



A REVIEW OF CELLULITIS MANAGEMENT AND TREATMENT WITH NOVEL DOSAGE FORMS

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Abstract:

Importance symptoms of cellulitis, an inflammation of the deep dermis and subcutaneous tissue, include swelling, tenderness, warmth, and spreading erythema. With more than 650,000 admissions each year in the United States alone, cellulitis is a prevalent health burden on the world's population.

Observations An estimated 14.5 million cases of cellulitis are reported each year in the US, costing \$3.7 billion just in ambulatory treatment. Since the bulk of cellulitis cases are nonculturable, the causing bacteria are not known. Numerous clinical diseases resemble one another and there are no reliable diagnostic techniques

Streptococcus and methicillin-sensitive *S. aureus* should be the first lines of defence in the treatment of primary and recurrent cellulitis, with an expansion for methicillin-resistant *S. aureus* (MRSA) in cases of cellulitis linked to particular risk factors, such as athletes, kids, men who have sex with men, prisoners, military recruits, residents of long-term care facilities, those who have previously been exposed to MRSA, and intravenous drug users. Treatment should last for five days, with extensions possible if symptoms do not get better. Recurrence risk can be reduced by addressing predisposing variables.

Verdicts and relevance Cellulitis is mainly diagnosed through a physical examination and history. Streptococcus and methicillin-sensitive *S aureus* should be targeted for treatment when treating simple cellulitis. Consideration should be given to resistant organisms, secondary conditions that resemble cellulitis, or underlying complicating conditions like immunosuppression, chronic liver disease, or chronic kidney disease if a patient's condition doesn't better after receiving the recommended first-line antibiotics.

Keywords: Cellulitis, risk factors, first line antibiotics, OPAT, infection.

Introduction:

Acute inflammation of the dermis and subcutaneous tissue, cellulitis is most frequently found causing a wound, ulcer or dermatosis. Localized discomfort, erythema, swelling, and heat characterise this pyogenic, spreading condition. The involved region lacks a clear distinction from the unaffected area, usually on the leg skin.

A superficial infection with noticeable lymphatic involvement known as erysipelas does have a border that is raised and indurated, distinguishing it from normal epidermis. These unique qualities to give off a "peau d'orange" look.

Cellulitis was recovered as the main diagnosis for 75,838 inpatient admissions with a median stay of 3 days and 114,190 completed consultant episodes in secondary care during the 2014 period. 63 is the average patient age. More cases are handled in basic care.

Etiology:

Cellulitis may result from native flora colonising the epidermis and appendages, such as *Staphylococcus aureus* and *Streptococcus pyogenes*, or it may result from other factors. many different exogenous microorganisms.

Bacteria enter the body in a variety of ways. The epidermis, burns, bites from insects, surgical incisions, intravenous (IV) All catheters could be routes. Cellulitis caused by *S. aureus* develops from a centrally located infection starts there and expands.

This disease may have as its focal point an abscess, folliculitis, or an infected foreign body, such as a splinter, prosthetic device, or IV tube. *S. pyogenes*-caused cellulitis has a distinctive pattern. It diffusely expands quickly and is frequently accompanied by fever and lymphangitis.

When chronic venous stasis or saphenous vein harvesting for coronary artery bypass operations are present, recurrent streptococcal cellulitis of the lower extremities frequently results from organisms from groups A, C, or G.

The most frequent pathogens in bacterial infections among drug users are streptococcal and staphylococcal species and infections that involve an unusual organism are frequently connected to a particular substance or method of drug use. Cellulitis is caused by numerous other microorganisms.

Young children's facial cellulitis caused by *Haemophilus influenzae* used to be a common illness, but the type B vaccine has made these infections uncommon. The pathogen in cellulitis caused by animal attacks, primarily cat bites, is *Pasteurella multocida*.

Clinical presentation:

The characteristics of cellulitis include rubor (redness), dolor (pain), tumour (swelling), and calor (heat). The range of severity varies from isolated erythema in a healthy system to patient to the fulminate sepsis and quickly spreading erythema seen in cases of necrotizing fasciitis.

Pain that is excessive compared to the clinical signs, especially if they are coupled with a history of rapid development should lead one to think about a necrotizing fasciitis. Groin discomfort and other systemic symptoms are frequent and may appear before skin changes. Skin abrasions, In cases of serious cellulitis, bullae or patches of necrotic tissue may be visible.

Risk elements: In case control studies, skin breaks, lymphedema, venous insufficiency, tinea pedis and obesity have all been linked to an increased chance of lower limb cellulitis.

Cellulitis mimics:

According to independent research, 30% of cellulitis patients receive the incorrect diagnosis. Frequently seen Eczema, lymphedema, and other conditions were also suspected. lipodermatosclerosis. 85% of people with incorrect diagnoses did not necessitate hospitalization, and 92% of needless care antibiotics.

Although the Eron classification of cellulitis is recommended by the UK Clinical Resource Efficiency Support Team (CREST) guidelines and the British Society for Antimicrobial Chemotherapy (BSAC) expert panel recommendations for use in grading cellulitis severity, the absence of a precise definition of systemic septicemia and ambiguous and potentially overlapping categories have limited its use in clinical practise.

In order to categorise patients into separate groups according to the presence or absence of specific systemic features of sepsis, the presence or absence of significant comorbidities, and their Standardised Early Warning Score, Marwick et al. modified the Eron classification (also known as the Dundee classification) (SEWS).

The SEWS is a standard early warning score that is derived from the patient's routine clinical observations. A threshold score of 4 was chosen to identify the patients who were the most seriously ill (class IV) and for whom a clinical review was required at the study location.

❖ Cellulitis severity classification

Class	Eron classification	Modified Dundee classification
Class 1	Comorbidities either absent or under management and overall	Neither sepsis nor comorbidities and SEWS<4
Class 2	Systemically ill without unmanaged comorbidities (such as obesity, peripheral artery disease, or venous insufficiency) or systemically well with badly managed	No sepsis, SEWS 4, and documentation of one or more serious conditions (such as obesity, peripheral vascular disease, or venous insufficiency).

	comorbidities, which may cause a delay in their recovery	
Class 3	marked systemic inflammatory response (alteration in mental status, tachypnea, tachycardia, hypotension, etc.) or may have extremely poorly controlled comorbidities that may affect their response to therapy or suffer from a limb-threatening illness as a result of vascular damage	SEWS<4 and sepsis
Class 4	Septic shock or potentially fatal manifestations like necrotizing fasciitis necessitating immediate critical care and surgery intervention	Sepsis and SEWS more than or equal to 4

Treatment:

The preferred treatment for cellulitis is a beta-lactam antibiotic with action against *S. aureus* that produces penicillinase because staphylococcal and streptococcal species account for the majority of cases. nafcillin, an antibiotic of the first generation, and cefazolin, third-generation ceftriaxone and synthesised penicillin against staphylococci.

All of the initial treatment choices include cephalosporin. If *S. aureus* is immune to methicillin, Vancomycin should be used if (MRSA) is detected or if the patient has a severe penicillin allergy, linezolid are the preferred medications, and both have comparable cure rates

	No penicillin allergy	Non severe penicillin allergy	Severe penicillin allergy
Initial PO therapy	Flucloxacillin 500 mg-1 g qds PO	As for severe penicillin allergy, or cephalexin 500 mg qds, PO	Clarithromycin 500 mg bd PO or Doxycycline 100 mg bd PO

Initial therapy	IV	Flucloxacillin 1–2 g, 6-hourly IV	Ceftriaxone 1-2 g, OD	Clindamycin 600 mg–1.2 g IV qds, IV or IV vancomycin
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Novel Approaches:

There are several novel approaches are developed nowadays like

1. Liposome:

Liposomes are concentric bi-layered vesicles in which the aqueous volume is completely surrounded by a membranous lipid bi-layer made primarily of phospholipids, either natural or manufactured. The solvents are enclosed inside the liposomes, which are spherical particles and are free to drift.

Main benefits: 1. is their excellent biocompatibility. 2. How simple it is to prepare. 3. The ability to load hydrophilic, amphiphilic, and lipophilic compounds due to chemical flexibility.

2. Ethosomes:

Phospholipids and ethanol in large concentrations are combined to form ethanosomes. This carrier's ability to thoroughly penetrate the skin will enhance drug delivery to the deeper layers of the skin and blood circulation. For the convenience of the patient, these formulations are helpful for topical delivery of alkaloids in the shape of gel and cream. By fluidizing the lipid domain of the skin, they demonstrate a rise in their permeability through the skin.

Advantages 1. Drug transdermal permeation through epidermis is improved by ethosomes. 2. Ethosomes serve as a vehicle for the delivery of numerous different types of drugs in significant quantities. 3. The semisolid state in which ethosomal drug is administered improves patient compliance.

3. Hydrogels

Three-dimensional, hydrophilic polymeric networks called hydrogels are able to absorb huge volumes of water or biological fluids. They serve as carriers in swellable and swelling-controlled release devices or are used to control medication release in reservoir-based controlled release systems.

4. Transferosomes

It is a complicated fat bilayer encasing an aqueous centre in a deformable vesicle. The makeup of the area and the bilayer's shape both affect the vesicle. self-control as well as self-improvement. This enables the client to successfully pass through various transmission barriers and subsequently serve as a non-intrusive target drug

transport agent. The delivery of medicinal substances and their ongoing discharge These components self-optimize. The ultra-flexible membrane can feed a drug consistently into or through it.

Transferosomes advantages:

1. One benefit of transferosomes is that they can create modest constriction (5–10 times smaller). Observable loss is limited to their own diameter.
2. They have a high capture efficiency of about 90% for lipophilic drugs.
3. The intact vesicles penetrate farther due to this high deformity.
4. Low- and high-molecular-weight medications, such as analgesics, can be supplied by them.

Prophylaxis:

An estimated 8-20% of patients with a history of cellulitis, especially in the lower extremities, will experience it again. Recurrent cellulitis patients should have any underlying conditions like dermatitis, tinea pedis, lymph oedema, or lower leg oedema thoroughly examined and treated if necessary.

So long as the predisposing factors continue to exist, patients who experience three to four cases of cellulitis per year despite addressing the predisposing factors may be candidates for prophylactic antimicrobial treatment.

A reduced incidence of recurrence was observed in the treatment group in a randomised controlled trial of phenoxymethylpenicillin prophylaxis in individuals with a history of recurrent cellulitis.

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