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PROTOCOL

Protocol No.	500
Subject	Skin and soft tissue infections
Effective Date	07-12-2021

GENERAL INTRODUCTION

The permanent dermal filler procedure devised and perfected by Dr. Loria through the years is a safe medical dermal filler procedure performed under the strictest guidelines to prevent any possible complications that inherently associated with all medically invasive procedures, regardless of the scope of intervention.

Although we may perform the procedure under rigorous guidelines and safety measures, the appearance of bacterial infection in an unavoidable truth that could occur at any moment, and it is our goal to first and foremost, reduce such risk to its minimal expression.

Local or regional microbial colonization of the teguments could be magnified or facilitated by a series of conditions and comorbidities, in addition to the beneficial or non-beneficial role that the patient himself plays in this post-procedure care protocol.

Infections could be classified by several factors as complicated and non-complicated as well, suppurative or non-suppurative, acute or chronic, among other things, and all these accounted factors will determine the approach, treatment, and essential follow up.

Initial treatment based predominantly in the clinical evaluation will be empirical, providing coverage to the most common microbial actors involved from the *Staphylococcus* and *Streptococcus* families. More specialized culture tests for example are reserved to chronic or difficult to treat infections that do not respond favorably enough to the empirical based on evidence therapy.

As a coadjutant therapy we cannot overlook the role that incision and drainage treatment or debridement procedures play as well. And it would be an understatement to mention the importance of treatment in immunocompromised patients. Methicillin-resistant bacteria are always a possibility that should be considered.

Most common symptoms are erythema, pain and/or sensibility or increase in the temperature. Systemic signs and symptoms such as fever or chills suggest a systemic dissemination, hemodynamic instability and such is extremely rare but should be treated in a hospital setting.

The strategy of antibiotic treatment must be oriented not only to prevent an acute infection after the procedure but also to prevent the formation of biofilm which is the most difficult to treat once it is installed.

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Treatment of biofilm infection requires sensitive and well-penetrating antibiotics to ensure a well enough effective concentration of antibiotic at the site of biofilm infection.

CLASSIFICATION

There is a classification that could be used according to the American Academy of Family Physicians, dividing the infection by severity in 4 distinctive classes.

- Class 1 - Simple infection with no systemic signs or symptoms indicating spread and no uncontrolled comorbidities that may complicate treatment, amenable to outpatient management with topical or oral antimicrobials.
- Class 2 - Infection with systemic signs or symptoms indicating spread or with stable comorbidities, or infection without systemic spread but with uncontrolled comorbidities; may require inpatient management or parenteral antibiotics.
- Class 3 - Infection with signs or symptoms of systemic spread or uncontrolled comorbidities; inpatient management with parenteral antibiotics required.
- Class 4 - Infection with signs of potentially fatal systemic sepsis requiring parenteral antibiotics; inpatient management (possibly in critical care unit) required, surgery may be indicated.

Suffice to say, the objective of the suspected bacterial infection protocol will be to treat Classes 1 & 2 as part of an outpatient effort. Classes 3 & 4 of infection severity should be treated in an adequate facility with a hospitalized patient. We have never seen a patient with any of these later classifications and you should not have the need either if treated promptly.

Simple infections would be considered all those that produce manifestations in the superficial tissues and complicated infections will be all those with possible loss of tissue due to necrosis, or that could affect the fascia of the penile shaft.

RISK FACTORS

Risk factors regarding infections will be similar to those of the general population (age, diabetes, obesity, tobacco use, etc.) with the addition of protocol non-compliance. Unfortunately, patients that incur in unprotected sexual intercourse (a predominant factor) while still in the healing process between the 35 days or without the use of a generous amount on an oil-based lubricant (to prevent dragging between the newly enhanced surfaces) and a prophylactic barrier (preventing micro-tears in the skin) up until day 90 are more propense to develop some bacterial infections, especially when the penetration involves the anal canal.

Late bacterial infections (post day 90) are rare in occurrence, although the risk factors will remain the same by all account.

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MICROBIOLOGY

As previously stated, most infections are caused by *Gram-positive cocci*, specifically *Staphylococcus aureus* and *streptococci*. *Streptococci* can be classified into several groups; group A particularly associated with necrotizing fasciitis, and group B often the causing agents of infections in diabetic patients. Methicillin-resistant *Staphylococcus aureus* (MRSA) could account for up to 59% of all infections.

The most common bacterial agents involved are...

- *Staphylococcus aureus,*
- *Streptococcus,*
- *Pepto-streptococcus*
- *Pseudomonas aeruginosa*
- *Beta-hemolytic streptococci*

PATHOGENESIS

Most infections occur by direct exposure to a microbial agent or by adjacency to an infectious site, with a breach in the continuity of the skin as the predisposing factor for entry that could be exacerbated by low tissue oxygenation or immunocompromise. Diabetes and other systemic conditions exacerbate the risks, although lymphatic and hematogenous dissemination is rare.

CLINICAL PRESENTATION

Early signs of infection should be recognized as soon as possible, and the intervention should be instated early as well. Early signs of infection include but are not limited as previously mentioned to...

- Erythema,
- Warmth,
- Edema,
- Pain

Deeper suspected infections could present as well...

- Induration
- Erysipelas and
- Cellulitis

Changes in coloration, cutaneous anesthesia, hemorrhage, abundant pus discharge or pain that does not correlate to the apparent severity of the infection are all warning signs suggestive of a necrotizing fasciitis, which requires aggressive antibiotic treatment and debridement.

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DIAGNOSIS

Will be and should be entirely clinical in nature, All and every paraclinical test that could be performed will be secondary to the best clinical judgement.

Blood or wound discharge cultures are not and should not be a pre-requisite to prescribe an appropriate empirical therapeutic regime, although these cultures and antibiogram could be used to later modify the treatment if needed. MRSA suspected infections that have had poor response to the empirical treatment could benefit from these cultures.

Imaging studies render no practical use in the diagnosis or treatment of these infections.

MANAGEMENT OF SUSPECTED BACTERIAL INFECTIONS

The treatment of suspected bacterial infections as you already know will greatly vary depending on a series of factors, including the severity, comorbidities, location, and extension of the infection. Needle drainage and debridement should always be considered when possible.

Most if not all mild superficial and localized infections in immunocompetent patients resolve completely with this measure alone, we do recommend prescription of oral or topical antibiotics as well.

- **Main Wrap Modifications**

  Due to the high importance of the wrap for shaping purposes, particularly on the early stages of the healing process, maintain the integrity of the wrap should be primordial. However, if the skin starts to develop a skin sore or cut with evident signs of infection, patients may need to transition into the simple retainer wrap sooner than the 35 expected days primarily to monitor the evolution of the affected area. This decision should not be taken lightly.

  Infections during this first 35 days post-procedure are rare since the patient should be taking the prescribed therapy. Anytime past day 35 the protocol should not vary as much, after this set day 35, patients are instructed to transition into the simple retainer wrap, a simplification (as the name implies) of the main wrap with only some sports pre-wrap or white gauze for comfort. Constant reevaluation and monitoring should take place, even on a daily basis.

  Primary infections, infections occurring during the first procedure and/or infections that occur during the first 35 days post-procedure, represent a challenge, infections occurring during a subsequent procedure make the transition more feasible. When and if the decision to transition into the simple retainer wrap must be made, we could stablish certain parameters dividing the whole healing period in thirds...

  - The first third, day 1 – day 11... You should avoid transitioning into the simple retainer wrap due to the proximity to the procedure day.

- The second third, day 12 – day 24... Transitioning into the simple retainer wrap should be done with caution and the patient should know that some minimal filler migration could occur.
- The last third, day 25 forward... You could transition into the simple retainer wrap with relative confidence.

It is important to notice that non-stick padding could be added to the wrap protocol in either stage, the main wrap or the simple retainer wrap stage, to cover any skin sore or ulcer that could have developed an infection, preventing the clothes from sticking to the tissues hampering the healing process or the cicatrization efforts.

Rewraps once transitioned into the simple retainer wrap, and within the first 90 days post procedure, will be done on a daily basis.

- **Physical Measures**

Among the wrap modifications and the pharmacological approach there are other physical measures that we could perform. This measure could not be practical with all patients though considering patients that might not be local to the medical office or have a limited availability schedule.

A physical treatment method that patients can apply at home is the use of hot Epsom salt baths, initially every other day or daily depending on the severity, for 45 minutes at a time. Magnesium chloride among other component dissolved in this solution will improve the local skin condition and has proven to be a good anti-inflammatory. While during the immersion hot Epsom salt baths drainage of the affected area is facilitated.

Needle drainages (incision and drainage) also fall into this category. The main advantage of the needle drainage is the possibility that patient could also perform the procedure at home if the visit to the medical office is not feasible. A protocol following simple step by step instructions could be followed by the vast majority of the patients.

Debridement in necrotizing infections should be initially performed at least once a week, twice a week if the patient is local, until you can see steady healing evolution. The act of debridement will limit the extension of the ulcer and promote early granulation. Non-necrotic infections will not benefit as much of this measure.

Facilitating the drainage of accumulated secretions not only speeds up the healing process reducing the bacterial load but also reduces the pressure from collected material under the tissues, becoming a pain management strategy as well.

Frequency of debridement procedures and needle drainage will depend on the clinical evolution of the infection. The need for multiple drainage procedures of this nature is infrequent though.

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- **Wound Dressings**

  Are not necessary for the management of simple and most complicated infections. The choosing of such dressings will vary depending on your own experience and best clinical judgement.

- **Topical Treatment**

  In close relation to the physical measures' topic, we could consider the local application of topical medication. There are several possible therapeutic combinations. The first line of treatment starting with the topical triple antibiotic, applied twice a day over the affected area. Application could start as early as the first local signs of infection are noticed, mostly when there is a necrotizing infection of any severity or extension.

  Triple antibiotic (bacitracin, polymyxin, and neomycin) should always cover and moisten open wounds and could be used in combination with Mupirocin 2% (75%-25% combination) for the same purpose.

  Maintaining wounds covered and moist with either topical agent or the combination promotes an optimal healing process preventing aberrant scarring.

  Pain management of the local infection site could also be facilitated with the addition of EMLA (lidocaine-prilocaine 2.5%-2.5%) cream to the aforementioned topical antibiotic agents.

  Nitro-Bid 2% application in the adjacent areas (not on the infected area itself) is indicated to increase blood flow and speed up the healing process. Topical steroids such as Betamethasone dipropionate is contraindicated as it could delay the healing process.

- **Oral Antibiotic Therapy**

  - **PRE-PROCEDURE TREATMENT**
  - **PATIENT ORAL AND IM TREATMENT IN OR:**

    Several combinations of antibiotics are provided as well considering documented allergic reactions. **Amoxicillin/Clavulanate (Augmentin)** 875/125 mg 2 tablets PO single dose.

    In addition, a single dose each of **Amikacin** 500mg IM and **Ceftriaxone** 1gr IM is also provided the same day of the procedure.

    Antibiotics that we are using have an excellent coverage for Gram (-), Gram (+) and anaerobic. Augmentin or Clindamycin + Ceftriaxone among the recommended oral antibiotics prescribed we can consider:

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- **Amoxicillin/clavulanate**

    - Gram-Positive Aerobes: *Staphylococcus aureus* (β-lactamase and non–β-lactamase–producing), *Staphylococci* which are resistant to methicillin/oxacillin must be considered resistant to amoxicillin/clavulanic acid. *Enterococcus faecalis, Staphylococcus epidermidis* (β-lactamase and non–β-lactamase–producing) *Staphylococcus saprophyticus* (β-lactamase and non–β-lactamase–producing) *Streptococcus pneumoniae, Streptococcus pyogenes, viridians* group *Streptococcus*.
    - Gram-Negative Aerobes: *Enterobacter* species, *Escherichia coli* (β-lactamase and non–β-lactamase–producing), *Haemophilus influenzae* (β-lactamase and non–β-lactamase–producing), *Klebsiella species, Moraxella catarrhalis* (β-lactamase and non–β-lactamase–producing). *Eikenella corrodens* (β-lactamase and non–β-lactamase–producing) *Neisseria gonorrhoeae*, (β-lactamase and non–β-lactamase–producing) *Proteus mirabilis*, (β-lactamase and non–β-lactamase–producing)
    - Anaerobic Bacteria: *Bacteroides* species, including *Bacteroides fragilis* (β-lactamase and non–β-lactamase–producing) *Fusobacterium species* (β-lactamase and non–β-lactamase–producing), *Pepto-streptococcus species*.
    - Common adverse effects: diarrhea, nausea, vomiting
    - Rare adverse effects: agranulocytosis, hepatorenal dysfunction, hypersensitivity reactions, pseudomembranous enterocolitis.

- **Ceftriaxone**

    - Aerobic gram-negative: *Acinetobacter calcoaceticus, Enterobacter aerogenes, Enterobacter cloacae, Escherichia coli, Haemophilus influenzae* (including ampicillin-resistant and beta-lactamase producing strains), *Haemophilus parainfluenzae, Klebsiella oxytoca, Klebsiella pneumoniae, Moraxella catarrhalis* (including beta-lactamase producing strains), *Morganella morganii, Neisseria gonorrhoeae* (including penicillinase- and non-penicillinase-producing strains), *Neisseria meningitidis, Proteus mirabilis, Proteus vulgaris, Serratia marcescens*. Ceftriaxone is also active against many strains of *Pseudomonas aeruginosa*.
    - Aerobic gram-positive: *Staphylococcus aureus* (including penicillinase-producing strains), *Staphylococcus epidermidis*, *Streptococcus pneumoniae, Streptococcus pyogenes, Viridans group streptococci*.
        - NOTE: *Methicillin-resistant staphylococci* are resistant to cephalosporins, including ceftriaxone. Most strains of Group D

streptococci and *enterococci*, e.g., *Enterococcus (Streptococcus) faecalis*, are resistant.
- Anaerobic microorganisms: *Bacteroides fragilis, Clostridium species, Pepto-streptococcus species*.
  - NOTE: Most strains of *Clostridium difficile* are resistant.

- **Amikacin**

  - Gram-Positive Bacteria: *Staphylococcus* species
  - Gram-Negative Bacteria: *Pseudomonas* species, *Escherichia coli, Proteus species* (indole-positive and indole-negative), *Klebsiella species, Enterobacter species, Serratia species, Acinetobacter species*.

- **POST-PROCEDURE TREATMENT**
- MEDICAL PRESCRIPTION TO TAKE AT HOME (STARTING ON DAY #1):

- **Amoxicillin/Potassium (Augmentin)** 875/125 mg Oral Tablet 1 Tablet by mouth every 12 hours for 10 days.
- **Clindamycin** 300 mg Capsule Take 1 capsules (300 mg) by mouth 2 times a day for 5 days, take a break and then resume for 5 additional days on day 11, and day 35.
  - With this combination we cover Gram (-), Gram (+). Anaerobic and MRSA.

- **Amoxicillin/Potassium (Augmentin)**

  - Gram-Positive Aerobes: *Staphylococcus aureus* (β-lactamase and non–β-lactamase – producing), *Staphylococci* which are resistant to methicillin/oxacillin must be considered resistant to amoxicillin/clavulanic acid. *Enterococcus faecalis, Staphylococcus epidermidis* (β-lactamase and non–β-lactamase–producing) *Staphylococcus saprophyticus* (β-lactamase and non–β-lactamase–producing) *Streptococcus pneumoniae, Streptococcus pyogenes, viridians* group *Streptococcus*.
  - Gram-Negative Aerobes: *Enterobacter* species, *Escherichia coli* (β-lactamase and non–β-lactamase–producing), *Haemophilus influenzae* (β-lactamase and non–β-lactamase–producing), *Klebsiella species, Moraxella catarrhalis* (β-lactamase and non–β-lactamase–producing). *Eikenella corrodens* (β-lactamase and non–β-lactamase–producing) *Neisseria gonorrhoeae*, (β-lactamase and non–β-lactamase–producing) *Proteus mirabilis*, (β-lactamase and non–β-lactamase–producing)

- Anaerobic Bacteria: *Bacteroides species*, including *Bacteroides fragilis* (β-lactamase and non–β-lactamase–producing) *Fusobacterium species* (β-lactamase and non–β-lactamase–producing), *Pepto-streptococcus species*.
- Alternatives for Penicillin Allergic Patients:
  - **Cephalexin (Keflex)** 500 mg oral capsule, 1 capsule by mouth 2 times per day for 10 days. (Understanding that the patient has already tolerated this. Cross-reactions with penicillin's are rare).
  - **Sulfamethoxazole/Trimethoprim (Bactrim)** 400/80 mg oral tablet, 2 tablets by mouth 2 times per day for 10 days, or **Bactrim DS** 800/160 mg oral tablet, 1 tablet by mouth 2 times per day for 10 days.
  - **Ciprofloxacin** 750 mg oral **t**ablet, take 1 tablet by mouth 2 times per day for 10 days.

- **Clindamycin**

  - Gram-positive: *Staphylococcus aureus* (methicillin-susceptible strains), *Streptococcus pneumoniae* (penicillin-susceptible strains), *Streptococcus pyogenes, Streptococcus viridians*.
  - Anaerobic: *Clostridium perfringens, Fusobacterium necrophorum, Fusobacterium nucleatum, Pepto-streptococcus anaerobius, Prevotella melaninogenica, Bacteriodes fragilis* group, *Bacteroides melaninogenicus, Bifidobacterium spp., Clostridium perfringens, Eubacterium spp, Fusobacterium spp, Peptococcus spp, Peptostreptococcus spp, Propionibacterium spp, Veillonella spp*.
  - Up to 50% of methicillin-susceptible *S. aureus* have been reported to be resistant to clindamycin in some areas. More than 90% of methicillin-resistant *S. aureus* (MRSA) are resistant to clindamycin and it should not be used while awaiting susceptibility test results if there is any suspicion of MRSA.

- **<u>Suspected Bacterial Infection</u>**

  Once we have stablished the clinical diagnosis of a suspected bacterial infection there are a couple of key elements to consider when prescribing the treatment.

  - We must choose effective antibiotics against MRSA.
  - MRSA is resistant to all penicillin (including nafcillin and dicloxacillin), ß-lactamase inhibitor combinations (including Augmentin), and all cephalosporins.

Some antibiotics available in oral formulations are treatment options for MRSA:

- First-line therapy: Trimethoprim-Sulfamethoxazole (TMP-SMX). This agent has been shown to be 95% effective.
- Second-line therapy: Clindamycin. Keep in mind that the organism may develop resistance to this drug, particularly if it is resistant to erythromycin. Also remember that patients exposed to clindamycin are at risk for infection with *Clostridium difficile*.
- Third-line therapy: tetracycline or doxycycline/minocycline. This agent is administered for 21 days.
- Fourth-line therapy: linezolid.
- Rifampin (Rifadin) may also be used. It is typically effective in combination with other drugs. Because rifampin achieves high concentrations in mucosal surfaces, its inclusion in a regimen to treat MRSA is theoretically beneficial.

- **Drugs to be avoided in suspected MRSA**

  Erythromycin and Cephalexin are ineffective against MRSA, and ciprofloxacin and levofloxacin are to be avoided because rates of MRSA infection are increased in hospitalized patients treated with quinolones. Bacitracin and neomycin, two common ingredients in OTC antibacterial ointments, are not recommended for the treatment of MRSA, although a recent study indicates that they may be effective against a specific clone of MRSA.

FINAL THOUGHTS

Immunocompromised patients are understandably more prone to infections than other patients. In patients allergic to penicillin, a combination of trimethoprim/sulfamethoxazole or a quinolone with clindamycin can be used.

Simple infections that result from exposure to fresh water are treated empirically with a quinolone, whereas doxycycline is used for those that occur after exposure to salt water.

Constant communication and evaluation of the patient is key to readjust the treatment and to ease all the patients concerns. It is important that patients understand we cannot control how their body will/could react to the filler formula, and such flare ups or inflammatory episodes escape our control.

Remission of the symptoms could last for a period of several months or even years, however, treatment will remain pretty much the same. Well educated patients will be able to spot these episodes, and this facilitates a prompt response and treatment.