Chapter

Streptococcal Skin and Skin-Structure Infections

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Abstract

Infections attributable to *Streptococcus* are protean. These range from mild skin and soft tissue infections to life-threatening conditions like meningitis, endocarditis and toxic shock syndrome. In addition, streptococcal infection can be associated with noninfectious sequelae like rheumatic fever and post-streptococcal glomerulonephritis. There is a wide range of *Streptococcus spp.* causing human infections and different classifications of these organisms have been described, the most quoted being the Lancefield classification based on cell-wall antigens. *Streptococci* can be studied based on their species: *S. pyogenes, S. pneumoniae, S. anginosus* etc. or by the Lancefield classification group A, B, C, D etc. or by the clinical syndromes associated with these bacteria. This chapter will describe clinical syndromes associated with streptococcal skin and soft tissue infections ranging from mild: cellulitis and lymphangitis which can be treated in the out-patient setting, to more aggressive manifestations that require hospitalization (sepsis and toxic shock syndrome) and even surgery (necrotizing fasciitis, myositis and gangrene), It will also provide clues to clinical diagnosis as well as suggest recommendations for optimized management of these conditions.

Keywords: *Streptococcus*, Skin and Skin-Structure Infections (SSTI), Necrotizing Fasciitis (NF), Toxic Shock syndrome (TSS)

1. Introduction

Streptococcal skin and skin-structure infection (SSTI) is associated with significant morbidity all over the world and the impact is felt predominantly in resource-poor areas with inadequate personal hygiene and over-crowded living conditions. While exact numbers are difficult to estimate on account of the lack of systematic reporting, a literature search conducted by Sims and colleagues [1] reported an estimated prevalence of 18 million cases, with an incidence rate of around 1.78 million cases per year of invasive *S. pyogenes* (*S. pyogenes*) infection in 2005, and more than 140 million cases of impetigo globally each year as reported in the 2010 Global Burden of Disease study. Rising numbers of cases of infectious diseases of the skin is also seen in Western nations, probably driven by drug abuse and homelessness [2, 3]. Increased cases result in increased costs from emergency room visits and hospital care, hence outpatient parenteral antibiotic therapy (OPAT) has proven to be a valuable alternative to hospitalization [4], and when patients are chosen appropriately, OPAT results

in very significant cost-savings without compromising outcomes [5]. Advances in pharmaceutical research has contributed to development of longer acting antibiotics that can be dosed once a day and in some cases once a week. There is ongoing research to determine the optimum duration of antibiotic therapy for these conditions.

Skin infections have been variously classified based on different criteria like depth of infection or the bacterial agents causing the infections or as primary infection in contrast to infection of pre-existing wounds or skin conditions. A very practical classification of patients hospitalized with skin infections (cellulitis versus abscess versus skin infections with additional complicating factors) has been described by Jenkins et al. [6]. The authors found in their study that cutaneous abscesses were primarily caused by *Staphylococcus aureus* and less often by the *Streptococcus spp*, in contrast with cellulitis which was caused primarily by *β-hemolytic streptococci* and less commonly by *Staphylococcus spp*. This differentiation is especially helpful when choosing the appropriate narrow spectrum antibiotic therapy for individual patients with these diagnoses. In contrast, "skin infections with additional complications" require more broad antibiotic coverage on account of mixed bacterial infection or infection with unusual organisms.

The clinical features of common streptococcal SSTIs and the antibiotics used in the management of these conditions will be further elaborated in this chapter.

2. Streptococcal pyoderma

Superficial skin infection has been described as **impetigo or pyoderma**. This is in contrast to more invasive diseases cellulitis and erysipelas. Impetigo (and the less precise term pyoderma) refers to superficial infection that begins in the form of a papule that progresses to a vesicle and pustule, ultimately forming crusted lesions (**Figure 1**). They resolve with hyper or hypopigmentation. These infections are caused either by *Staphylococcus* or *Streptococcus*, and one cannot clinically differentiate between the two causative organisms. They occur as a complication of underlying skin diseases

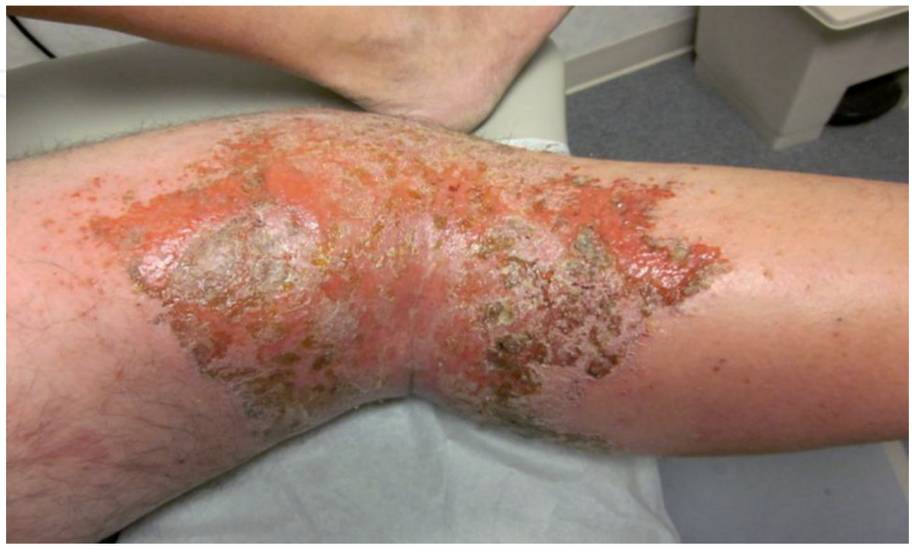

Figure 1.
Impetigo secondary to infected contact dermatitis.

like scabies [1] or contact dermatitis. The streptococci associated with these infections are most often group A (*S. pyogenes*). However other serotypes can also be isolated on cultures from these infections. Although considered benign, these infections could progress to more locally invasive cutaneous diseases (see below) and are associated with post-streptococcal complications like glomerulonephritis and acute rheumatic fever in resource limited populations (as reviewed in other chapters of this textbook).

3. Treatment of impetigo

Antiseptic soaks and antibacterial creams are the mainstay of therapy for impetigo. A wide variety of topical antimicrobial agents are available including silver-based products, iodides, hydrogen peroxide, zinc, chlorhexidine and potassium permanganate. There is very little data in the literature comparing benefits of one product versus the other [7, 8]. Antibacterial creams: mupirocin, Na-fusidate and bacitracin are also available for use in localized superficial skin infections [9]. Drawbacks of topical therapy include development of resistance, risk of irritant or allergic dermatitis (sensitization), and if used in high concentrations, these could cause burn injuries.

4. Invasive streptococcal infections: erysipelas and cellulitis

When skin infection results in erythematous (red in color), edematous (raised above the surface) and well demarcated (sharp boundary between involved and uninvolved skin) areas of involvement, it is referred to as **Erysipelas** (**Figure 2**). Erysipelas is characterized by marked edema in the skin, sometimes severe enough to cause skin blisters. While it could be seen at any age, it is more common in the very young and in older individuals. Classically described as occurring on the face, it can be seen in other parts of the body including the trunk and extremities. It is commonly associated with systemic symptoms like fever, chills and body ache, and blood cultures could be positive. Erysipelas is most commonly caused by *S. pyogenes* but could also be caused by other streptococci and less commonly by *S. aureus* [10]. Superficial skin culture should not be obtained, and causative organism can be established if blood cultures return positive. The diagnosis is usually clinical and it responds well to antibiotic therapy. However, in patients with uncontrolled diabetes or other immunocompromising conditions, the infection can spread deeper and the patient could develop sepsis and shock. Recurrences—especially on the extremities—are common in patients with underlying chronic lymphedema [11].

When streptococcal infection involves the skin as well as the subcutaneous tissue, it results in ill-defined areas of erythema that are rapidly spreading and this is called **Cellulitis.** The skin appears red with irregular spreading borders (**Figure 3**). The entry point for the infection is a break in the skin like a surgical wound or other skin trauma, underlying dermatoses like eczema and psoriasis or a fungal infection of the intertriginous areas like web spaces of the toes: "athlete's foot" (**Figure 4**). The area of the skin involved is tender to touch, and cellulitis is associated with systemic symptoms like fever, chills and body ache. Sometimes infection spreads along a lymphatic channel rather than the entire skin and this is called **streptococcal lymphangitis**.

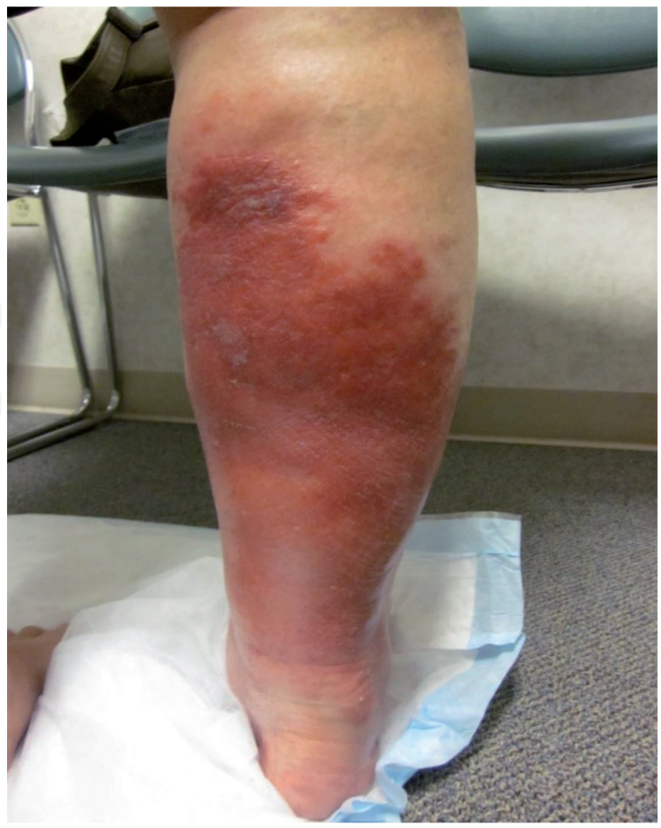

Figure 2.
Erysipelas with sharply-defined edematous red skin lesions.

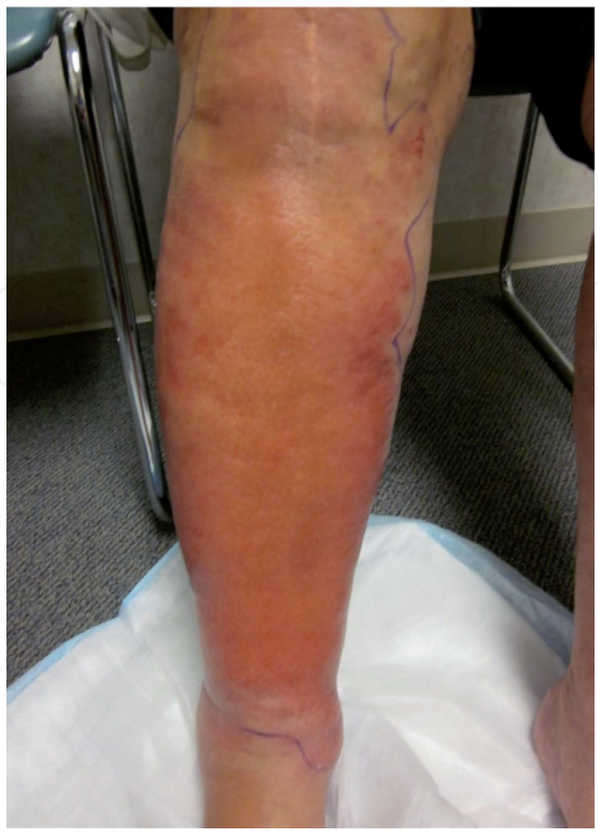

Figure 3.
Cellulitis with irregular and ill-defined borders.

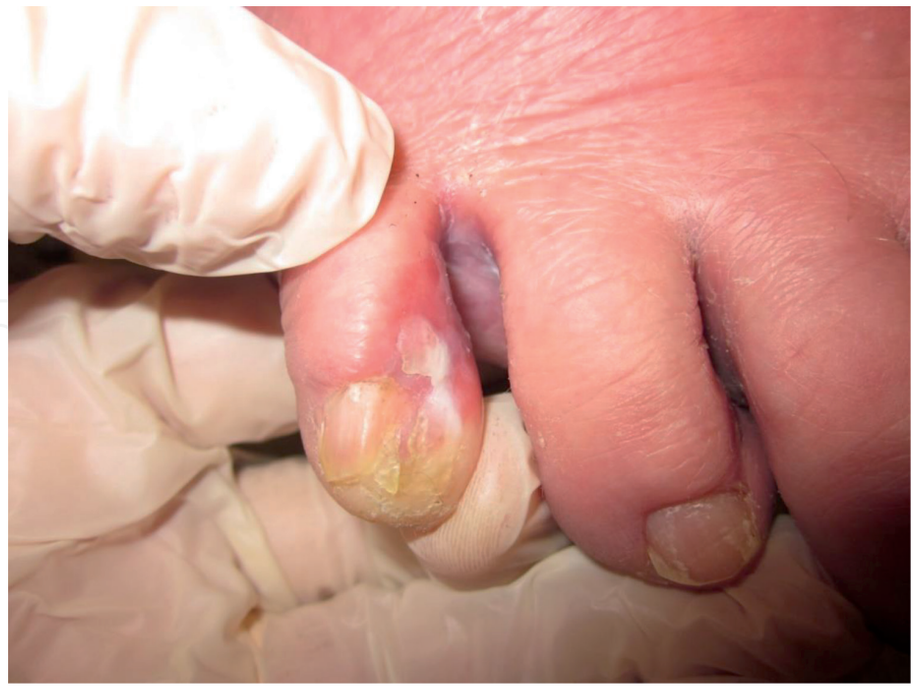

Figure 4.
Fungal infection in the webspace of the toes, also called "athlete's foot."

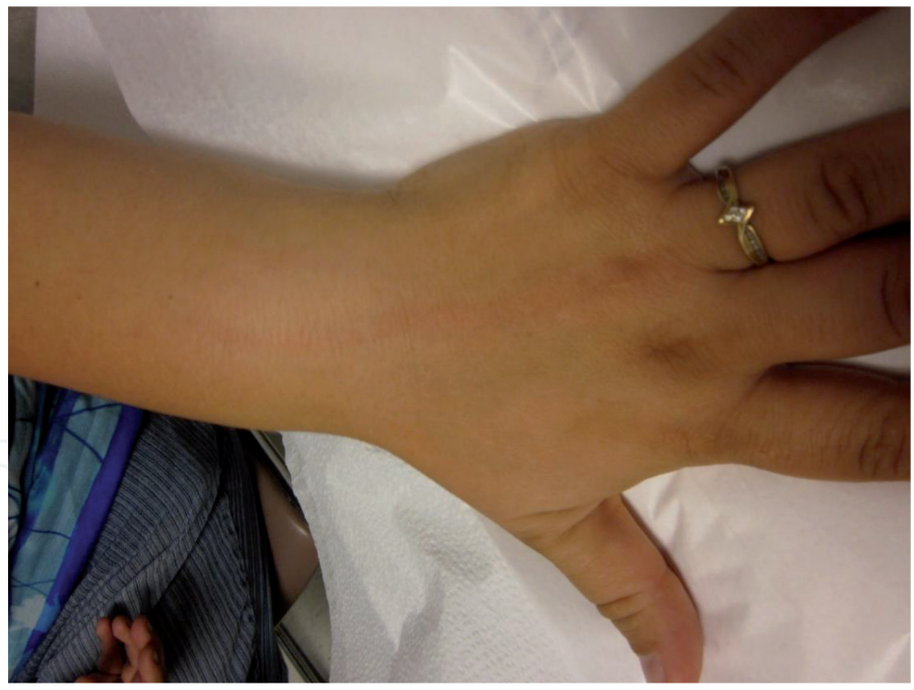

Figure 5.
Lymphangitic streaking of the upper extremity.

(**Figures 5** and **6**) Blood cultures are positive in around 10% of cases [12, 13] which include patients with more severe disease, older patients, patients with underlying liver cirrhosis [12] and diabetes [13]. The yield of blood cultures is higher if cultures are obtained at the time when the patient is experiencing fever and chills. Cellulitis responds very quickly to appropriate antibiotic therapy. As with erysipelas, recurrences are common in those with underlying risk factors, and left untreated, the infection can spread to deeper tissues and result in sepsis and shock.

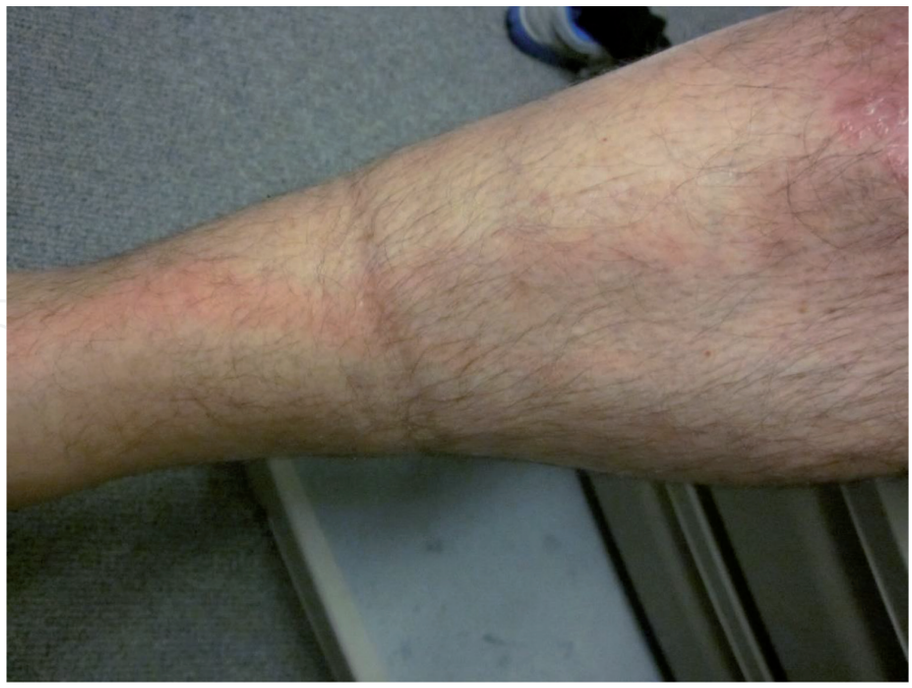

Figure 6.
Lymphangitic streaking (double) of the lower extremity.

In some patients there is an overlap between erysipelas and cellulitis and the clinical differences are not so clear. Importantly, management of both conditions is similar.

5. Treatment of cellulitis and erysipelas

Mild localized infections are treated with oral antibiotics, while more extensive infections or infections with systemic symptoms are treated with parenteral (intravenous) antibiotic therapy [14]. Patients with signs of sepsis: fever or hypothermia, tachycardia and hypotension, and patients with underlying conditions like uncontrolled diabetes, liver cirrhosis, severe peripheral vascular disease or severe lymphedema and patients with immunocompromising conditions like HIV, or patients on chemotherapy should be admitted to the hospital for antibiotics as well as aggressive management of the underlying conditions. Penicillins and β-lactams are considered the antibiotics of choice for treatment of streptococcal cellulitis. The addition of a second antibiotic like trimethoprim/sulfamethoxazole (TMP/SMX) or clindamycin has been shown to provide no additional benefit [6, 15–18]. Penicillins are available in the form of oral as well as intravenous preparations (**Table 1**). Extended spectrum penicillins: dicloxacillin, amoxicillin, ampicillin, oxacillin and nafcillin can be used if there is associated methicillin susceptible *S. aureus* (MSSA) infection. Cephalosporins are among the most commonly used β-lactams for the treatment of cellulitis. Different preparations are available both in the oral as well as the intravenous forms (**Table 2**). Physician preference and dosing convenience often define the choice of the antibiotic prescribed. Ceftaroline—one of the newest cephalosporins has excellent skin penetration and has activity against methicillin resistant *S. aureus* (MRSA) [19]. Patients who have an allergy to penicillin will require alternate agents. It should be noted here that there is increasing evidence in the literature

Name	Dosage	Comments
Oral agents		
Penicillin VK	250–500 mg, 4 times a day	
Dicloxacillin	250–500 mg, 4 times a day	Effective also against MSSA
Amoxicillin	500 mg, 3 times a day	Effective also against MSSA
Intravenous agents		
Penicillin G	2–4 million units, q 4–6 h	Also available as continuous infusion via pump
Ampicillin	2 g, q 4–6 h	Effective also against MSSA
Oxacillin, Nafcillin	1–2 g, q 4–6 h	Effective also against MSSA
Piperacillin-tazobactam*	4.5 g, q 8 h	Effective also against MSSA, *Pseudomona*, anaerobic bacteria

**Require dose adjustment in patients with kidney disease.*

Table 1.
Penicilins.

	Name	Dosage
Oral cephalosporins		
1st generation	cephalexin	500 mg, 4 time a day
2nd generation	cefaclor	500 mg, 3 times a day
	cefuroxime	500 mg, 2 times a day
3rd generation	cefpodoxime	200 mg, 2 times a day
Intravenous cephalosporins		
1st generation	cefazolin	1–2 g, q 8 h
3rd generation	ceftriaxone	1–2 g, q 24 h
5th generation	Ceftaroline	600 mg, q 12 h
Carbapenems (Intravenous)		
	Imipenem	0.5–1 g q 6 h
	Meropenem	1–2 g, q 8 h
	Ertapenem	1 g, q 24 h

Effective also against MSSA. Ceftaroline is also effective against MRSA.
All (except ceftriaxone) require dose adjustment in patients with kidney disease.

Table 2.
β-Lactam antibiotics used for streptococcal skin infections.

indicating patients who claim penicillin allergy may not have a true allergy and are able to tolerate β-lactams [20, 21]. TMP-SMX [22], doxycycline, linezolid, clindamycin and fluoroquinolones (**Table 3**) all have excellent skin penetration and may be used as alternate oral agents in patients with allergies to penicillin and β-lactams. Severe cellulitis in patients who have a true allergy to both penicillin and β-lactams is

Name	Drug class	Dose	Comments
Oral agents			
TMP/SMX* (160 mg/800 mg)	Sulphonamide	1–2 tabs, 2 times a day	Effective also against MSSA, MRSA
			Watch for rash, monitor cbc, creatinine
Doxycycline, Minocycline (100 mg)	Tetracycline derivative	1 tab, 2 times a day	Effective also against MSSA, MRSA
			Risk for sunburn, pill esophagitis
Linezolid (600 mg)	Oxazolidinone	1 tab, 2 times a day	Effective also against MSSA, MRSA
			Avoid co-administration with SSRI, MAO inhibitors
			Risk for cytopenias, neuropathy
			Excellent oral-parenteral bioavailability
Clindamycin (300 mg)	Lincosamide	300–450 mg, 4 times a day	Effective also against MSSA, MRSA
			Highest risk for CDiff infection
Ciprofloxacin, levofloxacin, moxifloxacin	Fluoroquinolone*	Different doses for different agents	Effective also against MSSA
			Risk for tendon injury, CNS side effects in the elderly, CDiff infection
Intravenous agents			Effective also against MSSA, MRSA
Vancomycin*	Glycopeptide	15–20 mg/kg q 12 h	Close monitoring of levels to avoid nephrotoxicity. Red-man syndrome if administered too fast
Daptomycin*	Cyclic lipopeptide	4–6 mg/kg q 24 h	Risk of rhabdomyolysis, Esosinophilic pneumonia
Linezolid	Oxazolidinone	600 mg q 12 h	Avoid co-administration with SSRI, MAO inhibitors
			Risk for cytopenias, neuropathy
Tigecycline	Tetracycline derivative (glycylcycline)	100 mg X 1, then 50 mg q 12 h	Effective also against anaerobes
			Risk for Nausea

**Require dose adjustment in patients with kidney disease.*

Table 3.
Non β-lactam antibiotics used for streptococcal skin infections.

treated with intravenous (IV) vancomycin. IV vancomycin requires close monitoring of levels to achieve optimized benefits while avoiding nephrotoxicity [23, 24], and often therapeutic levels are difficult to achieve in obese individuals [25]. Other alternatives to β-lactams are listed in **Table 3**. Daptomycin is a lipopeptide antibiotic that has excellent skin penetration. [26, 27]. It has the advantage of once- a- day

Name	Drug class	Dose	Comments
Dalbavancin	Lipo-glycopeptide	Intravenous: 1.5 g single dose	One dose IV provides 2 weeks of therapy
Oritavancin	Lipo-glycopeptide	Intravenous: 1.2 g single dose	One dose IV provides 2 weeks of therapy
Delafloxacin	Fluoroquinolone	Intravenous: 300 mg q 12 h Oral: 450 mg twice a day	Allows transition from IV to oral. Risks as with other FQ
Omadacycline	Tetracycline derivative	Intravenous: 200 mg X 1, then 100 mg daily Oral: 450 mg once a day for 2 days, then 300 mg once a day	Allows transition from IV to oral. Gastrointestinal side effects. Effective also against anaerobes
Tedizolid	Oxazolidinone	Intravenous: 200 mg, q 24 h Oral: 200 mg once a day	Allows transition from IV to oral. Risk for cytopenias, neuropathy

Effective also against MSSA, MRSA.

Table 4.
Newer antibiotics approved for treatment of skin infections.

dosing, making daptomycin a convenient agent for outpatient antibiotic therapy (OPAT). Other antibiotics with excellent skin penetration include linezolid [28, 29] and tigecycline [27, 30]. Both these antibiotics are dosed twice a day and hence less convenient for use as OPAT. Tigecycline is only available in the parenteral form and is recommended for patients hospitalized with severe infections. Linezolid is available in both parenteral as well as oral formulations. IV linezolid is used when a patient is hospitalized with severe cellulitis, and treatment can be completed with oral formulation once the patient improves. There are a number of newer agents approved for the management of SSTIs including long acting lipo-glycopeptide agents oritavancin and dalbavancin, extended-spectrum fluoroquinolone delafloxacin, and the new tetracycline derivative omadacycline [28, 29]. Important comments regarding the advantages as well as the potential side effects of these antibiotics are listed in **Tables 3** and **4**.

6. Streptococcal infection of deeper tissues

When streptococcal infection spreads deep beyond the subcutaneous tissue, it can result in extensive necrosis (gangrene) of the overlying skin and inflammation and necrosis of underlying fascia **(Streptococcal Necrotizing Fasciitis)** and even muscle (**Streptococcal Myositis).** These infections are considered surgical emergencies.

Necrotizing Fasciitis (NF) is characterized by rapidly (within hours) spreading infection of the skin, subcutaneous tissue and fascia with associated symptoms of fever, prostration, hypotension and shock. It carries a high mortality [31]. It could start as a benign appearing skin wound that rapidly spreads both on the surface as well as into deeper tissues and the entire limb or body-part could be involved in a matter of a few hours. Skin changes include a rapid progression from mild erythema to a dusky appearance followed by ecchymosis, purpura, blisters and tissue

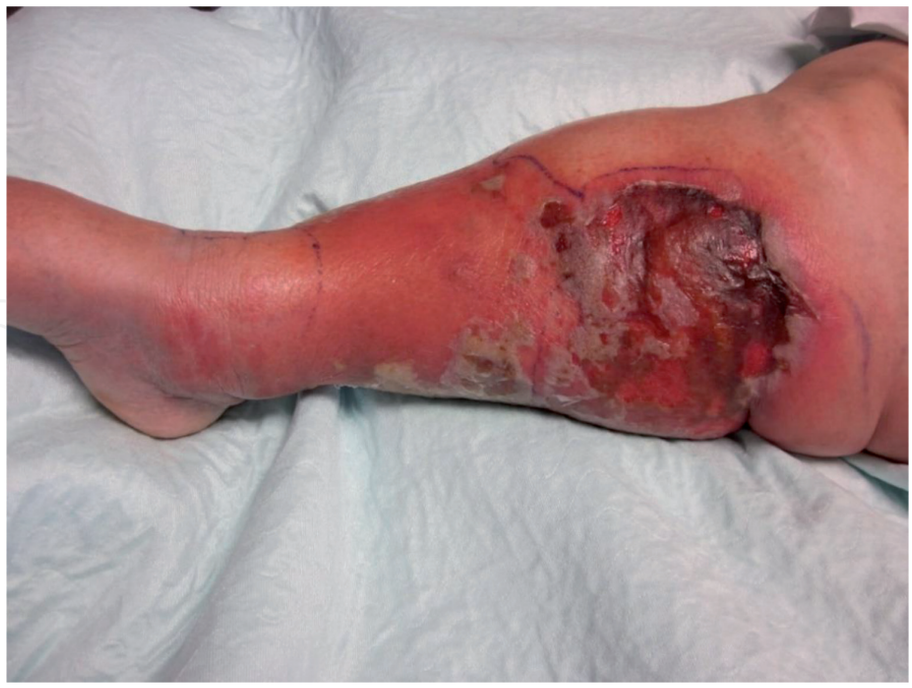

Figure 7.
Necrotizing fasciitis of the lower extremity.

necrosis—resulting in open wounds often discharging purulent or hemorrhagic fluid. (**Figures 7** and **8**) "Pain out of proportion to physical findings" is a characteristic sign of NF. In other words, there may be pain when palpating areas beyond the visible area of redness or in other cases even gentle palpation of involved area elicits excruciating pain. Some authorities divide NF into type I and type II. Type I is characterized by poly-microbial infection (involving both aerobic as well as anaerobic bacteria), while type II is characterized by mono-microbial infection of which

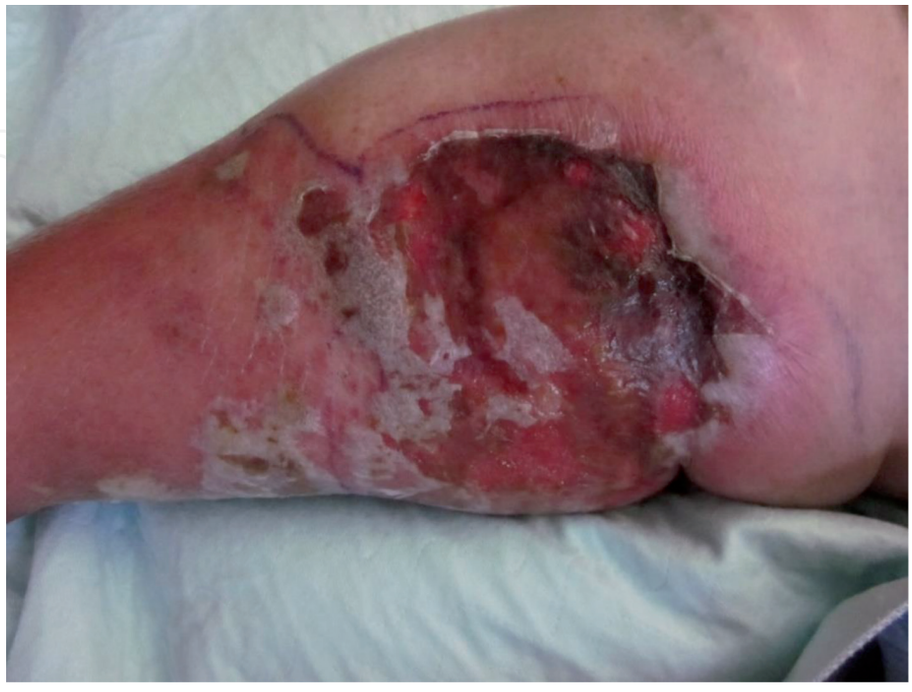

Figure 8.
Clinical photograph showing erythema, peeling skin, dusky hue and areas of necrosis.

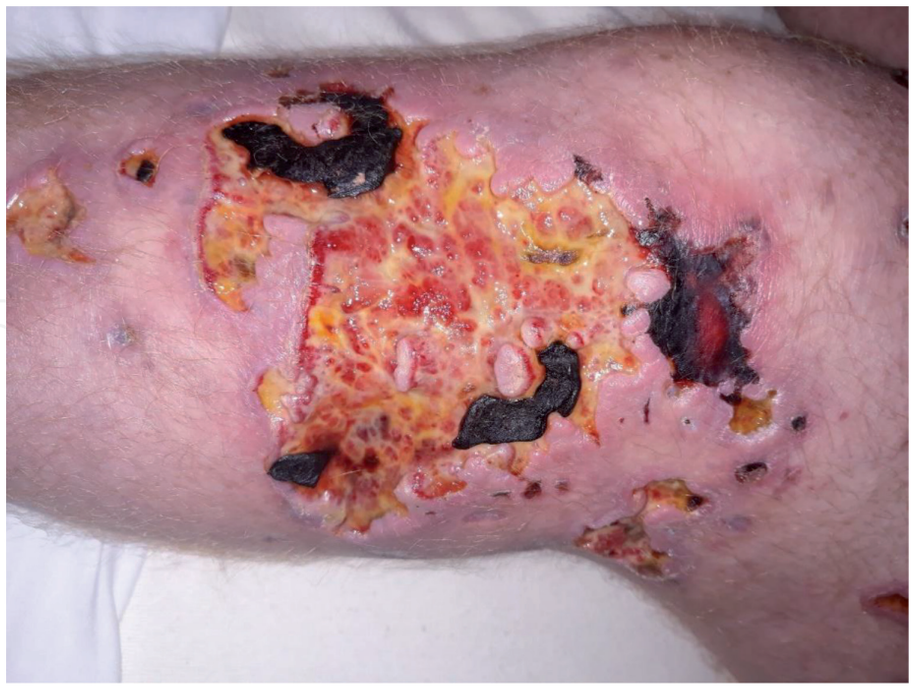

Figure 9.
Necrotic areas with skip lesions on leg of patient who is abusing self with injection drugs.

group A streptococcus is the most commonly implicated organism [32]. Mortality was found to be lower in *group A streptococcus*—associated NF (type II) compared to type I: 10% versus 20% in one large study [31]. NF may also be seen in persons who inject drugs. In these cases, multiple skip lesions are seen (**Figure 9**) and infection is usually poly-microbial. In addition to the skin lesions, the patient usually has systemic symptoms of sepsis including high fever, tachycardia, hypotension and may progress to have multi-organ failure. Streptococcal pyrogenic exotoxins

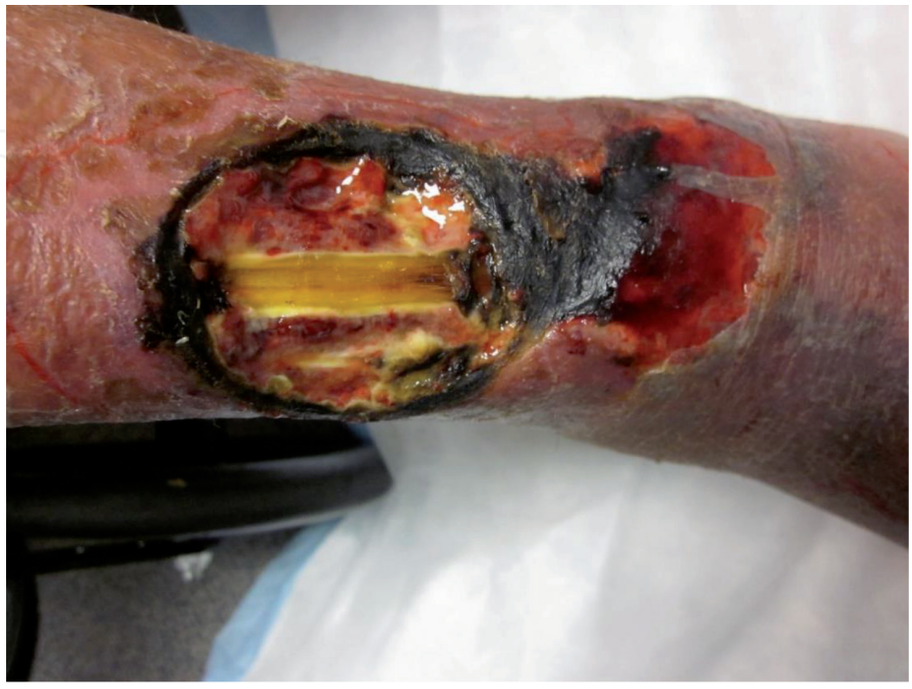

Figure 10.
Necrosis of skin, soft tissue and muscle with exposure of tendon.

(Spe) A, B and C are responsible for causing stimulation of a severe inflammatory cascade resulting in injury not only at the area of infection (local necrosis) but also to distant sites (lungs, kidneys, liver, central nervous system). Blood cultures are universally positive, and imaging of involved body-part (CT scan or MRI) will demonstrate edema and/or gas in the soft tissue planes and other changes consistent with this diagnosis [33].

When infection spreads beyond the fascial planes into the underlying muscles it is called myositis. **Streptococcal myositis** is often a complication of the overlying skin infection. Sometimes a deep tissue hematoma caused by blunt trauma [34] could get inoculated by the organism in a patient with bacteremia. This too is an emergency and requires rapid surgical intervention to relieve the pressure created by the severe inflammation in the muscle planes (**Figure 10**). Patients will also have systemic symptoms and signs of sepsis as seen in NF. There is often overlap of these two conditions in many patients.

7. Management of necrotizing fasciitis and streptococcal myositis

Patients need admission to the hospital often to the intensive care unit. They require management by a team of experts involving medical, surgical, infectious diseases and critical care specialties. They often present with septic shock and require pressors like epinephrine, norepinephrine and vasopressin to maintain adequate blood pressure in order to perfuse critical organs. Patients require broad spectrum antibiotic coverage, aggressive fluid resuscitation, as well as emergent aggressive debridement of the infected areas. Surgical removal of infected/necrotic tissue is essential in order to reduce bacterial burden and hence remove the source of toxins. Often patients require a second or even third visit to the operating room because of extensive tissue necrosis not amenable to removal in a single operation [14]. Operative tissue is sent for microbiology (cultures) to help determine the infectious agent and obtain an antibiotic sensitivity profile to help guide appropriate antibiotic choices. While awaiting the results of cultures, the antibiotics chosen should cover Gram-positive bacteria including *Streptococcus* and *S. aureus*, Gram-negative bacteria including drug-resistant bacteria like *Pseudomonas*, as well as anaerobic bacteria. Different combinations of antibiotics from **Tables 1–3** can be used. IV vancomycin (or IV daptomycin) plus cefepime (or fluoroquinolone) plus metronidazole, or IV vancomycin (or IV daptomycin) plus meropenem (or imipenem), or IV daptomycin plus piperacillin- tazobactam are some potential options for empiric therapy. Linezolid could be used in place of vancomycin and daptomycin in the above combinations. Vancomycin, daptomycin and linezolid provide Gram-positive coverage, cefepime and fluoroquinolones provide Gram-negative coverage. While metronidazole provides only anaerobic coverage, imipenem, meropenem and piperacillin-tazobactam provide Gram-negative as well as anaerobic coverage. Clindamycin is added in the initial critical stages of the infection on account of its antitoxin effect [14, 33]. If linezolid is used, additional clindamycin is not required because linezolid itself also has an antitoxin effect [33]. When culture results become available, antibiotics should be deescalated to target the organisms identified. Intravenous immunoglobulins (IVIG) is used at some centers as part of management of NF, however large studies have not shown a statistically significant benefit compared to those patients who did not receive IVIG [14, 33].

8. Toxic shock syndrome (TSS)

TSS is associated with a dramatic widespread skin rash and severe systemic symptoms. This condition is not due to direct inoculation of the skin with *Streptococcus,* but rather it is secondary to exotoxin [35] released by *Streptococcus* infection at a

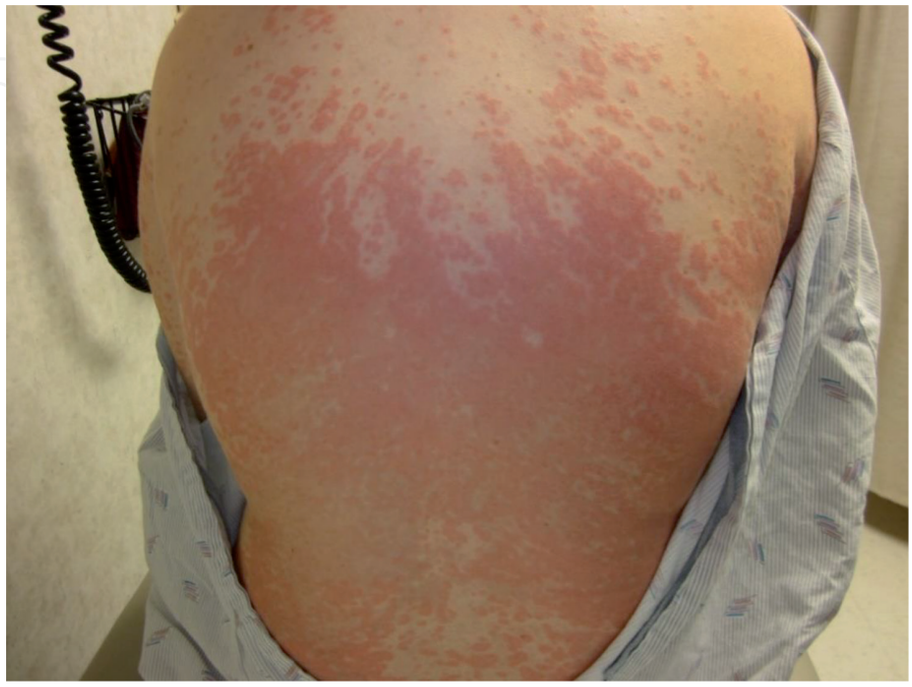

Figure 11.
Clinical photograph of sheet of erythema seen in acute phase of toxic shock syndrome.

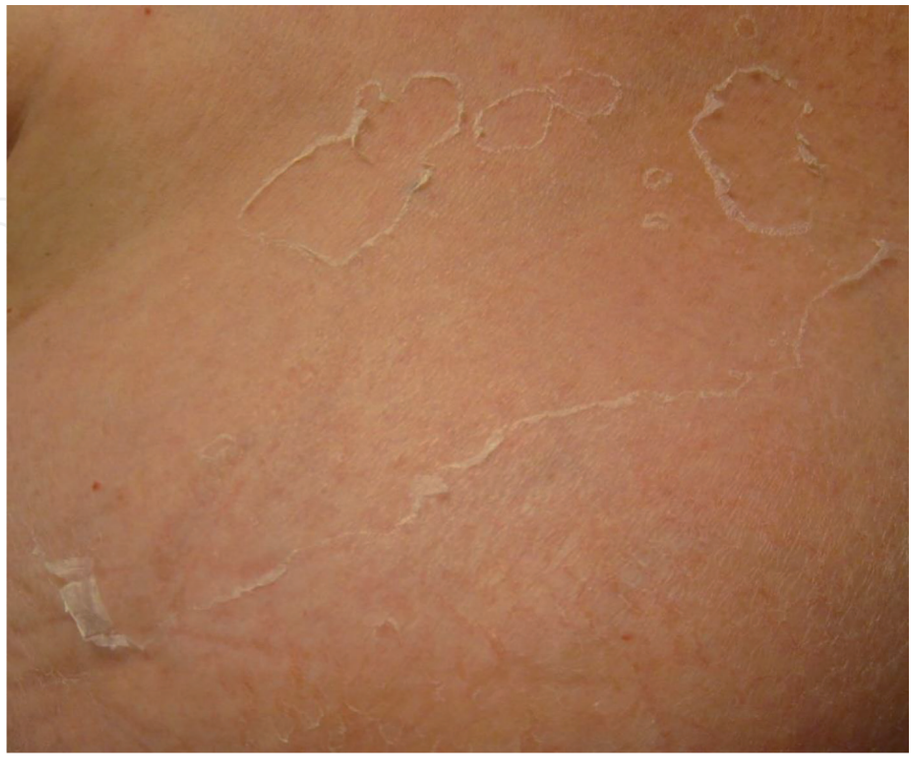

Figure 12.
Toxic shock syndrome with desquamation in the recovery phase.

distant site. Originally described in children with *S. aureus* infection, TSS is seen with *Streptococcus* and Clostridial infection in children as well as adults [36]. Patients present with widespread rash associated with fever, hypotension and multi-organ system involvement as a result of circulating streptococcal exotoxins A, B and C. The rash is described as sheets of erythema (**Figure 11**) involving the face, trunk as well as extremities, and it subsides with characteristic desquamation (**Figure 12**) when the patient recovers. A detailed examination is important to determine the source of infection: either retained foreign body like menstrual tampon or surgical sponge/dressing material, necrotizing infection in a deep space, post-operative wound infection or peritonitis. Rarely, streptococcal pharyngitis is the primary event. The circulating toxins (super-antigens) are responsible for injury to internal organs—lungs, kidneys, liver [35] and the disease can be fatal in 40 to 60% cases of streptococcal TSS especially when there is delay in the diagnosis and hence delayed initiation of appropriate antibiotics. Blood cultures may be positive, as are cultures from an identified focus of infection.

9. Management of TSS

As with other severe streptococcal infection, patients with TSS require admission to the hospital. If they are hypotensive or experience multi-organ failure, management is in the intensive care unit where patients are treated with aggressive fluid resuscitation, broad antibiotic therapy (choices similar to that as described for management of necrotizing fasciitis) and pressor support. Surgery may be required if a deep focus of infection is identified. Rarely patients do not respond to standard therapy and may require intravenous immunoglobulins (IVIG) [36].

10. Discussion on general principles of systemic antibiotic therapy

Streptococcal SSTIs respond very well to antibiotic therapy. A wide range of antibiotics with excellent skin penetration are now available as noted in **Table 1–4**. All antibiotics carry the potential for side effects like allergic reactions and gastrointestinal disturbances. There are some side effects that are unique to certain antibiotics and patients need to be monitored for these toxicities. For example: β-lactam antibiotics have the potential for hepatotoxicity, vancomycin is associated with nephrotoxicity, daptomycin can cause rhabdomyolysis and eosinophilic pneumonitis and clindamycin is one of the most common antibiotics associated with *Clostridioides difficile* (*C. Diff*) infection. In addition, inappropriate use of broad-spectrum antibiotics—and even prolonged use of narrow spectrum antibiotics—can result in collateral damage (destruction of protective normal bacterial flora of the skin and the gastrointestinal tract) and cause antibiotic-associated diarrhea and *C. Diff* infection [37, 38]. Indiscriminate use of broad-spectrum antibiotics has also contributed to the development of multidrug-resistant pathogens [39]. Therefore, judicious use of antibiotics is very important to reduce the risk of these complications. Streptococcal infections should be treated with narrow spectrum antibiotics like penicillin and β-lactams. When streptococcal cellulitis or erysipelas does not seem to be responding adequately within the first 2–3 days of β-lactam therapy, antibiotics with additional coverage against MRSA will need to be used.

11. Specific points regarding treatment of SSTIs

1. Mild infections should be treated with oral antibiotics.

2. Severe infections (severe local skin infection with systemic symptoms like fever, tachycardia, hypotension or leukocytosis and bacteremia, or more extensive skin infections even without systemic symptoms) will require parenteral therapy, with step-down to oral therapy as the patient improves [40]. Antibiotics like the floroquinolones: ciprofloxacin, levofloxacin, delafloxacin [41, 42], moxifloxacin [43], the oxazolidinones: linezolid, tedizolid and the new tetracycline: omadacycline [44] have excellent oral bioavailability and allow early conversion from intravenous to oral therapy.

3. In the most serious cases: sepsis, septic shock, necrotizing fasciitis, myositis, toxic shock syndrome: broad-spectrum antibiotics are required initially (most often with more than one antimicrobial agent) to cover *Streptococcus*, *S. aureus* including MRSA as well as gram-negative and anaerobic bacteria. "De-escalation" can be achieved once microbiology data (blood cultures, deep tissue and intraoperative cultures) are available to guide the final antibiotic choice targeting the bacteria identified.

4. Duration of antibiotics: This depends on the severity of the infection as well as the clinical response to therapy. Mild infections or even severe infections in an otherwise healthy host that respond rapidly to antibiotics could be treated for as short as 5 days [14, 45, 46]. More severe infections or infections with a delayed response to therapy may need longer courses like 7, 10 or 14 days, depending upon the clinical picture. Shorter courses may be possible with some of the newer antibiotics including single dose antibiotics like dalbavancin [47] and oritavancin [28]. Relapses are found to be more common in patients with shorter courses of therapy [45]. Patients with bacteremia are usually treated for 14 days.

5. Dose adjustments: Antibiotics are cleared by the liver or kidney and hence dosage needs to be reduced in patients with liver or kidney disease in order to avoid toxicity. Conversely, patients who are obese require a higher dose of the antibiotic to achieve therapeutic levels in the skin [25, 48].

6. Suppressive therapy is attempted for patients with multiple recurrences [45, 49, 50]. Oral penicillin twice daily showed a 70–80% reduction in episodes—but recurrences occurred after discontinuation of prophylaxis. Treatment of underlying factors like athlete's foot, chronic lymphedema, peripheral vascular disease and uncontrolled diabetes is also very important in the prevention of recurrences [11, 44, 45, 51].

12. Conclusions

Streptococcal skin infections cause significant morbidity all over the world, and severe infections like necrotizing fasciitis and toxic shock syndrome can be fatal. There is a wide spectrum of manifestations of skin infections ranging from mild superficial disease to deep necrotic and life-threatening infections. Skin infection is

one of the most common reasons for prescriptions of antibiotics in the community as well as in hospitalized patients. Some of the most commonly used antibiotics have excellent skin penetration and hence the armamentarium to treat skin infections is quite large. Over the last few years there have been multiple new antibiotics approved for the treatment of skin infections and these should be reserved for treatment of severe infections not responding to the common antibiotics and for infections with multi-drug-resistant organisms. A thorough understanding of the different types of skin infections, as well as a detailed knowledge of the different antibiotics are essential for the early diagnosis and selection of the most appropriate antibiotic for the management of simple as well as complex skin infections.

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