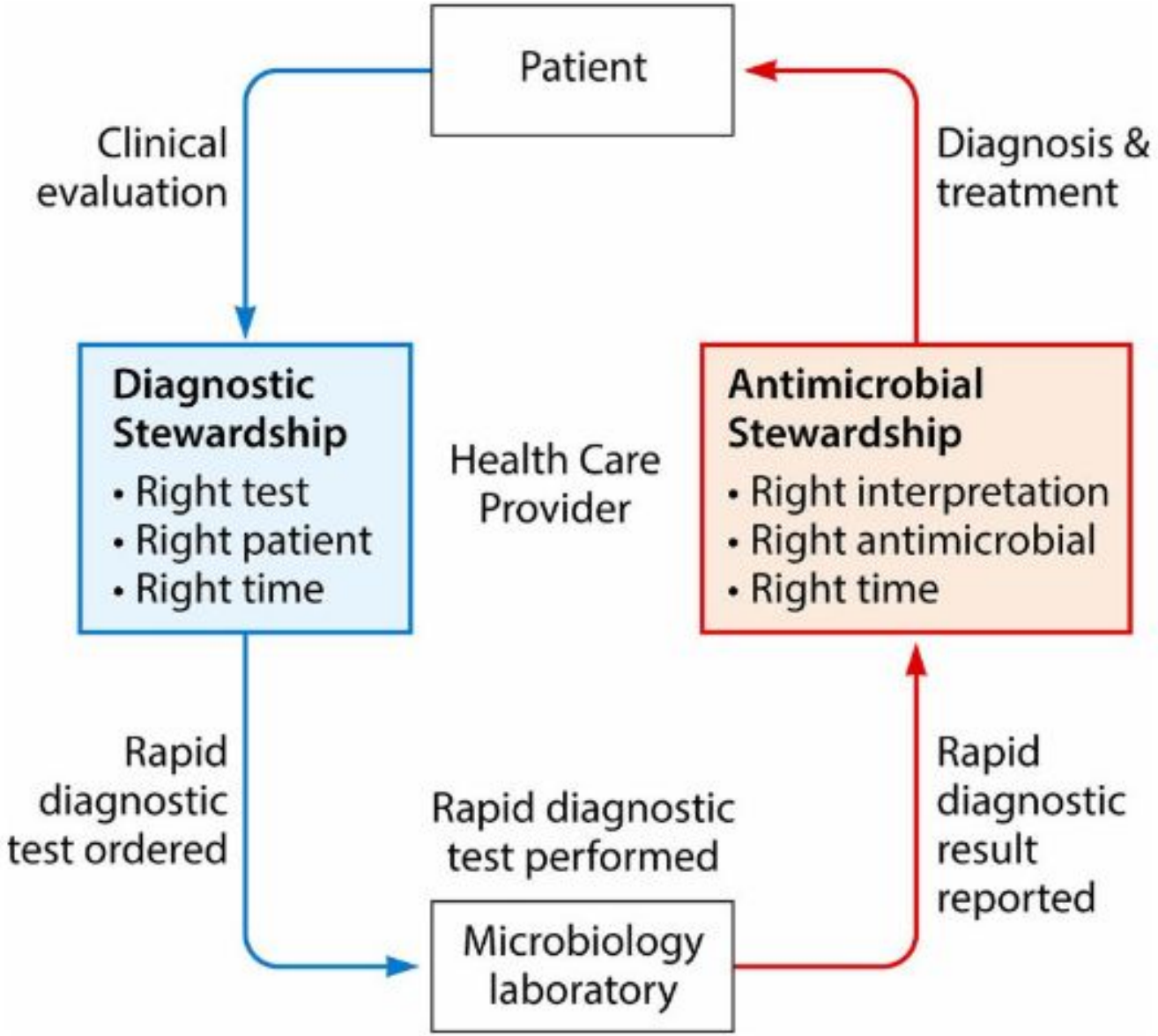
- Patient management guided by timely microbiological data to deliver safer and more effective and efficient patient care

- Accurate and representative AMR surveillance data to inform treatment guidelines, and AMR control strategies

Right test by right method within the right time

- Clinical Components:
  - Ordering Right Test (Indication)
  - Collecting Right Specimen at Right time

- Microbiological Components
  - Test by Right Method- accurate, reliable
  - Right Interpretation of test
  - Communicating report at the right time


Patient
Clinical evaluation
Diagnosis & treatment
Diagnostic Stewardship
• Right test
• Right patient
• Right time
Health Care Provider
Antimicrobial Stewardship
• Right interpretation
• Right antimicrobial
• Right time
Rapid diagnostic test ordered
Rapid diagnostic test performed
Rapid diagnostic result reported
Microbiology laboratory

PHASES

- Pre-analytics
- Analytic
- Post-analytic

Phase	Critical personal
Pre-Analytic	Clinician & Nursing officer
Analytic	Microbiologist
Post-Analytic	Clinician

Pre-analytic

- Specimen selection and collection
- Storage and transport

Sample collection and transport

- Results generated by lab is limited by the quality and condition of specimen on arrival in the laboratory.

- The proper collection of a sample → most important step of the recovery of the infectious agent causing disease.

- A poorly collected sample :

✔ may result in failure to recover causative microorganism

✔ may lead to incorrect or even harmful therapy if treatment is directed towards a commensal or containment.

COLLECTION

- The specimen must be collected with use of **strict aseptic technique** from anatomic sites most likely to yield pathogenic microorganisms.
- Specimens should be collected in such a way that contamination by indigenous flora is minimized.
- Collect the specimen before administration of antimicrobial agents as far as possible.
- **Sufficient material** must be submitted for cultures and other tests.
- Volume, while important for all specimens, is crucial for blood and for mycobacterial and fungal cultures of CSF and urine.
- Specimen should be collected at the appropriate phase of the disease.

- Persons collecting specimens should provide complete information on specimen requisition forms or in computerized order entry systems.

- Important information includes
  - The specific **site(s)** from which specimens were collected
  - Whether the patient was receiving **antimicrobial therapy** prior to specimen collection or at the time specimens were collected;
  - specific pathogens that are being sought;
  - the methods by which specimens were collected; and
  - whether the patient may be infected with pathogens known to be **hazardous to laboratory personnel** (e.g., *Brucella* or *Mycobacterium tuberculosis*).

SPECIMEN REQUISITION

- The specimen (or test) requisition is an order form that is sent to the laboratory along with a specimen.
- The requisition should contain as much information as possible.
- A complete requisition should include the following:-

- Patient's name
- Registration number
- Age /Sex
- Address
- OPD/IPD
- Collection date and time
- Source and type of specimen
- Tests requested
- Probable diagnosis
- Immunisation history
- Antimicrobial therapy

TRANSPORT

- Specimens collected should be transported in sterile specimen containers.
- Specimens for culture should be transported to the laboratory as promptly as possible for processing.
- Most specimens can be transported at room temperature.

STORAGE

- Refrigeration maintains the viability of pathogens and preserves them in the irrelative proportions.
- Refrigeration also minimizes the growth of contaminants.
- Specimens that should not be refrigerated include :
  - Blood, which should be kept at room temperature or in an incubator at 35°C
  - CSF, which, with the exception of that collected for viral cultures, should be transported at room temperature;

REJECTION CRITERIA

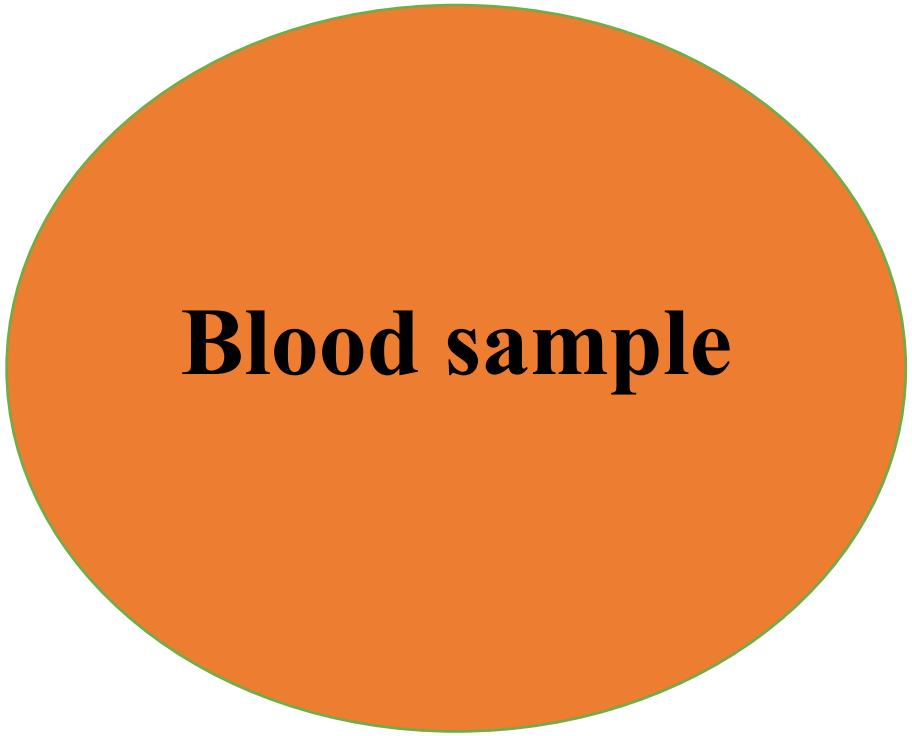
- Unlabelled or improperly labeled specimens
- Specimens received in leaking, cracked, or broken containers
- Specimens with obvious (visually apparent) contamination
- Unpreserved specimens received>12hours after being collected
- Specimens not appropriate for a particular test
- The specimen has been transported at improper temperature.
- The specimen has not been transported in the proper medium.

REJECTION CRITERIA

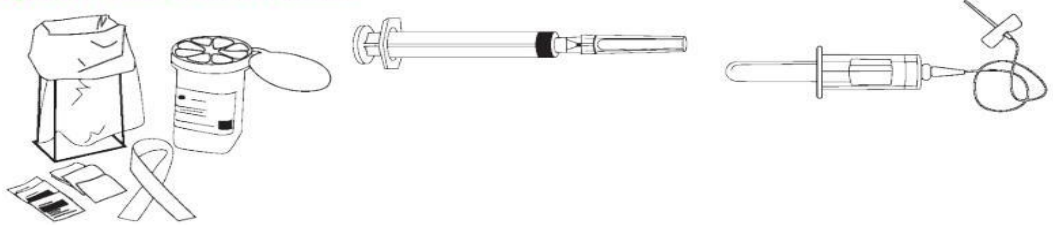
- The quantity of specimen is insufficient for testing (single swab submitted for multiple requests eg. aerobes, anaerobes, fungus, TB).
- The specimen is received in formalin.
- The specimen is dried up.
- Haemolysed /lipaemic / turbid serum samples.

 Effort should be made not to reject samples that are difficult to recollect such as CSF, pleural fluid, ascitic fluid etc.

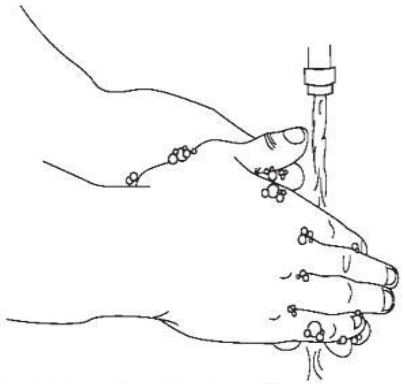
COLLECTION



- Blood should be collected before administration of antibiotics.
- Skin antisepsis is extremely important to reduce the risk of introducing contaminants into the blood culture media.
- Even with good collection technique, 1%-3% of blood cultures are found to be contaminated.
- Blood culture contamination rates can be minimized by strict adherence to aseptic collection technique and, whenever possible, collection of peripheral blood via venipuncture rather than via indwelling vascular catheters

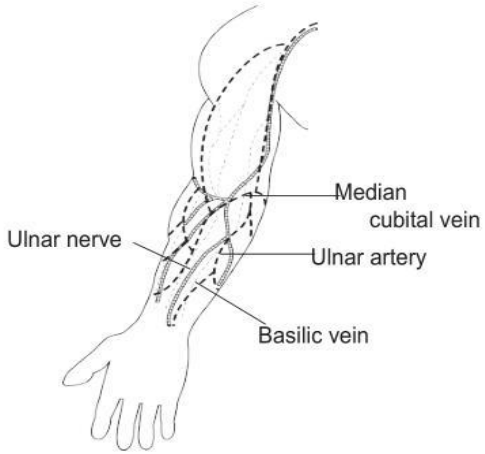


1. Assemble equipment and include needle and syringe or vacuum tube, depending on which is to be used.

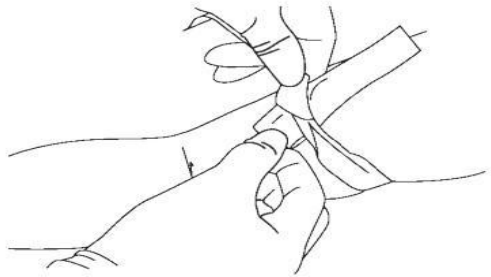


2. Perform hand hygiene (if using soap and water, dry hands with single-use towels).

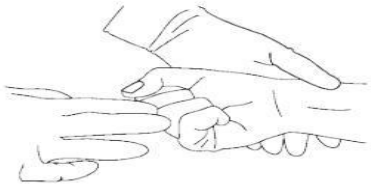
3. Identify and prepare the patient.



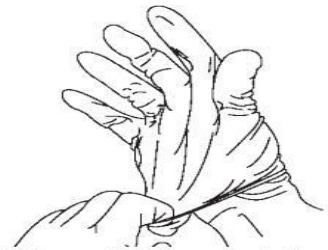
4. Select the site, preferably at the antecubital area (i.e. the bend of the elbow). Warming the arm with a hot pack, or hanging the hand down may make it easier to see the veins. Palpate the area to locate the anatomic landmarks. DO NOT touch the site once alcohol or other antiseptic has been applied.



5. Apply a tourniquet, about 4–5 finger widths above the selected venepuncture site.

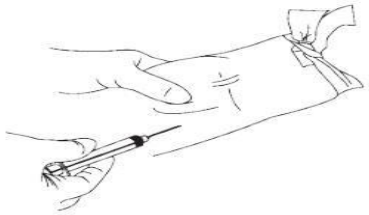


6. Ask the patient to form a fist so that the veins are more prominent.

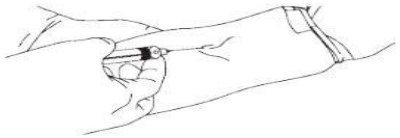


7. Put on well-fitting, non-sterile gloves.

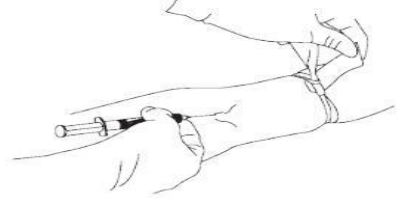
8. Disinfect the site using 70% isopropyl alcohol for 30 seconds and allow to dry completely (30 seconds).



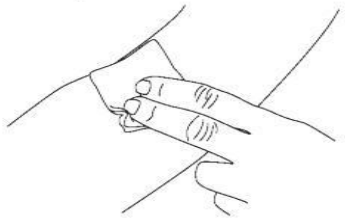
9. Anchor the vein by holding the patient's arm and placing a thumb BELOW the venepuncture site.



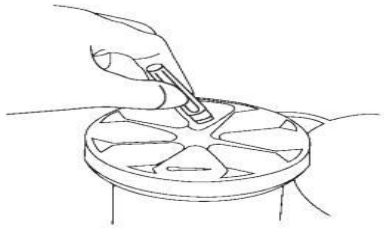
10. Enter the vein swiftly at a 30 degree angle.



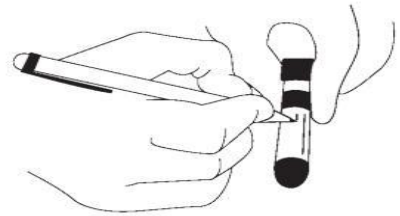
11. Once sufficient blood has been collected, release the tourniquet BEFORE withdrawing the needle.



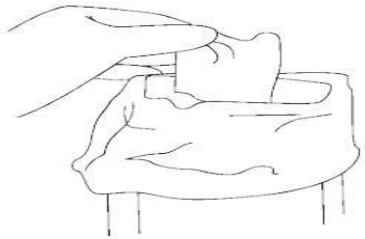
12. Withdraw the needle gently and then give the patient a clean gauze or dry cotton-wool ball to apply to the site with gentle pressure.



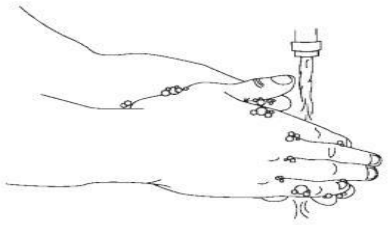
13. Discard the used needle and syringe or blood-sampling device into a puncture-resistant container.



14. Check the label and forms for accuracy.



15. Discard sharps and broken glass into the sharps container. Place items that can drip blood or body fluids into the infectious waste.



16. Remove gloves and place them in the general waste. Perform hand hygiene. If using soap and water, dry hands with single-use towels.

METHOD OF COLLECTION OF BLOOD SAMPLE

- Using 70% alcohol, the skin over the venipuncture site is cleaned in a circle approximately 5 cm in diameter by rubbing vigorously.
- 2% tincture of iodine or 10% povidone iodine or chlorhexidine (0.5% in 70% alcohol) are applied in circles and left for 1-2 minutes to dry.
- Iodine is removed by a 70% alcohol wash.
- If the site must again be palpated after the iodine - alcohol preparation, the finger must be disinfected or sterile gloves worn.
- Immediately after collection of blood The top of the blood culture bottle is cleaned with ethanol swab and blood is injected into the bottle aseptically.
- If a patient has an existing IV line, blood should be drawn below the existing line.
- Blood drawn above the line will be diluted by the fluid being infused.

VOLUME OF BLOOD

Table 6.2: Optimum volume to be collected in different age groups depending upon the body weight and body's total blood volume.[4,5]

Age group	Blood culture set	Volume per bottle	Total volume sampled per BC series*	Total blood volume of the patient	% of patient blood volume sampled
For neonates (<1 kg)	One BC set	1 mL	2 mL	50–99 mL	4%
For neonates (1–2 kg)	One pair of BC set	1 mL	4 mL	100–200 mL	4%
For infants (2–12 kg)	One pair of BC set	1.5 mL	6 mL	~200 mL	3%
For children (12–36 kg)	One pair of BC set	5 mL	20 mL	~800 mL	2.5%
For children (>36 kg)	Two to three pair of BC set	10 mL	40–60 mL	~2200 mL	1.8–2.7%
Adults	Two to three pair of BC set	10 mL	40–60 mL	5000 mL	0.8–1.2%

*Blood culture (BC) series is defined as one or more BC specimens obtained serially within a 24-hour period to detect a bloodstream infection (BSI) episode.

TIMING OF COLLECTION

- 2-3 samples may be taken at intervals of several hours from different venepuncture sites.
- The strategy depends upon the clinical condition and the degree of urgency to start antimicrobial treatment.

❖ For patients with suspected infective endocarditis , the results of three or four blood cultures may establish the presence of continuous bacteremia and help the physician determine the clinical relevance of the isolates that are recovered.

❖ For children, two or three blood specimens should be drawn.

❖ Single blood cultures for the detection of pathogens other than mycobacteria should not be done.

TRANSPORT AND STORAGE OF BLOOD SAMPLE

- Blood culture bottles should be transported immediately to the laboratory.
- If this is not possible, bottles can be kept at room temperature or in an incubator at a temperature of 35°C to 37°C.
- These bottles should never be refrigerated.

URINE SAMPLE

- All areas of the urinary tract above the urethra in a healthy human are sterile
- For microbiological examination 5-10 ml urine should be collected as clean catch midstream urine specimen.
- In a catheterised patient the soft rubber connector between the catheter and the collecting tube is cleaned vigorously with 70% ethanol and urine aspirated by a sterile syringe.
- Specimen should not be obtained from the collecting bag.
- Suprapubic aspiration is done for neonates and small children by disinfecting the skin over the bladder. Urine is aspirated by a 18-gauge short bevel spinal needle.

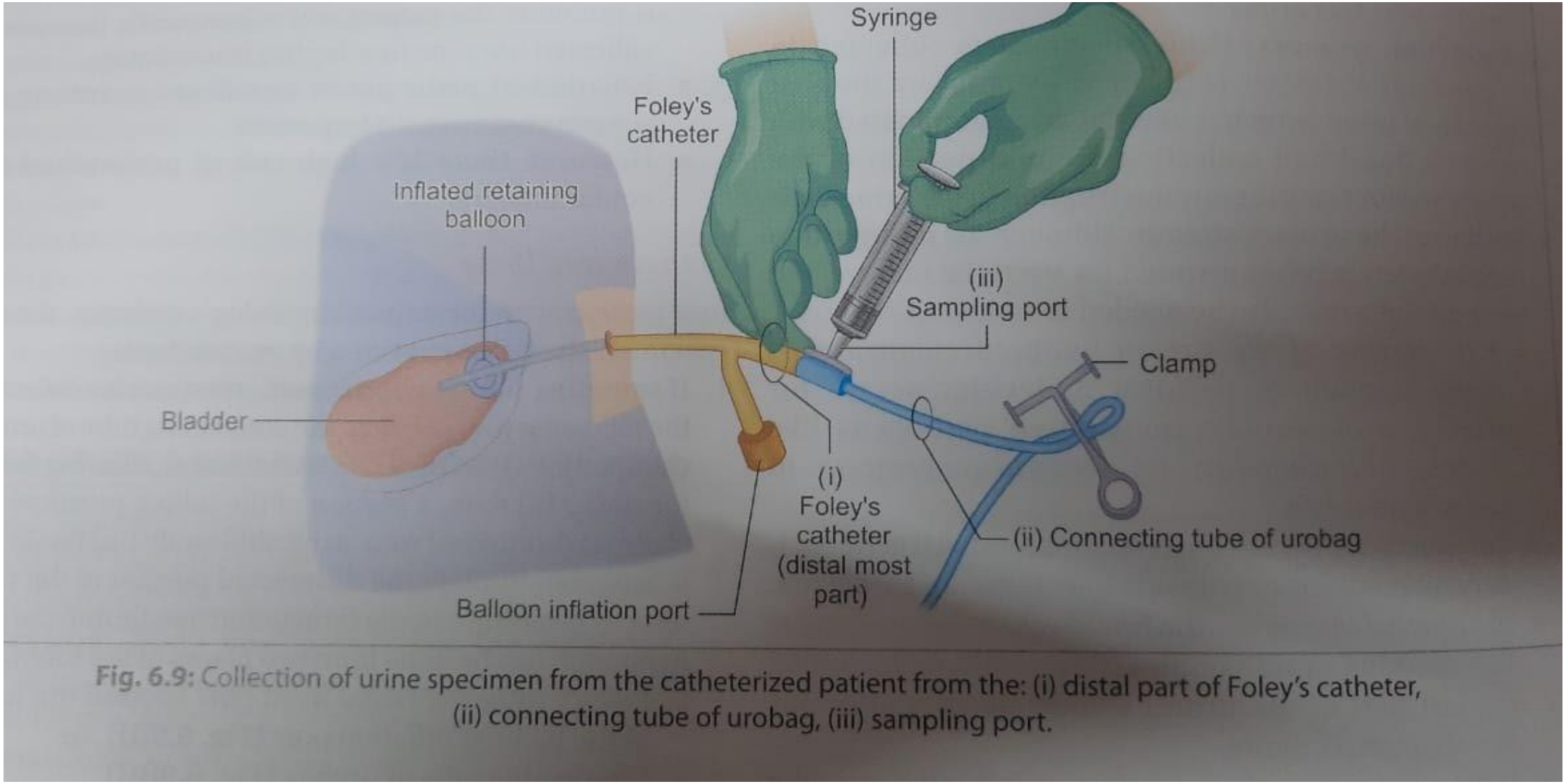


Fig. 6.9: Collection of urine specimen from the catheterized patient from the: (i) distal part of Foley's catheter, (ii) connecting tube of urobag, (iii) sampling port.

TRANSPORT

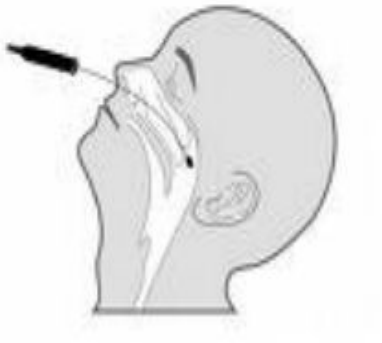
- Specimen should be processed within 2 hrs.
- In case of delay the specimen can be refrigerated for upto 6 hrs.
- In the absence of refrigeration boric acid in a concentration of 1.1% maintains bacterial counts in remote areas for upto 24 hrs.

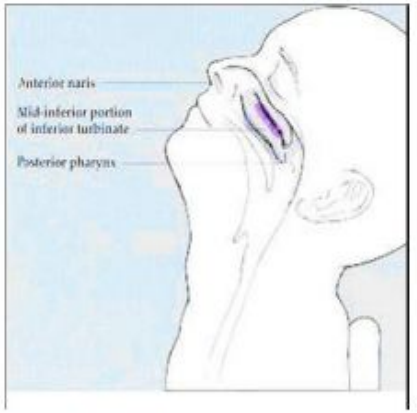
Throat swabs

- For bacteriological sampling, albumin coated or charcoal coated or plain cotton wool swabs should be used.
- A bright light should be focused into the oral cavity.
- The patient is instructed to tilt his or her head back and breathe deeply.
- The tongue is gently depressed with a tongue blade to visualise the tonsillar fossae and posterior pharynx.
- The patient is asked to make the sound 'ah' which serves to lift the uvula and helps prevent gagging.
- The inflamed areas of the throat, tonsils and then the pharynx are swabbed, taking care not to touch the lateral walls of the buccal cavity or the tongue to minimise contamination with commensal bacteria.

- Swabs should be sent to the laboratory within 4 hrs.
- In case of delay they should be refrigerated or sent in a transport media.
- While swabs have the advantage of being convenient and easy to use, they limit the volume of specimen that can be collected, they can compromise a direct gram stain, they become contaminated easily, and they can adversely affect recovery of certain microorganisms.

NASOPHARYNGEAL SWABS





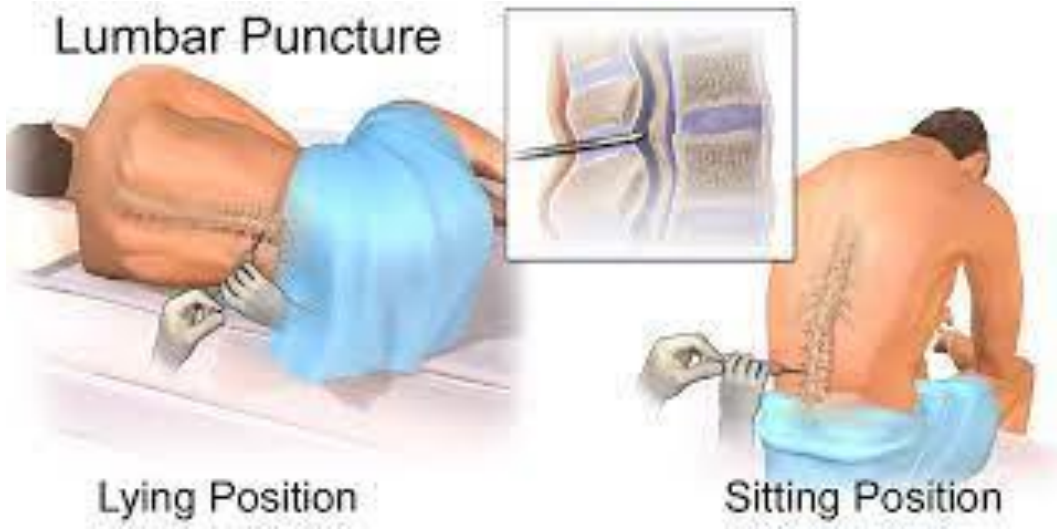
- Insert swab into one nostril.
- Rotate swab over surface of posterior nasopharynx.
- Withdraw swab from collection site; insert into saline transport tube
- Repeating procedure for the second nostril will deliver optimal combined sample.
- After collection, immediately transport specimen to the laboratory for viral testing and viral antigen detection. If transport is delayed, place specimen on ice or in refrigeration.

Cerebrospinal fluid (CSF)

- The specimen is collected aseptically only by a trained doctor/physician.
- The risk of contamination is low when the skin is adequately disinfected prior to lumbar puncture; either an iodophor or chlorhexidine can be used for disinfection.
- The following important precautions need to be taken for CSF collections and transportation.
  - CSF should be collected before administration of antibiotics as far as possible.
  - 3-10 ml of CSF should be collected in 3-4 sterile screw capped containers for microbiological and chemical studies.
  - It should be hand delivered immediately to the laboratory.
  - Specimens should never be refrigerated.
  - If CSF cannot be processed immediately it should be incubated at 37°C or left at room temperature.

CSF collection

- Skin disinfection LP needle with stylet is inserted at L3-L4, L4-L5 or L5-S1 interspace when subarachnoid space is reached, stylet is removed and CSF is slowly drained and collected in sterile containers.
- 1st container biochemical analysis
- 2nd container microbiological analysis
- 3rd container cytological analysis

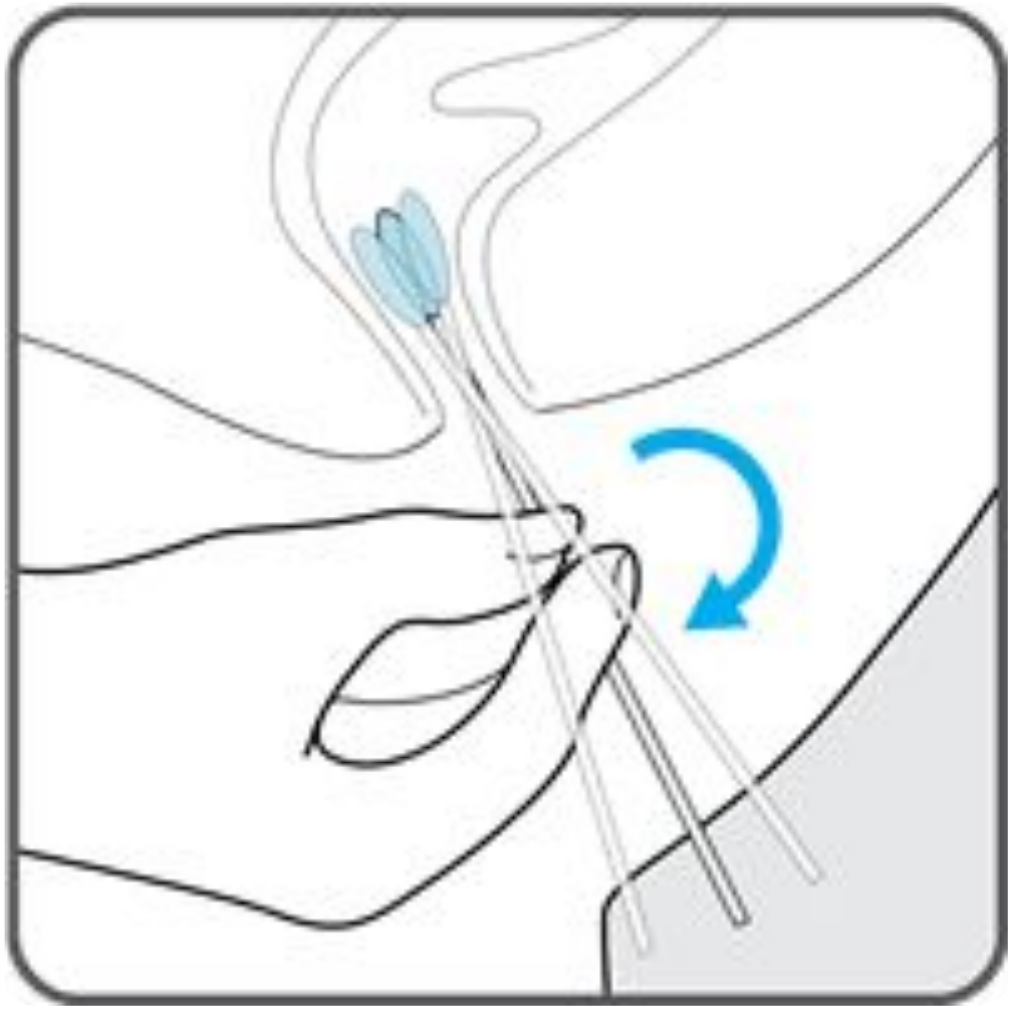


TRANSPORT AND STORAGE

- CSF specimens should be transported immediately to the laboratory.
- Systematic delays in transport should be identified and eliminated.
- Laboratories should strive to report the results of initial tests within 30 minutes of receipt of the specimen in the laboratory.
- From collection through processing, CSF specimens (except aliquots collected for viral cultures) should not be refrigerated until initial processing is completed.
- Laboratorians should consider using sequential testing to reduce the number of unnecessary CSF tests

STOOL SAMPLE

- Faeces for microbiological examination should be collected during the acute phase of diarrhoea.
- Specimen should be collected in a clean, dry, disinfectant free suitable wide mouthed container covered with a tight fitting lid.
- Contamination with urine should be avoided.
- Volume of stool to be collected liquid - 1 tsp (5ml), Formed stool pea sized (2 gm).
- Specimen should be delivered to the laboratory within 2 hours.
- In case of delay, specimen should be transported in transport media.

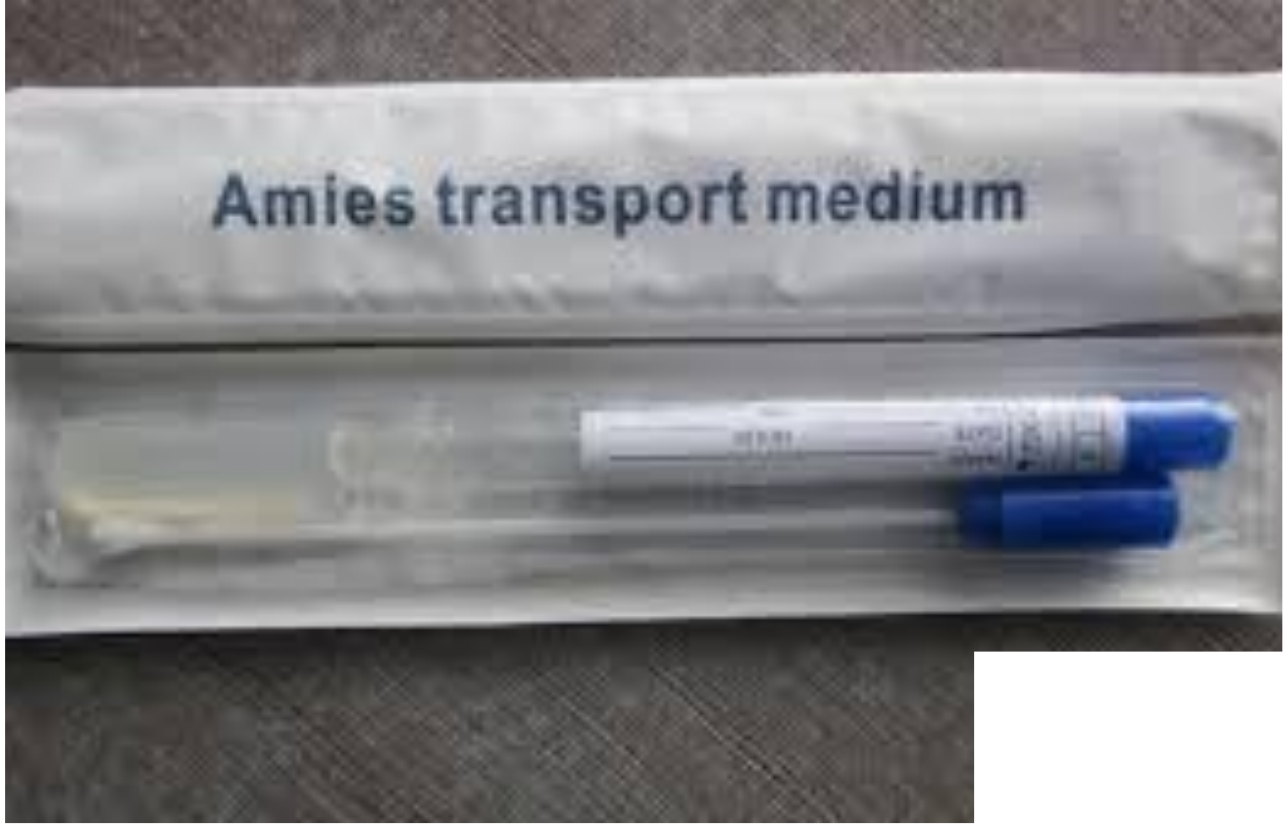


RECTAL SWABS

- Rectal swabs are used only if it is not possible to obtain faeces.
- Used for collecting samples in newborns or in severely debilitated patients.
- Swab should be inserted just beyond the anal sphincter and placed in transport medium, immediately to avoid drying

Wound, skin and deep sepsis

- Pus or exudate should be aspirated from the depths of wounds and abscesses with a sterile needle and syringe.
- Specimen should be transferred to a small sterile leak proof bottle or a firmly stoppered tube or sealed capillary tube.
- If material cannot be obtained with a needle and syringe, then a swab must be used.
- Two swabs one for direct microscopy and one for culture are taken from the depths of the wound or lesion and should be loaded well with the material.
- Transport : Specimen should be transported to the lab as soon as possible.
- In case of delay they should be transported in Amies and stuart's transport medium.


Amies transport medium

Sputum

- If possible sputum should be collected before any antibiotic therapy is begun.
- Sputum should be collected in a sterile wide mouthed container, preferably disposable and leak proof to prevent leakage or contamination during transport.
- The patients should be instructed, to inhale deeply 2-3 times, cough up deeply from the chest and spit in the specimen container by bringing it close to the mouth.
- Early morning sputum samples should be obtained as they contain pooled over night secretions.
- Staff collecting specimens should be instructed in how to obtain and recognise the correct material.

- Sputum from a bacterial infection is purulent containing yellow or green opaque material as well as clear mucoid secretion.

- Many patients may expectorate only saliva (watery fluid). Such samples should be discarded and a report sent to the physician stating that the specimen was mainly saliva and unsuitable for examination.

- Rejection criteria should be based on a microscopical as well as naked eye examination of the sample.

- The specimen should be delivered to the laboratory as quickly as possible, preferably within 2 hrs.

- In case of delay transport media should be used.

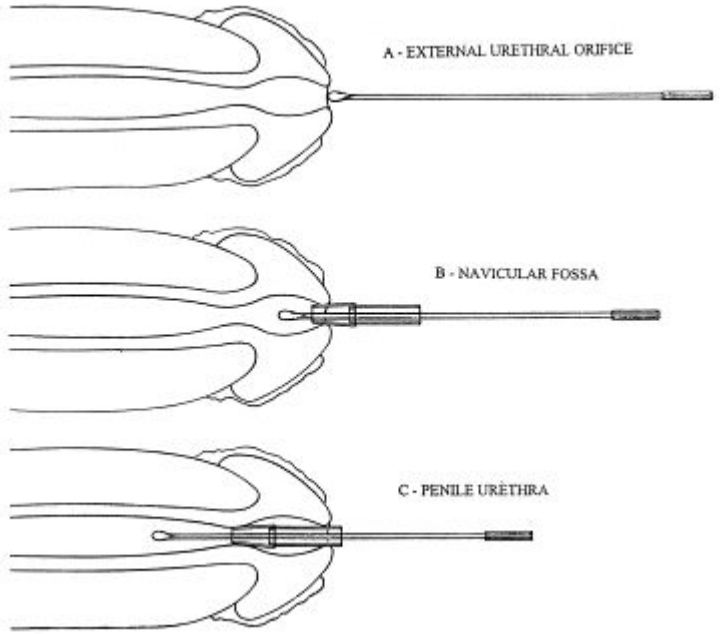
URETHRAL DISCHARGE

FROM MALE PATIENTS

- If possible collect the early morning sample before the patient passes urine or collection done atleast 1 hour after urination.
- Clean around the uretheral opening with sterile saline.
- Apply gentle pressure on the penis so that a drop of pus appears at the meatus.

If no pus appears, gently massage the urethra from above downwards.

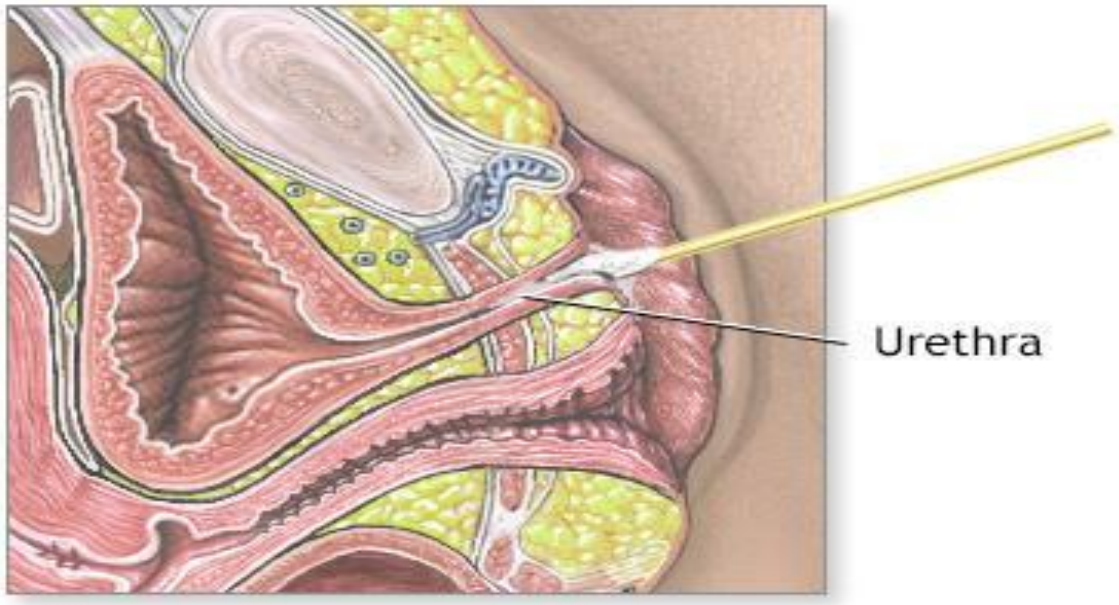
- If material is scanty, collect by inserting a narrow diameter cotton swab 2 cm into the anterior urethra.
- Two swabs are collected-one for direct microscopy and the second for culture.



FROM FEMALE PATIENT

- The specimen should be collected by a doctor or trained nurse with the aid of a speculum.

• Observe all the precautions as for collection of specimens in male and collect two swabs, as mentioned above.



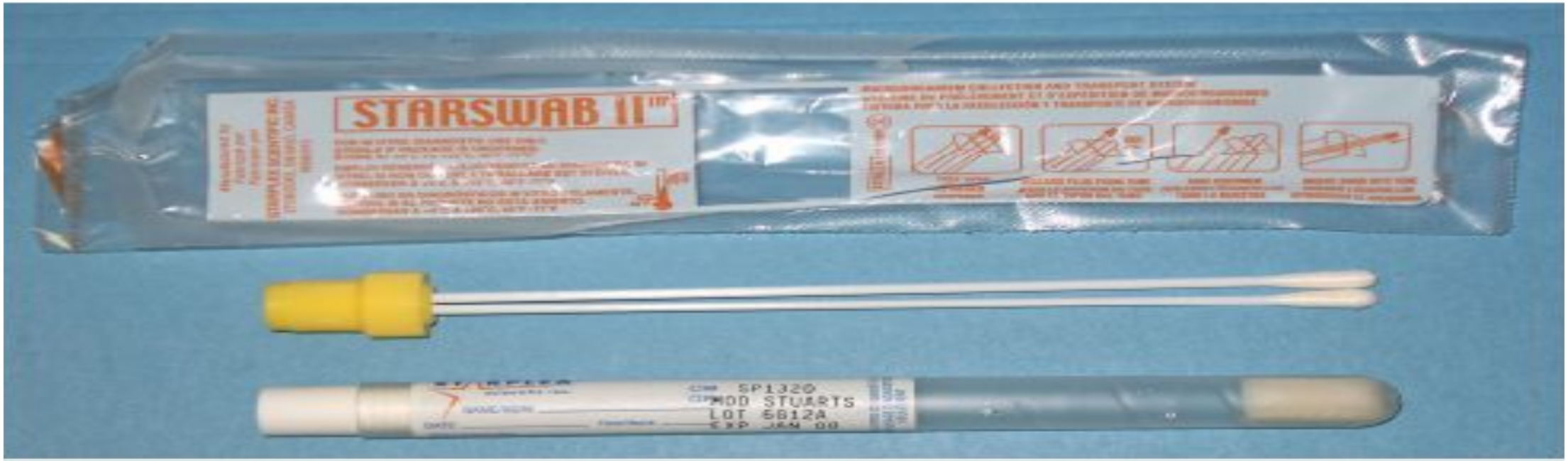
VAGINAL DISCHARGE

- The specimen should be collected by a doctor or trained nurse with the aid of a speculum.
- Swab mucosa high in the vaginal canal under direct visualization.
- Collect atleast two swabs.

GENITAL ULCER

- Wear protective gloves for this procedure.
- Clean the ulcer with a sterile gauze pad soaked in saline.
- Collect the exudate from the ulcer base with a sterile cotton swab.
- If there is no obvious serous fluid scrape the edge of the ulcer with a sterile flat edge of a scalpel blade till some blood is expressed.
- Blot the blood and then compress the ulcer gently with a gauze pad.
- Collect the exudate immediately on the slide and apply a coverslip.
- Transport should be done within 12 hrs.

Anaerobic Culture Collection Kit



Aerobic Culture Collection Kit:
Routine, Throat, Strep Screen A & B, Rapid Beta Strep, Genital

Turn around time (TAT)

- The local microbiology turnaround time (TAT) for each test is defined as the time of the receipt of the specimen into the laboratories to the time when the report is available to the requester

- TATs are specific to individual tests or specimen types

- This applies to preliminary results, such as gram-stain results, initial growth on plates and final results e. g. species identification and antimicrobial susceptibility

Turn around time	Definition: Duration between	Components	Reduced by
Laboratory TAT	Sample receipt and report signed	Culture →ID→AST	Automation Multi-stage reporting DST→AST ↕ Reporting frequency: Early, evening, holiday
Ward TAT	Sample collected and report received by ward	Sample transport time Report transport time	Live reporting

Analytics

- Identify the disease-causing organism and its susceptibility profile
- Proper documentation of specimen processing and reporting of results to clinicians
- Develop, implement and regularly update SOPs

Positive culture

Colonization

- Commensal microorganisms

Contamination

- Exogenous microorganisms introduced into a specimen

Infection

- Disease

Post Analytic

- Clinicians should expect to receive reports in a timely manner, including interpretive statements that enable the results to be easily and effectively applied for patient management

- Reports should be stored and be accessible in patient files, ideally also electronically

- Report negative results

Selective reporting

Selective reporting of AST results involves reporting results for specific antimicrobial agents while suppressing few others, based on different criteria :

- Organism isolation
- Mechanism of resistance
- Body site
- Clinical setting
- Patient demographics
- Aberrant results
- Unavailability of clinical breakpoint

Cascade reporting

- Involves reporting of the broader-spectrum and costlier agents only when the narrow-spectrum and cheaper are found to be non-susceptible.
- **First line agents:** usually of narrow spectrum, have oral formulations available, and/or cheaper and/or associated with fewer adverse events.
- **Second-line agents:** relatively broader-spectrum, available as parenteral/oral formulations, relatively expensive, &/or associated with fewer adverse events.
- **Restricted agents:** extensive-spectrum, mostly parenteral formulation, highly expensive &/or associated with severe adverse events, include agents reserved for management of MDROs.

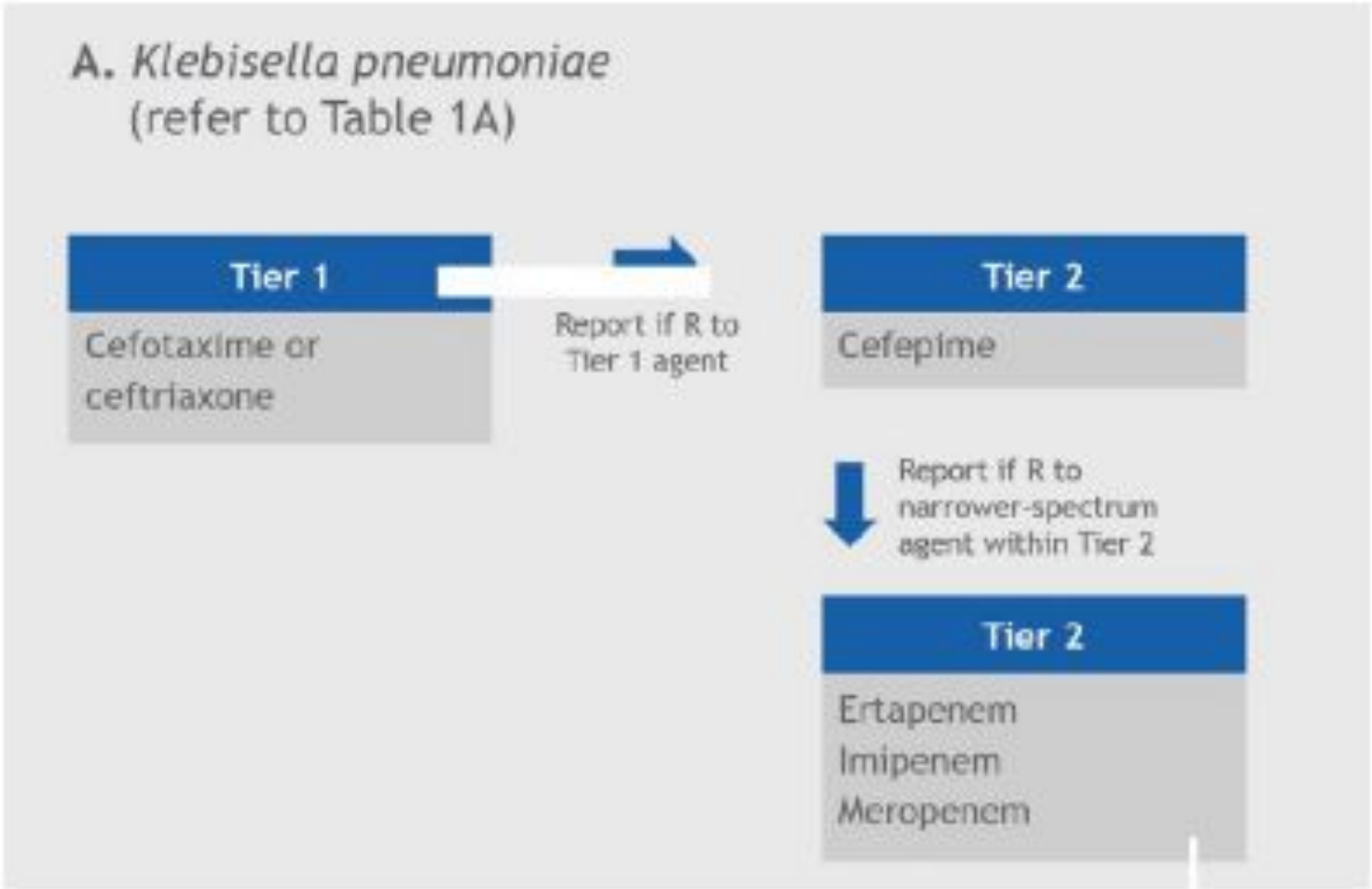
Tier based approach : CLSI 2023

- Clinical efficacy
- Prevalence of resistance
- Minimising emergence of resistance
- Cost
- Current recommendations on first line and alternative drugs

Tier Based Approach

CLSI Tier	Testing	Reporting
1	Routine	All
2 (General)	Routine	Cascade
3 (High risk for MDROs)	Routine or by request	Cascade
4	By request	By request
U only	Routine	As appropriate
Other (Mostly not in the list of first choice or alternative drugs)	By request	By request
Inv (No FDA approval)	By request	By request

Cascade reporting – Within Tiers

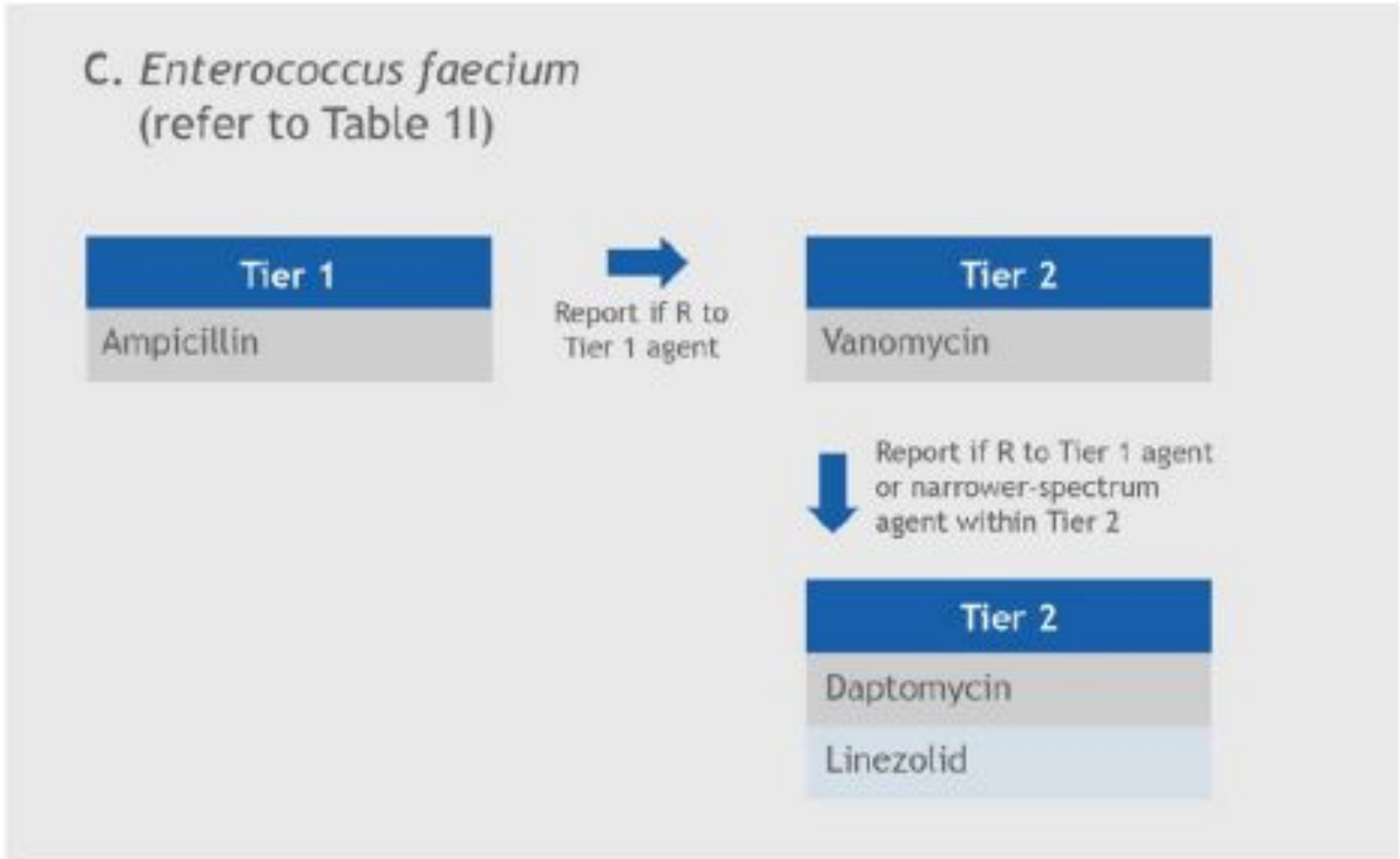


Cascade reporting – Between Tiers

B. *Klebisella pneumoniae*
(refer to Table 1A)

Tier 1	→ Report if R to Tier 1 agent	Tier 2	→ Report if R to Tier 1 and Tier 2 agents	Tier 3
Cefotaxime or ceftriaxone		Cefepime		Cefiderocol
		Ertapenem Imipenem Meropenem		Ceftazidime-avibactam Imipenem-relebactam Meropenem-vaborbactam

Cascade reporting – Within Tiers



All India Institute of Medical Sciences
Rishikesh

LABORATORY OBSERVATION REPORT

UHID:	20230159462	**Reg. Date:**	05/11/2023 03:29 AM
Patient Name:	[redacted]	**Ward Name:**	231 OUTBORN NICU
Sex:	Male	**Age:**	8 days
Order By:	Dr. Sriparna Basu	**Order Date:**	08/11/2023
Unit Name:	1	**Unit In-charge:**	Dr. Sriparna Basu
Sample Collection Date:	09/11/2023 09:37 AM	**Sample Received Date:**	
Lab Name:	MICROBIOLOGY	**Lab Ref No:**	
Department:	Neonatology	**Report Upload Date:**	11/11/2023 01:04 PM

Sample Details : 09112300053 (Blood) /Microbiology Lab Clinical Details :

Test Name : BLOOD CULTURE (AEROBIC)PAEDIATRIC/ ADULT AND AST (Template : 2023 BLOOD Methicillin-resistant Staphylococcus aureus (MRSA))

AEROBIC BACTERIAL CULTURE & SENSITIVITY

SAMPLE: ***BLOOD***

ORGANISM:*Methicillin-resistant Staphylococcus aureus (MRSA)*

ANTIBIOTICS	SUSCEPTIBILITY
Tier 1	
Erythromycin	R
Clindamycin	R
Oxacillin	R
Cefoxitin*	R
Tetracycline	**S**
Trimethoprim sulphamethoxazole	R
Vancomycin	**S**
Tier 2	
Linezolid	**S**
Daptomycin	**S**
Tier 3	
Ciprofloxacin	R
Levofloxacin	R
Gentamicin	**S**

Note: Cascade reporting (CR) is a strategy of reporting antimicrobial susceptibility test results in which secondary agents are only reported if an organism is resistant to primary, narrow spectrum agents within a drug class; to prevent antimicrobial resistance and better antibiotic stewardship. Tier 1 drugs must be preferred. Tier 2/3/4 drugs to be given if Tier 1 or subsequent Tier drugs resistant.

Tier 1: Primary and routine testing; Tier 2: Tested routinely but reported following cascade reporting; Tier 3: Tested routinely but reported following cascade reporting; Tier 4: tested and reported on request/ ffollowing cascade reporting.

Oxacillin (or cefoxitin) results can be applied to other penicillinase-stable penicillins (cloxacillin ,dicloxacillin, methicillin,nafcillin). Oxacillin (or cefoxitin) susceptible staphylococci can be considered susceptible to:

- β-lactam/β-lactamase inhibitor combinations (amoxiclav, ampicillin-sulbactam, piperacillin-tazobactam).
- Oral cephems
- Parentral cephems including cephalosporins I, II, III, IV gen.
- Carpapenems.
- Oxacillin resistant staphylococci are resistant to all currently available β-lactam antimicrobial agents, with the exception of the newer Cephalosporin with Anti-MRSA activity (as per CLSI 2023 guidelines)

NOTE:

- **Susceptible (S)**: Isolates can be inhibited by the usually achievable concentrations of antimicrobial agent with the dosages recommended.
- **Susceptible Dose Dependent (SDD)**: It is a category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosage regimen that is used in the patient. To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either MICs or zone diameters) are in the SDD category, it is necessary to use a dosage regimen (i.e. higher doses, more frequent doses or both) that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint. Consideration should be given to the maximum, literature-supported dosage regimen, because higher exposure gives the highest probability of adequate coverage of an SDD isolate.
- **Intermediate (I)**: Denotes clinical efficiency in body sites where drugs are physiologically concentrated or when a higher than normal dosage of drug can be used.
- **Resistant (R)**: Isolates are not inhibited by the usually achievable concentration of the agent with normal dosage schedules.

******* End of Report*******

***This is a computer generated report. No signature required.**

Dr. Vanya Singh (Consultant) **Dr. Balram ji Omar (Consultant)**

Lab Technologist

Verified by
(Dr.Balram Ji Omar)

Definitions	
MIC	• Minimum concentration of an antibiotic needed to inhibit visible growth of a single isolate of an organism • Important for definitive treatment of an individual patient - Inhibition of growth
MBC: Minimum Bactericidal Concentration	Lowest concentration of antibacterial agent required to kill a particular bacterium over a fixed (extended period), 18-24 hours - Microbial death
Breakpoint	• Discriminatory concentrations used in the interpretation of results of susceptibility testing to define isolates as susceptible, intermediate, or resistant (determined by various organizations - FDA, CLSI, EUCAST)

Interpretive category

- Category derived from microbiological characteristics, pharmacokinetic/pharmacodynamic parameters, and clinical outcome data, when available;

- MIC or zone diameter value breakpoints and interpretive categories are established per CLSI document M234 for categories of susceptible, intermediate, and resistant (and susceptible-dose dependent and non-susceptible, when appropriate).

- **susceptible (S)** – a category defined by a breakpoint that implies that isolates with an MIC at or below or a zone diameter at or above the susceptible breakpoint are inhibited by the usually achievable concentrations of antimicrobial agent when the dosage recommended to treat the site of infection is used, resulting in likely clinical efficacy.

susceptible-dose dependent (SDD) –

- a category defined by a breakpoint that implies that susceptibility of an isolate depends on the dosage regimen that is used in the patient.
- To achieve levels that are likely to be clinically effective against isolates for which the susceptibility testing results (either MICs or zone diameters) are in the SDD category, it is necessary to use a dosage regimen (ie, higher doses, more frequent doses, or both) that results in higher drug exposure than that achieved with the dose that was used to establish the susceptible breakpoint.

- **Intermediate (I)** – a category defined by a breakpoint that includes isolates with MICs or zone diameters within the intermediate range that approach usually attainable blood and tissue levels and/or for which response rates may be lower than for susceptible isolates;

Resistant (R)

- A category defined by a breakpoint that implies that isolates with an MIC at or above or a zone diameter at or below the resistant breakpoint are not inhibited by the usually achievable concentrations of the agent with normal dosage schedules

  and/or

- that demonstrate MICs or zone diameters that fall in the range in which specific microbial resistance mechanisms are likely,

  and

- clinical efficacy of the agent against the isolate has not been reliably shown in treatment studies.

- Resistant strain are not inhibited by the usually attainable concentrations of the agent with normal dosage schedules

- The breakpoint is the highest effective concentration of the antimicrobial at the site of infection, following systemic administration at established doses.

- MIC values above or equal to the breakpoint are considered indicative of resistance.

- The breakpoint and range of dilutions differ by drug and bacterial species.
- Therefore, comparing MICs of different antibiotics is not based solely on the numerical value but on how far the MIC is from the breakpoint, the site of the infection, and other considerations, such as the age, species, and health of the animal.
- Possible side-effects of the drug, price, frequency, and route of administration are also crucial factors.

Which antibiotic should you use?

Antibiotic	Mic	Interpretation
Aztreonam	8	S
Ceftriaxone	> 32	R
Ceftazidime	4	S
Ciprofloxacin	<=1	S
Gentamicin	2	S
Meropenem	< =1	S
Piperacillin-tazobactam	<=16	S

RULE #1

ALWAYS START WITH A BETA-LACTAM IF POSSIBLE, ESPECIALLY IN SEVERE INFECTIONS

- They have the best data supporting their use and are in general excellent drugs

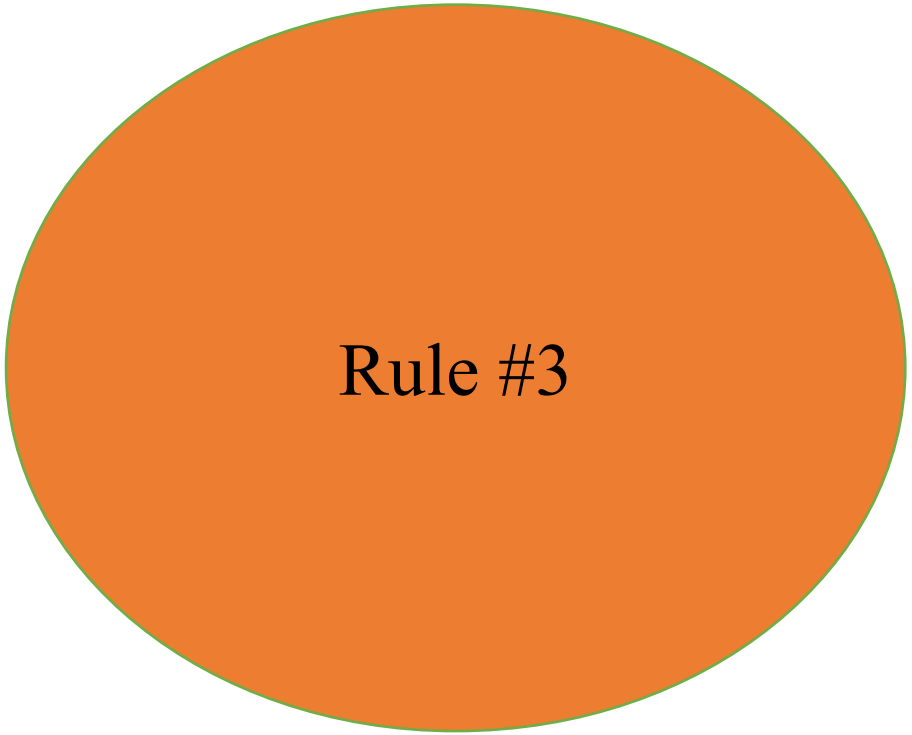
- Exception: atypical infections

Rule #2

- DO NOT COMPARE MICS BETWEEN DRUGS

- **Each antibiotic has different pharmacokinetics**
- **Different serum concentrations**
- **Different tissue concentrations**

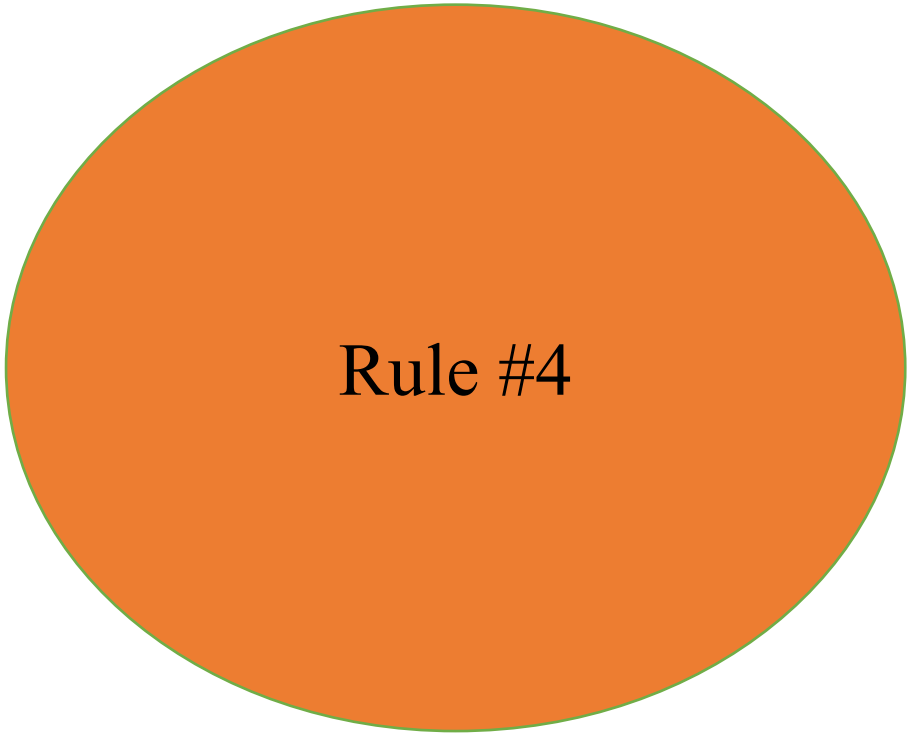
- **Each antibiotic has different goal pharmacodynamic parameters**
- **Time vs concentration vs AUC/MIC dependent**



IF “≤” YOU CAN USE THE DRUG

Exceptions

- Drug doesn’t get to the site of action
- Drug doesn’t achieve its goal pharmacodynamics parameters
- Drug doesn’t have inducible resistance
- Patient-specific factors
- Drug cost



- MICROBIOLOGY MAY HAVE MORE INFORMATION THAN WHAT IS REPORTED
- They may have results before they are reported in the computer
- Antibiotics may be suppressed
- They can perform additional testing

Therapeutic Index (TI)

- A ratio that compares the blood concentration at which a drug becomes toxic and the concentration at which the drug is effective. The larger the therapeutic index (TI), the safer the drug is.

Concept of MIC therapeutic index

Clinicians usually select best antimicrobial agent for therapy based on MIC of the antimicrobial agents

antimicrobial agent with lowest raw MIC value is often considered as the drug of choice by the treating physician

Antimicrobials may vary in their susceptibility breakpoint for the said organism

The actual effectiveness depends up on the number of folds the MIC value of a drug is lower than its susceptible breakpoint.

Concept of MIC therapeutic index

MIC therapeutic index = Susceptible clinical breakpoint for that drug/bug (as given by CLSI/EUCAST/etc) / Actual MIC of the test isolate obtained on AST

KLEBSIELLA PNEUMONIAE

Antimicrobial	MIC(ug/mL)	AST-VITEK Interpretation	S	I	R	Therapeutic Index
Cefepime	1.0	S	≤ 2	4-8	≥16	**2 / 1**
Cefoperazone sulbactum	8.0	S				
Piperacillin tazobactam	4.0	S	≤ 16	32-64	≥128	**16 / 4**
Amikacin	2.0	S	≤ 16	32	≥64	**16 / 2**

Parameters to be considered while choosing anbx

- 1st: Anbx line
- 2nd: TI filter

Other factors to consider in parallel:

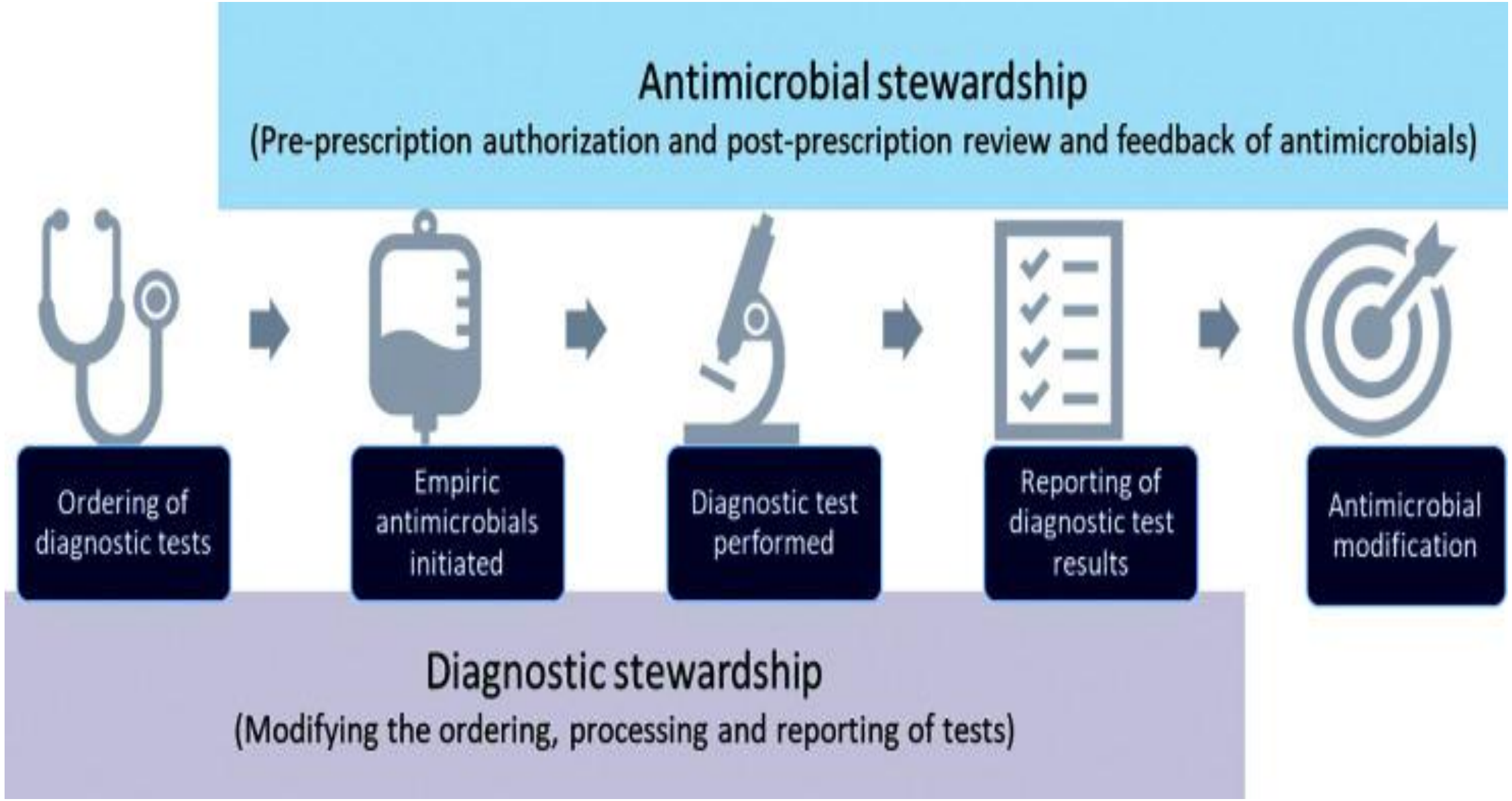
- Renal parameters and safety
- Age
- Site specific action
- Other culture reports

Molecular diagnostics and point-of-care assay

- Advocated as the solution for antimicrobial resistance (MDR/PanDR)
- More expensive compared with classical culture-based methodology
- But they are faster and more sensitive

Impact

- To decide proper guided antibiotic therapy for correct dosing and duration for the same
- Prevent misuse of antibiotics and preserve second line/broad spectrum antibiotics for future
- Identify and isolate MDR/XDR/PDR patients there by helping in enforcing HIC


Antimicrobial stewardship
(Pre-prescription authorization and post-prescription review and feedback of antimicrobials)
Ordering of diagnostic tests
Empiric antimicrobials initiated
Diagnostic test performed
Reporting of diagnostic test results
Antimicrobial modification
Diagnostic stewardship
(Modifying the ordering, processing and reporting of tests)


Thank You