Discharge antibiotic stewardship & tackling beta-lactam allergies

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Background

- Community-acquired pneumonia (CAP), urinary tract infection (UTI), and skin and soft tissue infections (SSTIs) rank among the most common indications for hospitalizations
- Antimicrobial stewardship initiatives at the point of discharge are relatively unexplored as compared to inpatient settings
- Previous literature reports an estimated 50-70% of discharge antimicrobial prescriptions are inappropriate in drug choice, dose, or duration

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Background

- Impact of short duration of therapy guide: 2019-2020
- N=205

	Pre-Implementation	Post-Implementation
Inpatient antibiotic days, median (IQR)		
CAP	4 (2)	5 (3)
UTI	4 (2)	3 (3)
Bacteremia	5 (5.5)	5 (2)
Post-discharge antibiotic days, median (IQR)		
CAP	5 (2.8)	3 (5)
UTI	3 (5)	4 (5)
Bacteremia	7 (7.5)	4 (5)

Recommended duration of therapy for CAP for patients who clinically improve quickly: 5 days

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ASP pharmacist

- Theradoc
  - Alerts are based on positive cultures, labs, DDIs, types of antibiotics (ex: duplicate coverage, >/=3 antibiotics etc.)
    - Patients with CAP & cellulitis very rarely have positive cultures
  - Durations of therapy report includes patients on antibiotics >/= 4 days
    - CAP & cellulitis patients could be discharged within this window
- Even when a recommendation was made and implemented on the inpatient side, it is possible that a provider may accidentally select a longer duration on a discharge script

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Discharge antibiotic stewardship initiative: Phase 1

- Who: south tower & north tower med rec pharmacists
- What: review and make interventions on patients with community-acquired pneumonia to recommend an optimal antibiotic regimen (drug, dose, frequency, and duration) for discharge
- Why: improve appropriateness of discharge prescriptions for CAP

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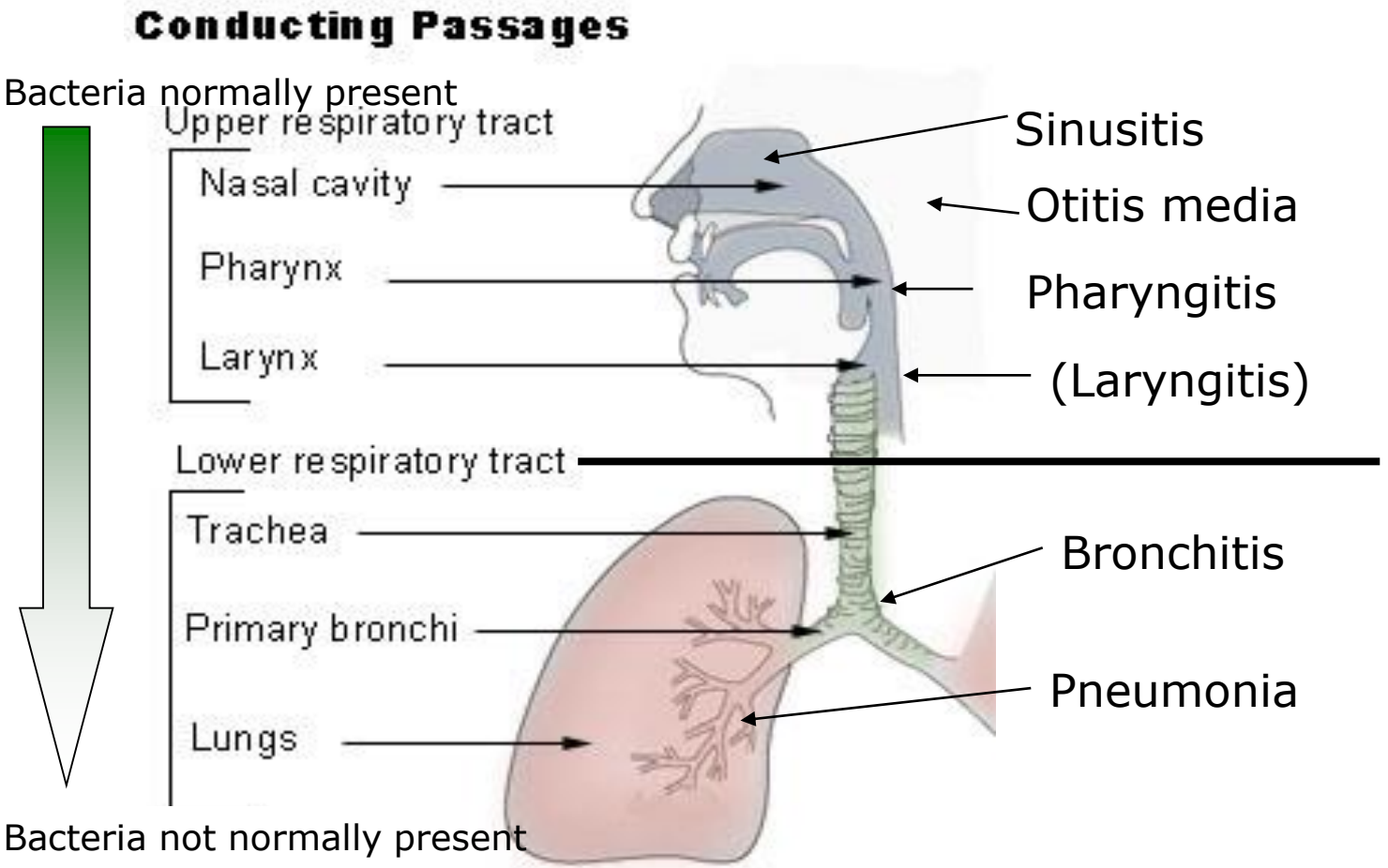
CAP: a refresher!



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Diagnosis

- Chest X-ray
  - Highly sensitive to rule out pneumonia
- Obtaining a sample – challenging (see table)
- And despite cultures being ordered less than half of patients with CAP have pathogens identified

SAMPLE	PROCEDURE	PROS	CONS
Blood culture	-Draw blood via venipuncture	-Easy to obtain for ED/inpatient -Identifies invasive pathogens -Good *specificity*	-Difficult for outpatients -Poor *sensitivity*
Sputum culture	-Deep cough sample -Good sample: many WBCs & few epithelial cells on Gram stain	-Noninvasive -Easy to obtain	-Poor *sensitivity* (can't get to lower airways) -Poor *specificity* (contamination with upper respiratory organisms)
Endotracheal aspirate (ETA)	-Suction of secretions in intubated patient	-Noninvasive & easy to obtain (if you're on a vent) -Moderate *sensitivity*	-Poor specificity (contamination with ET tube colonizers)
Broncho-alveolar lavage (BAL)	-Endoscopy guided or blind (mini-BAL) flexible tube into lower airways	-Good *sensitivity* -Good *specificity*	-Invasive -Requires intubation, sedation, expertise

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Common Pathogens - Pneumonia

- Community-acquired
  - *S. pneumoniae*
  - *H. influenza/ Moraxella catarrhalis*
  - *Legionella pneumophilia*
  - *Chlamydia pneumoniae*
  - *Mycoplasma pneumoniae*

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Treatment recommendations

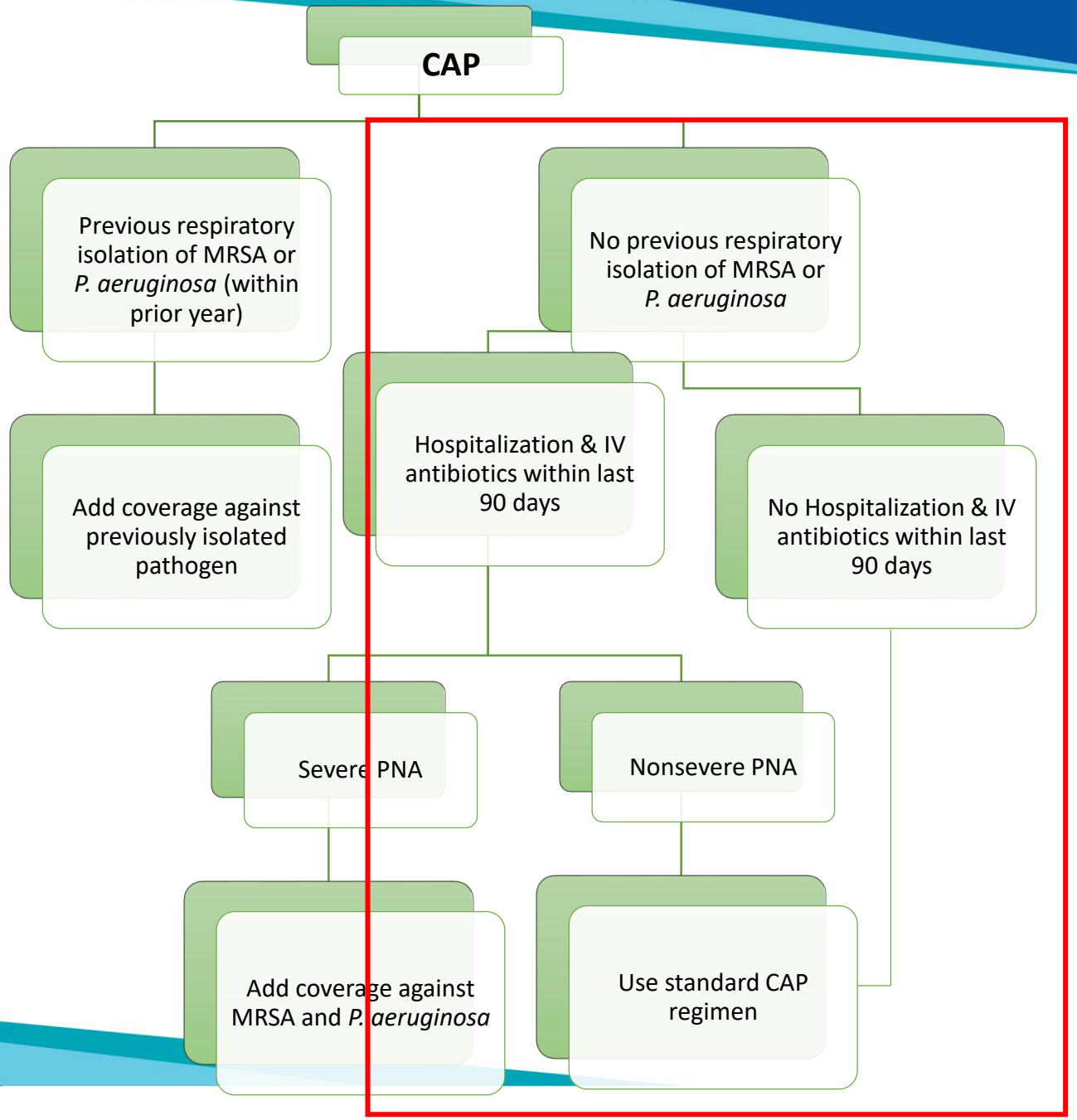
Severe PNA: 1 major criterion or ≥ 3 minor criteria

Major:

- Septic shock w/ vasopressor need
- Resp failure requiring mechanical ventilation

Minor:

- Respiratory rate ≥ 30 breaths/min
- PaO2/FiO2 ratio ≤ 250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (BUN level ≥ 20)
- Leukopenia (WBC < 4k)
- Thrombocytopenia (Platelet <100k)
- Hypothermia (temp <36°C)
- Hypotension requiring fluid resuscitation



Remember HCAP?

- Any o[illegible]actors:
  - [illegible]in a nursing hom[illegible]her [illegible]e facilities
  - [illegible]ospitaliz[illegible]> 2 days in last [illegible]ays
  - [illegible]ome infusion
  - [illegible]ronic dialysis
  - [illegible]wound care
  - Fa[illegible]ibiotic-resista[illegible]

- Our resp. culture data 2109
  - MRSA: 92/1576 (6%)
  - P. aeruginosa: 93/1576 (6%)
  - Ceftriaxone R gram negative: 135/1576 (9%)

- Our CAP patient data 2020
  - Risk factors for true infections with MDR pathogens are the same as current IDSA guidelines

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Antibiotic Recommendations

- CAP Standard Regimens:
  - Ceftriaxone 1g IV q24 + azithromycin 500mg IV/PO daily x 5 days OR
  - Levofloxacin 750mg IV/PO q24
- CAP w/ previous (within 1 year) isolation of MRSA:
  - Standard Regimen + IV vancomycin pharmacy to dose
- CAP w/ previous (within 1 year) isolation of *Pseudomonas spp*:
  - Cefepime 1g IV q6 or Pip/tazo 3.375/4.5g IV q8 extended infusion + azithromycin 500mg IV/PO daily x 5 days
- CAP w/ hospitalization & IV abx in past 90 days:
  - Nonsevere: Standard CAP regimen
  - Severe: Cefepime 1g IV q6 + IV vancomycin pharmacy to dose + azithromycin 500mg IV/PO daily x 5 days

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Switching to oral therapy

<u>Switch to PO antibiotics</u>

When:

-Hemodynamically stable

-Able to ingest/absorb PO drugs

- “In switching from parenteral to oral antibiotics, either the same agent or the same drug class should be used”
- No need to continue atypical coverage with azithromycin at the point of switching to PO therapy unless patient has been diagnosed with an atypical PNA

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Duration of therapy

Question 15: In Outpatient and Inpatient Adults with CAP Who Are Improving, What Is the Appropriate Duration of Antibiotic Treatment?

Recommendation. We recommend that the duration of antibiotic therapy should be guided by a validated measure of clinical stability (resolution of vital sign abnormalities [heart rate, respiratory rate, blood pressure, oxygen saturation, and temperature], ability to eat, and normal mentation), and antibiotic therapy should be continued until the patient achieves stability and for no less than a total of 5 days (strong recommendation, moderate quality of evidence).

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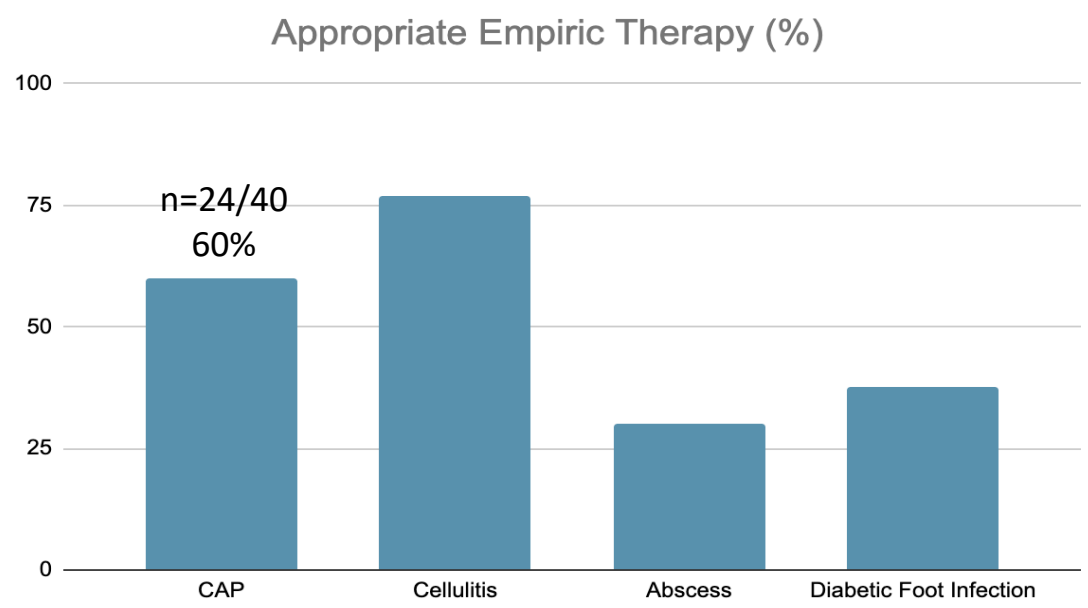
Background

- Assessment of guideline compliance PNA & SSTI: 2022
- N=76



Secondary Endpoints	
CABP	9(7)
Cellulitis	9(6.8)
Abscess	10.5(5)
DFI	11(3.8)
CABP	5(2)
Cellulitis	4(3)
Abscess	7(4)
DFI	5(5)
ad-spectrum antibiotics, n (%)	27/32(84%)
row spectrum antibiotics, n (%)	5/32(16%)
IV to oral antibiotic switch, if appropriate*, in patients with CABP, n (%)	1/38(2.6%)

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Summary

1. CAP is 1 of the most common reasons for hospitalization
2. Most patients with CAP can be treated with standard therapy
    a. But, many patients are mislabeled as having “HCAP” and treated with broader spectrum antibiotics
3. Respiratory cultures are notoriously challenging to obtain and can be unreliable
    a. Sometimes MRSA nasal swabs are ordered in patients without validated risk factors for MRSA
    b. A positive MRSA nasal swab does not definitively mean your patient has MRSA pneumonia. It’s positive predictive value is around 40%
4. Patients are prescribed longer than necessary durations
5. Patients are rarely switched from IV to PO inpatient

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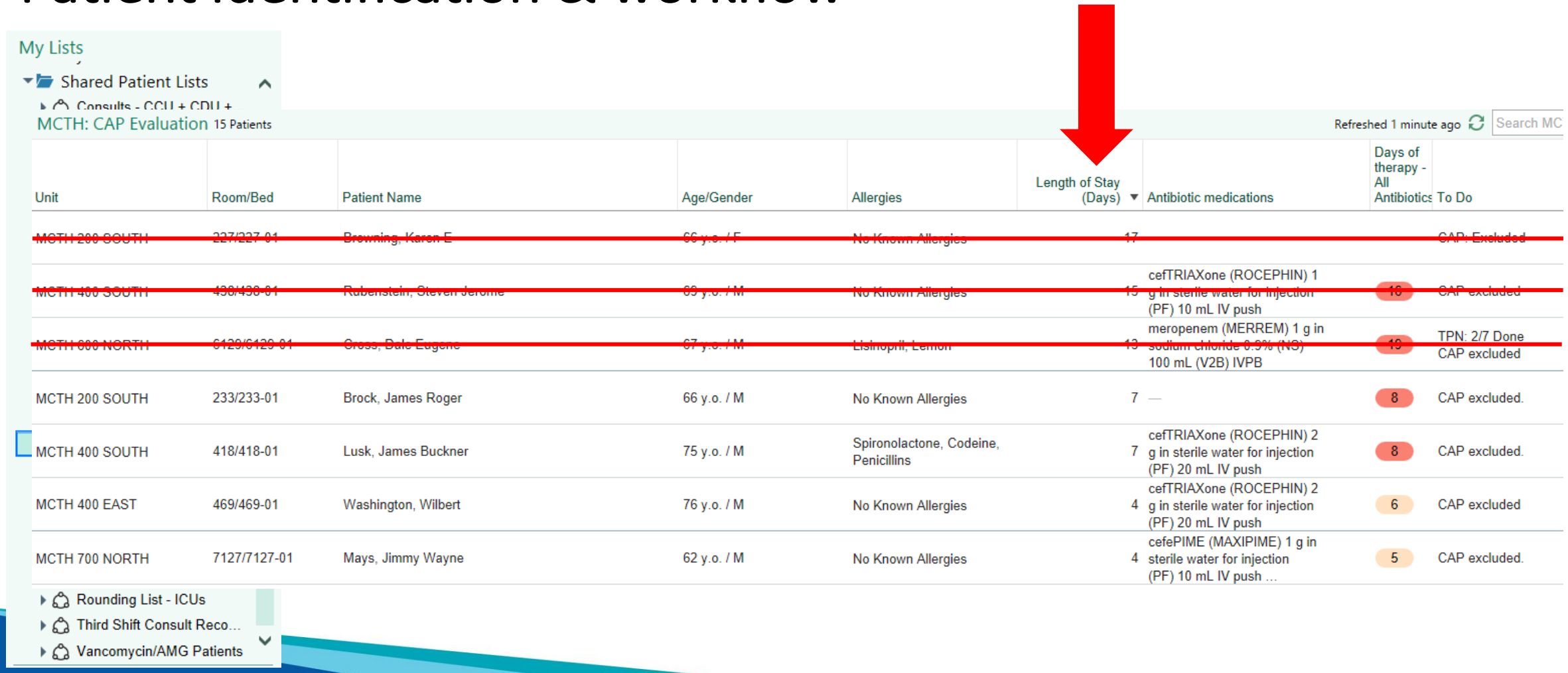
Patient identification & workflow



Unit	Room/Bed	Patient Name	Age/Gender	Allergies	Length of Stay (Days)	Antibiotic medications	Days of therapy - All Antibiotics	To Do
~~MCTH 200 SOUTH~~	~~227/227-01~~	~~Browning, Karen E~~	~~66 y.o. / F~~	~~No Known Allergies~~	~~17~~			~~CAP: Excluded~~
~~MCTH 400 SOUTH~~	~~438/438-01~~	~~Rubenstein, Steven Jerome~~	~~69 y.o. / M~~	~~No Known Allergies~~	~~15~~	~~cefTRIAXone (ROCEPHIN) 1 g in sterile water for injection (PF) 10 mL IV push~~	~~10~~	~~CAP excluded~~
~~MCTH 600 NORTH~~	~~6129/6129-01~~	~~Gross, Dale Eugene~~	~~67 y.o. / M~~	~~Lisinopril, Lemon~~	~~13~~	~~meropenem (MERREM) 1 g in sodium chloride 0.9% (NS) 100 mL (V2B) IVPB~~	~~10~~	~~TPN: 2/7 Done CAP excluded~~
MCTH 200 SOUTH	233/233-01	Brock, James Roger	66 y.o. / M	No Known Allergies	7	—	8	CAP excluded.
MCTH 400 SOUTH	418/418-01	Lusk, James Buckner	75 y.o. / M	Spironolactone, Codeine, Penicillins	7	cefTRIAXone (ROCEPHIN) 2 g in sterile water for injection (PF) 20 mL IV push	8	CAP excluded.
MCTH 400 EAST	469/469-01	Washington, Wilbert	76 y.o. / M	No Known Allergies	4	cefTRIAXone (ROCEPHIN) 2 g in sterile water for injection (PF) 20 mL IV push	6	CAP excluded
MCTH 700 NORTH	7127/7127-01	Mays, Jimmy Wayne	62 y.o. / M	No Known Allergies	4	cefePIME (MAXIPIME) 1 g in sterile water for injection (PF) 10 mL IV push ...	5	CAP excluded.

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Patient identification & workflow

MCTH 200 SOUTH	233/233-01	Brock, James Roger	66 y.o. / M	No Known Allergies	7	8	CAP excluded.
MCTH 400 SOUTH	418/418-01	Lusk, James Buckner	75 y.o. / M	Spironolactone, Codeine, Penicillins	7	cefTRIAXone (ROCEPHIN) 2 g in sterile water for injection (PF) 20 mL IV push	8	CAP excluded.
MCTH 400 EAST	469/469-01	Washington, Wilbert	76 y.o. / M	No Known Allergies	4	cefTRIAXone (ROCEPHIN) 2 g in sterile water for injection (PF) 20 mL IV push	6	CAP excluded
MCTH 700 NORTH	7127/7127-01	Mays, Jimmy Wayne	62 y.o. / M	No Known Allergies	4	cefePIME (MAXIPIME) 1 g in sterile water for injection (PF) 10 mL IV push ...	5	CAP excluded.
MCTH CLINICAL DECISION UNIT	CDU1/CDU1-11	Simons, Wanda Sue	67 y.o. / F	Percocet [Oxycodone-acetaminop... Codeine, Doxycycline	3	—	5	CAP: abx completed
MCTH CLINICAL DECISION UNIT	CDU2/CDU2-28	Campbell, Felix Undre	50 y.o. / M	No Known Allergies	3	cefTRIAXone (ROCEPHIN) 1 g in sterile water for injection (PF) 10 mL IV push	5	CAP: abx to end on 2/8
MCTH 100 SOUTH	108/108-01	Davis, Tommie L	86 y.o. / M	No Known Allergies	2	AZITHROmycin (ZITHROMAX) 500 mg in sodium chloride 0.9% (NS) 250 mL (V2B) IVPB	3	CAP: re-eval 2/9 (pending repeat blood cx)

- Review EPIC i-vents & pharmacy handoff prior to reviewing case

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Inclusion & Exclusion Criteria

Inclusion criteria:

- Patients who are admitted to the hospital from the community (includes nursing home patients) with a clinical diagnosis of pneumonia
- Meets criteria for clinical stability (next slide)

Exclusion criteria:

- Hospital-acquired pneumonia (diagnosis >48 hours after hospital admission)
- Ventilator associated pneumonia
- Failed standard therapy for CAP
- Empyema, lung abscess, or other complications including bacteremia
- Pneumonia caused by or suspected to be caused by MRSA, Pseudomonas, or a multi-drug resistant gram negative rod
- Receiving antibiotics during admission for non-pneumonia indication

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Criteria for clinical stability

- Afebrile for 48 hours
- No more than 1 sign of clinical instability
  - SBP < 90mmhHg
  - HR > 100/min
  - RR > 24/min
  - Arterial O2 <90% or PaO2 <60 mmHg at room air (unless requires O2 at baseline)

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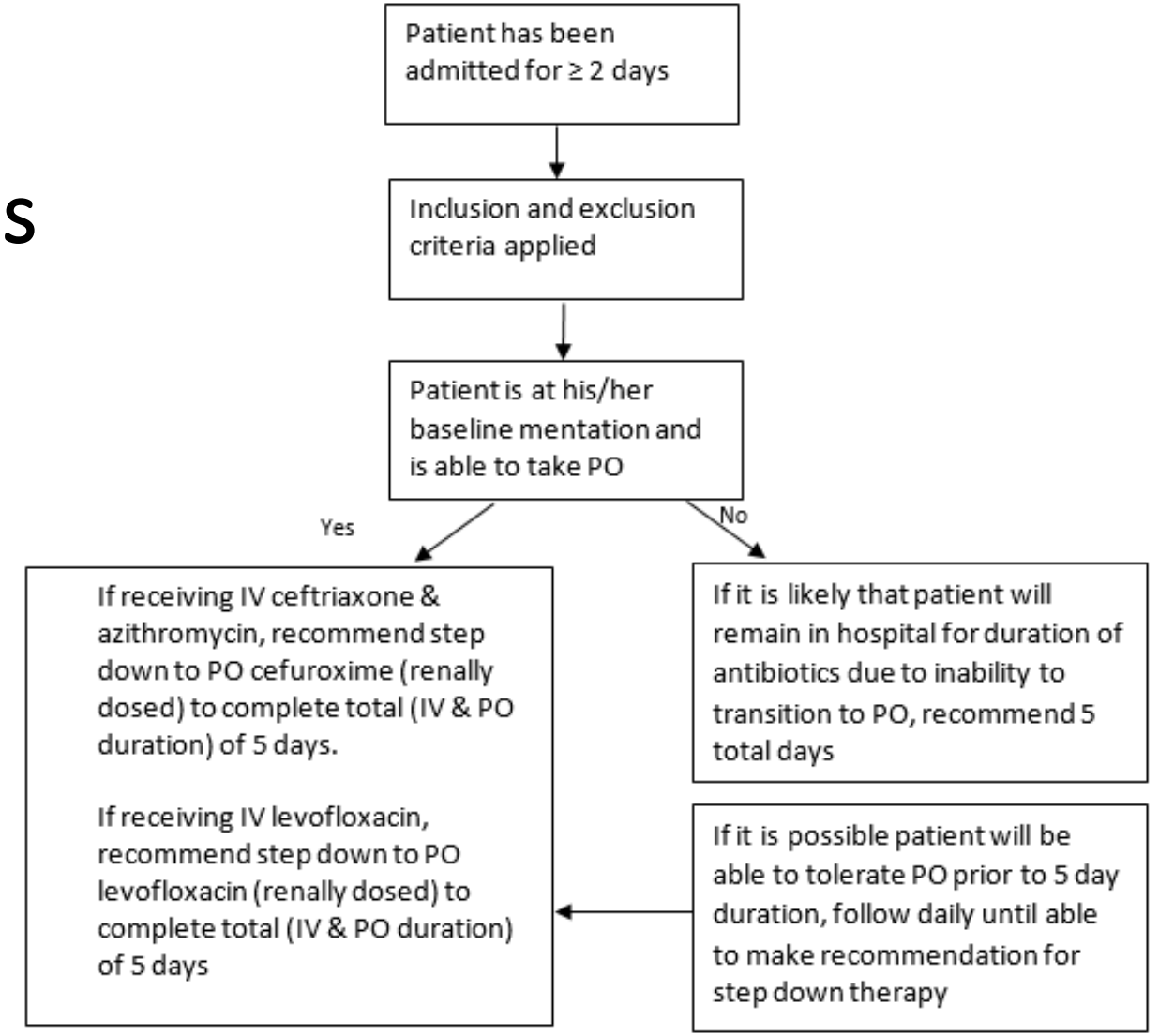
Evaluation & Intervention suggestions



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Patient identification & workflow

- If able to make an intervention to provider, please do so and enter an i-vent in EPIC (Type: Antimicrobial Stewardship; Subtype: whichever is felt to be relevant for the intervention you made). In Pharmacy handoff, pharmacy to do – write “CAP intervention made”
- If unable to make an intervention to provider at that time, please jot down any handoff notes in pharmacy summary and/or a quick note in the to do section to help tomorrow’s pharmacist
- When verifying a discharge antibiotic for a patient with CAP, review patient handoff &/or i-vent to determine if an intervention has been made and if not and a change needs to happen, please recommend an appropriate change

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When making recommendations:

- Please keep in mind that our top priority is ensuring that discharge antibiotic prescriptions are appropriate, particularly with regards to duration of therapy. Make recommendations at the most impactful time during a patient's stay (ex: when they are able to transition to PO, when it appears they are close to discharge etc.)
- When recommending only a duration of therapy, calculate how many more days of therapy patient would need and ask if you may go ahead and place an end date in EPIC (to ensure the intervention is followed through)

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When making recommendations:

- For switching to PO therapy, please include drug, route, dose, frequency, and days remaining in your communications to the provider (ex: Rm 411 has received 2 days of IV ceftriaxone & azithromycin for CAP. Based on clinical improvement, she is a good candidate for a 5 day total duration. Would consider switch to PO cefuroxime 500mg BID x 3 days to complete 5 day course.)
- If the provider is reluctant to use a 5 day duration, recommend 7 days

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Beta-lactam allergy guideline (formweb)

Patient allergy assessment tool

1. What is the name of the antibiotic you are allergic to?
2. Please describe the details of the reaction.
3. Was it immediate or a few days after taking it?
4. When did your allergy occur?
    1. < 1 year ago, 1-10 years ago, >10 years ago
5. How was the reaction managed and what happened?
6. Have you taken any other antibiotics since (amoxicillin, augmentin, keflex, ceftin etc.)?

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Beta-lactam allergy guideline (formweb)

Type of reaction and Action Plan

Dermatological			Respiratory or Systemic		Unknown Reaction	
Clinical manifestation		Severity or Allergy type	Clinical manifestation	Severity or Allergy type	Clinical manifestation	Severity or Allergy type
Childhood rash		Unlikely to be significant	Laryngeal Involvement ("throat tightness", "hoarse voice")	Severe	Unknown reaction ≤ 10 years ago	Unknown
Diffuse rash or localized rash/swelling with no other symptoms	>10 years ago or unknown	Non-severe	Respiratory compromise ("shortness of breath")	Severe	Unknown reaction >10 years or family history	Unlikely to be significant
	≤ 10 years ago	Non-severe				
Angioedema ("lip, facial, or tongue swelling")		Severe	Anaphylaxis, unexplained collapse	Severe	**Renal**	
Generalized swelling (outside of angioedema)		Severe	**Hematological**		Severe renal injury, failure, or AIN	Potential immune mediated
Urticaria ("wheals and hives")		Non-severe	Low platelets, neutrophils, hemoglobin, eosinophilia	Potential immune mediated	Mild renal impairment	Unlikely immune mediated
Mucosal ulceration ("mouth, eye, or genital ulcers")		Severe			Severe liver injury, failure	Potential immune mediated
Pustular, blistering or desquamating rash ("skin shedding")		Severe			Mild hepatic enzyme elevation	Unlikely immune mediated

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Beta-lactam allergy guideline (formweb)

Reaction Risk (Color Coded) & Action Plan		Gastrointestinal or Neurological	
Appropriate for oral re-challenge or direct de-labeling	Low Risk	GI symptoms (nausea, vomiting, diarrhea)	Unlikely immune mediated
Appropriate for oral re-challenge or using full dose beta-lactam with dissimilar side chain (Appendix 3)	Low Risk	Mild neurological symptoms (headache, depression, mood disorder)	Unlikely immune mediated
May be appropriate for test dose of beta-lactams with dissimilar side chains* or penicillin skin test	Moderate risk		
Not appropriate for allergy testing	High risk	Severe neurological manifestation (seizures, psychosis)	Unknown or unclear mechanism

*If moderate risk penicillin reaction, can consider test dose of cefazolin, 3rd, 4th, 5th generation cephalosporins or carbapenem.

If moderate risk cephalosporin reaction, can consider test dose of cephalosporins with dissimilar side chains (Appendix 3), penicillin (if reaction to 3rd, 4th, or 5th generation cephalosporin), or carbapenem.

Aztreonam full dose can be administered unless reaction was to ceftazidime

Adapted from Devchand *et al*. 2018

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Beta-lactam allergy guideline (formweb)

Cross-reactivity matrix

	Penicillin	Amoxicillin	Ampicillin	Piperacillin	Cefazolin	Cefadroxil/ Cephalexin	Cefoxitin	Cefuroxime	Ceftriaxone	Ceftazidime	Cefepime	Ceftaroline	Ceftolozane
Penicillin	=						*						
Amoxicillin		=	*	*		*							
Ampicillin		*	=	*		*							
Piperacillin		*	*	=		*							
Cefazolin					=								
Cefadroxil/ Cephalexin		*	*	*		=							
Cefoxitin	*						=	*					
Cefuroxime							*	=	*	*	*		*
Ceftriaxone								*	=	*	*		*
Ceftazidime								*	*	=	*		*
Cefepime								*	*	*	=		*
Ceftaroline												=	
Ceftolozane								*	*	*	*		=

A box with (*) Indicates that the two antibiotics share a similar or identical side chain and that there is a risk of cross-reactivity between them. Empty boxes indicate a lack of side-chain similarity and a lower risk for cross-reactivity. Cefazolin and Ceftaroline have dissimilar side chains to all other penicillins and cephalosporins.

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Beta-lactam allergy guideline (formweb)

Test Dose Procedure

Note: This procedure is NOT meant to be used for patients with Type II-IV reactions including SJS/TEN, DRESS/DISH, serum sickness, drug-induced cytopenias, other significant laboratory abnormalities such as nephrotoxicity or delayed reactions

1) Utilize Appendix 2 to identify appropriate candidates for the test dose
2) Review patient's current medications to ensure no antihistamines, famotidine, high dose steroids were given in the last 24 hours as these may mask an allergic reaction
3) Obtain patient's verbal consent prior to procedure
4) Drug order & monitoring
    a. Oral rechallenge for de-labeling
        i. Single dose penicillin VK 250mg (if reported allergy penicillin) or amoxicillin 250mg (if reported allergy amoxicillin or ampicillin)
        ii. Perform observation every 30 mins for 1 hour post oral challenge
    b. Test dose of beta-lactam that you intend to use
        i. Give patient 1/10th of full standard treatment dose (ex: for ceftriaxone (standard dose: 1-2g), formulate 1g dose in 50mL of normal saline and give 1st 5 mins of dose ~160mg)
        ii. Monitor for 30 minutes. If the patient remains asymptomatic, give the full dose.
        iii. Monitor patient for 60 more minutes to ensure no reaction
        iv. Subsequent doses can be given as per hospital's standard protocol
5) Profile Anaphylaxis & Acute Drug Hypersensitivity Protocol MCT to be available during the test dose procedure