Chapter 21

Skin and Eye Infections

Figure 21.1 The skin is an important barrier to pathogens, but it can also develop infections. These raised lesions (left) are typical of folliculitis, a condition that results from the inflammation of hair follicles. Acne lesions (right) also result from inflammation of hair follicles. In this case, the inflammation results when hair follicles become clogged with complex lipids, fatty acids, and dead skin cells, producing a favorable environment for bacteria.

Chapter Outline

21.1 Anatomy and Normal Microbiota of the Skin and Eyes
21.2 Bacterial Infections of the Skin and Eyes
21.3 Viral Infections of the Skin and Eyes
21.4 Mycoses of the Skin
21.5 Protozoan and Helminthic Infections of the Skin and Eyes

Introduction

The human body is covered in skin, and like most coverings, skin is designed to protect what is underneath. One of its primary purposes is to prevent microbes in the surrounding environment from invading underlying tissues and organs. But in spite of its role as a protective covering, skin is not itself immune from infection. Certain pathogens and toxins can cause severe infections or reactions when they come in contact with the skin. Other pathogens are opportunistic, breaching the skin’s natural defenses through cuts, wounds, or a disruption of normal microbiota resulting in an infection in the surrounding skin and tissue. Still other pathogens enter the body via different routes—through the respiratory or digestive systems, for example—but cause reactions that manifest as skin rashes or lesions.

Nearly all humans experience skin infections to some degree. Many of these conditions are, as the name suggests, “skin deep,” with symptoms that are local and non-life-threatening. At some point, almost everyone must endure conditions like acne, athlete’s foot, and minor infections of cuts and abrasions, all of which result from infections of the skin. But not all skin infections are quite so innocuous. Some can become invasive, leading to systemic infection or spreading over large areas of skin, potentially becoming life-threatening.
21.1 Anatomy and Normal Microbiota of the Skin and Eyes

Learning Objectives

• Describe the major anatomical features of the skin and eyes
• Compare and contrast the microbiomes of various body sites, such as the hands, back, feet, and eyes
• Explain how microorganisms overcome defenses of skin and eyes in order to cause infection
• Describe general signs and symptoms of disease associated with infections of the skin and eyes

Human skin is an important part of the innate immune system. In addition to serving a wide range of other functions, the skin serves as an important barrier to microbial invasion. Not only is it a physical barrier to penetration of deeper tissues by potential pathogens, but it also provides an inhospitable environment for the growth of many pathogens. In this section, we will provide a brief overview of the anatomy and normal microbiota of the skin and eyes, along with general symptoms associated with skin and eye infections.

Layers of the Skin

Human skin is made up of several layers and sublayers. The two main layers are the epidermis and the dermis. These layers cover a third layer of tissue called the hypodermis, which consists of fibrous and adipose connective tissue (Figure 21.2).

The epidermis is the outermost layer of the skin, and it is relatively thin. The exterior surface of the epidermis, called the stratum corneum, primarily consists of dead skin cells. This layer of dead cells limits direct contact between the outside world and live cells. The stratum corneum is rich in keratin, a tough, fibrous protein that is also found in hair and nails. Keratin helps make the outer surface of the skin relatively tough and waterproof. It also helps to keep the surface of the skin dry, which reduces microbial growth. However, some microbes are still able to live on the surface of the skin, and some of these can be shed with dead skin cells in the process of desquamation, which is the shedding and peeling of skin that occurs as a normal process but that may be accelerated when infection is present.

Beneath the epidermis lies a thicker skin layer called the dermis. The dermis contains connective tissue and embedded structures such as blood vessels, nerves, and muscles. Structures called hair follicles (from which hair grows) are located within the dermis, even though much of their structure consists of epidermal tissue. The dermis also contains the two major types of glands found in human skin: sweat glands (tubular glands that produce sweat) and sebaceous glands (which are associated with hair follicles and produce sebum, a lipid-rich substance containing proteins and minerals).

Clinical Focus

Part 1

Sam, a college freshman with a bad habit of oversleeping, nicked himself shaving in a rush to get to class on time. At the time, he didn’t think twice about it. But two days later, he noticed the cut was surrounded by a reddish area of skin that was warm to the touch. When the wound started oozing pus, he decided he had better stop by the university’s clinic. The doctor took a sample from the lesion and then cleaned the area.

• What type of microbe could be responsible for Sam’s infection?

Jump to the next Clinical Focus box.
Perspiration (sweat) provides some moisture to the epidermis, which can increase the potential for microbial growth. For this reason, more microbes are found on the regions of the skin that produce the most sweat, such as the skin of the underarms and groin. However, in addition to water, sweat also contains substances that inhibit microbial growth, such as salts, lysozyme, and antimicrobial peptides. Sebum also serves to protect the skin and reduce water loss. Although some of the lipids and fatty acids in sebum inhibit microbial growth, sebum contains compounds that provide nutrition for certain microbes.

Figure 21.2  (a) A micrograph of a section through human skin shows the epidermis and dermis. (b) The major layers of human skin are the epidermis, dermis, and hypodermis. (credit b: modification of work by National Cancer Institute)

Check Your Understanding

• How does desquamation help with preventing infections?

Normal Microbiota of the Skin

The skin is home to a wide variety of normal microbiota, consisting of commensal organisms that derive nutrition from skin cells and secretions such as sweat and sebum. The normal microbiota of skin tends to inhibit transient-microbe colonization by producing antimicrobial substances and outcompeting other microbes that land on the surface of the skin. This helps to protect the skin from pathogenic infection.

The skin’s properties differ from one region of the body to another, as does the composition of the skin’s microbiota. The availability of nutrients and moisture partly dictates which microorganisms will thrive in a particular region of the skin. Relatively moist skin, such as that of the nares (nostrils) and underarms, has a much different microbiota than the dryer skin on the arms, legs, hands, and top of the feet. Some areas of the skin have higher densities of sebaceous glands. These sebum-rich areas, which include the back, the folds at the side of the nose, and the back of the neck, harbor distinct microbial communities that are less diverse than those found on other parts of the body.
Different types of bacteria dominate the dry, moist, and sebum-rich regions of the skin. The most abundant microbes typically found in the dry and sebaceous regions are Betaproteobacteria and Propionibacteria, respectively. In the moist regions, Corynebacterium and Staphylococcus are most commonly found (Figure 21.3). Viruses and fungi are also found on the skin, with Malassezia being the most common type of fungus found as part of the normal microbiota. The role and populations of viruses in the microbiota, known as viromes, are still not well understood, and there are limitations to the techniques used to identify them. However, Circoviridae, Papillomaviridae, and Polyomaviridae appear to be the most common residents in the healthy skin virome. 

**Figure 21.3** The normal microbiota varies on different regions of the skin, especially in dry versus moist areas. The figure shows the major organisms commonly found in different locations of a healthy individual’s skin and external mucosa. Note that there is significant variation among individuals. (credit: modification of work by National Human Genome Research Institute)

**Check Your Understanding**

- What are the four most common bacteria that are part of the normal skin microbiota?

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Infections of the Skin

While the microbiota of the skin can play a protective role, it can also cause harm in certain cases. Often, an opportunistic pathogen residing in the skin microbiota of one individual may be transmitted to another individual more susceptible to an infection. For example, methicillin-resistant *Staphylococcus aureus* (MRSA) can often take up residence in the nares of health care workers and hospital patients; though harmless on intact, healthy skin, MRSA can cause infections if introduced into other parts of the body, as might occur during surgery or via a post-surgical incision or wound. This is one reason why clean surgical sites are so important.

Injury or damage to the skin can allow microbes to enter deeper tissues, where nutrients are more abundant and the environment is more conducive to bacterial growth. Wound infections are common after a puncture or laceration that damages the physical barrier of the skin. Microbes may infect structures in the dermis, such as hair follicles and glands, causing a localized infection, or they may reach the bloodstream, which can lead to a systemic infection.

In some cases, infectious microbes can cause a variety of rashes or lesions that differ in their physical characteristics. These rashes can be the result of inflammation reactions or direct responses to toxins produced by the microbes. Table 21.1 lists some of the medical terminology used to describe skin lesions and rashes based on their characteristics; Figure 21.4 and Figure 21.5 illustrate some of the various types of skin lesions. It is important to note that many different diseases can lead to skin conditions of very similar appearance; thus the terms used in the table are generally not exclusive to a particular type of infection or disease.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>abscess</td>
<td>localized collection of pus</td>
</tr>
<tr>
<td>bulla (pl., bullae)</td>
<td>fluid-filled blister no more than 5 mm in diameter</td>
</tr>
<tr>
<td>carbuncle</td>
<td>deep, pus-filled abscess generally formed from multiple furuncles</td>
</tr>
<tr>
<td>crust</td>
<td>dried fluids from a lesion on the surface of the skin</td>
</tr>
<tr>
<td>cyst</td>
<td>encapsulated sac filled with fluid, semi-solid matter, or gas, typically located just below the upper layers of skin</td>
</tr>
<tr>
<td>folliculitis</td>
<td>a localized rash due to inflammation of hair follicles</td>
</tr>
<tr>
<td>furuncle (boil)</td>
<td>pus-filled abscess due to infection of a hair follicle</td>
</tr>
<tr>
<td>macules</td>
<td>smooth spots of discoloration on the skin</td>
</tr>
<tr>
<td>papules</td>
<td>small raised bumps on the skin</td>
</tr>
<tr>
<td>pseudocyst</td>
<td>lesion that resembles a cyst but with a less defined boundary</td>
</tr>
<tr>
<td>purulent</td>
<td>pus-producing; suppurative</td>
</tr>
<tr>
<td>pustules</td>
<td>fluid- or pus-filled bumps on the skin</td>
</tr>
<tr>
<td>pyoderma</td>
<td>any suppurative (pus-producing) infection of the skin</td>
</tr>
<tr>
<td>suppurative</td>
<td>producing pus; purulent</td>
</tr>
<tr>
<td>ulcer</td>
<td>break in the skin; open sore</td>
</tr>
<tr>
<td>vesicle</td>
<td>small, fluid-filled lesion</td>
</tr>
<tr>
<td>wheal</td>
<td>swollen, inflamed skin that itches or burns, such as from an insect bite</td>
</tr>
</tbody>
</table>

Table 21.1
Figure 21.4  (a) Acne is a bacterial infection of the skin that manifests as a rash of inflamed hair follicles (folliculitis). The large whitehead near the center of the cheek is an infected hair follicle that has become purulent (or suppurative), leading to the formation of a furuncle. (b) An abscess is a pus-filled lesion. (credit b: modification of work by Bruce Blaus)

Figure 21.5  Numerous causes can lead to skin lesions of various types, some of which are very similar in appearance. (credit: modification of work by Bruce Blaus)

Check Your Understanding

• How can asymptomatic health care workers transmit bacteria such as MRSA to patients?

Anatomy and Microbiota of the Eye

Although the eye and skin have distinct anatomy, they are both in direct contact with the external environment. An important component of the eye is the nasolacrimal drainage system, which serves as a conduit for the fluid of the eye, called tears. Tears flow from the external eye to the nasal cavity by the lacrimal apparatus, which is composed of
the structures involved in tear production (Figure 21.6). The lacrimal gland, above the eye, secretes tears to keep the eye moist. There are two small openings, one on the inside edge of the upper eyelid and one on the inside edge of the lower eyelid, near the nose. Each of these openings is called a lacrimal punctum. Together, these lacrimal puncta collect tears from the eye that are then conveyed through lacrimal ducts to a reservoir for tears called the lacrimal sac, also known as the dacrocyst or tear sac.

From the sac, tear fluid flows via a nasolacrimal duct to the inner nose. Each nasolacrimal duct is located underneath the skin and passes through the bones of the face into the nose. Chemicals in tears, such as defensins, lactoferrin, and lysozyme, help to prevent colonization by pathogens. In addition, mucins facilitate removal of microbes from the surface of the eye.

![Figure 21.6](credit: modification of work by "Evidence Based Medical Educator Inc."/YouTube)

The surfaces of the eyeball and inner eyelid are mucous membranes called conjunctiva. The normal conjunctival microbiota has not been well characterized, but does exist. One small study (part of the Ocular Microbiome project) found twelve genera that were consistently present in the conjunctiva. These microbes are thought to help defend the membranes against pathogens. However, it is still unclear which microbes may be transient and which may form a stable microbiota.

Use of contact lenses can cause changes in the normal microbiota of the conjunctiva by introducing another surface into the natural anatomy of the eye. Research is currently underway to better understand how contact lenses may impact the normal microbiota and contribute to eye disease.

The watery material inside of the eyeball is called the vitreous humor. Unlike the conjunctiva, it is protected from contact with the environment and is almost always sterile, with no normal microbiota (Figure 21.7).

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Infections of the Eye

The conjunctiva is a frequent site of infection of the eye; like other mucous membranes, it is also a common portal of entry for pathogens. Inflammation of the conjunctiva is called **conjunctivitis**, although it is commonly known as pinkeye because of the pink appearance in the eye. Infections of deeper structures, beneath the cornea, are less common (Figure 21.8). Conjunctivitis occurs in multiple forms. It may be acute or chronic. Acute purulent conjunctivitis is associated with pus formation, while acute hemorrhagic conjunctivitis is associated with bleeding in the conjunctiva. The term **blepharitis** refers to an inflammation of the eyelids, while **keratitis** refers to an inflammation of the cornea (Figure 21.8); **keratoconjunctivitis** is an inflammation of both the cornea and the conjunctiva, and **dacryocystitis** is an inflammation of the lacrimal sac that can often occur when a nasolacrimal duct is blocked.

Infections leading to conjunctivitis, blepharitis, keratoconjunctivitis, or dacryocystitis may be caused by bacteria or viruses, but allergens, pollutants, or chemicals can also irritate the eye and cause inflammation of various structures. Viral infection is a more likely cause of conjunctivitis in cases with symptoms such as fever and watery discharge that occurs with upper respiratory infection and itchy eyes. **Table 21.2** summarizes some common forms of conjunctivitis and blepharitis.
### Types of Conjunctivities and Blepharitis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
<th>Causative Agent(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute purulent conjunctivitis</td>
<td>Conjunctivitis with purulent discharge</td>
<td>Bacterial (<em>Haemophilus</em>, <em>Staphylococcus</em>)</td>
</tr>
<tr>
<td>Acute hemorrhagic conjunctivitis</td>
<td>Involves subconjunctival hemorrhages</td>
<td>Viral (<em>Picornaviridae</em>)</td>
</tr>
<tr>
<td>Acute ulcerative blepharitis</td>
<td>Infection involving eyelids; pustules and ulcers may develop</td>
<td>Bacterial (<em>Staphylococcal</em>) or viral (<em>herpes simplex, varicella-zoster, etc.</em>)</td>
</tr>
<tr>
<td>Follicular conjunctivitis</td>
<td>Inflammation of the conjunctiva with nodules (dome-shaped structures that are red at the base and pale on top)</td>
<td>Viral (adenovirus and others); environmental irritants</td>
</tr>
<tr>
<td>Dacryocystitis</td>
<td>Inflammation of the lacrimal sac often associated with a plugged nasolacrimal duct</td>
<td>Bacterial (<em>Haemophilus</em>, <em>Staphylococcus</em>, <em>Streptococcus</em>)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>Inflammation of cornea</td>
<td>Bacterial, viral, or protozoal; environmental irritants</td>
</tr>
<tr>
<td>Keratoconjunctivitis</td>
<td>Inflammation of cornea and conjunctiva</td>
<td>Bacterial, viral (adenoviruses), or other causes (including dryness of the eye)</td>
</tr>
<tr>
<td>Nonulcerative blepharitis</td>
<td>Inflammation, irritation, redness of the eyelids without ulceration</td>
<td>Environmental irritants; allergens</td>
</tr>
<tr>
<td>Papillary conjunctivitis</td>
<td>Inflammation of the conjunctiva; nodules and papillae with red tops develop</td>
<td>Environmental irritants; allergens</td>
</tr>
</tbody>
</table>

Table 21.2

#### Check Your Understanding

- How does the lacrimal apparatus help to prevent eye infections?

### 21.2 Bacterial Infections of the Skin and Eyes

#### Learning Objectives

- Identify the most common bacterial pathogens that cause infections of the skin and eyes
- Compare the major characteristics of specific bacterial diseases affecting the skin and eyes

Despite the skin’s protective functions, infections are common. Gram-positive *Staphylococcus* spp. and *Streptococcus* spp. are responsible for many of the most common skin infections. However, many skin conditions are not strictly associated with a single pathogen. Opportunistic pathogens of many types may infect skin wounds, and individual cases with identical symptoms may result from different pathogens or combinations of pathogens.

In this section, we will examine some of the most important bacterial infections of the skin and eyes and discuss how biofilms can contribute to and exacerbate such infections. Key features of bacterial skin and eye infections are also summarized in the Disease Profile boxes throughout this section.
Staphylococcal Infections of the Skin

*Staphylococcus* species are commonly found on the skin, with *S. epidermidis* and *S. hominis* being prevalent in the normal microbiota. *S. aureus* is also commonly found in the nasal passages and on healthy skin, but pathogenic strains are often the cause of a broad range of infections of the skin and other body systems.

*S. aureus* is quite contagious. It is spread easily through skin-to-skin contact, and because many people are chronic nasal carriers (asymptomatic individuals who carry *S. aureus* in their nares), the bacteria can easily be transferred from the nose to the hands and then to fomites or other individuals. Because it is so contagious, *S. aureus* is prevalent in most community settings. This prevalence is particularly problematic in hospitals, where antibiotic-resistant strains of the bacteria may be present, and where immunocompromised patients may be more susceptible to infection. Resistant strains include methicillin-resistant *S. aureus* (MRSA), which can be acquired through healthcare settings (hospital-acquired MRSA, or HA-MRSA) or in the community (community-acquired MRSA, or CA-MRSA). Hospital patients often arrive at health-care facilities already colonized with antibiotic-resistant strains of *S. aureus* that can be transferred to health-care providers and other patients. Some hospitals have attempted to detect these individuals in order to institute prophylactic measures, but they have had mixed success (see **Eye on Ethics: Screening Patients for MRSA**).

When a staphylococcal infection develops, choice of medication is important. As discussed above, many staphylococci (such as MRSA) are resistant to some or many antibiotics. Thus, antibiotic sensitivity is measured to identify the most suitable antibiotic. However, even before receiving the results of sensitivity analysis, suspected *S. aureus* infections are often initially treated with drugs known to be effective against MRSA, such as trimethoprim-sulfamethoxazole (TMP/SMZ), clindamycin, a tetracycline (doxycycline or minocycline), or linezolid.

The pathogenicity of staphylococcal infections is often enhanced by characteristic chemicals secreted by some strains. Staphylococcal virulence factors include hemolysins called *staphylolysins*, which are cytotoxic for many types of cells, including skin cells and white blood cells. Virulent strains of *S. aureus* are also coagulase-positive, meaning they produce coagulase, a plasma-clotting protein that is involved in abscess formation. They may also produce leukocidins, which kill white blood cells and can contribute to the production of pus and Protein A, which inhibits phagocytosis by binding to the constant region of antibodies. Some virulent strains of *S. aureus* also produce other toxins, such as toxic shock syndrome toxin-1 (see **Virulence Factors of Bacterial and Viral Pathogens**).

To confirm the causative agent of a suspected staphylococcal skin infection, samples from the wound are cultured. Under the microscope, gram-positive *Staphylococcus* species have cellular arrangements that form grapelike clusters; when grown on blood agar, colonies have a unique pigmentation ranging from opaque white to cream. A catalase test is used to distinguish *Staphylococcus* from *Streptococcus*, which is also a genus of gram-positive cocci and a common cause of skin infections. *Staphylococcus* species are catalase-positive while *Streptococcus* species are catalase-negative.

Other tests are performed on samples from the wound in order to distinguish coagulase-positive species of *Staphylococcus* (CoPS) such as *S. aureus* from common coagulase-negative species (CoNS) such as *S. epidermidis*. Although CoNS are less likely than CoPS to cause human disease, they can cause infections when they enter the body, as can sometimes occur via catheters, indwelling medical devices, and wounds. Passive agglutination testing can be used to distinguish CoPS from CoNS. If the sample is coagulase-positive, the sample is generally presumed to contain *S. aureus*. Additional genetic testing would be necessary to identify the particular strain of *S. aureus*.

Another way to distinguish CoPS from CoNS is by culturing the sample on mannitol salt agar (MSA). *Staphylococcus* species readily grow on this medium because they are tolerant of the high concentration of sodium chloride (7.5% NaCl). However, CoPS such as *S. aureus* ferment mannitol (which will be evident on a MSA plate), whereas CoNS such as *S. epidermidis* do not ferment mannitol but can be distinguished by the fermentation of other sugars such as lactose, malonate, and raffinose (**Figure 21.9**).
Figure 21.9  (a) A mannitol salt agar plate is used to distinguish different species of staphylococci. In this plate, *S. aureus* is on the left and *S. epidermidis* is in the right. Because *S. aureus* is capable of fermenting mannitol, it produces acids that cause the color to change to yellow. (b) This scanning electron micrograph shows the characteristic grapelike clusters of *S. aureus*. (credit a: modification of work by “ScienceProfOnline”/YouTube; credit b: modification of work by Centers for Disease Control and Prevention)

**Screening Patients for MRSA**

According to the CDC, 86% of invasive MRSA infections are associated in some way with healthcare, as opposed to being community-acquired. In hospitals and clinics, asymptomatic patients who harbor MRSA may spread the bacteria to individuals who are more susceptible to serious illness.

In an attempt to control the spread of MRSA, hospitals have tried screening patients for MRSA. If patients test positive following a nasal swab test, they can undergo decolonization using chlorhexidine washes or intranasal mupirocin. Some studies have reported substantial reductions in MRSA disease following implementation of these protocols, while others have not. This is partly because there is no standard protocol for these procedures. Several different MRSA identification tests may be used, some involving slower culturing techniques and others rapid testing. Other factors, such as the effectiveness of general hand-washing protocols, may also play a role in helping to prevent MRSA transmission. There are still other questions that need to be addressed: How frequently should patients be screened? Which individuals should be tested? From where on the body should samples be collected? Will increased resistance develop from the decolonization procedures?

Even if identification and decolonization procedures are perfected, ethical questions will remain. Should patients have the right to decline testing? Should a patient who tests positive for MRSA have the right to decline the decolonization procedure, and if so, should hospitals have the right to refuse treatment to the patient? How do we balance the individual’s right to receive care with the rights of other patients who could be exposed to disease as a result?
Superficial Staphylococcal Infections

*S. aureus* is often associated with pyoderma, skin infections that are purulent. Pus formation occurs because many strains of *S. aureus* produce leukocidins, which kill white blood cells. These purulent skin infections may initially manifest as folliculitis, but can lead to furuncles or deeper abscesses called carbuncles.

Folliculitis generally presents as bumps and pimples that may be itchy, red, and/or pus-filled. In some cases, folliculitis is self-limiting, but if it continues for more than a few days, worsens, or returns repeatedly, it may require medical treatment. Sweat, skin injuries, ingrown hairs, tight clothing, irritation from shaving, and skin conditions can all contribute to folliculitis. Avoidance of tight clothing and skin irritation can help to prevent infection, but topical antibiotics (and sometimes other treatments) may also help. Folliculitis can be identified by skin inspection; treatment is generally started without first culturing and identifying the causative agent.

In contrast, furuncles (boils) are deeper infections (Figure 21.10). They are most common in those individuals (especially young adults and teenagers) who play contact sports, share athletic equipment, have poor nutrition, live in close quarters, or have weakened immune systems. Good hygiene and skin care can often help to prevent furuncles from becoming more infective, and they generally resolve on their own. However, if furuncles spread, increase in number or size, or lead to systemic symptoms such as fever and chills, then medical care is needed. They may sometimes need to be drained (at which time the pathogens can be cultured) and treated with antibiotics.

When multiple boils develop into a deeper lesion, it is called a carbuncle (Figure 21.10). Because carbuncles are deeper, they are more commonly associated with systemic symptoms and a general feeling of illness. Larger, recurrent, or worsening carbuncles require medical treatment, as do those associated with signs of illness such as fever. Carbuncles generally need to be drained and treated with antibiotics. While carbuncles are relatively easy to identify visually, culturing and laboratory analysis of the wound may be recommended for some infections because antibiotic resistance is relatively common.

Proper hygiene is important to prevent these types of skin infections or to prevent the progression of existing infections.

![Figure 21.10](image)

**Figure 21.10** Furuncles (boils) and carbuncles are infections of the skin often caused by *Staphylococcus* bacteria. (a) A furuncle contains pus and exhibits swelling. (b) A carbuncle is a pus-filled lesion that is typically deeper than the furuncle. It often forms from multiple furuncles. (credit a: modification of work by “Mahdouch”/Wikimedia Commons; credit b: modification of work by “Drvgaikwad”/Wikimedia Commons)

Staphylococcal scalded skin syndrome (SSSS) is another superficial infection caused by *S. aureus* that is most commonly seen in young children, especially infants. Bacterial exotoxins first produce erythema (redness of the skin) and then severe peeling of the skin, as might occur after scalding (Figure 21.11). SSSS is diagnosed by examining characteristics of the skin (which may rub off easily), using blood tests to check for elevated white blood cell counts, culturing, and other methods. Intravenous antibiotics and fluid therapy are used as treatment.
Impetigo

The skin infection impetigo causes the formation of vesicles, pustules, and possibly bullae, often around the nose and mouth. Bullae are large, fluid-filled blisters that measure at least 5 mm in diameter. Impetigo can be diagnosed as either nonbullous or bullous. In nonbullous impetigo, vesicles and pustules rupture and become encrusted sores. Typically the crust is yellowish, often with exudate draining from the base of the lesion. In bullous impetigo, the bullae fill and rupture, resulting in larger, draining, encrusted lesions (Figure 21.12).

Especially common in children, impetigo is particularly concerning because it is highly contagious. Impetigo can be caused by S. aureus alone, by Streptococcus pyogenes alone, or by coinfection of S. aureus and S. pyogenes. Impetigo is often diagnosed through observation of its characteristic appearance, although culture and susceptibility testing may also be used.

Topical or oral antibiotic treatment is typically effective in treating most cases of impetigo. However, cases caused by S. pyogenes can lead to serious sequelae (pathological conditions resulting from infection, disease, injury, therapy, or other trauma) such as acute glomerulonephritis (AGN), which is severe inflammation in the kidneys.

Nosocomial S. epidermidis Infections

Though not as virulent as S. aureus, the staphylococcus S. epidermidis can cause serious opportunistic infections. Such infections usually occur only in hospital settings. S. epidermidis is usually a harmless resident of the normal
skin microbiota. However, health-care workers can inadvertently transfer *S. epidermidis* to medical devices that are inserted into the body, such as catheters, prostheses, and indwelling medical devices. Once it has bypassed the skin barrier, *S. epidermidis* can cause infections inside the body that can be difficult to treat. Like *S. aureus*, *S. epidermidis* is resistant to many antibiotics, and localized infections can become systemic if not treated quickly. To reduce the risk of nosocomial (hospital-acquired) *S. epidermidis*, health-care workers must follow strict procedures for handling and sterilizing medical devices before and during surgical procedures.

**Check Your Understanding**

- Why are *Staphylococcus aureus* infections often purulent?

**Streptococcal Infections of the Skin**

*Streptococcus* are gram-positive cocci with a microscopic morphology that resembles chains of bacteria. Colonies are typically small (1–2 mm in diameter), translucent, entire edge, with a slightly raised elevation that can be either nonhemolytic, alpha-hemolytic, or beta-hemolytic when grown on blood agar (Figure 21.13). Additionally, they are facultative anaerobes that are catalase-negative.

![Figure 21.13](credit: modification of work by Centers for Disease Control and Prevention)

The genus *Streptococcus* includes important pathogens that are categorized in serological Lancefield groups based on the distinguishing characteristics of their surface carbohydrates. The most clinically important streptococcal species in humans is *S. pyogenes*, also known as group A streptococcus (GAS). *S. pyogenes* produces a variety of extracellular enzymes, including streptolysins O and S, hyaluronidase, and streptokinase. These enzymes can aid in transmission and contribute to the inflammatory response. *S. pyogenes* also produces a capsule and **M protein**, a streptococcal cell wall protein. These virulence factors help the bacteria to avoid phagocytosis while provoking a substantial immune response that contributes to symptoms associated with streptococcal infections.

*S. pyogenes* causes a wide variety of diseases not only in the skin, but in other organ systems as well. Examples of diseases elsewhere in the body include pharyngitis and scarlet fever, which will be covered in later chapters.

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Cellulitis, Erysipelas, and Erythema Nosodum

Common streptococcal conditions of the skin include cellulitis, erysipelas, and erythema nodosum. An infection that develops in the dermis or hypodermis can cause cellulitis, which presents as a reddened area of the skin that is warm to the touch and painful. The causative agent is often *S. pyogenes*, which may breach the epidermis through a cut or abrasion, although cellulitis may also be caused by staphylococci. *S. pyogenes* can also cause erysipelas, a condition that presents as a large, intensely inflamed patch of skin involving the dermis (often on the legs or face). These infections can be suppurative, which results in a bullous form of erysipelas. Streptococcal and other pathogens may also cause a condition called erythema nodosum, characterized by inflammation in the subcutaneous fat cells of the hypodermis. It sometimes results from a streptococcal infection, though other pathogens can also cause the condition. It is not suppurative, but leads to red nodules on the skin, most frequently on the shins (Figure 21.14).

In general, streptococcal infections are best treated through identification of the specific pathogen followed by treatment based upon that particular pathogen’s susceptibility to different antibiotics. Many immunological tests, including agglutination reactions and ELISAs, can be used to detect streptococci. Penicillin is commonly prescribed for treatment of cellulitis and erysipelas because resistance is not widespread in streptococci at this time. In most patients, erythema nodosum is self-limiting and is not treated with antimicrobial drugs. Recommended treatments may include nonsteroidal anti-inflammatory drugs (NSAIDs), cool wet compresses, elevation, and bed rest.

Necrotizing Fasciitis

Streptococcal infections that start in the skin can sometimes spread elsewhere, resulting in a rare but potentially life-threatening condition called necrotizing fasciitis, sometimes referred to as flesh-eating bacterial syndrome. *S. pyogenes* is one of several species that can cause this rare but potentially-fatal condition; others include *Klebsiella*, *Clostridium*, *Escherichia coli*, *S. aureus*, and *Aeromonas hydrophila*.

Necrotizing fasciitis occurs when the fascia, a thin layer of connective tissue between the skin and muscle, becomes infected. Severe invasive necrotizing fasciitis due to *Streptococcus pyogenes* occurs when virulence factors that are responsible for adhesion and invasion overcome host defenses. *S. pyogenes* invasins allow bacterial cells to adhere to tissues and establish infection. Bacterial proteases unique to *S. pyogenes* aggressively infiltrate and destroy host tissues, inactivate complement, and prevent neutrophil migration to the site of infection. The infection and resulting tissue death can spread very rapidly, as large areas of skin become detached and die. Treatment generally requires debridement (surgical removal of dead or infected tissue) or amputation of infected limbs to stop the spread of the infection; surgical treatment is supplemented with intravenous antibiotics and other therapies (Figure 21.15).

Necrotizing fasciitis does not always originate from a skin infection; in some cases there is no known portal of entry. Some studies have suggested that experiencing a blunt force trauma can increase the risk of developing streptococcal necrotizing fasciitis.\(^7\)
Figure 21.15  (a) The left leg of this patient shows the clinical features of necrotizing fasciitis. (b) The same patient’s leg is surgically debrided to remove the infection. (credit a, b: modification of work by Piotr Smuszkiewicz, Iwona Trojanowska, and Hanna Tomczak)

Check Your Understanding

• How do staphylococcal infections differ in general presentation from streptococcal infections?

Clinical Focus

Part 2

Observing that Sam’s wound is purulent, the doctor tells him that he probably has a bacterial infection. She takes a sample from the lesion to send for laboratory analysis, but because it is Friday, she does not expect to receive the results until the following Monday. In the meantime, she prescribes an over-the-counter topical antibiotic ointment. She tells Sam to keep the wound clean and apply a new bandage with the ointment at least twice per day.

• How would the lab technician determine if the infection is staphylococcal or streptococcal? Suggest several specific methods.
• What tests might the lab perform to determine the best course of antibiotic treatment?

Jump to the next Clinical Focus box. Go back to the previous Clinical Focus box.

Pseudomonas Infections of the Skin

Another important skin pathogen is Pseudomonas aeruginosa, a gram-negative, oxidase-positive, aerobic bacillus that is commonly found in water and soil as well as on human skin. P. aeruginosa is a common cause of opportunistic infections of wounds and burns. It can also cause hot tub rash, a condition characterized by folliculitis that frequently afflicts users of pools and hot tubs (recall the Clinical Focus case in Microbial Biochemistry). P. aeruginosa is also the cause of otitis externa (swimmer’s ear), an infection of the ear canal that causes itching, redness, and discomfort, and can progress to fever, pain, and swelling (Figure 21.16).

Figure 21.16  (a) Hot tub folliculitis presents as an itchy red rash. It is typically caused by *P. aeruginosa*, a bacterium that thrives in wet, warm environments such as hot tubs. (b) Otitis externa (swimmer’s ear) may also be caused by *P. aeruginosa* or other bacteria commonly found in water. Inflammation of the outer ear and ear canal can lead to painful swelling. (credit b: modification of work by Klaus D. Peter)

Wounds infected with *P. aeruginosa* have a distinctive odor resembling grape soda or fresh corn tortillas. This odor is caused by the 2-aminoacetophenone that is used by *P. aeruginosa* in quorum sensing and contributes to its pathogenicity. Wounds infected with certain strains of *P. aeruginosa* also produce a blue-green pus due to the pigments **pyocyanin** and **pyoverdin**, which also contribute to its virulence. Pyocyanin and pyoverdin are siderophores that help *P. aeruginosa* survive in low-iron environments by enhancing iron uptake. *P. aeruginosa* also produces several other virulence factors, including phospholipase C (a hemolysin capable of breaking down red blood cells), exoenzyme S (involved in adherence to epithelial cells), and exotoxin A (capable of causing tissue necrosis). Other virulence factors include a slime that allows the bacterium to avoid being phagocytized, fimbriae for adherence, and proteases that cause tissue damage. *P. aeruginosa* can be detected through the use of cetrimide agar, which is selective for *Pseudomonas* species (Figure 21.17).

Figure 21.17  (a) These *P. aeruginosa* colonies are growing on xylose lysine sodium deoxycholate (XLD) agar. (b) *Pseudomonas* spp. can produce a variety of blue-green pigments. (c) *Pseudomonas* spp. may produce fluorescein, which fluoresces green under ultraviolet light under the right conditions. (credit a: modification of work by Centers for Disease Control and Prevention)

*Pseudomonas* spp. tend to be resistant to most antibiotics. They often produce β-lactamases, may have mutations affecting porins (small cell wall channels) that affect antibiotic uptake, and may pump some antibiotics out of the cell, contributing to this resistance. Polymyxin B and gentamicin are effective, as are some fluoroquinolones. Otitis externa is typically treated with ear drops containing acetic acid, antibacterials, and/or steroids to reduce inflammation; ear drops may also include antifungals because fungi can sometimes cause or contribute to otitis externa. Wound
infections caused by *Pseudomonas* spp. may be treated with topical antibiofilm agents that disrupt the formation of biofilms.

Check Your Understanding

- Name at least two types of skin infections commonly caused by *Pseudomonas* spp.

### Acne

One of the most ubiquitous skin conditions is **acne**. Acne afflicts nearly 80% of teenagers and young adults, but it can be found in individuals of all ages. Higher incidence among adolescents is due to hormonal changes that can result in overproduction of sebum.

Acne occurs when hair follicles become clogged by shed skin cells and sebum, causing non-inflammatory lesions called comedones. Comedones (singular “comedo”) can take the form of whitehead and blackhead pimples. Whiteheads are covered by skin, whereas blackhead pimples are not; the black color occurs when lipids in the clogged follicle become exposed to the air and oxidize (**Figure 21.18**).

![Figure 21.18](image)

**Figure 21.18** (a) Acne is characterized by whitehead and blackhead comedones that result from clogged hair follicles. (b) Blackheads, visible as black spots on the skin, have a dark appearance due to the oxidation of lipids in sebum via exposure to the air. (credit a: modification of work by Bruce Blaus)

Often comedones lead to infection by *Propionibacterium acnes*, a gram-positive, non-spore-forming, aerotolerant anaerobic bacillus found on skin that consumes components of sebum. *P. acnes* secretes enzymes that damage the hair follicle, causing inflammatory lesions that may include papules, pustules, nodules, or pseudocysts, depending on their size and severity.

Treatment of acne depends on the severity of the case. There are multiple ways to grade acne severity, but three levels are usually considered based on the number of comedones, the number of inflammatory lesions, and the types of lesions. Mild acne is treated with topical agents that may include salicylic acid (which helps to remove old skin cells) or retinoids (which have multiple mechanisms, including the reduction of inflammation). Moderate acne may be treated with antibiotics (erythromycin, clindamycin), acne creams (e.g., benzoyl peroxide), and hormones. Severe acne may require treatment using strong medications such as isotretinoin (a retinoid that reduces oil buildup, among other effects, but that also has serious side effects such as photosensitivity). Other treatments, such as phototherapy and laser therapy to kill bacteria and possibly reduce oil production, are also sometimes used.
Check Your Understanding

• What is the role of *Propionibacterium acnes* in causing acne?

Clinical Focus

Resolution

Sam uses the topical antibiotic over the weekend to treat his wound, but he does not see any improvement. On Monday, the doctor calls to inform him that the results from his laboratory tests are in. The tests show evidence of both *Staphylococcus* and *Streptococcus* in his wound. The bacterial species were confirmed using several tests. A passive agglutination test confirmed the presence of *S. aureus*. In this type of test, latex beads with antibodies cause agglutination when *S. aureus* is present. *Streptococcus pyogenes* was confirmed in the wound based on bacitracin (0.04 units) susceptibility as well as latex agglutination tests specific for *S. pyogenes*.

Because many strains of *S. aureus* are resistant to antibiotics, the doctor had also requested an antimicrobial susceptibility test (AST) at the same time the specimen was submitted for identification. The results of the AST indicated no drug resistance for the *Streptococcus* spp.; the *Staphylococcus* spp. showed resistance to several common antibiotics, but were susceptible to cefoxitin and oxacillin. Once Sam began to use these new antibiotics, the infection resolved within a week and the lesion healed.

Go back to the previous Clinical Focus box.

Anthrax

The zoonotic disease *anthrax* is caused by *Bacillus anthracis*, a gram-positive, endospore-forming, facultative anaerobe. Anthrax mainly affects animals such as sheep, goats, cattle, and deer, but can be found in humans as well. Sometimes called wool sorter’s disease, it is often transmitted to humans through contact with infected animals or animal products, such as wool or hides. However, exposure to *B. anthracis* can occur by other means, as the endospores are widespread in soils and can survive for long periods of time, sometimes for hundreds of years.

The vast majority of anthrax cases (95–99%) occur when anthrax endospores enter the body through abrasions of the skin. This form of the disease is called cutaneous anthrax. It is characterized by the formation of a nodule on the skin; the cells within the nodule die, forming a black *eschar*, a mass of dead skin tissue (Figure 21.19). The localized infection can eventually lead to bacteremia and septicemia. If untreated, cutaneous anthrax can cause death in 20% of patients. Once in the skin tissues, *B. anthracis* endospores germinate and produce a capsule, which prevents the bacteria from being phagocytized, and two binary exotoxins that cause edema and tissue damage. The first of the two exotoxins consists of a combination of protective antigen (PA) and an enzymatic lethal factor (LF), forming lethal toxin (LeTX). The second consists of protective antigen (PA) and an edema factor (EF), forming edema toxin (EdTX).

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Figure 21.19  (a) Cutaneous anthrax is an infection of the skin by *B. anthracis*, which produces tissue-damaging exotoxins. Dead tissues accumulating in this nodule have produced a small black eschar. (b) Colonies of *B. anthracis* grown on sheep’s blood agar. (credit a, b: modification of work by Centers for Disease Control and Prevention)

Less commonly, anthrax infections can be initiated through other portals of entry such as the digestive tract (gastrointestinal anthrax) or respiratory tract (pulmonary anthrax or inhalation anthrax). Typically, cases of noncutaneous anthrax are more difficult to treat than the cutaneous form. The mortality rate for gastrointestinal anthrax can be up to 40%, even with treatment. Inhalation anthrax, which occurs when anthrax spores are inhaled, initially causes influenza-like symptoms, but mortality rates are approximately 45% in treated individuals and 85% in those not treated. A relatively new form of the disease, injection anthrax, has been reported in Europe in intravenous drug users; it occurs when drugs are contaminated with *B. anthracis*. Patients with injection anthrax show signs and symptoms of severe soft tissue infection that differ clinically from cutaneous anthrax. This often delays diagnosis and treatment, and leads to a high mortality rate.[10]

*B. anthracis* colonies on blood agar have a rough texture and serrated edges that eventually form an undulating band (Figure 21.19). Broad spectrum antibiotics such as penicillin, erythromycin, and tetracycline are often effective treatments.

Unfortunately, *B. anthracis* has been used as a biological weapon and remains on the United Nations’ list of potential agents of bioterrorism.[11] Over a period of several months in 2001, a number of letters were mailed to members of the news media and the United States Congress. As a result, 11 individuals developed cutaneous anthrax and another 11 developed inhalation anthrax. Those infected included recipients of the letters, postal workers, and two other individuals. Five of those infected with pulmonary anthrax died. The anthrax spores had been carefully prepared to aerosolize, showing that the perpetrator had a high level of expertise in microbiology.[12]

A vaccine is available to protect individuals from anthrax. However, unlike most routine vaccines, the current anthrax vaccine is unique in both its formulation and the protocols dictating who receives it.[13] The vaccine is administered through five intramuscular injections over a period of 18 months, followed by annual boosters. The US Food and Drug Administration (FDA) has only approved administration of the vaccine prior to exposure for at-risk adults, such as individuals who work with anthrax in a laboratory, some individuals who handle animals or animal products (e.g., some veterinarians), and some members of the United States military. The vaccine protects against cutaneous and


inhalation anthrax using cell-free filtrates of microaerophilic cultures of an avirulent, nonencapsulated strain of *B. anthracis*.\(^{[14]}\) The FDA has not approved the vaccine for routine use after exposure to anthrax, but if there were ever an anthrax emergency in the United States, patients could be given anthrax vaccine after exposure to help prevent disease.

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**Check Your Understanding**

- What is the characteristic feature of a cutaneous anthrax infection?

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**Disease Profile**

**Bacterial Infections of the Skin**

Bacterial infections of the skin can cause a wide range of symptoms and syndromes, ranging from the superficial and relatively harmless to the severe and even fatal. Most bacterial skin infections can be diagnosed by culturing the bacteria and treated with antibiotics. Antimicrobial susceptibility testing is also often necessary because many strains of bacteria have developed antibiotic resistance. Figure 21.20 summarizes the characteristics of some common bacterial skin infections.

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### Bacterial Infections of the Skin

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Antimicrobial Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td><em>Propionibacterium acnes</em></td>
<td>Comedones (whiteheads, blackheads); papules, pustules, nodules, or pseudocysts</td>
<td>Not transmissible; clogged pores become infected by normal skin microbiota (<em>P. acnes</em>)</td>
<td>Erythromycin, clindamycin</td>
</tr>
<tr>
<td>Anthrax (cutaneous)</td>
<td><em>Bacillus anthracis</em></td>
<td>Eschar at site of infection; may lead to sepsicaemia and can be fatal</td>
<td>Entry of <em>B. anthracis</em> endospores through cut or abrasion</td>
<td>Penicillin, erythromycin, or tetracycline</td>
</tr>
<tr>
<td>Cellulitis</td>
<td><em>Streptococcus pyogenes</em></td>
<td>Localized inflammation of dermis and hypodermis; skin red, warm, and painful to the touch</td>
<td>Entry of <em>S. pyogenes</em> through cut or abrasion</td>
<td>Oral or intravenous antibiotics (e.g., penicillin)</td>
</tr>
<tr>
<td>Erysipelas</td>
<td><em>S. pyogenes</em></td>
<td>Inflamed, swollen patch of skin, often on face; may be suppurative</td>
<td>Entry of <em>S. pyogenes</em> through cut or abrasion</td>
<td>Oral or intravenous antibiotics (e.g., penicillin)</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td><em>S. pyogenes</em></td>
<td>Small red nodules, often on shins</td>
<td>Associated with other streptococcal infection</td>
<td>None or anti-inflammatory drugs for severe cases</td>
</tr>
<tr>
<td>Impetigo</td>
<td><em>Staphylococcus aureus</em>, <em>S. pyogenes</em></td>
<td>Vesicles, pustules, and sometimes bullae around nose and mouth</td>
<td>Highly contagious, especially via contact</td>
<td>Topical or oral antibiotics</td>
</tr>
<tr>
<td>Necrotizing fasciitis</td>
<td><em>S. pyogenes</em>, <em>Klebsiella</em>, <em>Clostridium</em>, others</td>
<td>Infection of fascia and rapidly spreading tissue death; can lead to septic shock and death</td>
<td>Entry of bacteria through cut or abrasion</td>
<td>Intravenous broad-spectrum antibiotics</td>
</tr>
<tr>
<td>Otitis externa</td>
<td><em>Pseudomonas aeruginosa</em></td>
<td>Itching, redness, discomfort of ear canal, progressing to fever, pain, swelling</td>
<td><em>P. aeruginosa</em> enters ear canal via pool or other water</td>
<td>Acidic ear drops with antibiotics, antifungals, steroids</td>
</tr>
<tr>
<td>Staphylococcal scalded skin syndrome (SSSS)</td>
<td><em>S. aureus</em></td>
<td>Erythema and severe peeling of skin</td>
<td>Infection of skin and mucous membranes, especially in children</td>
<td>Intravenous antibiotics, fluid therapy</td>
</tr>
<tr>
<td>Wound infections</td>
<td><em>P. aeruginosa</em>, others</td>
<td>Formation of biofilm in or on wound</td>
<td>Exposure of wound to microbes in environment; poor wound hygiene</td>
<td>Polymyxin B, gentamicin, fluoroquinolones, topical anti-biofilm agents</td>
</tr>
</tbody>
</table>

### Bacterial Conjunctivitis

Like the skin, the surface of the eye comes in contact with the outside world and is somewhat prone to infection by bacteria in the environment. Bacterial conjunctivitis (pinkeye) is a condition characterized by inflammation of the conjunctiva, often accompanied by a discharge of sticky fluid (described as acute purulent conjunctivitis) (Figure 21.21). Conjunctivitis can affect one eye or both, and it usually does not affect vision permanently. Bacterial conjunctivitis is most commonly caused by *Haemophilus influenzae*, but can also be caused by other species such as *Moraxella catarrhalis*, *S. pneumoniae*, and *S. aureus*. The causative agent may be identified using bacterial cultures, Gram stain, and diagnostic biochemical, antigenic, or nucleic acid profile tests of the isolated pathogen. Bacterial conjunctivitis is very contagious, being transmitted via secretions from infected individuals, but it is also self-limiting.
Bacterial conjunctivitis usually resolves in a few days, but topical antibiotics are sometimes prescribed. Because this condition is so contagious, medical attention is recommended whenever it is suspected. Individuals who use contact lenses should discontinue their use when conjunctivitis is suspected. Certain symptoms, such as blurred vision, eye pain, and light sensitivity, can be associated with serious conditions and require medical attention.

**Figure 21.21** Acute, purulent, bacterial conjunctivitis causes swelling and redness in the conjunctiva, the membrane lining the whites of the eyes and the inner eyelids. It is often accompanied by a yellow, green, or white discharge, which can dry and become encrusted on the eyelashes. (credit: “Tanalai”/Wikimedia Commons)

**Neonatal Conjunctivitis**

Newborns whose mothers have certain sexually transmitted infections are at risk of contracting *ophthalmia neonatorum* or *inclusion conjunctivitis*, which are two forms of neonatal conjunctivitis contracted through exposure to pathogens during passage through the birth canal. Gonococcal ophthalmia neonatorum is caused by *Neisseria gonorrhoeae*, the bacterium that causes the STD gonorrhea (Figure 21.22). Inclusion (chlamydial) conjunctivitis is caused by *Chlamydia trachomatis*, the anaerobic, obligate, intracellular parasite that causes the STD chlamydia.

To prevent gonococcal ophthalmia neonatorum, silver nitrate ointments were once routinely applied to all infants’ eyes shortly after birth; however, it is now more common to apply antibacterial creams or drops, such as erythromycin. Most hospitals are required by law to provide this preventative treatment to all infants, because conjunctivitis caused by *N. gonorrhoeae*, *C. trachomatis*, or other bacteria acquired during a vaginal delivery can have serious complications. If untreated, the infection can spread to the cornea, resulting in ulceration or perforation that can cause vision loss or permanent blindness. As such, neonatal conjunctivitis is treated aggressively with oral or intravenous antibiotics to stop the spread of the infection. Causative agents of inclusion conjunctivitis may be identified using bacterial cultures, Gram stain, and diagnostic biochemical, antigenic, or nucleic acid profile tests.

**Figure 21.22** A newborn suffering from gonococcal ophthalmia neonatorum. Left untreated, purulent discharge can scar the cornea, causing loss of vision or permanent blindness. (credit: Centers for Disease Control and Prevention)

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**Check Your Understanding**

- Compare and contrast bacterial conjunctivitis with neonatal conjunctivitis.
Trachoma

Trachoma, or granular conjunctivitis, is a common cause of preventable blindness that is rare in the United States but widespread in developing countries, especially in Africa and Asia. The condition is caused by the same species that causes neonatal inclusion conjunctivitis in infants, *Chlamydia trachomatis*. *C. trachomatis* can be transmitted easily through fomites such as contaminated towels, bed linens, and clothing and also by direct contact with infected individuals. *C. trachomatis* can also be spread by flies that transfer infected mucous containing *C. trachomatis* from one human to another.

Infection by *C. trachomatis* causes chronic conjunctivitis, which leads to the formation of necrotic follicles and scarring in the upper eyelid. The scars turn the eyelashes inward (a condition known as trichiasis) and mechanical abrasion of the cornea leads to blindness (Figure 21.23). Antibiotics such as azithromycin are effective in treating trachoma, and outcomes are good when the disease is treated promptly. In areas where this disease is common, large public health efforts are focused on reducing transmission by teaching people how to avoid the risks of the infection.

![Figure 21.23](credit b: modification of work by Otis Historical Archives National Museum of Health & Medicine)

(a) If trachoma is not treated early with antibiotics, scarring on the eyelid can lead to trichiasis, a condition in which the eyelashes turn inward. (b) Trichiasis leads to blindness if not corrected by surgery, as shown here. (credit b: modification of work by Otis Historical Archives National Museum of Health & Medicine)

**Check Your Understanding**

- Why is trachoma rare in the United States?

**Micro Connections**

**SAFE Eradication of Trachoma**

Though uncommon in the United States and other developed nations, trachoma is the leading cause of preventable blindness worldwide, with more than 4 million people at immediate risk of blindness from trichiasis. The vast majority of those affected by trachoma live in Africa and the Middle East in isolated rural or desert communities with limited access to clean water and sanitation. These conditions provide an environment
conducive to the growth and spread of *Chlamydia trachomatis*, the bacterium that causes trachoma, via wastewater and eye-seeking flies.

In response to this crisis, recent years have seen major public health efforts aimed at treating and preventing trachoma. The Alliance for Global Elimination of Trachoma by 2020 (GET 2020), coordinated by the World Health Organization (WHO), promotes an initiative dubbed “SAFE,” which stands for “Surgery, Antibiotics, Facial cleanliness, and Environmental improvement.” The Carter Center, a charitable, nongovernment organization led by former US President Jimmy Carter, has partnered with the WHO to promote the SAFE initiative in six of the most critically impacted nations in Africa. Through its Trachoma Control Program, the Carter Center trains and equips local surgeons to correct trichiasis and distributes antibiotics to treat trachoma. The program also promotes better personal hygiene through health education and improves sanitation by funding the construction of household latrines. This reduces the prevalence of open sewage, which provides breeding grounds for the flies that spread trachoma.

**Bacterial Keratitis**

Keratitis can have many causes, but bacterial keratitis is most frequently caused by *Staphylococcus epidermidis* and/or *Pseudomonas aeruginosa*. Contact lens users are particularly at risk for such an infection because *S. epidermidis* and *P. aeruginosa* both adhere well to the surface of the lenses.

Risk of infection can be greatly reduced by proper care of contact lenses and avoiding wearing lenses overnight. Because the infection can quickly lead to blindness, prompt and aggressive treatment with antibiotics is important. The causative agent may be identified using bacterial cultures, Gram stain, and diagnostic biochemical, antigenic, or nucleic acid profile tests of the isolated pathogen.

**Check Your Understanding**

- Why are contact lens wearers at greater risk for developing keratitis?

**Biofilms and Infections of the Skin and Eyes**

When treating bacterial infections of the skin and eyes, it is important to consider that few such infections can be attributed to a single pathogen. While biofilms may develop in other parts of the body, they are especially relevant to skin infections (such as those caused by *S. aureus* or *P. aeruginosa*) because of their prevalence in chronic skin wounds. Biofilms develop when bacteria (and sometimes fungi) attach to a surface and produce extracellular polymeric substances (EPS) in which cells of multiple organisms may be embedded.

When a biofilm develops on a wound, it may interfere with the natural healing process as well as diagnosis and treatment.

Because biofilms vary in composition and are difficult to replicate in the lab, they are still not thoroughly understood. The extracellular matrix of a biofilm consists of polymers such as polysaccharides, extracellular DNA, proteins, and lipids, but the exact makeup varies. The organisms living within the extracellular matrix may include familiar pathogens as well as other bacteria that do not grow well in cultures (such as numerous obligate anaerobes). This presents challenges when culturing samples from infections that involve a biofilm. Because only some species grow *in vitro*, the culture may contain only a subset of the bacterial species involved in the infection.

Biofilms confer many advantages to the resident bacteria. For example, biofilms can facilitate attachment to surfaces on or in the host organism (such as wounds), inhibit phagocytosis, prevent the invasion of neutrophils, and sequester host antibodies. Additionally, biofilms can provide a level of antibiotic resistance not found in the isolated cells and colonies that are typical of laboratory cultures. The extracellular matrix provides a physical barrier to antibiotics, shielding the target cells from exposure. Moreover, cells within a biofilm may differentiate to create subpopulations of dormant cells called persister cells. Nutrient limitations deep within a biofilm add another level of resistance, as stress responses can slow metabolism and increase drug resistance.
Bacterial Infections of the Eyes

A number of bacteria are able to cause infection when introduced to the mucosa of the eye. In general, bacterial eye infections can lead to inflammation, irritation, and discharge, but they vary in severity. Some are typically short-lived, and others can become chronic and lead to permanent eye damage. Prevention requires limiting exposure to contagious pathogens. When infections do occur, prompt treatment with antibiotics can often limit or prevent permanent damage. Figure 21.24 summarizes the characteristics of some common bacterial infections of the eyes.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Antimicrobial Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute bacterial conjunctivitis</td>
<td>Haemophilus influenzae</td>
<td>Inflammation of conjunctiva with purulent discharge</td>
<td>Exposure to secretions from infected individuals</td>
<td>Broad-spectrum topical antibiotics</td>
</tr>
<tr>
<td>Bacterial keratitis</td>
<td>Staphylococcus epidermidis, Pseudomonas aeruginosa</td>
<td>Redness and irritation of eye, blurred vision, sensitivity to light; progressive corneal scarring, which can lead to blindness</td>
<td>Exposure to pathogens on contaminated contact lenses</td>
<td>Antibiotic eye drops (e.g., with fluoroquinolones)</td>
</tr>
<tr>
<td>Neonatal conjunctivitis</td>
<td>Chlamydia trachomatis, Neisseria gonorrhoeae</td>
<td>Inflammation of conjunctiva, purulent discharge, scarring and perforation of cornea; may lead to blindness</td>
<td>Neonate exposed to pathogens in birth canal of mother with chlamydia or gonorrhea</td>
<td>Erythromycin</td>
</tr>
<tr>
<td>Trachoma (granular conjunctivitis)</td>
<td>C. trachomatis</td>
<td>Chronic conjunctivitis, trichiasis, scarring, blindness</td>
<td>Contact with infected individuals or contaminated fomites; transmission by eye-seeking flies</td>
<td>Azithromycin</td>
</tr>
</tbody>
</table>

Figure 21.24

21.3 Viral Infections of the Skin and Eyes

Learning Objectives

- Identify the most common viruses associated with infections of the skin and eyes
- Compare the major characteristics of specific viral diseases affecting the skin and eyes

Until recently, it was thought that the normal microbiota of the body consisted primarily of bacteria and some fungi. However, in addition to bacteria, the skin is colonized by viruses, and recent studies suggest that Papillomaviridae, Polyomaviridae and Circoviridae also contribute to the normal skin microbiota. However, some viruses associated with skin are pathogenic, and these viruses can cause diseases with a wide variety of presentations.

Numerous types of viral infections cause rashes or lesions on the skin; however, in many cases these skin conditions result from infections that originate in other body systems. In this chapter, we will limit the discussion to viral skin
infections that use the skin as a portal of entry. Later chapters will discuss viral infections such as chickenpox, measles, and rubella—diseases that cause skin rashes but invade the body through portals of entry other than the skin.

**Papillomas**

Papillomas (warts) are the expression of common skin infections by human papillomavirus (HPV) and are transmitted by direct contact. There are many types of HPV, and they lead to a variety of different presentations, such as common warts, plantar warts, flat warts, and filiform warts. HPV can also cause sexually-transmitted genital warts, which will be discussed in *Urogenital System Infections*. Vaccination is available for some strains of HPV.

Common warts tend to develop on fingers, the backs of hands, and around nails in areas with broken skin. In contrast, plantar warts (also called foot warts) develop on the sole of the foot and can grow inwards, causing pain and pressure during walking. Flat warts can develop anywhere on the body, are often numerous, and are relatively smooth and small compared with other wart types. Filiform warts are long, threadlike warts that grow quickly.

In some cases, the immune system may be strong enough to prevent warts from forming or to eradicate established warts. However, treatment of established warts is typically required. There are many available treatments for warts, and their effectiveness varies. Common warts can be frozen off with liquid nitrogen. Topical applications of salicylic acid may also be effective. Other options are electrosurgery (burning), curettage (cutting), excision, painting with cantharidin (which causes the wart to die so it can more easily be removed), laser treatments, treatment with bleomycin, chemical peels, and immunotherapy (Figure 21.25).

![Figure 21.25](image)

(a) Multiple plantar warts have grown on this toe. (b) A filiform wart has grown on this eyelid.

**Oral Herpes**

Another common skin virus is herpes simplex virus (HSV). HSV has historically been divided into two types, HSV-1 and HSV-2. HSV-1 is typically transmitted by direct oral contact between individuals, and is usually associated with oral herpes. HSV-2 is usually transmitted sexually and is typically associated with genital herpes. However, both HSV-1 and HSV-2 are capable of infecting any mucous membrane, and the incidence of genital HSV-1 and oral HSV-2 infections has been increasing in recent years. In this chapter, we will limit our discussion to infections caused by HSV-1; HSV-2 and genital herpes will be discussed in *Urogenital System Infections*.

Infection by HSV-1 commonly manifests as cold sores or fever blisters, usually on or around the lips (Figure 21.26). HSV-1 is highly contagious, with some studies suggesting that up to 65% of the US population is infected; however, many infected individuals are asymptomatic. Moreover, the virus can be latent for long periods, residing in the trigeminal nerve ganglia between recurring bouts of symptoms. Recurrence can be triggered by stress or
environmental conditions (systemic or affecting the skin). When lesions are present, they may blister, break open, and crust. The virus can be spread through direct contact, even when a patient is asymptomatic.

While the lips, mouth, and face are the most common sites for HSV-1 infections, lesions can spread to other areas of the body. Wrestlers and other athletes involved in contact sports may develop lesions on the neck, shoulders, and trunk. This condition is often called herpes gladiatorum. Herpes lesions that develop on the fingers are often called herpetic whitlow.

HSV-1 infections are commonly diagnosed from their appearance, although laboratory testing can confirm the diagnosis. There is no cure, but antiviral medications such as acyclovir, penciclovir, famiciclovir, and valacyclovir are used to reduce symptoms and risk of transmission. Topical medications, such as creams with n-docosanol and penciclovir, can also be used to reduce symptoms such as itching, burning, and tingling.

Figure 21.26  This cold sore was caused by HSV-1. (credit: Centers for Disease Control and Prevention)

Check Your Understanding

- What are the most common sites for the appearance of herpetic lesions?

Roseola and Fifth Disease

The viral diseases roseola and fifth disease are somewhat similar in terms of their presentation, but they are caused by different viruses. Roseola, sometimes called roseola infantum or exanthem subitum (“sudden rash”), is a mild viral infection usually caused by human herpesvirus-6 (HHV-6) and occasionally by HHV-7. It is spread via direct contact with the saliva or respiratory secretions of an infected individual, often through droplet aerosols. Roseola is very common in children, with symptoms including a runny nose, a sore throat, and a cough, along with (or followed by) a high fever (39.4 ºC). About three to five days after the fever subsides, a rash may begin to appear on the chest and abdomen. The rash, which does not cause discomfort, initially forms characteristic macules that are flat or papules that are firm and slightly raised; some macules or papules may be surrounded by a white ring. The rash may eventually spread to the neck and arms, and sometimes continues to spread to the face and legs. The diagnosis is generally made based upon observation of the symptoms. However, it is possible to perform serological tests to confirm the diagnosis. While treatment may be recommended to control the fever, the disease usually resolves without treatment within a week after the fever develops. For individuals at particular risk, such as those who are immunocompromised, the antiviral medication ganciclovir may be used.

Fifth disease (also known as erythema infectiosum) is another common, highly contagious illness that causes a distinct rash that is critical to diagnosis. Fifth disease is caused by parvovirus B19, and is transmitted by contact.

with respiratory secretions from an infected individual. Infection is more common in children than adults. While approximately 20% of individuals will be asymptomatic during infection,\(^{[16]}\) others will exhibit cold-like symptoms (headache, fever, and upset stomach) during the early stages when the illness is most infectious. Several days later, a distinct red facial rash appears, often called “slapped cheek” rash (Figure 21.27). Within a few days, a second rash may appear on the arms, legs, chest, back, or buttocks. The rash may come and go for several weeks, but usually disappears within seven to twenty-one days, gradually becoming lacy in appearance as it recedes.

In children, the disease usually resolves on its own without medical treatment beyond symptom relief as needed. Adults may experience different and possibly more serious symptoms. Many adults with fifth disease do not develop any rash, but may experience joint pain and swelling that lasts several weeks or months. Immunocompromised individuals can develop severe anemia and may need blood transfusions or immune globulin injections. While the rash is the most important component of diagnosis (especially in children), the symptoms of fifth disease are not always consistent. Serological testing can be conducted for confirmation.

![Figure 21.27](a) Roseola, a mild viral infection common in young children, generally begins with symptoms similar to a cold, followed by a pink, patchy rash that starts on the trunk and spreads outward. (b) Fifth disease exhibits similar symptoms in children, except for the distinctive “slapped cheek” rash that originates on the face.

**Check Your Understanding**

- Identify at least one similarity and one difference between roseola and fifth disease.

**Viral Conjunctivitis**

Like bacterial conjunctivitis viral infections of the eye can cause inflammation of the conjunctiva and discharge from the eye. However, viral conjunctivitis tends to produce a discharge that is more watery than the thick discharge associated with bacterial conjunctivitis. The infection is contagious and can easily spread from one eye to the other or to other individuals through contact with eye discharge.
Viral conjunctivitis is commonly associated with colds caused by adenoviruses; however, other viruses can also cause conjunctivitis. If the causative agent is uncertain, eye discharge can be tested to aid in diagnosis. Antibiotic treatment of viral conjunctivitis is ineffective, and symptoms usually resolve without treatment within a week or two.

**Herpes Keratitis**

Herpes infections caused by HSV-1 can sometimes spread to the eye from other areas of the body, which may result in keratoconjunctivitis. This condition, generally called herpes keratitis or herpetic keratitis, affects the conjunctiva and cornea, causing irritation, excess tears, and sensitivity to light. Deep lesions in the cornea may eventually form, leading to blindness. Because keratitis can have numerous causes, laboratory testing is necessary to confirm the diagnosis when HSV-1 is suspected; once confirmed, antiviral medications may be prescribed.

### Disease Profile

**Viral Infections of the Skin and Eyes**

A number of viruses can cause infections via direct contact with skin and eyes, causing signs and symptoms ranging from rashes and lesions to warts and conjunctivitis. All of these viral diseases are contagious, and while some are more common in children (fifth disease and roseola), others are prevalent in people of all ages (oral herpes, viral conjunctivitis, papillomas). In general, the best means of prevention is avoiding contact with infected individuals. Treatment may require antiviral medications; however, several of these conditions are mild and typically resolve without treatment. Figure 21.28 summarizes the characteristics of some common viral infections of the skin and eyes.
21.4 Mycoses of the Skin

Learning Objectives

- Identify the most common fungal pathogens associated with cutaneous and subcutaneous mycoses
- Compare the major characteristics of specific fungal diseases affecting the skin

Many fungal infections of the skin involve fungi that are found in the normal skin microbiota. Some of these fungi can cause infection when they gain entry through a wound; others mainly cause opportunistic infections in immunocompromised patients. Other fungal pathogens primarily cause infection in unusually moist environments that promote fungal growth; for example, sweaty shoes, communal showers, and locker rooms provide excellent breeding grounds that promote the growth and transmission of fungal pathogens.

Fungal infections, also called mycoses, can be divided into classes based on their invasiveness. Mycoses that cause superficial infections of the epidermis, hair, and nails, are called cutaneous mycoses. Mycoses that penetrate the epidermis and the dermis to infect deeper tissues are called subcutaneous mycoses. Mycoses that spread throughout the body are called systemic mycoses.
Tineas

A group of cutaneous mycoses called tineas are caused by dermatophytes, fungal molds that require keratin, a protein found in skin, hair, and nails, for growth. There are three genera of dermatophytes, all of which can cause cutaneous mycoses: Trichophyton, Epidermophyton, and Microsporum. Tineas on most areas of the body are generally called ringworm, but tineas in specific locations may have distinctive names and symptoms (see Table 21.3 and Figure 21.29). Keep in mind that these names—even though they are Latinized—refer to locations on the body, not causative organisms. Tineas can be caused by different dermatophytes in most areas of the body.

Some Common Tineas and Location on the Body

<table>
<thead>
<tr>
<th>Tinea corporis (ringworm)</th>
<th>Body</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinea capitis (ringworm)</td>
<td>Scalp</td>
</tr>
<tr>
<td>Tinea pedis (athlete's foot)</td>
<td>Feet</td>
</tr>
<tr>
<td>Tinea barbae (barber's itch)</td>
<td>Beard</td>
</tr>
<tr>
<td>Tinea cruris (jock itch)</td>
<td>Groin</td>
</tr>
<tr>
<td>Tinea unguium (onychomycosis)</td>
<td>Toenails, fingernails</td>
</tr>
</tbody>
</table>

Table 21.3

Dermatophytes are commonly found in the environment and in soils and are frequently transferred to the skin via contact with other humans and animals. Fungal spores can also spread on hair. Many dermatophytes grow well in moist, dark environments. For example, tinea pedis (athlete’s foot) commonly spreads in public showers, and the causative fungi grow well in the dark, moist confines of sweaty shoes and socks. Likewise, tinea cruris (jock itch) often spreads in communal living environments and thrives in warm, moist undergarments.

Tineas on the body (tinea corporis) often produce lesions that grow radially and heal towards the center. This causes the formation of a red ring, leading to the misleading name of ringworm recall the Clinical Focus case in The Eukaryotes of Microbiology.

Several approaches may be used to diagnose tineas. A Wood’s lamp (also called a black lamp) with a wavelength of 365 nm is often used. When directed on a tinea, the ultraviolet light emitted from the Wood’s lamp causes the fungal elements (spores and hyphae) to fluoresce. Direct microscopic evaluation of specimens from skin scrapings, hair, or nails can also be used to detect fungi. Generally, these specimens are prepared in a wet mount using a potassium hydroxide solution (10%–20% aqueous KOH), which dissolves the keratin in hair, nails, and skin cells to
allow for visualization of the hyphae and fungal spores. The specimens may be grown on Sabouraud dextrose CC (chloramphenicol/cyclohexamide), a selective agar that supports dermatophyte growth while inhibiting the growth of bacteria and saprophytic fungi (Figure 21.30). Macroscopic colony morphology is often used to initially identify the genus of the dermatophyte; identification can be further confirmed by visualizing the microscopic morphology using either a slide culture or a sticky tape prep stained with lactophenol cotton blue.

Various antifungal treatments can be effective against tineas. Allylamine ointments that include terbinafine are commonly used; miconazole and clotrimazole are also available for topical treatment, and griseofulvin is used orally.

Figure 21.30  To diagnose tineas, the dermatophytes may be grown on a Sabouraud dextrose CC agar plate. This culture contains a strain of \textit{Trichophyton rubrum}, one of the most common causes of tineas on various parts of the body. (credit: Centers for Disease Control and Prevention)

Check Your Understanding

• Why are tineas, caused by fungal molds, often called ringworm?

\textbf{Cutaneous Aspergillosis}

Another cause of cutaneous mycoses is \textit{Aspergillus}, a genus consisting of molds of many different species, some of which cause a condition called aspergillosis. Primary cutaneous aspergillosis, in which the infection begins in the skin, is rare but does occur. More common is secondary cutaneous aspergillosis, in which the infection begins in the respiratory system and disseminates systemically. Both primary and secondary cutaneous aspergillosis result in distinctive eschars that form at the site or sites of infection (Figure 21.31). Pulmonary aspergillosis will be discussed more thoroughly in \textit{Respiratory Mycoses).
Primary cutaneous aspergillosis usually occurs at the site of an injury and is most often caused by *Aspergillus fumigatus* or *Aspergillus flavus*. It is usually reported in patients who have had an injury while working in an agricultural or outdoor environment. However, opportunistic infections can also occur in health-care settings, often at the site of intravenous catheters, venipuncture wounds, or in association with burns, surgical wounds, or occlusive dressing. After candidiasis, aspergillosis is the second most common hospital-acquired fungal infection and often occurs in immunocompromised patients, who are more vulnerable to opportunistic infections.

Cutaneous aspergillosis is diagnosed using patient history, culturing, histopathology using a skin biopsy. Treatment involves the use of antifungal medications such as voriconazole (preferred for invasive aspergillosis), itraconazole, and amphotericin B if itraconazole is not effective. For immunosuppressed individuals or burn patients, medication may be used and surgical or immunotherapy treatments may be needed.

**Check Your Understanding**

- Identify the sources of infection for primary and secondary cutaneous aspergillosis.

**Candidiasis of the Skin and Nails**

*Candida albicans* and other yeasts in the genus *Candida* can cause skin infections referred to as cutaneous candidiasis. *Candida* spp. are sometimes responsible for *intertrigo*, a general term for a rash that occurs in a skin fold, or other localized rashes on the skin. *Candida* can also infect the nails, causing them to become yellow and harden (Figure 21.32).
Candidiasis of the skin and nails is diagnosed through clinical observation and through culture, Gram stain, and KOH wet mounts. Susceptibility testing for anti-fungal agents can also be done. Cutaneous candidiasis can be treated with topical or systemic azole antifungal medications. Because candidiasis can become invasive, patients suffering from HIV/AIDS, cancer, or other conditions that compromise the immune system may benefit from preventive treatment. Azoles, such as clotrimazole, econazole, fluconazole, ketoconazole, and miconazole; nystatin; terbinafine; and naftifine may be used for treatment. Long-term treatment with medications such as itraconazole or ketoconazole may be used for chronic infections. Repeat infections often occur, but this risk can be reduced by carefully following treatment recommendations, avoiding excessive moisture, maintaining good health, practicing good hygiene, and having appropriate clothing (including footwear).

*Candida* also causes infections in other parts of the body besides the skin. These include vaginal yeast infections (see *Fungal Infections of the Reproductive System*) and oral thrush (see *Microbial Diseases of the Mouth and Oral Cavity*).

### Check Your Understanding

- What are the signs and symptoms of candidiasis of the skin and nails?

### Sporotrichosis

Whereas cutaneous mycoses are superficial, subcutaneous mycoses can spread from the skin to deeper tissues. In temperate regions, the most common subcutaneous mycosis is a condition called *sporotrichosis*, caused by the fungus *Sporothrix schenkii* and commonly known as rose gardener’s disease or rose thorn disease (recall *Case in Point: Every Rose Has Its Thorn*). Sporotrichosis is often contracted after working with soil, plants, or timber, as the fungus can gain entry through a small wound such as a thorn-prick or splinter. Sporotrichosis can generally be avoided by wearing gloves and protective clothing while gardening and promptly cleaning and disinfecting any wounds sustained during outdoor activities.

*Sporothrix* infections initially present as small ulcers in the skin, but the fungus can spread to the lymphatic system and sometimes beyond. When the infection spreads, nodules appear, become necrotic, and may ulcerate. As more lymph nodes become affected, abscesses and ulceration may develop over a larger area (often on one arm or hand). In severe cases, the infection may spread more widely throughout the body, although this is relatively uncommon.
Sporothrix infection can be diagnosed based upon histologic examination of the affected tissue. Its macroscopic morphology can be observed by culturing the mold on potato dextrose agar, and its microscopic morphology can be observed by staining a slide culture with lactophenol cotton blue. Treatment with itraconazole is generally recommended.

**Check Your Understanding**

- Describe the progression of a Sporothrix schenkii infection.

**Disease Profile**

**Mycoses of the Skin**

Cutaneous mycoses are typically opportunistic, only able to cause infection when the skin barrier is breached through a wound. Tineas are the exception, as the dermatophytes responsible for tineas are able to grow on skin, hair, and nails, especially in moist conditions. Most mycoses of the skin can be avoided through good hygiene and proper wound care. Treatment requires antifungal medications. Figure 21.33 summarizes the characteristics of some common fungal infections of the skin.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Antimicrobial Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillosis (cutaneous)</td>
<td>Aspergillus fumigatus, Aspergillus flavus</td>
<td>Distinctive eschars at site(s) of infection</td>
<td>Entry via wound (primary cutaneous aspergillosis) or via the respiratory system (secondary cutaneous aspergillosis); commonly a hospital-acquired infection</td>
<td>Itraconazole, voriconazole, amphotericin B</td>
</tr>
<tr>
<td>Candidiasis (cutaneous)</td>
<td>Candida albicans</td>
<td>Intertrigo, localized rash, yellowing of nails</td>
<td>Overgrowth of normal skin microbiota, especially in moist, dark areas</td>
<td>Azoles</td>
</tr>
<tr>
<td>Sporotrichosis (rose gardener’s disease)</td>
<td>Sporothrix schenkii</td>
<td>Subcutaneous ulcers and abscesses; may spread to a large area, e.g., hand or arm</td>
<td>Entry via thorn prick or other wound</td>
<td>Itraconazole</td>
</tr>
<tr>
<td>Tineas</td>
<td>Trichophyton spp., Epidermophyton spp., Microsporum spp.</td>
<td>Itchy, ring-like lesions (ringworm) at sites of infection</td>
<td>Contact with dermatophytic fungi, especially in warm, moist environments conducive to fungal growth</td>
<td>Terbinafine, miconazole, clotrimazole, griseofulvin</td>
</tr>
</tbody>
</table>

*Figure 21.33*
21.5 Protozoan and Helminthic Infections of the Skin and Eyes

Learning Objectives

• Identify two parasites that commonly cause infections of the skin and eyes
• Identify the major characteristics of specific parasitic diseases affecting the skin and eyes

Many parasitic protozoans and helminths use the skin or eyes as a portal of entry. Some may physically burrow into the skin or the mucosa of the eye; others breach the skin barrier by means of an insect bite. Still others take advantage of a wound to bypass the skin barrier and enter the body, much like other opportunistic pathogens. Although many parasites enter the body through the skin, in this chapter we will limit our discussion to those for which the skin or eyes are the primary site of infection. Parasites that enter through the skin but travel to a different site of infection will be covered in other chapters. In addition, we will limit our discussion to microscopic parasitic infections of the skin and eyes. Macroscopic parasites such as lice, scabies, mites, and ticks are beyond the scope of this text.

Acanthamoeba Infections

*Acanthamoeba* is a genus of free-living protozoan amoebae that are common in soils and unchlorinated bodies of fresh water. (This is one reason why some swimming pools are treated with chlorine.) The genus contains a few parasitic species, some of which can cause infections of the eyes, skin, and nervous system. Such infections can sometimes travel and affect other body systems. Skin infections may manifest as abscesses, ulcers, and nodules. When acanthamoebae infect the eye, causing inflammation of the cornea, the condition is called *Acanthamoeba* keratitis. Figure 21.34 illustrates the *Acanthamoeba* life cycle and various modes of infection.

While *Acanthamoeba* keratitis is initially mild, it can lead to severe corneal damage, vision impairment, or even blindness if left untreated. Similar to eye infections involving *P. aeruginosa*, *Acanthamoeba* poses a much greater risk to wearers of contact lenses because the amoeba can thrive in the space between contact lenses and the cornea. Prevention through proper contact lens care is important. Lenses should always be properly disinfected prior to use, and should never be worn while swimming or using a hot tub.

*Acanthamoeba* can also enter the body through other pathways, including skin wounds and the respiratory tract. It usually does not cause disease except in immunocompromised individuals; however, in rare cases, the infection can spread to the nervous system, resulting in a usually fatal condition called granulomatous amoebic encephalitis (GAE) (see *Fungal and Parasitic Diseases of the Nervous System*). Disseminated infections, lesions, and *Acanthamoeba* keratitis can be diagnosed by observing symptoms and examining patient samples under the microscope to view the parasite. Skin biopsies may be used.

*Acanthamoeba* keratitis is difficult to treat, and prompt treatment is necessary to prevent the condition from progressing. The condition generally requires three to four weeks of intensive treatment to resolve. Common treatments include topical antiseptics (e.g., polyhexamethylene biguanide, chlorhexidine, or both), sometimes with painkillers or corticosteroids (although the latter are controversial because they suppress the immune system, which can worsen the infection). Azoles are sometimes prescribed as well. Advanced cases of keratitis may require a corneal transplant to prevent blindness.
Acanthamoeba spp. are waterborne parasites very common in unchlorinated aqueous environments. As shown in this life cycle, Acanthamoeba cysts and trophozoites are both capable of entering the body through various routes, causing infections of the eye, skin, and central nervous system. (credit: modification of work by Centers for Disease Control and Prevention)

Figure 21.34

(a) An Acanthamoeba cyst. (b) An Acanthamoeba trophozoite (c) The eye of a patient with Acanthamoeba keratitis. The fluorescent color, which is due to sodium fluorescein application, highlights significant damage to the cornea and vascularization of the surrounding conjunctiva. (credit a: modification of work by Centers for Disease Control and Prevention; credit b, c: modification of work by Jacob Lorenzo-Morales, Naveed A Kahn and Julia Walochnik)

Check Your Understanding

- How are Acanthamoeba infections acquired?
Loiasis

The helminth *Loa loa*, also known as the African eye worm, is a nematode that can cause loiasis, a disease endemic to West and Central Africa (Figure 21.36). The disease does not occur outside that region except when carried by travelers. There is evidence that individual genetic differences affect susceptibility to developing loiasis after infection by the *Loa loa* worm. Even in areas in which *Loa loa* worms are common, the disease is generally found in less than 30% of the population.[17] It has been suggested that travelers who spend time in the region may be somewhat more susceptible to developing symptoms than the native population, and the presentation of infection may differ.[18]

The parasite is spread by deerflies (genus *Chrysops*), which can ingest the larvae from an infected human via a blood meal (Figure 21.36). When the deerfly bites other humans, it deposits the larvae into their bloodstreams. After about five months in the human body, some larvae develop into adult worms, which can grow to several centimeters in length and live for years in the subcutaneous tissue of the host.

The name “eye worm” alludes to the visible migration of worms across the conjunctiva of the eye. Adult worms live in the subcutaneous tissues and can travel at about 1 cm per hour. They can often be observed when migrating through the eye, and sometimes under the skin; in fact, this is generally how the disease is diagnosed. It is also possible to test for antibodies, but the presence of antibodies does not necessarily indicate a current infection; it only means that the individual was exposed at some time. Some patients are asymptomatic, but in others the migrating worms can cause fever and areas of allergic inflammation known as Calabar swellings. Worms migrating through the conjunctiva can cause temporary eye pain and itching, but generally there is no lasting damage to the eye. Some patients experience a range of other symptoms, such as widespread itching, hives, and joint and muscle pain.

Worms can be surgically removed from the eye or the skin, but this treatment only relieves discomfort; it does not cure the infection, which involves many worms. The preferred treatment is diethylcarbamazine, but this medication produces severe side effects in some individuals, such as brain inflammation and possible death in patients with heavy infections. Albendazole is also sometimes used if diethylcarbamazine is not appropriate or not successful. If left untreated for many years, loiasis can damage the kidneys, heart, and lungs, though these symptoms are rare.

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Figure 21.36  This *Loa loa* worm, measuring about 55 mm long, was extracted from the conjunctiva of a patient with loiasis. The *Loa loa* has a complex life cycle. Biting deerflies native to the rain forests of Central and West Africa transmit the larvae between humans. (credit a: modification of work by Eballe AO, Epée E, Koki G, Owono D, Mvogo
Describe the most common way to diagnose loiasis.

See a video (https://openstax.org/l/22microfilvid) of a live *Loa loa* microfilaria under the microscope.

The protozoan *Acanthamoeba* and the helminth *Loa loa* are two parasites capable of causing infections of the skin and eyes. Figure 21.37 summarizes the characteristics of some common fungal infections of the skin.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Pathogen</th>
<th>Signs and Symptoms</th>
<th>Transmission</th>
<th>Antimicrobial Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acanthamoeba</em> keratitis</td>
<td><em>Acanthamoeba</em></td>
<td>Inflammation and damage to cornea; vision impairment or blindness</td>
<td>Exposure to pathogens in contaminated water or on contact lenses</td>
<td>Polyhexamethylene biguanide, chlorhexidine, azoles</td>
</tr>
<tr>
<td>Loiasis</td>
<td><em>Loa loa</em></td>
<td>Recurring fever and localized Calabar swelling, itching, and skin or eye pain during subcutaneous migration of worms</td>
<td>Larvae transmitted between humans by deerfly vector</td>
<td>Diethylcarbamazine, albendazole</td>
</tr>
</tbody>
</table>

**Summary**

**21.1 Anatomy and Normal Microbiota of the Skin and Eyes**

- Human skin consists of two main layers, the **epidermis** and **dermis**, which are situated on top of the **hypodermis**, a layer of connective tissue.
- The skin is an effective physical barrier against microbial invasion.
• The skin’s relatively dry environment and normal microbiota discourage colonization by transient microbes.
• The skin’s normal microbiota varies from one region of the body to another.
• The conjunctiva of the eye is a frequent site for microbial infection, but deeper eye infections are less common; multiple types of conjunctivitis exist.

21.2 Bacterial Infections of the Skin and Eyes
• *Staphylococcus* and *Streptococcus* cause many different types of skin infections, many of which occur when bacteria breach the skin barrier through a cut or wound.
• *S. aureus* are frequently associated with purulent skin infections that manifest as *folliculitis, furuncles,* or *carbuncles.* *S. aureus* is also a leading cause of staphylococcal scalded skin syndrome (SSSS).
• *S. aureus* is generally drug resistant and current MRSA strains are resistant to a wide range of antibiotics.
• Community-acquired and hospital-acquired staphylococcal infections are an ongoing problem because many people are asymptomatic carriers.
• **Group A streptococci** (*GAS*), *S. pyogenes,* is often responsible for cases of *cellulitis,* *erysipelas,* and *erythema nodosum.* GAS are also one of many possible causes of *necrotizing fasciitis.*
• *P. aeruginosa* is often responsible for infections of the skin and eyes, including wound and burn infections, *hot tub rash,* *otitis externa,* and bacterial *keratitis.*
• *Acne* is a common skin condition that can become more inflammatory when *Propionibacterium acnes* infects hair follicles and pores clogged with dead skin cells and sebum.
• Cutaneous *anthrax* occurs when *Bacillus anthracis* breaches the skin barrier. The infection results in a localized black *eschar* on skin. Anthrax can be fatal if *B. anthracis* spreads to the bloodstream.
• Common bacterial *conjunctivitis* is often caused by *Haemophilus influenzae* and usually resolves on its own in a few days. More serious forms of conjunctivitis include gonococcal *ophthalmia neonatorum,* inclusion *conjunctivitis* (chlamydial), and *trachoma,* all of which can lead to blindness if untreated.
• *Keratitis* is frequently caused by *Staphylococcus epidermidis* and/or *Pseudomonas aeruginosa,* especially among contact lens users, and can lead to blindness.
• Biofilms complicate the treatment of wound and eye infections because pathogens living in biofilms can be difficult to treat and eliminate.

21.3 Viral Infections of the Skin and Eyes
• *Papillomas* (warts) are caused by human papillomaviruses.
• *Herpes simplex virus* (especially HSV-1) mainly causes *oral herpes,* but lesions can appear on other areas of the skin and mucous membranes.
• *Roseola* and *fifth disease* are common viral illnesses that cause skin rashes; roseola is caused by HHV-6 and HHV-7 while fifth disease is caused by parvovirus 19.
• *Viral conjunctivitis* is often caused by adenoviruses and may be associated with the common cold. *Herpes keratitis* is caused by herpesviruses that spread to the eye.

21.4 Mycoses of the Skin
• *Mycoses* can be *cutaneous,* *subcutaneous,* or *systemic.*
• Common cutaneous mycoses include *tineas* caused by *dermatophytes* of the genera *Trichophyton,* *Epidermophyton,* and *Microsporum.* *Tinea corporis* is called *ringworm.* Tineas on other parts of the body have names associated with the affected body part.
• *Aspergillosis* is a fungal disease caused by molds of the genus *Aspergillus.* Primary cutaneous aspergillosis enters through a break in the skin, such as the site of an injury or a surgical wound; it is a common hospital-acquired infection. In secondary cutaneous aspergillosis, the fungus enters via the respiratory system and disseminates systemically, manifesting in lesions on the skin.
• The most common subcutaneous mycosis is *sporotrichosis* (rose gardener’s disease), caused by *Sporothrix schenckii.*
• Yeasts of the genus *Candida* can cause opportunistic infections of the skin called *candidiasis*, producing *intertrigo*, localized rashes, or yellowing of the nails.

### 21.5 Protozoan and Helminthic Infections of the Skin and Eyes

• The protozoan *Acanthamoeba* and the helminth *Loa loa* are two parasites that can breach the skin barrier, causing infections of the skin and eyes.

• *Acanthamoeba keratitis* is a parasitic infection of the eye that often results from improper disinfection of contact lenses or swimming while wearing contact lenses.

• *Loiasis*, or eye worm, is a disease endemic to Africa that is caused by parasitic worms that infect the subcutaneous tissue of the skin and eyes. It is transmitted by deerfly vectors.

### Review Questions

**Multiple Choice**

1. ___________ glands produce a lipid-rich substance that contains proteins and minerals and protects the skin.
   a. Sweat
   b. Mammary
   c. Sebaceous
   d. Endocrine

2. Which layer of skin contains living cells, is vascularized, and lies directly above the hypodermis?
   a. the stratum corneum
   b. the dermis
   c. the epidermis
   d. the conjunctiva

3. *Staphylococcus aureus* is most often associated with being
   a. coagulase-positive.
   b. coagulase-negative.
   c. catalase-negative.
   d. gram-negative

4. M protein is produced by
   a. *Pseudomonas aeruginosa*
   b. *Staphylococcus aureus*
   c. *Propionibacterium acnes*
   d. *Streptococcus pyogenes*

5. ___________ is a major cause of preventable blindness that can be reduced through improved sanitation.
   a. Ophthalmia neonatorum
   b. Keratitis
   c. Trachoma
   d. Cutaneous anthrax

6. Which species is frequently associated with nosocomial infections transmitted via medical devices inserted into the body?
   a. *Staphylococcus epidermidis*
   b. *Streptococcus pyogenes*
   c. *Propionibacterium acnes*
   d. *Bacillus anthracis*

7. Warts are caused by
   a. human papillomavirus.
   b. herpes simplex virus.
   c. adenoviruses.
   d. parvovirus B19.

8. Which of these viruses can spread to the eye to cause a form of keratitis?
   a. human papillomavirus
   b. herpes simplex virus 1
   c. parvovirus 19
   d. circoviruses

9. Cold sores are associated with:
   a. human papillomavirus
   b. roseola
   c. herpes simplex viruses
   d. human herpesvirus 6

10. Which disease is usually self-limiting but is most commonly treated with ganciclovir if medical treatment is needed?
    a. roseola
    b. oral herpes
    c. papillomas
    d. viral conjunctivitis

11. Adenoviruses can cause:
    a. viral conjunctivitis
    b. herpetic conjunctivitis
    c. papillomas
    d. oral herpes
12. __________ is a superficial fungal infection found on the head.
   a. Tinea cruris
   b. Tinea capitis
   c. Tinea pedis
   d. Tinea corporis

13. For what purpose would a health-care professional use a Wood’s lamp for a suspected case of ringworm?
   a. to prevent the rash from spreading
   b. to kill the fungus
   c. to visualize the fungus
   d. to examine the fungus microscopically

14. Sabouraud dextrose agar CC is selective for:
   a. all fungi
   b. non-saprophytic fungi
   c. bacteria
   d. viruses

15. The first-line recommended treatment for sporotrichosis is:
   a. itraconazole
   b. clindamycin
   c. amphotericin
   d. nystatin

16. Which of the following is most likely to cause an Acanthamoeba infection?
   a. swimming in a lake while wearing contact lenses
   b. being bitten by deerflies in Central Africa
   c. living environments in a college dormitory with communal showers
   d. participating in a contact sport such as wrestling

17. The parasitic Loa loa worm can cause great pain when it:
   a. moves through the bloodstream
   b. exits through the skin of the foot
   c. travels through the conjunctiva
   d. enters the digestive tract

18. A patient tests positive for Loa loa antibodies. What does this test indicate?
   a. The individual was exposed to Loa loa at some point.
   b. The individual is currently suffering from loiasis.
   c. The individual has never been exposed to Loa loa.
   d. The individual is immunosuppressed.

Fill in the Blank

20. The ________ is the outermost layer of the epidermis.

21. The mucous membrane that covers the surface of the eyeball and inner eyelid is called the ________.
22. A purulent wound produces ________.
23. Human herpesvirus 6 is the causative agent of ________.
24. The most common subcutaneous mycosis in temperate regions is ________.
25. Eye worm is another name for ________.
26. The ________ is the part of the eye that is damaged due to *Acanthamoeba* keratitis.

**Short Answer**

27. What is the role of keratin in the skin?
28. What are two ways in which tears help to prevent microbial colonization?
29. Which label indicates a sweat gland?

![Figure 21.38](credit: modification of work by National Cancer Institute)

30. How are leukocidins associated with pus production?
31. What is a good first test to distinguish streptococcal infections from staphylococcal infections?
32. Compare and contrast bacterial and viral conjunctivitis.
33. What yeasts commonly cause opportunistic infections?

**Critical Thinking**

34. Explain why it is important to understand the normal microbiota of the skin.
35. Besides the presence or absence of ulceration, how do acute ulcerative and nonulcerative blepharitis differ?
36. What steps might you recommend to a patient for reducing the risk of developing a fungal infection of the toenails?
37. Why might a traveler to a region with *Loa loa* worm have a greater risk of serious infection compared with people who live in the region?
38. What preventative actions might you recommend to a patient traveling to a region where loiasis is endemic?