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Mini Review

Antibiotic Selection and Dosage in Dermatology: A Primer

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Abstract

Antibiotics remain a cornerstone in dermatological practice, particularly in conditions associated with barrier disruption, secondary bacterial infections, and systemic sepsis. Dermatological emergencies such as pemphigus vulgaris, toxic epidermal necrolysis, erythroderma, and infected ulcers often require prompt empirical antimicrobial therapy before culture and sensitivity reports become available. This review provides a concise and clinically oriented overview of commonly used antibiotics in dermatology, emphasizing their mechanisms of action, antimicrobial spectrum, dosage regimens, adverse effects, and renal dose modifications. Major antibiotic classes discussed include penicillins, cephalosporins, carbapenems, fluoroquinolones, tetracyclines, aminoglycosides, macrolides, glycopeptides, and other reserve antimicrobials used in multidrug-resistant infections. Emerging concerns regarding antimicrobial resistance, including methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant organisms, carbapenem-resistant Enterobacteriaceae, and pan-resistant Pseudomonas and Klebsiella species are highlighted. The review also outlines practical antibiotic selection strategies for dermatological emergencies and severe cutaneous infections. Judicious antibiotic use guided by local antibiograms, culture sensitivity reports, and infectious disease consultation is strongly recommended to combat the growing burden of antimicrobial resistance.

Abbreviations

MRSA: Methicillin-Resistant Staphylococcus aureus; VRSA: Vancomycin-Resistant Staphylococcus aureus; VRE: Vancomycin-Resistant Enterococci; ESBL: Extended Spectrum Beta Lactamase; PEAK: Pseudomonas, Escherichia coli Acinetobacter Klebsiella; CDC: Centers for Disease Control and Prevention; SCCM: Society of Critical Care Medicine; MIC: Minimum Inhibitory Concentration; eGFR: Estimated Glomerular Filtration Rate; DRESS: Drug Reaction with Eosinophilia and Systemic Symptoms; OPD: Outpatient Department; IV: Intravenous; IM: Intramuscular

Introduction

Antibacterial drugs are often required in those conditions where breach of the skin barrier function is accompanied by signs and symptoms of infections. While standard guidelines recommend deciding antibiotics decided by culture and sensitivity reports, they are often time consuming and are not available for the first three days (that is, 72 hours). During this time, empirical antibiotics must be considered. As any dermatologist can testify, conditions such as Pemphigus vulgaris with a large body surface area, Toxic epidermal necrolysis and certain erythroderms are extremely prone to get infected and quickly progress to sepsis. The following primer will help the dermatology internist select an appropriate antibiotic and its proper dosage.

Classification of antibiotics based on Mechanism of Action

1. **Cell Wall Inhibitors:** They inhibit formation of bacterial cell wall. They are frequently bactericidal. Classic Examples include: Bacitracin, Tobramycin, Beta Lactam antibiotics (including cephalosproins), Cephalosporins, Vancomycin.

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2. **Protein Synthesis Inhibitors:** They bind to mRNA and rRNA and inhibit one step of protein synthesis. They are broadly divided into:

   i. **Binding to 30 S Subunit:** Aminoglycosides and Tetracyclines

   ii. **Binding to 50S Subunit:** Streptograminins, Macrolides, Lincoamides and Linezolid.

The penicillins

In today's dermatological acute skin care, their use has considerably declined due to rapid emergence of resistance. They are classical cell wall inhibitors with a central B lactam ring. The availability of orally active agents such as Amoxycillin with a Beta lactamase inhibitor confers a reasonable option particularly for management in outpatient basis when only oral drugs can be used. Their spectrum primarily includes Gram positive organisms like Staphylococcus (excluding MRSA). The use of other penicllins like Penicllin G or Benzathine Penicillin is now obsolete, except in select settings such as treatment of syphilis. The rapid advent of Beta Lactamase producing bacteria have limited their use. While initially considered a domain of Gram negative pathogens, Beta lactamase production by staphylococcus has become almost universal. Major β-lactamase families include plasmid-mediated extended-spectrum β-lactamases (ESBLs), AmpC cephalosporinases, and carbapenemases [1]. There exist considerable geographic variations in the spectrum of Beta lactamase inhibitors which KPC Serine carbapenemase being detected more in the Americas whereas metalloproteinase B lactamases found distinctively more commonly in the Indian subcontinent, which varies from 70% to 85% [2]. Pharmacokinetics data should dictate the dosage modifications in the elderly and those with chronic kidney disease [Table 1].

Most penicillins do not need dose adjustments in chronic Kidney disease for loading dose, however maintenance dose may require dose adjustment as per estimated GFR. For Amoxycillin the doses are CrCl 10-30: 500 mg q12h

Table 1:

Drug	Spectrum	Dose	Side Effects
Amoxycillin	Gram positive cocci (Staphylococcus aureus and Streptococcus). Gram negative coverage variable	500 mg thrice daily	Gastroenteritis Antibiotic associated diarrhoea
Benzathine Penicillin	Gram positive cocci, spirochetas (like Treponema pallidum)	For Syphilis (Early): 2.4 Million Units stat intramuscularly For Late Syphilis: 2.4 million Units	Gastroenteritis Anaphylaxis Anaphylactoid reactions
Cloxacillin	Gram Positive occi	500 mg thrice to four times a day	Same
Piperaciilin Tazobactam	Gram Positive cocci and Gram Negative bacilli. Excludes MRSA but includes Pseudomonas, some strains of Klebsiella	3.375 - 4.5 mg intravenous four times daily	Rash Antibiotic-associated diarrhoea

CrCl <10: 500 mg q24h [3]. Similar dosage modifications for other Aminopeniiilins are available in many primers [3].

The carbepenems [1-2]

Main Spectrum: Gram Negative. Highly useful for PEAK pathogens (Pseudomonas, Enterobacter, Acinetobacter, Klebsiella). However the higher prevalence of Carbepenem resistance across many tertiary care centres in India have limited their. Use. Resistosome analyses of the six major Carbapenem resistance pathogens have been performed, which showed an overall prevalcence of 24% with Acinetobacter baumanii showing upto 48% resistance, closely followed by Klebsiella pneumoniae at 12% [4]. IPM-MEM resistance discrepancies were found in *Citrobacter* and *Proteus* species. Gene profiling of resistant strains revealed the predominance of bla_{NDM}, bla_{VIM} in *all organism. Common types of Carbapenemases include KPC (Class A), NDM, VIM, IMP (Class B), and OXA-48 (Class D).* If resistance is suspected it is preferable to get guided by culture sensitivity results – however for empiric therapy, use of Collistin, Tigecycline and Fosfomycin Trometamol or switching over to Tazoactam-Vaborbactam has been helpful [5,6].

Dose Adjustment should always be done as per creatinine clearance since accumulation to toxic levels is associated with increased risk of seizures [3].

Table 2: The Cephalosporins

3rd generation cephalosporins are broad spectrum with mainly Gram Negative coverage including PEAK pathogens with significant extension into gram positive coverage. Useful in combination with other antimicrobials for PEAK pathogens. The prevalence of 3rd generation cephalosporinase producing Excherichia coli has surprisingly decreased to 10% [7] in 2015 as compared to 2010. Production of Beta Lactamases, production of efflux proteins, compensatory overproduction of cell wall peptides, sequestration of bacteria inside debris where antibiotic cannot penetrate are some of the mechanisms of widespread cephalosporin resistance [7]. As with other gram negative bacterial resistance, coverage guided by culture sensitivity values should help. Since plasmid borne resistance is rapidly spread and it may not always be prudent to wait for sensitivity values, switching over to Carbapenems and in extreme cases the vintage antibiotics such as Collistin, polymyxin, aminoglycosides should help. Some cephalosporins are associated with risk of hepatotoxicity: They include: Cephalzoline, Cefuroxime, Ceftriaxone, Cefnidir, Cefepime, Cefotetan and Cefoxitin. Documented reports of hepatic injury have ranged from asymptomatic cholestatsis to fulminant hepatic failure [8]. Of note, dose adjustment in case of renal failure is needed for all cephalosproins except Ceftriaxone which is metabolized by liver and Cefoperazone.

Table 3: The Fluoroquinolones [9]

These are helpful in infections caused by suspected gram negative bacilli such as PEAK pathogens. They are classic Gyrase inhibitors, a critical enzyme needed for uncoling

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Table 2:

Drug	Spectrum	Dosage	Indications	Side Effects
Imipinem	1. Gram Positive: Staphylococcus aureus (Except MRSA and VRSA), Staphylococcus epidermidis and saprophyticus, Streptococcus 2. Gram Negative: Enterobactericaea sp, Pseudomonas aeruginosa, Listeria 3. Anaerobes	Imipenem + Cilastin combination 0.5 g intravenously every 6 hourly Maximum daily dose is 4 g per day	1. Infected Pemphigus 2. Infection over Toxic Epidermal Necrolysis and Erythema Multiform Major 3. Sepsis (Secondary to any of the conditions listed above) 4. Diabetic foot/ gangrene	1. Can induce seizures particularly in high doses 2. GI intolerance – Nausea, vomiting, diarrhoea 3. Can itself induce Maculopapular drug rash (Rarely DRESS)
Meropenem	Same as above	10 – 40 mg/ kg intravenously slowly as infusion every 8th hour	Same as above	1. Does not induce Seizure 2. GI intolerance
Faropenem	Same as above	Orally active. 150 – 300 mg Thrice Daily	Same as above but can be used on OPD basis (as it is orally active)	1. GI Intolerance 2. Maculopapular Drug Rash
Doripenem	Same as above but activity more against Pseudomonas	Inj 500 mg intravenously every 8th hour	Same as above	GI Intolerance Maculopapular Drug Rash

Table 3:

Drug	Spectrum	Dosage [6]	Side Effects
3rd Gen Cephalosporins			
1. Cefotaxime	1. Aerobic Gram Negative organisms like HACEK group 2, Gram Positive organisms (See Exceptions) NOT effective against Pseudomonas, Staph Aureus and Bacteroides fragilis	1 – 2gm iv 6 hourly Children: 50 -100 mg/ kg/day	GI intolerance Maculopapular drug rash
2 Ceftriaxone	Same	1 – 2 gm iv or im per day	Bleeding and Hypoprothrombinemia
3. Ceftazidime	Highly effective against Pseduomonas	0.5 – 2 gm iv or im every 8 hurly	Neutropenia, Thrombocytopenia, Transaminase elevations
4.Cefopodoxime	Orally active Highly effective aginst Enterobactericeae and Staph aureus. Also inhibits gram negative organism	Orally 200 mg Twice daily (Can be hiked upto 800 mg per day)	Maculopapular drug rash DRESS GI intolerance
2nd Gen Cephalosporins			
5. Cefuroxime ascetil	Gram Negative Organisms except Pesudomonas Not very reliable	Orally Tab 250 – 500 mg twice daily	Diarrhoea, Nausea, vomiting etc
6. Cefuroxime	Gram Negative including PPNG	Inj 1.5 gm im stat for Gonorrhoea Iv 0.75 – 1.5 gm every 8 hourly Children 30 – 100 mg/kg/day	GI Intolerance Maculopapular rash

the double helix structure of DNA needed for bacterial replication. Fluoroquinolone resistance is common in E coli and M tuberculosis (where it is often used as a second line drug). Prevalence has ranged from 30% to over 50% [10]. Of note, Nesisseria gonorrhoea, which can case disseminated gonococcus infection and where fluoroquinolones used to be a recommendation by the CDC guidelines, have recently shown upto 100% resistance and is no longer recommended as 1st line. Dose adjustment is needed in renal failure as per estimated GFR [3] [Table 4].

Table 4 – The Tetracyclines and Macrolides

In today's dermatological practice, the primary use of these drugs is for their anti inflammatory effect, rather than for their antibiotic effect. Notable uses include acne (specially with pustules), bullous pemphigoid, cicatricial alopecias like folliculitis decalvans, erosive pustular dermatoses of the scalp. Tetarcyclines bind to 30S subunit of rRNA and thereby inhibit the complex formation necessary for translation. Unfortunately prevalence of resistance is increasing at a dramatic pace. Alternation of binding site at 30S subunit, development of efflux pumps and alternate splicing mechanisms account for some of the resistance patterns to tetracyclines. For Propionibacterium acnes, the prevalence of resistance to the Tetracyclines are as follows: Minocycline 0.2%- 0.5%, Tetracycline 2% – 5%, Doxycycline 2.4% – 8%. In these cases, it is preferable to switch over to a retinoid or an alternate tetracyclines [11]. Of note, both Indian Association of Dermatologists Venereologists and Leprologists guidelines and other guidelines have recommended against the monotherapy with tetracyclines in the treatment of acne vulgaris [11-13]. Even low dose doxycycline as low as 40 mg once daily have been found to be therapeutically effective for acne [13]. Of note, Doxycycline is one of the drugs used in syndromic management of Sexually Transmitted Infections. Also Doycyline is one antibiotic of the class which can be used if renal status is no known since it is not nephrotoxic. All other tetrcyclines need dose adjustment in renal failure as per eGFR [3]. Also chloramphenicol cannot be used in neonates since it may cause gray baby syndrome due to hepatic insufficiency [Table 5].

Aminoglycosides

These group of drugs are very valuable particularly when dealing with sepsis in Pemphigus or Toxic epidermal necrolysis

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Table 4:

Drug	Spectrum	Dosage	Side Effects
Ciprofloxacin	Aerobic Gram Negative bacilli like Klebsiella pneumoniae, Pseudomonas Bacillus anthracis	500 mg twice daily IV dose: 400 mg twice daily	Photosensitivity Rash GI intolerance Tendinitis
Moxifloxacin	Same	400 mg once daily	Same
Levofloxacin	Same	500 mg Once Daily	Same
Pefloxacin	Same	400 mg Twice Daily	Same

Table 5:

Drug	Spectrum	Dosage [8]	Side Effects
Tetracycline	MRSA Streptococcus pyogenes Gram Positive Bacilli like Clostridia sp Treponemes including Treponema pallidum Propionibacterium acnes	Orally 500 mg upto 4 times a day	Liver toxicity Renal Damage Tooth and bone damage and discoloration Phototoxicity
Doxycycline	Same Also used for Syndromic management of Sexually transmitted infections.	Orally 100 to 200 mg per day Low dose 40 mg once daily is effective for treatment of acne [13]	More phototoxicity Lacks renal toxicity
Minocycline	Same	Orally Cap 100 mg once daily Inj Minocycline 100 mg vial for life threatening sepsis	More Renal and Cochlear toxicity Pigmentation
Lymecycline	Same It is a newer analogue of Tertacylcine with lesser resistance	Orally Cap 408 mg once daily OR Cap 204 mg Once daily	Less Phototoxic
Oxytetracycline	Same	Orally 500 mg capsules	Same as Tetracycline
Chloramphenicol	Mostly restricted to Gonorrhea in dermatological practice	500 mg 6 hourly (Maximum 100 mg/kg/day)	Bone Marrow Suppression Aplastic crisis Induction of Leukemias Gray baby syndrome

patients with Pseudomonas or other PEAK (Pseudomonas, Escherichia coli, Acinetobacter baumanii, Klebsiella pneumoniae). Like Tetracylicnes, they bind to 30 S subunit of ribosomes and halt the protein translation. Renal modified dosage must be used in those with sepsis induced acute kidney injury. Hospital acquired pneumonia in these patients also respond well. Spectinomycin is an aminoglycoside antibiotic which has been recommended by CDC Atlanta for management of drug resistant gonorrhoea. Unfortunately it is not available in India. Dose adjustment is needed for renal failure as per eGFR [3] [Table 6].

Macrolides

These were main stay in the management of acne and related conditions but the rapid development of resistance have made their use obsolete in acne and have been superceeded by tetracycline group of antibiotics. They are also very valuable in management of sexually transmitted infections caused by bacteria without a cell wall as in Chlamydia trachomatis and Gardenerella vaginalis where they serve as alternate agents. For the dermatology internist, their use is limited in the treatment of minor skin and soft tissue infections. ROM regimen which featured Rifampicin, Ofloxacin and Minocycline has been used as an alternate regimen to leprosy, particularly in those with Rifampicin resistance. In Rifamicin Resistance, as per WHO recommendations one is supposed to choose from two of these agents: Ofloxacin, Minocycline or Clarithromycin given together with compulsory Clofazimine for a period of 6 months. For the next 18 months, one of the aforementioned (in place of two) is chosen and combined with clofazimine for the rest of the 18 months [14] [Table 7].

Selecting an appropriate antibiotic regimen: Situation specific guidelines

1. **Infected Pemphigus and Toxic Epidermal Necrolysis with large body surface areas:**

Since the commonest infecting organisms are Gram positive cocci which are skin commensals such as Staphylococcus aureus followed by Gram negative organisms like Klebsiella, Pseudomonas, Acinetobacter and others, a proper regimen is one antibiotic for gram positive coverage with 2 antibiotics for Gram negative coverage [3,4]. An example of this regimen is Amoxycillin-Clavulanate with Levofloxacin and imipenem or other carbepenems.

Another possible regimen is using a 3rd Generation cephalosporin such as Cefotaxime or Ceftriaxone with a Fluoroquinolone with an Aminoglycoside. While dealing with Pemphigus, due consideration should be always given to hospital acquired infections, such as MRSA, Pseudomonas, Klebsiella and Acinetobacter. Some clues to their possibility, prior to the availability of culture sensitivity reports are a history of prior admission to a hospital, prolonged hospital stay, sudden worsening of sepsis or sudden increase in pus

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Table 6:

Drug	Spectrum	Dosage	Side Effects
Gentamycin/ Tobramycin/ Sisomycin/ Netilmycin	Gram Negative Bacilli notably Klebsiella pneumoniae, Escherichia coli, Proteus, Pseudomonas auruginosa	3 – 5 mg/kg/day by slow infusion	Ototoxicity Nephrotoxicity
Amikacin/ Streptomycin/ Kanamycin	Same	7.5 – 15 mg/kg/day by slow infusion	Same

Table 7:

Drug	Spectrum	Dose	Adverse effects
Erythromycin	Streptococcus pneumoniae, Gardenerella vaginalis, Chlamydia trachomatis	250 – 500 mg every 6 hourly, orally. Maximum daily dose not to exceed 4 g per day	Nausea, vomiting, diarrhoea, QTc prolongation and ventricular arrythmias
Azithromycin	Same	500 mg once daily	Same but less QTc prolongation
Clarithromycin	Predominantly used for Leprosy and for H pylori eradication in Chronic Urticaria patients	500 mg per day orally	Same but lesser QTc prolongation
Telithromycin	Predominant use for Gonococcus	800 mg per day orally	Same but lesser QTc
Clindamycin	Gram positive cocci Except MRSA Anerobes – like Bacteroides fragilis	300 mg four times a day orally 3 – 6 mg/kg/day Intravenous: 600 mg every 8 hourly	Rashes, Urticaria, abdominal pain, nausea, vomiting, pseudomembranous colitis
Vancomycin	MRSA sepsis – predominant use in infected pemphigus	Inj 500 mg every 6 hourly	Ototoxic and Nephrotoxic
Linezolid	MRSA, VRSA sepsis VRE sepsis	600 mg Twice daily orally or injection by slow iv infusion	Hematological toxicity – Bone marrow suppression for > 2 weeks
Tedizolid	MRSA, VRSA sepsis, VRE sepsis	200 mg once daily	GI intolerance
Spectinomycin	Multi drug resistant Gonorrhoea	2 gm intramuscular stat	Anemia, renal and hepatotoxicity
Quinupristine-Dalfopristine	Sepsis by MRSA, MRE (But not E faecalis), VRSA	7.5 mg per kg every 8 hourly administered in 60 minute dose	Muscle, Joint, Injection site pain
Daptomycin	Sepsis by MRSA, VRSA, Multidrug resistant enterococci	4 mg/ kg intravenous once daily	Abdominal pain, arthralgia etc
Polymyxin B	Gram Negative organisms	Topically	Contact hypersentitivity
Collistin	Gram Negative including Pseudomonas	Topically	Contact Hypersentivity

discharge, sudden spikes of fever or hypothermia, formation of greenish colonies on denuded skin.

2. **The problem of pan resistant organisms**

Our experience in a tertiary care centre suggests most isolates in infected patients are pan resistant – predominantly pan resistant Klebsiella and Pseudomonas. Both organisms are notoriously difficult to treat.

Pan resistant klebsiella

One algorithm for pan resistant Klebsiella is combining high dose Tigecycline with colistin [5]. Another such algorithm is combing two carbepenems given above with colistin [6]. Other options include combination of ceftazidime-avibactam plus aztreonam, or cefiderocol as monotherapy, if carbapenemase testing results are not available [7].

Pan resistant pseudomonas

It is defined as *P. aeruginosa* exhibiting non-susceptibility to all of the following: piperacillin-tazobactam, ceftazidime, cefepime, aztreonam, meropenem, imipenem-cilastatin, ciprofloxacin, and levofloxacin [20].

The IDSA recommends an aminoglycoside in combination with either ceftolozane-tazobactam, ceftazidime-avibactam, or imipenem-cilastatin-relebactam, preferentially selecting the β-lactam-β-lactamase inhibitor agent for which the MIC is closest to its susceptibility breakpoint [15-20].

How long to continue antibiotics?

Because of poor penetration, most infected pemphigus patients require 10 – 14 days of therapy. For sepsis, as per Surviving Sepsis Campaign, the continuation antibiotics beyond defervescence and clinical improvement must be decided by procalcitonin levels.

Conclusion

With the advent of pan resistant organisms, the dermatologist must familiarize themselves with the proper antibiotic selection and proper dosage. Wherever possible, antibiotic selection must be guided by proper sensitivity testing and the help of a relevant infectious disease physician should be sought.

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