



# **Is it Infected? How do I know?**

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## Is it infected? How do I really know?

Objectives: At the conclusion of this program, the participant will be able to:

- Identify common characteristics of contaminated and infected wounds.
- Recognize when interventions are required to decrease bacteria levels in wounds.

### I. Bacteria

- A. In utero, the skin is sterile, but after birth environmental microbes rapidly start to colonize the stratum corneum eventually developing into a complex microbial ecosystem that is in homeostasis with its host.<sup>46</sup>
  1. It is estimated that over 100 distinct species making up a total of 1 million microorganisms colonize each square centimeter of our skin.<sup>1,44</sup>
  2. This flora is also referred to as the skin microbiome.<sup>45</sup>
  3. These microorganisms vary between individuals and between different sites on the skin.
  4. Most are found in the superficial layers of the epidermis and the upper parts of hair follicles.
- B. When skin integrity is breached, the wound quickly becomes contaminated with bacteria.<sup>2</sup>
  1. Healthy persons have immunity against their own bacteria, but if someone becomes immunocompromised, or if there are large amounts of bacteria or virulent bacteria present, infection can occur.<sup>47</sup>
  2. All chronic wounds have bacteria residing in them, determining how much and how severe is an important factor for healing and for some it can mean the difference between life and death.
  3. Bio-burden – presence of micro-organisms on or in a wound.

### II. Effects of Bacteria in Wounds

- A. Delayed Healing
  1. Infection at the wound site will ensure that the healing process remains in the inflammatory phase. Pathogenic microbes in the wound compete with macrophages and fibroblasts for limited resources and may cause further necrosis in the wound bed.
- B. An increased bacterial burden in a wound can also affect tissue oxygen availability.<sup>3</sup>
  1. Leukocytes are needed in the wound bed to kill phagocytic bacteria-by mechanisms that involve the consumption of significant amounts of molecular oxygen.
  2. This increased oxygen consumption by inflammatory cells can act as a sump, "stealing" oxygen required for basic wound metabolism.
- C. Bacteria produce endotoxins and exotoxins that destroy or alter normal cellular activities, such as collagen deposition and cross-linking.<sup>60</sup>
  1. Wound endotoxins and other inflammatory mediators may be associated with pain.<sup>62</sup>
- D. Biofilms
  1. In vulnerable tissue, biofilms are created by planktonic bacteria attaching and forming a protective community before they are killed by the patient's immune system, antibiotics, or by debridement.<sup>53</sup>
  2. Bacterial biofilms are sessile colonies of single bacterial or fungal species, or more commonly, polymicrobial organisms (bacterial, fungal, and possibly, viral) which are often symbiotic.<sup>5,6,53</sup> These biofilm colonies produce a protective coating to protect the colonies from host defenses.<sup>4,53</sup>
  3. Biofilms have high levels of tolerance to antibodies, antibiotics, disinfectants, and phagocytic inflammatory cells.<sup>4</sup>

4. 60%-70% of chronic wounds have a biofilm present, while only 6% of acute wounds have documented biofilm. <sup>7,8,49</sup>
  5. Biofilms can impair healing in chronic wounds. <sup>4,9,10</sup>
    - a. The presence of a biofilm stimulates a low-grade and persistent inflammatory response from the body in an attempt to remove the biofilm from the wound which impairs both epithelialization and granulation tissue formation. <sup>52</sup>
    - b. This inflammatory response results in high levels of proteases (matrix metalloproteinases (MMPs) and elastases. The proteases can help to break down the attachments between biofilms and the tissue; however, they also damage normal and healing tissues, proteins, and immune cells thus delaying/stalling wound healing. <sup>4,9,10</sup>
  6. Reproduction is carried out by the biofilm breaking down portions of itself and releasing fragments which contain cells incased in matrix material. <sup>50</sup> These detachment fragments have the ability to attach to a suitable surface, become metabolically active, and reform a biofilm community. <sup>51</sup>
  7. Implications of biofilms for wound management are uncertain because means of diagnosing biofilm infections in wounds are not yet well developed and effective treatment strategies are not established. <sup>4</sup>
    - a. Traditional Lab Data is Designed to find planktonic bacteria (non-attached, free floating)
    - b. DO NOT measure bacteria in biofilms or anaerobic bacteria
    - c. Specialized microscopy is needed—i.e., confocal laser scanning microscope
  8. Bio-film based Wound Care <sup>4,48</sup>
    - a. Goal: Reduce the biofilm bioburden and Prevent reforming of the biofilm
    - b. Physical disruption <sup>4,48</sup>
      - 1) (aggressive/ sharp debridement is generally agreed to be the best method of removing biofilm)
      - 2) Regular debridement to reduce the biofilm potential for regrowth <sup>4,48</sup>
      - 3) Accompanied by vigorous physical cleansing (such as irrigation or ultrasound) <sup>4,48</sup>
    - c. Prevention of biofilm reconstitution
      - 1) Use appropriate wound dressings to prevent further wound contamination <sup>4,48</sup>
      - 2) Use of a topical broad-spectrum antimicrobial (silver, iodine, honey, PHMB) to kill planktonic microorganisms <sup>4,48</sup>
      - 3) Change to a different antimicrobial if there is a lack of progress <sup>4,48</sup>
  9. Ways to Determine Resolution
    - a. It is not possible to categorically state when a wound is biofilm-free, because there is a lack of definitive clinical signs and available laboratory tests. <sup>48</sup>
    - b. The most likely clinical indicator is progression of healing, with reduction in exudate and slough. <sup>48</sup>
- E. Even though it is virtually inevitable that most wounds contain bacteria, many heal successfully. The potential for bacteria to produce harmful effects is influenced by the:
1. Ability of the patient's immune system to combat the bacteria (host resistance) <sup>11,54</sup>
    - a. The most important factor
    - b. Systemic and local factors can decrease host resistance
    - c. Adequate blood supply is needed for the wound to heal as a decreased or inadequate blood supply favors bacterial proliferation and damage that may prevent or delay healing. <sup>54</sup>
    - d. Individuals with diabetes have at least a 10-fold greater risk of being hospitalized for soft tissue and bone infections of the foot than nondiabetic individuals. <sup>54</sup>

- e. Uncontrolled edema, smoking, poor nutrition, excess alcohol intake, drugs that interfere with the immune system, or immunodeficiency diseases may all challenge wound healing.<sup>54</sup>
  - 2. Number of bacteria introduced – higher numbers are more likely to overcome host resistance
  - 3. Type of bacteria introduced:
    - a. Some bacteria have greater disease-producing ability (virulence) than others, and may be able to cause disease in relatively low numbers
    - b. Benign residents in one body site may cause disease if transferred elsewhere.
- III. Continuum of Bacterial Bioburden
- A. The presence of bacteria in a wound may result in:
1. Contamination – the bacteria do not increase in number or cause clinical problems
    - a. Most bacteria enter the wound bed through external contamination from the environment, dressings, the patient’s body fluids, or the hands of the patient or health care provider.<sup>54</sup>
    - b. If the surface organisms attach to the tissue and multiply, colonization is established but a bacterial balance remains.<sup>54</sup>
  2. Colonization – the bacteria multiply, but wound tissues are not damaged
    - a. Some of these colonizers may be involved in a mutually beneficial relationship with the host preventing the adherence of more virulent organisms in the wound bed.<sup>55,56</sup>
    - b. These organisms include *Corynebacterium* species, coagulase-negative staphylococci, and viridans streptococci.<sup>55-57</sup>
  3. Critical Colonization - The presence of replicating (reproducing) microorganisms on the surface of the wound, which are attached to the wound surface but there is no invasion of the tissues by the bacteria.<sup>14,51,54,57,59</sup>
    - a. Amount of bacteria inhibits wound healing but host does not exhibit classic signs of infection.
    - b. Critical Colonization may be suspected if 3 or more of the signs and symptoms of NERDS: Non-healing, Exudate, Red friable tissue, Debris, Smell are present.<sup>14,54,59</sup>
    - c. The treatment of critical colonization often takes 2 to 4 weeks in a healable wound where the cause has been corrected and patient-centered concerns have been addressed.<sup>59</sup>
  4. Infection –is the invasion and multiplication of microorganisms in the wound tissue beneath the wound surface. The bacteria multiply, healing is disrupted and wound tissues are damaged (local infection).<sup>14,51,54,56,57,59</sup>
    - a. The presence of microorganisms in wound necrotic tissue, or slough isn’t evidence of tissue invasion.<sup>57</sup> These nonviable substances are known to support bacterial growth, for an infection to be present, the microorganisms must be present in viable tissue.<sup>57,58</sup>
    - b. Bacteria may produce problems nearby (spreading infection) or cause systemic illness (systemic infection)
    - c. Gold standard diagnosis - Lab results 100,000 organisms/gm of tissue, a.k.a. 10<sup>5</sup> guideline.<sup>12</sup>
    - d. With more than one species of bacteria in a wound, an infection can develop with fewer organisms, due to interaction between the organisms.<sup>13</sup>
    - e. Greater than 90% of chronic wounds have polymicrobial flora containing up to four species.<sup>14</sup>
    - f. In addition, some bacteria, such as beta-hemolytic streptococci, are injurious at levels far below 10<sup>5</sup>.<sup>15,16</sup>

- g. Infection may produce different signs and symptoms in wounds of different types and etiologies. <sup>9,11,15,17</sup>
    - h. Kravitz proposes a new definition of infection, “the presence of bacteria in any quantity sufficient to prevent the wound from healing,”<sup>18</sup>
  - B. Wound infection occurs in wound tissue, not on the surface of the wound bed. Wound infection occurs in viable wound tissue; it isn’t a phenomenon of necrotic tissue, eschar, or other debris contained in the wound bed.
- IV. Signs and Symptoms of Bacteria in Wounds
  - A. Classic symptoms
    - 1. Erythema
      - a. Inflammation <sup>63</sup>
        - 1) Usually presents with well-defined borders.
        - 2) Not as intense in color.
        - 3) May be seen as skin discoloration in dark-skinned persons, such as a purple or gray hue to the skin or a deepening of normal ethnic color.
      - b. Infection<sup>63</sup>
        - 1) Edges of erythema or skin discoloration may be diffuse and indistinct.
        - 2) May present as very intense erythema or discoloration with well demarcated and distinct borders.
        - 3) Red stripes or streaking up or down from the area indicates infection
    - 2. Pain
      - a. Inflammation
        - 1) Variable
        - 2) In acute stages, may be very tender and painful
      - b. Infection
        - 1) Pain is persistent and continues for unusual amount of time.
        - 2) Pain level increases
        - 3) Pain in neuropathic extremity
        - 4) Increasing pain and wound breakdown
    - 3. Heat
      - a. Inflammation
        - 1) Usually noted as palpable increase in temperature at wound site and surrounding tissues.
      - b. Infection
        - 1) Systemic fever may be present
        - 2) Evidence shows a 3°F (1.7°C) temperature difference between the wound margin and mirror image skin was 8 times more likely to be associated with deep and surrounding infection.<sup>62</sup> In a study of leg ulcers, temperature was able to identify deep and surrounding infection in 19 of 22 subjects when used as a sole criterion.<sup>61</sup>
    - 4. Swelling/Edema around the wound
      - a. Inflammation
        - 1) May be slight swelling, firmness at wound edge.
      - b. Infection
        - 1) Edema and induration with warmth
    - 5. Increased or purulent drainage
      - a. Result of bacterial exotoxins recruiting white blood cells to the wound.
      - b. Exudate may be serous, seropurulent or purulent.
    - 6. Odor from the wound

- a. Odor may be present due to necrotic tissue, liquefaction of necrotic tissue, or wound product not necessarily infection<sup>63</sup>
  - b. Odors that point to infection may be sweet, pungent, foul, strong, fecal or musty.<sup>64</sup>
    - 1) Pseudomonas – sweet odor
    - 2) Proteus – ammonia odor
- B. Delayed healing - Healing progresses at a slower rate than expected. As a guide:
  - 1. In open surgical wounds healing mainly by epithelialization, the epithelial margin advances at about 5mm per week.<sup>17</sup>
  - 2. Clean pressure ulcers with adequate blood supply and innervation should show signs of healing within two to four weeks.<sup>25</sup>
  - 3. A reduction in venous leg ulcer surface area of >30% during the first two weeks of treatment is predictive of healing.<sup>26</sup>
  - 4. If has not healed 50% in first 4 weeks of treatment there is only a 9% chance it will go on to healing in 3 months.<sup>27</sup>
  - 5. Lack of healing after 2 weeks of Topical Therapy
- C. Discoloration of the tissues in the wound, change in color of the wound bed
- D. Friable granulation tissue – crumbly, bleeds easily
  - 1. Due to bacterial stimulation of vascular endothelial growth factor, an excess of blood vessels forms over collagen, resulting in red friable bleeding tissue upon dressing removal.<sup>62</sup>
- E. Absent or abnormal granulation tissue
- F. Systemic Infection
  - 1. Elevated white blood cell count
  - 2. Elevated body temperature
  - 3. Chills
  - 4. Confusion or agitation in older adults
  - 5. Red streaks from wound
- G. Exceptions to the Classic Signs
  - 1. Diabetes
    - a. Signs of infection in diabetic foot ulcers are likely to be “masked” as people with diabetes may not show typical inflammatory response to infection (pain, erythema, swelling, and leucocytosis).<sup>30</sup>
    - b. Diabetic patient with an infected foot ulcer and peripheral neuropathy, pain may not be a prominent feature.<sup>9</sup>
    - c. Clinicians should also be aware that in the diabetic foot, inflammation is not necessarily indicative of infection. For example, inflammation may be associated with Charcot’s arthropathy.<sup>9</sup>
    - d. At least 50% of diabetic patients ‘with a limb-threatening infection do not manifest systemic signs or symptoms.<sup>31</sup>
  - 2. The classic local signs of infection may be muted or absent when the inflammatory response is impaired:<sup>32</sup>
    - a. Malnutrition
    - b. Steroid therapy
    - c. Immunosuppression
    - d. Wound Chronicity
  - 3. Burns and skin graft rejection; pain is not always a feature of infection in full thickness burns.<sup>11</sup>

4. In Chronic Wounds; new, increased, or altered pain or delayed (or stalled) healing are individually highly indicative of infection.<sup>11,15</sup>

#### V. Clinical Indications of Wound Infection

- A. In practice, wound infection is identified and diagnosed based on clinical signs and symptoms of infection or on the findings from wound cultures. Diagnosing infection in a chronic wound is a difficult clinical task with poor consensus even among experts in the field as the lack of clear guidelines regarding the number of signs and symptoms that need to be present to constitute infection.<sup>56</sup>
- B. Clinicians may find the mnemonics, or enablers, NERDS\* and STONES\* helpful in making wound infection assessments.<sup>54,59,62</sup>
  1. For superficial infection, think of NERDS:<sup>54,59,62</sup>
    - a. N = Non-healing wound: Wound is not 30% smaller over the last 4 weeks.
    - b. E = Exudative wound
    - c. R = Red and bleeding wound: Friable granulation tissue
    - d. D = Debris: Dead cells on the surface of the wound represented by yellow or brown-tinged slough.
    - e. S = Smell from the wound
  2. STONES define clinical signs of deep and surrounding wound infection.<sup>54,59,62</sup>
    - a. S = Size Bigger: Expanding wounds invades the sides of the wound or develops a deeper base through destruction of the wound base or both.
    - b. T = Temperature Increased
    - c. O = Os: Latin word for "bone." Exposed or probing to bone has been documented in previous studies to be a reliable and valid clinical test for osteomyelitis.<sup>65,66</sup>
    - d. N = New breakdown: As wounds deteriorate, they expand laterally. Often, small islands of tissue break down in the wound margins, and then they join up to become confluent with the original wound.
    - e. E = Exudate, Edema, & Erythema: Otherwise known as cellulitis.
    - f. S = Smell: Usually indicates the invasion of gram-negative and anaerobic organisms after the wound has been primarily compromised with the more virulent gram-positive organisms.
    - g. If 3 or more STONES criteria are present, treatment with a systemic agent should be initiated.<sup>62</sup>
- C. Wound Specific Symptoms that indicate infection<sup>35</sup>
  1. Pressure Ulcer - crepitus
  2. Neuropathic/diabetic ulcers – phlegmon(spreading diffuse inflammatory process with formation of suppurative/purulent exudate or pus)
  3. Venous Ulcers - increase in local skin temperature
  4. Arterial Disease - dry necrosis, which may turn moist and boggy at the edges of the necrotic tissue
- D. Cellulitis
  1. Cellulitis is defined as a spreading bacterial infection of the skin and underlying soft tissue.
  2. Cellulitis involves the deep dermis, extending into the subcutaneous tissue and fat.
  3. Infection is most common in the lower extremities.
  4. Cellulitis is typically unilateral
  5. Major findings
    - a. Local erythema of the skin: presents as either red streaking (lymphangitis) or broad areas of redness. It may be difficult to diagnose cellulitis from observation in people with darker skin



- b. Skin is hot, red, and edematous
  - c. Skin surface appearance resembling the skin of an orange (peau d'orange)
  - d. inflammation is diffuse with ill-defined borders
  - e. Petechiae are common; large areas of ecchymosis are rare.
  - f. Vesicles and bullae may develop and rupture, occasionally with necrosis of the involved skin.
6. Cellulitis with rapid spread of infection, rapidly increasing pain, hypotension, delirium, or skin sloughing, particularly with bullae and fevers, suggests life-threatening sepsis.
- E. Erysipelas<sup>72</sup>
- 1. Erysipelas is a bacterial infection affecting the upper dermis and characterized by bright red skin with induration (hardness) and sharply demarked edges.
  - 2. Superficial form of Cellulitis caused by streptococci involving the upper dermis that characteristically extends into the superficial cutaneous lymphatics.
    - a. Most facial infections are attributed to group A streptococci, while an increasing percentage of lower extremity infections are being caused by non-group A streptococci.<sup>73</sup>
  - 3. Predominantly affects the skin of the lower limbs, but when it involves the face it can have a characteristic butterfly distribution on the cheeks and bridge of the nose.
  - 4. Usually abrupt in onset and begins as a small erythematous patch that progresses to a fiery-red, indurated, tense, and shiny plaque.
  - 5. Intensely erythematous, indurated plaque with a sharply demarcated border. Its well-defined margin can help differentiate it from other skin infections.
  - 6. The affected skin is red, firm, swollen and may be finely dimpled (peau d'orange).
  - 7. It may be blistered.
  - 8. Bleeding into the skin may cause purpura
  - 9. Malaise, chills, and high fever, often begin before the onset of the skin lesions and, if present, usually occur within 48 hours of cutaneous involvement. Pruritus, burning, tenderness, and swelling are typical complaints.
- F. Sepsis
- 1. Sepsis is a systemic response to an overwhelming inflammatory process caused by an infection.
    - a. Approximately one in four people who develop sepsis will die directly linked to delayed diagnosis and initiation of treatment.
    - b. In 2012, there were over 1,665,000 patients diagnosed with sepsis in the United States.
    - c. sepsis is the number one cause of death in the ICU and the 11th-leading cause of death in the United States
  - 2. Sepsis or bacteremia is caused by anaerobes and gram-negative bacteria and can occur in any susceptible wound.
    - 1) Assessment for presence of sepsis should include consideration of erythema, warmth, edema, purulent or increased drainage, induration, increased tenderness or pain, and crepitus or fluctuance at wound/incision.
  - 3. Assessment for the presence of sepsis should include suspected or documented infection plus some of the following:<sup>71</sup>
    - a. General variables of sepsis
      - 1) heart rate >90 beats/min
      - 2) temperature >101° F (38.3° C) or <96.8° F (36° C)
      - 3) altered mental status
      - 4) significant edema or positive fluid balance (>20 mL/kg over 24 hours)

- 5) hyperglycemia (plasma glucose >140 mg/dL in the absence of diabetes)
- b. Inflammatory variables
  - 1) white blood cell (WBC) count >12,000/mm<sup>3</sup> or <4,000/mm<sup>3</sup>
  - 2) normal WBC count with >10% immature forms (bands)
  - 3) plasma C-reactive protein more than two standard deviations above the normal value
  - 4) plasma procalcitonin more than two standard deviations above the normal value
- c. Hemodynamic variables
  - 1) systolic BP <90 mm Hg or
  - 2) mean arterial pressure <70 mm Hg or
  - 3) systolic BP decrease >40 mm Hg in adults or less than two standard deviations below normal for age
- d. Organ dysfunction variables
  - 1) arterial hypoxemia (partial pressure of oxygen dissolved in arterial blood [PaO<sub>2</sub>]/fraction of inspired oxygen [FiO<sub>2</sub>] <300)
  - 2) acute oliguria (urine output <0.5 mL/kg/hr for at least 2 hours despite adequate fluid resuscitation)
  - 3) serum creatinine increase >0.5 mg/dL
  - 4) coagulation abnormalities (INR >1.5 or aPTT >60 seconds)
  - 5) ileus (absent bowel sounds)
  - 6) thrombocytopenia (platelet count <100,000/mm<sup>3</sup>)
  - 7) hyperbilirubinemia (plasma total bilirubin >4 mg/dL)
- e. Tissue perfusion variables
  - 1) serum lactate >1 mmol/L
  - 2) decreased capillary refill or mottling

## VI. Diagnosis of Wound Infection

- A. Emphasis is currently being placed on holistic assessment with clinical signs and symptoms playing key roles in diagnosis of chronic wound infection.<sup>11,19</sup>
- B. The diagnosis of wound infection is made mainly on clinical grounds. Assessment should include:<sup>11</sup>
  - 1. Evaluation of the patient
  - 2. The tissues around the wound and the wound itself for the signs and symptoms of wound infection
  - 3. Factors likely to increase the risk and severity of infection.<sup>11</sup>
    - a. Any factor that debilitates the patient, impairs immune resistance or reduces tissue perfusion
      - 1) Comorbidities - diabetes mellitus, immunocompromised status, hypoxia/poor tissue perfusion due to anemia or arterial/cardiac/respiratory disease, renal impairment, malignancy, rheumatoid arthritis, obesity, malnutrition
      - 2) Medication – corticosteroids, cytotoxic agents, immunosuppressants
      - 3) Psychosocial factors – hospitalization/institutionalization, poor personal hygiene, unhealthy lifestyle choices
    - b. Poor standards of wound care related hygiene.
    - c. Acute wounds
      - 1) Contaminated surgery
      - 2) Long operative procedure
      - 3) Trauma with delayed treatment
      - 4) Necrotic tissue or foreign body

- d. Chronic Wounds
    - 1. Necrotic tissue or foreign body
    - 2. Prolonged duration
    - 3. Large in size and/or deep
    - 4. Anatomically situated near a site of potential contamination, e.g. anal area
  - e. Age is considered an important factor, with neonates and the elderly at particular risk of infection.
- C. Initial assessment may indicate the need for microbiological analysis, blood tests or imaging investigations to confirm the diagnosis, detect complications such as osteomyelitis, and guide management.
- 1. It is inappropriate to culture all wounds.<sup>20, 21,22</sup>
  - 2. When to culture:<sup>11,20</sup>
    - a. Acute wounds with signs of infection
    - b. Chronic wounds with signs of spreading or systemic infection
    - c. Infected chronic wounds that have not responded to or are deteriorating despite appropriate antimicrobial treatment.
    - d. As required by local surveillance protocols for drug resistant micro-organisms
    - e. High-risk chronic wounds with signs of localized infection, e.g. delayed (or stalled) healing, in patients who have diabetes mellitus or peripheral arterial disease, or who are taking immunosuppressants or corticosteroids.
  - 3. In patients showing signs of sepsis, blood cultures are important, and cultures of other likely sites of infection should be considered.
  - 4. Sampling techniques include wound swabbing, needle aspiration and wound biopsy.
    - a. Wound biopsy (considered the gold standard) provides the most accurate information about type and quantity of pathogenic bacteria, but is invasive, skill-intensive and unavailable in many settings. Used most often for wounds that are failing to heal despite treatment for infection.<sup>56</sup>
    - b. Swab culture
      - 1) The most common swab techniques are the Levine and Z techniques.
      - 2) The Levine technique detects more organisms in acute wounds, as well as in chronic wounds, than the Z technique.<sup>69</sup>
      - 3) Comparing both with the biopsy as criterion standard, the diagnostic accuracy to diagnose a chronic wound infection by the Levine technique was higher in comparison to the Z technique.<sup>69</sup>
      - 4) Levine's technique provides culture findings most comparable to tissue specimens because this technique attempts to sample microorganisms from within the wound tissue, not just from the wound surface.<sup>56</sup>
    - c. Levine Swab Culture ( Most frequently used method)<sup>11,23</sup>
      - 1) Clean wound (non-antiseptic solution)
      - 2) Rotate swab over a 1cm<sup>2</sup> area with sufficient pressure to express fluid from within wound tissue.
      - 3) Concentrate on areas of the wound of greatest clinical concern.
- D. Molecular diagnostic medicine
- 1. Molecular genetics-based pathogen diagnostics are based upon the identification of unique DNA sequence of each type of microorganism.
    - a. DNA sequencing and quantitative PCR now allow the identification and quantification of both known and previously unknown microbial species.

- b. Antibiotic resistance factors can be identified by their genetic signatures in clinical specimens.
- c. Microbial composition of wounds can be determined in hours as opposed to days using quantitative PCR
- 2. Results of molecular analyses study were also compared to those obtained using traditional culture-based diagnostics.<sup>5</sup>
  - d. Study revealed approximately 60% of the bacterial species present in chronic pressure ulcers and approximately 30% of those found in diabetic ulcers were strict anaerobic bacteria, and in fact many bacterial species were present that had never been reported before in cultures of chronic wounds.<sup>5</sup>
  - e. This data suggests that many of the bacteria present in chronic wound biofilms could never be successfully cultured in a standard clinical microbiology laboratory due to obligate cooperation with other bacteria, creating unique environmental conditions in a polymicrobial community (the biofilm itself).<sup>24</sup>
- 3. Cost of PCR-based testing is often cited as a barrier to these tests. Although the individual tests can be expensive, they are comparable to classical microbiological culture (approximately \$200 vs. \$300) and provide clinicians with far more clinical information. In addition, most insurers are now accustomed to these types of testing technologies and they are also reimbursable by Medicare in most cases.<sup>70</sup>
- 4. PathoGenius - State of the art CLIA and CAP certified Molecular Diagnostic Facility offering molecular pathogen diagnostics for both Chronic Wound Infections and for Ear, Nose, and Throat pathogens. Information: [www.pathogenius.com](http://www.pathogenius.com)

#### VII. Surgical site infection (SSI)

- A. Local signs of pain, swelling, erythema, and purulent drainage provide the most reliable information in diagnosing an SSI.<sup>68</sup>
- B. Surgical site infections rarely occur during the first 48 hours after surgery, and fever during that period usually arises from noninfectious or unknown causes.<sup>67</sup>
  - 1. SSIs that do occur in this time frame are almost always due to *S. pyogenes* or *Clostridium* species.<sup>68</sup>
  - 2. After 48 hours, SSI is a more common source of fever, and careful inspection of the wound is indicated; by 4 days after surgery, a fever is equally likely to be caused by an SSI or by another infection or other unknown sources.<sup>68</sup>
  - 3. In surgical wounds, inflammation occurs after wounding but should subside within 5 days.<sup>56</sup>
- C. There are 3 different types of surgical site infections (SSI) defined by the Centers for Disease Control and Prevention (CDC):
  - 1. Superficial incisional (involving only skin or subcutaneous tissue of the incision).<sup>74</sup>
  - 2. Deep incisional (involving fascia and/or muscular layers).
    - a. Deep incision primary (DIP)—SSI identified in a primary incision in a patient who has had an operation with 1 or more incisions.<sup>74</sup>
    - b. Deep incision secondary (DIS)—SSI identified in a secondary incision in a patient who has had an operation with more than 1 incision.<sup>74</sup>
  - 3. Organ/space (involving any part of the body opened or manipulated during the procedure, excluding skin incision, fascia, or muscle layers).<sup>74</sup>
- D. National Nosocomial Infection Surveillance System (NNIS) is an ongoing collaborative surveillance system sponsored by the Centers for Disease Control (CDC) to obtain national data on nosocomial infections. The CDC uses the data that are reported voluntarily by participating hospitals to estimate the magnitude of the nosocomial infection problem in the United States

and to monitor trends in infections and risk factors. New criteria published in January 2017 for Surgical Site Infection (SSI) Event <https://www.cdc.gov/nhsn/ambulatory-surgery/ssi/>

- E. CDC and Healthcare Infection Control Practices Advisory Committee guideline for the prevention of surgical site infection was updated in 2014. Details can be found at <https://www.cdc.gov/nhsn/ambulatory-surgery/ssi/>

#### VIII. Diabetic Foot Infection

- A. Diabetic foot infections (DFIs) typically begin in a wound, most often a neuropathic ulceration.<sup>35</sup>
- B. Most diabetic foot infections are polymicrobial, with aerobic gram-positive cocci (GPC), and especially staphylococci, the most common causative organisms.<sup>35</sup>
- C. Aerobic gram-negative bacilli are frequently co-pathogens in infections that are chronic or follow antibiotic treatment, and obligate anaerobes may be co-pathogens in ischemic or necrotic wounds.<sup>35</sup>
- D. Infectious Diseases Society of America Clinical Practice Guideline for the Diagnosis and Treatment of Diabetic Foot Infections 2012 <https://academic.oup.com/cid/pdf-lookup/54/12/e132>

#### IX. Osteomyelitis

- A. Infection, inflammatory process of the bone resulting from spread of infection from an adjacent soft tissue focus.
- B. Most common - Staphylococcus aureus, Staphylococcus epidermis and Pseudomonas aeruginosa<sup>36</sup>
- C. Consider Osteomyelitis<sup>35</sup>
  - 1. In deep or extensive ulcers, especially if chronic and over a bony prominence
  - 2. Ulcer does not heal after 6 weeks of appropriate care
  - 3. Ulcer with bone visible or easily palpable
  - 4. Swollen foot in patient with history of foot ulceration, a “sausage toe”
  - 5. Unexplained high WBC or inflammatory markers
  - 6. X-ray evidence of bone destruction beneath ulcer
  - 7. Wound closes and re-opens repeatedly
  - 8. Osteomyelitis has been reported in up to 32% of patients with pressure ulcers.<sup>37</sup>
- D. Diagnosis
  - 1. Perform Erythrocyte sedimentation rate (ESR) and C-reactive protein (CR-P) to assist in confirmation of diagnosis.<sup>31,38</sup>
    - a. Acute osteomyelitis
      - 1) The CBC count usually reveals leukocytosis, and the ESR is moderately or highly elevated.<sup>39</sup>
      - 2) Blood culture results are usually negative. When positive, the findings most frequently indicate the presence of S aureus.<sup>40</sup>
    - b. Chronic osteomyelitis
      - 1) The CBC count is often within the reference range. Usually, the ESR is very highly elevated; it may exceed 100 mm/h.<sup>39</sup>
      - 2) The platelet count is often elevated in chronic osteomyelitis.
      - 3) Blood culture results are usually negative in patients with chronic osteomyelitis.<sup>40</sup>
  - 2. Imaging Studies
    - a. When osteomyelitis is a possibility, obtain plain radiographs.<sup>31</sup>
      - 1) Soft tissue swelling and periosteal elevation are the earliest signs of acute osteomyelitis on a plain radiograph.

- 2) If these radiographs show no evidence of pathological findings in bone, the patient should be treated for 2 weeks for the soft-tissue infection. If suspicion of osteomyelitis persists, perform plain radiography again 2–4 weeks later.<sup>31</sup>
  - b. If findings of radiography are only consistent with, but not characteristic of, osteomyelitis, one of the following choices should be considered:<sup>31</sup>
    - 1) Additional imaging studies. MRI is the preferred imaging study, with nuclear medicine scans.
    - 2) Empirical treatment. Provide antibiotic therapy for another 2–4 weeks and then perform radiograph again to determine whether bony changes have progressed (which would suggest infection).
    - 3) Bone biopsy.
  - c. Bone scan findings are positive within 24 hours in acute osteomyelitis. A bone scan is preferred to gallium or indium scans in the assessment of acute osteomyelitis.<sup>40</sup>
  - d. Radiologic changes may lag behind the clinical presentation of osteomyelitis as long as two weeks.<sup>38,41</sup>
  - e. MRI is the most accurate imaging study for defining bone infection, and it also provides the most reliable image of deep soft-tissue infections. MRI is usually not needed to diagnose osteomyelitis in a patient with observable or palpable bone and plain radiographs suggestive of osteomyelitis in that location.<sup>35</sup>
  - f. When osteomyelitis becomes chronic, plain radiographic findings are invariably abnormal.<sup>40</sup>
  3. Magnetic Resonance Imaging has demonstrated the presence of osteomyelitis with 98% sensitivity and 89% specificity.<sup>42,43</sup> and is the preferred technology for diagnosis.<sup>37</sup>
- X. Summary – Is It Infected?
- A. Diagnosis of infection is a clinical diagnosis
  - B. Lab cultures used to confirm correct antibiotics
  - C. It is important to know the signs and symptoms of bacterial burden in wounds
  - D. Treat locally infected wounds locally and systemic infections both locally and systemically
  - E. Biofilms delay wound healing – recommendation is to physically remove
  - F. Diabetics often lack classic signs of infection and may not show elevated WBCs when infected.

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