

# Training aimed at nurses

## Infection of chronic wounds

### Diagnosis and treatment

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## 1 | Introduction

The infection of chronic wounds is an issue that is increasingly under the spotlight within the medical and scientific community. The era in which antibiotic treatment was given on the basis of inadequate clinical evidence, erroneously backed up by bacteriological samples of no value, has come and gone.

Some microorganisms exploited the situation to mutate and have become resistant to numerous antibiotics, a phenomenon that is extremely worrying in terms of future treatment options.

Today, we have a better understanding of the bacterial ecology of wounds and the relationships between a potentially pathogenic microorganism and its host lie at the very heart of the problem: will there be a confrontation and who is likely to come out on top?

Will the microorganism simply pass through, contaminating the wound only briefly, will it settle in quietly without any need for the host to react, will it try to establish itself with determination prompting the host to put up barriers, or will it seek to conquer, infiltrate and overcome the host's defences, ultimately winning the battle and extending its harmful effects beyond the original battlefield?

Will the host be robust enough to repel the attack of microorganisms? Are there sufficient numbers of microorganisms and do they have the arsenal required to invade?

In other words: the host's defence systems and the virulence of microorganisms are the key determining factors in the development and severity of an infection.

This is the core of the debate and there are many issues to be resolved: from what point can a wound be said to be infected? What criteria should be used to make a diagnosis and, consequently, determine the appropriate treatment to be implemented?

Finally, should these be based solely on clinical factors or should other biological or bacteriological criteria also be taken into account?

In clinical practice, a number of signs lead nursing staff to suspect that a wound may be infected: when the dressing removed has become dirty, if exudates are thicker than usual or suspect in colour, the presence of a clearly purulent discharge with a highly inflammatory reaction around the edges of the wound, or if there is fistulisation of an abscess in a febrile context, to name but a few examples.

This module will address all these questions, but the conclusion remains as follows: a diagnosis of infection of a chronic wound is, above all, a clinical diagnosis, made on the basis of early identification criteria, which, when combined, are highly suggestive of infection. This is the case with inflammatory signs, for example, which reflect a reaction by the host and must be very carefully interpreted by means of tests repeated frequently enough to detect their extension, which would indicate a process that has become invasive.

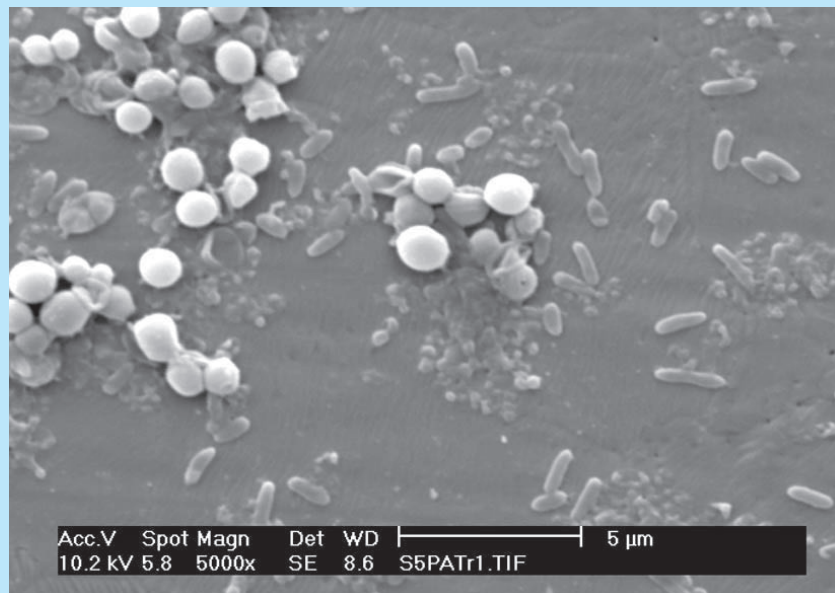
Nursing staff are on the front line when it comes to wounds and their healing course. Consequently, they form the first crucial link in a diagnostic chain, on the look-out for early signs suggestive of wound infection and working in close cooperation with doctors and bacteriological laboratories if the suspected diagnosis is confirmed.

## 2 | The bacterial ecosystem of the skin

➤ The skin is not sterile and is home to numerous microorganisms from our environment. The **skin barrier** constitutes the body's first line of defence against pathogenic microorganisms. This barrier is a **physical** one, linked to the inherent nature of the epidermis, which is pluristratified and keratinised and is subject to constant desquamation, contributing the mechanical elimination of surface microorganisms. The acidic pH of its surface also plays a role, acting as a **chemical barrier**, as does the release of toxic lipids produced by sebaceous secretions.

Finally, a **microbiological barrier** prevents colonisation by pathogenic bacteria. This consists of the skin's permanent **normal flora** (*Staphylococcus epidermidis*, corynebacteria) and temporary bacterial flora, known as **transient flora**, from our environment, the gastrointestinal tract (enterobacteria) or the rhinopharynx, including the nasal cavities, for *Staphylococcus aureus*.

**This bacterial flora is said to be commensal** in that it consists of different species that live together peacefully without attacking one another and, above all, without any adverse effects for the host (concept of **balance** between the microorganisms and the host).



Colonies of cocci in the form of strings of *Staphylococcus aureus* and bacilli in the form of rods of *Pseudomonas aeruginosa*. (SEM X 5000)

# 3 | A break in the skin: from contamination to colonisation

### ▶ Contamination of a wound

- ▶ Contamination of a wound means the **straightforward transfer** of microorganisms from the surrounding skin into the wound when the skin is broken. In the case of a chronic wound, the intrusion of a microorganism via contamination does not necessarily mean that it will persist and multiply in the wound.

A number of conditions must be met, including the structural capacities of the bacterial wall **to bind and adhere** to the cells of the wound and the presence of favourable **nutritional conditions**. In addition, the contaminant microorganism may be expelled from the wound during wound cleaning procedures or following the application of an absorbent dressing.

### ▶ Colonisation of a wound

- ▶ Colonisation of a wound is considered to be a normal phase following contamination by microorganisms from the normal or transient flora.

The most frequently encountered microorganisms are *S. epidermidis*, *coagulase negative staphylococci*, *Corynebacterium* sp, anaerobic microorganisms, such as *Peptostreptococcus* but also aerobic contaminant microorganisms from the transient flora, such as *Pseudomonas aeruginosa* (pyocyanic bacillus) or *S. aureus*, aero-anaerobic microorganisms, such as *E. coli*, or strictly anaerobic microorganisms such as *Bacteroides fragilis* from the colonic flora.

**Two conditions** define straightforward colonisation of a wound: **strictly localised** proliferation of non-pathogenic microorganisms at the surface of the wound, with **no invasion** of underlying or peripheral tissue and the **absence of any host reaction**.

This commonplace proliferation of microorganisms belonging **to non or low-pathogenic flora** remains a **surface phenomenon**, perfectly tolerated by the host in the absence of any species virulence.

## 4 | Pathogenic capacity, virulence and host defences

### ▶ Pathogenic capacity of bacteria

- ▶ The pathogenic capacity of a bacterium defines its capacity **to cause infection** in the host. The bacteria responsible for wound infection are **opportunistic** since they take advantage of a **weakening of the host's immune defences** to exert their **pathogenic capacity**.

The microorganisms most commonly involved are Gram-positive cocci (*Staphylococcus aureus*, group A *Streptococcus pyogenes*), Gram-negative bacilli (enterobacteria including *E. coli*, *Pseudomonas aeruginosa*) to cite but a few.

A number of factors influence the pathogenic capacity of bacteria: their invasive power or virulence and their capacity to produce local toxins.

### ▶ Concept of virulence

- ▶ Virulence defines the properties of a microorganism **to penetrate the tissues and multiply** within them despite the defensive mechanisms mobilised by the host.

**Binding** of the microorganism to the wound is the first requirement, via branched extensions from its cytoplasmic membrane (pili) or thanks to a structural organisation in the form of biofilms (see below). The bacterium must also be capable of **protecting** itself against the host's defences and hence **phagocytosis** through the synthesis of hydrolytic **local toxins**.

Some virulent bacteria have **enzymatic equipment** that helps them invade tissues: this is the case for *Staphylococcus*, which can produce a **coagulase** enabling it to hide in the centre of a coagulum and protect itself against phagocytosis, and then a **fibrinolysin** to dissolve clots and spread. Finally, a diffusion enzyme (**hyaluronidase**) deconstructs the connective tissue and allows the bacteria to penetrate between the tissues. Other microorganisms produce local **collagenases** that alter granulation tissue, making it fragile and friable and causing delayed healing.

**The virulence of a microorganism is also a quantitative notion** because virulence genes are only expressed from a certain level of colonisation. It is generally accepted that below an infectious dose of  $10^5$  microorganisms, an infection has little chance of spreading. It will be seen that the literature adopts this level of  **$10^5$  microorganisms per gram of tissue** to define an infected wound (except for *Streptococcus A* where the virulence level is lowered to  $10^3$ ).

# Infection of chronic wounds

## 4 | Pathogenic capacity, virulence and host defences

- The concept of **quorum sensing** refers to a system of communication between bacteria above a certain bacterial density. This interactive biological language system is based on the diffusion of small molecules outside the bacteria in order to coordinate the latter's behaviour. Beyond a certain critical mass of bacteria, the quantity of these molecules (homoserine lactones for Gram-negative bacteria) reaches a concentration level that activates the transcription of numerous genes involved in the virulence of microorganisms. (Cooper R.A. L'identification des critères d'infection des plaies, EWMA 2005).

This same quorum sensing mechanism is also reported in the formation of bacterial biofilms (Decho A.W. Trends microbiol. 2010; 18 (2)).

Where the **resistance of a microorganism to antibiotics** is concerned, this does not constitute a virulence factor of the microorganism. **This is the case for MRSA** (Methicillin-resistant *Staphylococcus aureus*), which may be present in a wound following previous inappropriate antibiotic therapy that has failed or after because the patient acquired the microorganism during a recent hospital stay, most frequently. However, if this microorganism were to become virulent, its resistance to methicillin would pose antibiotic therapy sensitivity problems in addition to the inherent invasive potential of pathogenic staphylococci.

## ▶ The host's defence mechanisms

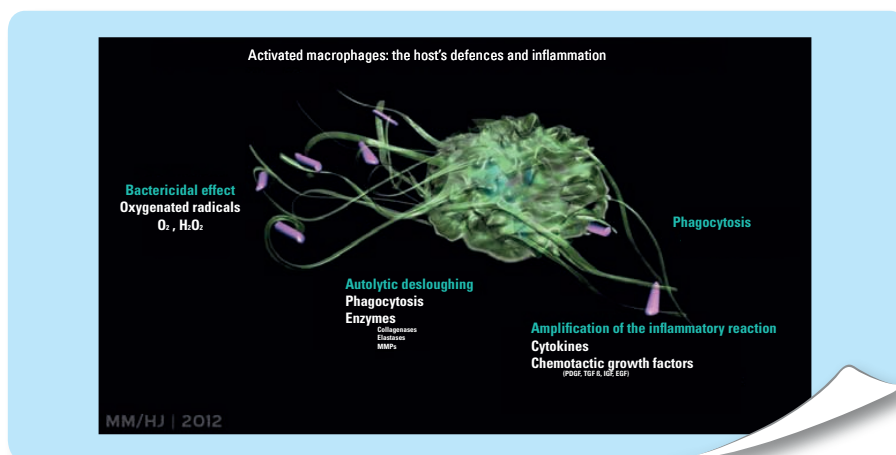
- The **host's susceptibility** in response to a bacterial attack is the main influence on the virulence of microorganisms.

The host reacts via the triggering of an **inflammatory reaction** mediated by an **influx of phagocytic cells** (neutrophils, monocytes) to perform the physical **destruction** of microorganisms by **phagocytosis**.

The presence of a pathogenic microorganism in a wound does not necessarily mean that an infection will follow: **the great majority of colonised wounds do not become infected** despite the discovery of a potentially pathogenic microorganism in surface bacteriological samples.

Patients usually suffer secondary infection of their wound following a **weakening in their general condition and immune responses**. Age is an important factor, as is under-nutrition in terms of protein and calorie intake, the existence of diabetes, peripheral arterial disease (PAD), hypoxia due to anaemia and iatrogenic immune depression (induced by corticosteroids or chemotherapy).

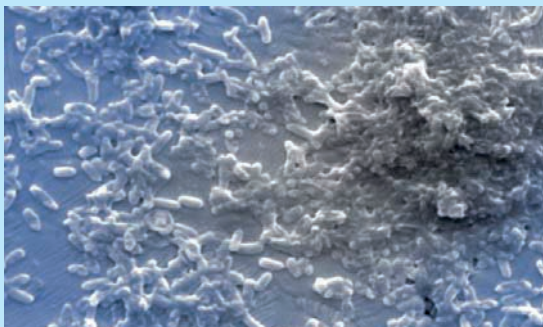
Local factors also play a role in reducing the host's immune defences: the size and depth of the wound, the presence of necrotic tissue, local ischaemia.



# Infection of chronic wounds

## 4 | Pathogenic capacity, virulence and host defences

### ► Organisation of microorganisms in the form of bacterial biofilms



Adhesion of initially free pyocyanic bacilli (planktonic cells) then colonisation by irreversible attachment of replicative bacteria to the medium.

On the right, formation of a bacterial community anchored within an adherent and protective extracellular matrix (slime). (SEM X 5000)

► **Binding of potentially pathogenic microorganisms** is one of the prerequisites for tissue invasion. The notion of organisation of bacterial communities in the form of **biofilms** describes a **polymicrobial organisation strongly and irreversibly bound to the surface of the wound** thanks to the secretion of a polysaccharide extracellular matrix, called slime, by the bacteria themselves. This **protective matrix** binds the biofilm to the surface of the wound and forms a **physical protection** against attack by antibacterial agents (Costerton J.W. *et al.* Science 99).

Bacterial organisation in the form of biofilms is one of **the causes of delayed healing** in chronic wounds. One study estimates that biofilms may be involved in more than 60% of chronic wounds (James G.A. *et al.* Wound Repair Regen 2008).

This continuous presence of adherent bacteria maintains an inflammatory defensive reaction against the aggressor, mobilises non-specific immune response cells and diverts them from their pro-healing inflammatory purpose, explaining the delay in healing and the occurrence of recurrent episodes of infection.

**Clinically**, diagnosis of a bacterial biofilm on the surface of a chronic wound remains difficult and some authors report the presence of a shiny, thick viscous coating on the surface of slow-to-heal wounds, corresponding to slime that is mature and thick enough to have become visible (Fromantin I., Soins 2012-762: 53).

**Preventing the formation of a biofilm** above all requires regular wound cleaning and desloughing, essential to remove fibrinous waste which are foci for an increase in local bacterial load.

Consequently, local antibacterial agents must now demonstrate their bactericidal efficacy against isolated microorganisms as well as their ability to deconstruct biofilms *in vitro*, in addition to demonstrating their clinical efficacy in the healing of highly colonised wounds (TLC-Silver).



## 5 | Concept of critical colonisation

➤ In the event of quantitatively very significant colonisation as a result of local conditions promoting bacterial retention or replication (deep or raw wound, inadequate desloughing or necrosis), **the host-bacterial colonisation balance** evolves either towards a “**compensated**” stage, thanks to the deployment of the host’s still efficient resistance mechanisms, or towards a “**decompensated**» stage due to progressive erosion of this resistance, opening the doors to infection in the event of virulent microorganisms.

**The host’s level of resistance therefore constitutes the key factor** determining whether or not simple colonisation progresses towards infection.

This notion of **strong bacterial colonisation still compensated for by efficient immune resistance** led to the emergence of the **critical colonisation** concept to define a stage following on from simple colonisation but **without an inevitable continuum towards infection** (Edwards R, Harding K. Curr Opin Infect Dis 2004 -17).

However, while the notion of critical colonisation does not allow us to assume an inevitable progression towards infection, it is currently widely accepted that it is predictive of **delayed healing** linked to excessive surface colonisation.

This intense and prolonged bacterial presence induces permanent defensive leukocyte recruitment, macrophage hyperactivity, and an **inflammatory reaction that stagnates** at the amplification stage (cytokines, chemotactic factors, MMPs) and **does not progress towards the resolution phase enabling granulation**.

Hence some authors now describe the critical colonisation stage as a **strictly local infection** given that it induces delayed healing of the colonised wound (Meaume S. Soins 762,2012).

➤ **Clinically**, the critical colonisation stage can be defined by the following triad: signs of surface bacterial multiplication, reactive inflammatory signs and delayed healing. However, there are no signs of diffusion into the tissues from the port of entry, i.e. the wound.

-The wound may be dirty, due to thick, foul-smelling exudates of suspect colour.

- The wound margins are inflammatory, erythematous and slight oedematous, but **with no extension of the process on subsequent frequent examinations**, reflecting an inflammatory reaction to superficial colonisation only.

- Absence of signs of remote bacterial diffusion: no extensive erythema, no tight, painful cellulitis, no lymphangitis or systemic signs of infection.

- Delayed or interrupted healing but no tissue lysis (increase in wound size, necrosis).

## 6 | Infected wounds

- The disruption of the host/bacteria balance leads to modification of the flora, now composed of **virulent microorganisms** (*S. aureus*, *Streptococci*, *E. coli*, anaerobic microorganisms, *Pseudomonas*) capable of invading the tissues from the wound surface and exerting their harmful effects there, which the body will attempt to counter, usually unsuccessfully.

**The local signs are evident, the inflammatory reaction intense and extensive, as are the regional and systemic signs.**

Infection is conventionally defined using Altemeier's formula: 
$$\frac{\text{Bacterial load} \times \text{Virulence}}{\text{Host resistance}}$$

Diagnosing secondary infection of a chronic wound is not always easy, however, particularly in the case of slow-healing or recurrent wounds with tissues remodelled by sclerosis, all factors that are liable to mask the intensity of the inflammatory reaction (lipodermatosclerosis in leg ulcers, diabetic foot ulcers).

Too often, diagnosing an infected wound is based on a bundle of arguments, leading to clinical suspicion on the basis of still-to-be-validated criteria.

As we will see, microbiological criteria may prove insufficient and laboratory tests may only provide some guidance.

### ▶ Clinical diagnosis

- Clinically, clear signs of local infection with a **marked tissue reaction** reflecting bacterial invasion remain highly suggestive of infection. This is the case of an **abscess** that may cause a **continuous purulent discharge** in the wound, **cellulitis** indicating that the bacteria have spread into the subcutaneous tissues distant from the wound and, in the worst case scenario, leading to the worrying condition of **necrotising fasciitis**, **the emergence of a secondary wound** indicating remote abscess formation, or a clinical picture of **osteo-arthritis**.  
In less acute cases, the **presence of pus** at the surface of the wound in a reactive context of **extensive redness** (> 2cm) that is tight, oedematous, warm to the touch and painful, is suggestive of local infection.

In conditions remodelled by a chronic course, an **increase in wound size** due to bacterial cytolysis, the development of **necrotic zones** (staphylococci) or **zones of skin sloughing** in a context of increased exudates, which have become thick, delayed healing due to **alteration of granulation tissue, which appears pale or dull, fragile and friable** are also elements suggestive of infection.

In conclusion, the clinical pictures are very disparate and the diagnostic criteria have varying values, between the discovery of clear local abscess formation and delayed healing in the context of a dirty wound.

# Infection of chronic wounds

## 6 | Infected wounds

### ► Systemic signs and biology

► The **development of a fever or, conversely, hypothermia** (<36°C) remains highly indicative in the absence of any other cause for this change in temperature.

- Isolated **hyperleukocytosis** is of limited indicative value.

- Among the various biological markers of inflammation, **CRP** appears to be the best marker for some authors, making it possible to differentiate between infection and simple colonisation and, more specifically, the Procalcitonin/CRP pairing in diabetic foot ulcers (Jeandrot A *et al.* Diabetologia 2007).

### ► Microorganisms involved and role of bacteriological samples in the diagnosis of infection

► For pressure ulcers and leg ulcers, globally there are no major differences with respect to the bacteriology of these wounds. The ecosystem is always **polymicrobial**.

- **In leg ulcers**, *S. aureus* is the most frequently encountered pathogen but other microorganisms are also present, including *Pseudomonas* spp, enterobacteria and anaerobic microorganisms, with the latter being found in 50% of cases in a context of synergy of cultures between species. The presence of yeasts is rare (Hansson, Acta Clin Scand 1988).

- **In pressure ulcers**, the flora is also polymicrobial, with a prevalence of aerobic microorganisms and faecal flora microorganisms: *S. aureus*, streptococci, *Pseudomonas*, as well as *E. coli*, *Proteus*, etc. On average, four species are found per sample, including one anaerobic microorganism (*Peptostreptococcus* spp, *Bacteroides fragilis*) (Chow. J Infect Dis. 1977).

- **In malum perforans pedis and diabetic foot ulcers**, the flora is much more varied (Wheat L. Arch Int Med 1986).

- **In malum perforans pedis**, *S. aureus* is found in almost half of all cases, and enterococci, *Pseudomonas aeruginosa* and *Streptococcus* sp in 20% of samples. Anaerobic microorganisms are remarkably prevalent, including *Peptostreptococcus* (35%) and *Bacteroides* sp (16%).

As regards microorganisms from **deep samples** in diabetic foot ulcers, it is mainly Gram-negative bacilli and anaerobic microorganisms that are isolated in Wagner stage 4 and 5 lesions, in contrast with the Gram-positive cocci found more superficially (Van der Meer, Diabet Med 1996).

**For all these wounds, MRSA and Gram-negative bacilli resistant to narrow-spectrum antibiotics** are frequently encountered, the price of failed previous antibiotic treatments.

# Infection of chronic wounds

## 6 | Infected wound

- Consequently, this **polymicrobism** of chronic wounds means that **surface samples** are always positive, without it necessarily being possible to interpret the results unless the microorganism responsible in the case of infection can be isolated. Performed by **simple swabbing**, these samples **test positive to numerous microorganisms**, primarily aerobic and superficial, whereas the microorganisms related to infection are mainly deep Gram-negative bacilli or anaerobic microorganisms if we take the example of stage 4 or 5 diabetic foot ulcers.

Given its ease of use in clinical practice, the risk of superficial swabbing, particularly in community medicine settings, is that it may lead to the conclusion that the microorganism isolated is the sole culprit and inappropriate antibiotic treatment may therefore be prescribed, leading to a risk of **emergence of multi-resistant strains** and treatment failure.

According to certain recent studies, wound cleaning and desloughing before any superficial samples are taken may lead to more reliable results. (Meaume S. Soins 762, 2012).

- **Deep tissue samples** (curettage-swabbing, needle aspiration, biopsy) require prior preparation of the wound to avoid superficial wound contamination. It should be cleaned and desloughed before taking the tissue sample by scraping with curette (curettage). (Lavigne J.P, Sotto A. Spectra Biologie 2007,159).

**Thin needle aspiration** requires the same prior wound preparation, and antiseptics of the surrounding skin since the puncture must be made in healthy skin and reach an area of deep infection or a pus collection.

**Tissue biopsy** requires several fragments of tissue to be sampled from non-adjacent areas on the wound. Biopsy should be favoured in the case of a deep tissue lesion. However, tissue biopsy requires close cooperation with the Bacteriology department, controlled sample transport methods and thorough training of the operator.

It is important not to forget **aero-anaerobic blood cultures** in the event of sepsis.

The notion of a quantitative threshold of  $10^5$  microorganisms per gram of tissue on biopsy enabling a diagnosis of an infected wound to be made is based on only one study and is currently being questioned.

## 7 | Clinical characteristics

### ► Pressure ulcers

► Only stage III or IV pressure ulcers involving the entire skin thickness down to the adipose cell tissues or going beyond the fascias into the underlying tissues are at high risk of infection. These are usually complex wounds with zones of sloughing, cavity extensions and the presence of necrotic and fibrinous tissue, all factors that promote bacterial retention and multiplication «in a vacuum».

Furthermore, in the case of a sacral or pelvic pressure ulcer in an elderly patient, the pressure ulcer is exposed to a permanent risk of contamination as a result of incontinence - particularly faecal - carrying enterobacteria, including *E. coli* primarily (108 per gram of faeces).

Consequently, pressure ulcers are complex, deep wounds, extensively colonised by a polymicrobial flora (an average of 4 bacterial species per sample), including faecal microorganisms, containing necrotic tissue promoting microbial retention and proliferation, with a high risk of progression to infection.

Old age and fragility, under-nutrition and immune deficiency all combined to reduce the host's defences in response to bacterial attack.

Only the development of **cellulitis** going beyond the wound edges or the formation of an **abscess** constitute signs highly suggestive of infection. Less important signs include, according to some authors, the exacerbation or onset of **local pain**, an increase in the amount of exudates or thickening of exudates and peripheral erythema with local heat (Sanada H *et al.* L'identification des critères d'infection des plaies, EWMA 2005).

Other signs, such as an **increase in the size of the wound** despite offloading, the persistence of a foul-smelling odour resistant to absorbent draining dressings, and fragile, friable granulation tissue have a lower predictive value.

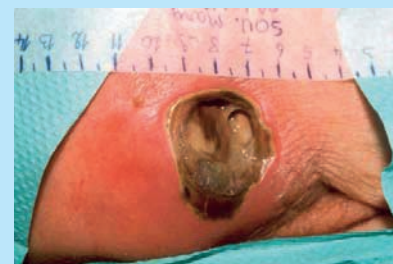
Other criteria that have been inadequately evaluated but are frequently reported in case studies are worth mentioning, including the development of unexplained behavioural disturbances, such as **confusion**, withdrawal, loss of appetite, preceding the development of local signs.

The infection may extend to functionally important structures, such as the serous bursa over which the gluteal muscles slide at their trochanteric insertion (**infectious bursitis**) and then be complicated by osteitis of the trochanter, or **osteo-arthritis** of the knee in the case of a pressure ulcer on the condyles, to cite just a few examples.

In this scenario, the prognosis remains poor in the very elderly, with an imminent risk of death in a context of septic shock.



Pressure ulcer on the heel: pyocyanic bacterial colonisation following inadequate wound desloughing.



Infected sacral pressure ulcer. More evident and foul-smelling through a necrotic zone, with signs of cellulitis at the lower part in a context of a deterioration in general condition.



Infected pressure ulcer soe over the Achilles tendon. Clear signs of pyocyanic infection. Very intense inflammatory reaction from the wound edges, signalling invasion of the surrounding tissues.

# Infection of chronic wounds

## 7 | Clinical characteristics

### ► Infected diabetic foot ulcers

- Infection is a particularly detrimental factor that adversely affects the wound healing prognosis in diabetics and often compromises the capacity to save the anatomical segment involved since it is responsible for around **25 to 50% of foot amputations**.

An **imbalance in the host's defences** in diabetics is linked to impairment of the bactericidal properties of the neutrophils, exacerbated by local hypoxia in the event of associated arterial disease, poor glucose balance and the absence of early offloading when the wound begins (Jourdan N and Rodier M. Le pied diabétique. Collection JPC 2002).

**The specific anatomical characteristics of the foot** and the pressure exerted promote the spread of infection: there are numerous muscles, which slide within four longitudinal compartments as far as the toes. Adipose cell separation spaces and the plantar pad contribute to the extension of cellulitis in the **absence of offloading**.

The contaminant flora in diabetics differs from that in other chronic wounds: presence of more virulent gram-positive cocci, including *Staphylococcus aureus* and  $\beta$ -haemolytic *Streptococcus A*.

**Superficial infections** that do not go beyond the subcutaneous adipose tissue are responsible for cellulitis, with peripheral extension of erythema of more than 2 cm around the wound and the possible presence of pus. Heat and pain may be absent in the event of peripheral arterial disease and neuropathy.

**Deep infections** present a dual risk: **spread of the infection** that may require extensive desloughing procedures and **bone involvement** with osteitis.

In diabetics, these severe signs may have no biological signals: inconstant fever, no leukocyte reaction, no systematic elevation in CRP.

Hence, regular examination of wound to look for any **visible bone structures** or bone contact by exploration using a sterile probe has a highly predictive value when it comes to osteitis (Jourdan N et Rodier M. Le pied diabétique. Collection JPC 2002).

For a toe, a **"sausage-like" appearance**, in which the toe is swollen by oedema, red and tight, is suggestive of underlying osteoarthritis.

**Necrotising fasciitis** constitutes a very specific clinical picture given its terrible prognosis. It consists of an **infectious cellulitis with necrosis** of the superficial aponeurosis leading to **rapid spread** of the infection above the muscle fascia. The microorganisms involved are  $\beta$ -haemolytic group A streptococci, as well as *Staphylococcus aureus*, anaerobic microorganisms or Gram-negative bacteria.

Tissue necrosis is linked to the cytotoxic effect of toxins and bacterial enzymes (hyaluronidases, DNAases), the formation of extensive, purulent micro-thromboses and compression of the fascia by oedema.

Fatal in 30 to 50% of cases in a context of severe sepsis, its treatment combines intensive care for septic shock, extensive excision of necrotic tissue and parenteral antibiotic therapy initiated whenever the bacteriological samples have been taken.



Abscess of the plantar surface of the forefoot, with clear pus discharge.



Ulceration due to lateral pressure on the outside surfaces of the toes. Yellow-green colour of moist necrosis and inflammatory reaction at the base of the toe, with diffusion of the infection towards the forefoot.



Collar button abscess on the big toe triggered by a small wound covered by reformed keratosis. Highly inflammatory appearance of the toe contrasting with the adjacent toe. Invasive deep infection.

# Infection of chronic wounds

## 7 | Clinical characteristics

### ➤ Bacteriological criteria

Bacteriological samples are only **indicated in the presence of local clinical signs suggestive of an infected wound**, otherwise there is a risk of identifying simple colonisation microorganisms.

Swab samples that are too superficial may only find colonising flora, whereas the microorganisms involved (including certain Gram-negative bacilli and anaerobic microorganisms) are present deep in the wound.

In the case of anaerobic bacteria, it is important to remember that the time taken to isolate and identify these is particularly long, requiring specific culture media. Given the time required, therapists usually end up initiating **probabilistic antibiotic treatment** before obtaining the bacteriological result, with a drug that is active on both aerobic and anaerobic microorganisms given that 80% of anaerobic microorganisms are mixed.

It is therefore preferable to take deep samples where possible and when the benefit is judged to outweigh the trauma of the procedure: curettage, needle aspiration and tissue biopsy for qualitative and quantitative analysis (per gram of tissue) of the microorganisms.

Despite these precautions, it is often difficult to interpret the responsibility of a microorganism that has apparently been identified in the development of an infection.

### ➤ Contribution of imaging procedures

If osteitis is suspected, **standard x-ray** is still the first imaging exam that should be performed, although there is a risk that it might miss very early osteitis given the delay of around a fortnight between bone lysis and radiographic recognition.

**Nuclear Magnetic Resonance imaging** effectively visualises bone structures and soft tissues, with a sensitivity of close to 100%.

If a doubt persists relative to the diagnosis, the use of isotopic tests (CT scans) should be discussed with the radiologist on the basis of the sensitivity and specificity of the different techniques.

### ➤ The broad treatment lines

**Offloading** is essential, since relieving pressure limits the spread of an infectious process towards adjacent cavities and cell spaces.

**Surgical desloughing** in the event of infected necrotic tissue helps eliminate this and control tissue invasion. It also makes it easier to take deep bacteriological samples and drain an abscess.

Initiation of **antibiotic therapy** must take into account the severity of the wound, factors linked to diabetes (renal insufficiency and liver toxicity, peripheral arterial disease and local diffusion) and the pharmacodynamic (spectrum) and pharmacokinetic (distribution) properties of the drugs selected.

In the event of severe infection, antibiotic therapy is empirical and broad-spectrum, initiated intravenously in a hospital setting and combining several drugs selected for their good bone diffusion, in a context of close cooperation between the diabetes specialist and the microbiologist.

In the event of significant bacterial colonisation with no clinical signs of wound infection, occlusive dressings are contraindicated; instead, dressings with good absorption, drainage and microorganism-trapping properties, possibly incorporating an antibacterial agent such as Silver, should be used (Jourdan N and Rodier M. Le pied diabétique. Collection JPC 2002).



**Surgical desloughing and removal of a collection of pus.**

# Infection of chronic wounds

## 7 | Clinical characteristics

### ▶ Venous leg ulcers

- Venous leg ulcers are wounds that are systematically colonised but, in contrast with other chronic wounds, spread of the infection to the underlying tissues (osteitis) remains rare, whereas a more superficial extension (infectious cellulitis, erysipelas) is more frequently encountered, especially in the event of an underlying condition favouring this (concomitant diabetes, drug-induced immune suppression, etc.).

Among the various specific infections that are possible, **tetanus** must be mentioned first of all: leg ulcers are highly tetanogenic wounds since 20% of tetanus patients present a **leg ulcer as the port of entry**, with a mortality rate of around 5%.

Leg ulcer wounds are usually colonised by more than two bacterial species, including an anaerobic microorganism in 50% of samples, and the most commonly encountered microorganisms are *S. aureus*, *S. epidermidis*, *Pseudomonas* spp, enterobacteria and anaerobic microorganisms.

Yeasts are not exceptional, but are rarer (10% of microorganisms). It has already been stressed that high local colonisation of a chronic wound is not predictive of the risk of developing an infection (concept of critical colonisation). In the absence of microorganisms with a high level of virulence, **ulcers are capable of tolerating large numbers of microorganisms**, with however, **a clearly detrimental effect on healing**. This is the case for *Staphylococcus*, even Methicillin-resistant strains, and, stereotypically, for *Pseudomonas aeruginosa*, which can be easily recognised by the blue-green colour (cyan) of the exudates, the liquefied slough and dressings with a characteristic fruity odour. In the absence of local signs suggestive of infection, careful desloughing of the ulcer bed, along with the use of local antibacterial agents and absorbent dressings are sufficient to reduce and then eliminate colonisation with pyocyanic microorganisms.

Hence, the notion of **critical colonisation** due to a high level of bacterial multiplication may be likened, by extension, to a **strictly local and superficial infection**, the primary risk of which is to cause delayed healing (Meaume S. Soins 762,2012).

In the absence of a purulent surface coating, diagnosis is based on a set of criteria, the simultaneous presence of which remains indicative: peripheral **inflammatory signs** in a context of limited, non-extensive erythema with local pain and increased temperature at the wound edges, **increase in thicker, more intensely colour, foul-smelling exudates, delayed healing** or increase in ulcer size with pale or, conversely, abnormally dark, fragile granulation tissue.

A delay in healing despite appropriate wound bed management and effective compression is a good indicative sign. When associated with the presence of peripheral inflammatory signs, it responds well to local antibacterial treatment, as demonstrated with Silver dressings in the lipido-colloid range (TLC-Ag). (Lazareth I. *et al.* JPC 2008-66).



Leg ulcer demonstrating delayed healing. Reappearance of slough liquefied by the exudate, with a shiny, viscous surface coating.



Pyocyanic bacterial colonisation. Absence of peripheral inflammatory signs suggestive of infection. Desloughing and antibacterial dressings.



Extension of a leg ulcer (lower wound), with reappearance of small zones of necrosis, suspect colour of slough, fragility of granulation tissue with bleeding and an inflammatory reaction limited to the edges. Suspected critical colonisation with an impact on the course of the wound.



# Infection of chronic wounds

## 7 | Clinical characteristics

➤ **An infected ulcer** mainly involves two clinical pictures: erysipelas and cellulitis.

**Erysipelas** is an acute, **non-necrotising** cellulitis, primarily due to  $\beta$ -haemolytic group A streptococcus, causing a febrile, red, enlarged leg. It presents as a large erythematous patch, with relatively clearly defined borders, tight, fiery, infiltrated and hot, with inguinal drainage adenopathy. Systemic signs are evident, with a fever at 39-40°C, general malaise and chills.

Erysipelas is a serious complication of leg ulcers, sensitive to penicillin G, which remains the first-line antibiotic treatment.

The term **infectious cellulitis** has now been replaced by a new nosological classification, necrotising bacterial cellulitis and necrotising fasciitis, in contrast with erysipelas. These deep skin infections are classified according to their depth relative to the superficial aponeurosis. Their seriousness and management have already been described.

In the context of leg ulcers, the discovery of **less spectacular and subacute forms**, with the appearance of an erysipeloid patch with an inaugural fever but no signs of shock, requires careful management, marking of the edges of the erythema with a felt pen and then very regular re-examination and trial treatment with antibiotic therapy once bacteriological samples and blood cultures have been performed in order not to miss progression to necrotising fasciitis.



Acute febrile enlarged leg: erysipelas with a leg ulcer as the port of entry.



Infected leg ulcer in a diabetic patient. Highly inflammatory erythema suggestive of active bacterial invasion.

# 8 | Treatment of infected and highly colonised wounds

- The broad lines for the treatment of infected wounds have been covered during a presentation of the various wound types. Immediate systemic antibiotic therapy is justified to combat and eliminate the diffusion of virulent microorganisms within the tissues, along with their systemic spread.

This is the case for bacterial cellulitis in leg ulcers, extensive cellulitis in pressure ulcers, and deep infections with osteitis in diabetic foot ulcers. Close cooperation between medical, bacteriological and surgical teams is usually necessary in the case of necrotising fasciitis or for the surgical desloughing - sometimes as an emergency - of a deep infection of the foot.

- **A high level of bacterial colonisation of a chronic wound** (or strictly local and superficial infection, also fitting the concept of critical colonisation in the sense that it constitutes a healing delay factor) only requires **local treatment, aimed at reducing the bacterial load and the inflammatory reaction** in order to restart the healing process.

- **Careful preparation of the wound bed** remains essential to reduce the local bacterial load and is hinged around two main strategies: **regular cleaning and careful desloughing** to quickly eliminate adherent slough or slough that is liquefying under the action of bacterial enzymes.

- **Selecting the most appropriate dressing** contributes to absorption and drainage of bacterial waste and slough residue. Occlusive dressings are not indicated in infectious contexts or in the event of deep, cavity or sloughy wounds; **alginate or related dressings** should be preferred for their drainage and bacteria-trapping capacities.

- **Local antibacterial agents** include a set of products with differing levels of evidence in terms of their value in the treatment of wounds infected by superficial colonisation.

- **Antiseptics** have not been proven to be effective in the event of long-term treatment: many of these have a reduced activity in the presence of organic matter and are cytotoxic, some are allergenic (iodine antiseptics, chlorhexidine) and others irritant (antiseptics containing chlorine). However, although their routine use is not recommended, the debate concerning their restricted, rational use in certain specific clinical situations is still ongoing. New cleaning solutions (or gels) combining an antibacterial agent and a surfactant (for example PMBH + betaine), and octenidine demonstrate an activity on «free» bacteria and biofilms but, to date, their benefit has mainly been evaluated in vitro (Andriessen A.E. *et al.* Wounds 2008; 20 (6)).

- **Local antibiotics** have no longer been recommended for a number of years due to the risk of inducing selective resistant microorganism pressure and the absence of any demonstrated efficacy.

- **Among Silver dressings**, therapists may now only choose products with demonstrated efficacy on the **only clinically relevant criterion**: wound healing.

This is the case for TLC-Silver range dressings (Urgotul® Ag/Silver and UrgoCell® Ag/Silver) in a sequential comparative trial versus a neutral dressing (Lazareth *et al.* JPC 2008 - 66).

## 9 | Conclusion

➤ **Understanding the mechanisms underlying the infection of wounds requires fundamental biological and microbiological knowledge. An infection can only occur when the microorganisms take advantage of a favourable environment to act as opportunistic pathogens when the host's immune defences are lowered.**

**Throughout this presentation, the pathological situations outlined demonstrate this lowering of the host's immune defences, influencing the pathogenic capacity of bacteria: old age and fragility, diabetes, immune suppression, local ischaemia.**

**Knowing how to intervene locally to deal with the causes of excessive bacterial colonisation, identifying the signs suggestive of local infection at an early stage, and seeking to provide bacteriological documentation of a clinically probable infection using reliable samples are all essential prerequisites in order to initiate the most appropriate treatment for the situation encountered as quickly as possible.**

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