Skin Antisepsis in Venipuncture

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Course Objectives

At the end of this course, you will be able to:

1. Discuss the development of antisepsis throughout history

2. Define various terms related to antisepsis

3. Understand the role of skin and its normal flora in bodily defense

4. Explain the significance of pathogenic microbes

5. Discuss the current guidelines for skin cleansing in venipuncture

6. List some common antiseptics used in venipuncture

Introduction: The Development of Antisepsis

Throughout history and across different cultures, healers have relied on various methods to treat wounds and prevent what would later come to be understood as infection. Early civilizations made use of remedies such as medicinal herbs, honey, milk, and beer. In ancient Greece the physician Hippocrates, widely regarded as the father of modern medicine, administered wine and vinegar to treat wounds. Although such remedies demonstrated a certain efficacy, it would be many centuries before science would discover the actual cause of infection.

In 1546 the Italian physician and scholar Girolamo Fracastoro theorized that tiny organisms were responsible for spreading infections, though at the time he had no means to prove their existence. What came to be known as the *Germ Theory of Disease* was initially rejected by the scientific community. Proof of microbial life finally came in the 1660s – 70s, when microscopic observations of fungi and bacteria were made by Robert Hooke and Antonie van Leeuwenhoek respectively. Scientists then came to accept the presence of living things which were invisible to the naked eye, although their link to infection was not yet realized.

In the 1840s Hungarian obstetrician Ignaz Semmelweis theorized that doctors and medical students who performed autopsies prior to delivering babies were transmitting some form of contaminated matter in their hands, causing mothers to die at childbirth. He was able to drastically reduce the number of deaths at his maternity clinic by having medical staff wash their hands with a chlorinated lime solution between patient contacts. Although this was an early example of the effectiveness of hand hygiene, it still did not establish the germ-killing property of chemical antiseptics.

More conclusive evidence emerged from the study of Microbiology in 1857. French scientist Louis Pasteur proved that microorganisms cause fermentation of fluids. He went on to devise a way of preventing bacterial contamination of wine and milk by using sufficient heat, a process now known as pasteurization. Pasteur suggested that applying germ-killing chemicals to a wound might likewise stop infection.

Joseph Lister, a Scottish surgeon, decided to apply Germ Theory in an effort to prevent surgical infections, with his findings published in 1867. He experimented with carbolic acid, using it as a chemical barrier (which he called an antiseptic) between a surgical wound and the environment. He went on to develop an antisepsis system: a set of techniques to prevent germs from coming into contact with a wound. This included chemically treating surgeons' hands, surgical materials, instruments, even the air around the patient with an antiseptic barrier. These methods resulted in decreased incidence of infections, and they gradually gained acceptance.

As Germ Theory became widely recognized, the field of Bacteriology emerged in the 1880s. Robert Koch, a German scientist, developed criteria for establishing the microbial causes of diseases such as tuberculosis and cholera. He demonstrated that dry heat and steam were just as effective at killing germs as chemical methods. Gustav Neuber, a German surgeon, used these findings to pioneer the sterilization and aseptic techniques seen in modern surgical procedures, including wearing sterile gowns, disinfection of surfaces, and autoclaved instruments. In 1886, Neuber opened what is considered the world's first aseptic hospital. Johns Hopkins Hospital became the first to use sterile operating gloves in 1894.

All of the research and innovation stemming from Germ Theory proved that infectious diseases are spread by microorganisms (also called microbes), particularly those which are pathogenic (disease-causing). These *pathogens* include bacteria, viruses, parasites, and fungi. More importantly, pioneering work by scientists and physicians demonstrated that infection could be prevented by eliminating pathogens from the body and its immediate environment. *Skin antisepsis*, the removal of microorganisms from the skin's surface, is part of the modern techniques they created which are now indispensable to infection prevention and control in the healthcare field.

The Skin, its Normal Flora, and Pathogenic Microbes

The skin is the body's largest organ, serving as a natural covering that separates the body from its outer environment. It is the first line of defense against injury, regulates temperature and moisture levels, contains pigment which blocks ultraviolet rays, and provides the sense of touch. The skin also defends the body by preventing the entry of pathogenic microorganisms. Aside from serving as a physical barrier, intact skin is acidic (i.e., has a low water content), contains specialized immune cells, and secretes antimicrobial substances. All of these properties contribute to warding off infection. (Swaney and Kalan)

Normal Flora

A host of bacteria, viruses and fungi have adapted to survive on the skin's surface and underlying layers. These *normal flora* naturally colonize the skin and are not harmful under ordinary circumstances. In fact, they compete with pathogens for available space and resources on the skin, (Dockery) and can also directly reduce the growth of specific skin pathogens. (Swaney and Kalan)

Staphylococcus epidermidis is the most common skin flora, comprising more than 90% of skin's resident bacteria. S. epidermidis has been found to augment the skin's defense mechanisms by stimulating specific immune cells and providing protection from harmful fungi. (NIH)

Pathogenic Microbes

However, normal flora can become harmful if they are allowed to pass through the skin. For example, *Staphylococcus epidermidis* becomes opportunistic and can cause serious complications when allowed to proliferate in the body. It is a known contaminant of medical prosthetic devices, central lines, and catheters, and is believed to be one of the most common causes of nosocomial (healthcare-related) infections in the U.S. (Lee and Anjum) Such infections can lead to prolonged hospital stays and higher healthcare costs.

Pathogenic skin microbes cause harmful infections when they invade body. The skin can be exposed to pathogens either by direct person-to-person contact, by indirect means, such as contact with contaminated surfaces, or by contaminated medical devices placed within the body. The most common bacterial skin pathogens are *Staphylococcus aureus* and group A β-hemolytic streptococci. (Aly)

Staphylococcus aureus is found on the skin and in the nose of about 30% of individuals (CDC). This bacteria can enter the body through breaks in the skin, causing a variety of localized skin infections. It can also cause more serious, potentially fatal systemic infections if it gains access to the bloodstream. Antibiotic resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) are much more difficult to treat and are a common cause of nosocomial infections. Staphylococcus aureus infections are associated with almost half a million hospitalizations and 50,000 deaths in the U.S. annually. (Schlecht, et. al.)

The Risk for Infection in Venipuncture

Any break in the skin can compromise its ability to defend against microbial invasion. Cuts and scrapes, especially those contaminated with dirt or other foreign matter, can serve as an entry point for disease-causing organisms if not adequately cleaned and treated.

Being an invasive procedure (i.e., a needle must puncture the skin and be inserted deep enough to penetrate a vein), venipuncture carries the risk of infection. Since microbes are ubiquitous on the skin's surface, they can contaminate the needle as it is being inserted, and gain access to the deeper tissues. Conditions such as phlebitis (inflammation of a vein) and cellulitis (diffuse inflammation of the subcutaneous connective tissue) are possible infectious complications of venipuncture. Both are considered to trigger serious local reactions, including pain, swelling, tenderness, and fever. Either of these conditions can lead to more severe complications if not adequately treated. (Insert pictures of phlebitis and cellulitis)

Cleansing the patient's skin prior to inserting the needle is part of standard practice in venipuncture to prevent infectious complications. Thorough and appropriate skin cleansing decreases the number of surface microbes, thereby decreasing the chance of contamination and infection. The U.S. Food and Drug Administration (FDA) states that "the use of antiseptics by health care providers in the hospital setting is considered an essential component of hospital infection control measures. Hospital-acquired infections can result in prolonged hospital stays, additional medical treatment, adverse clinical outcomes, and increased health care costs."

Contamination of Blood Cultures due to Inadequate Antisepsis

Blood cultures are commonly used to provide important diagnostic information to determine the presence of bacteremia. Blood cultures can become contaminated with microorganisms (from either the skin or the environment), which multiply inside the culture bottle, giving the false impression that these organisms are present in the blood. Contamination of blood cultures can lead to unnecessary antibiotic treatment and prolonged hospital stays. The frequency of contamination can be reduced by following established protocols for blood culture collection. The CLSI defines an acceptable contamination rate as less than 3% false positives with all blood cultures collected. When faced with a positive blood culture result, clinicians must decide whether the finding represents contamination or sepsis.

Terminology associated with Infection Control

The goal of infection control is to prevent the spread of infectious diseases (caused by microorganisms such as bacteria, viruses, parasites, and fungi) in the healthcare setting. Achieving this goal involves the use of precautions, equipment and procedures that can drastically decrease the presence of microorganisms on both living and non-living surfaces. This includes adequate cleansing of the skin especially prior to any medical procedure.

However, the degree of cleaning required depends on the type of procedure to be performed. The CDC states, "Because sterilization of all patient-care items is not necessary, health-care policies must identify, primarily on the basis of the items' intended use, whether *cleaning*, *disinfection*, or *sterilization* is indicated."

When discussing infection control, there are several terms used to describe the elimination of microbes. Sometimes they are used interchangeably due to their overlapping definitions. Nonetheless, it is important for healthcare practitioners to distinguish each. One important difference between these terms is whether a process is meant to be performed on living tissue or inanimate (non-living) surfaces.

- **Decontamination** removes pathogenic microorganisms from objects, so they are safe to handle, use, or discard. Cleaning, disinfection, and sterilization are all forms of decontamination.
- **Sanitizing** is the lowering the number of microbes on a surface to a safe level, using *cleaning, disinfecting, or both*. The level of safety is determined by public health standards or requirements in the workplace.
- **Cleaning** is the process of physically removing visible soil (organic and inorganic matter) and debris from the surfaces of objects. It includes the use of soap and water. Cleaning removes some microbes from the cleaned surface, but not all microbes are removed or killed.
- **Disinfection** is the use of chemicals which can kill microbes on inanimate surfaces and objects. Disinfectants must be allowed to maintain contact with the surface for a specified time in order to be effective. Disinfection does not necessarily remove dirt or completely eliminate germs from surfaces, including bacterial spores.
- **Sterilization** renders a surface completely free of microbial life, including the destruction of bacterial spores (dormant forms of bacteria which are

resistant to heat and common antimicrobials). It is the highest level of decontamination.

- **Antisepsis** is the removal of microbes from living surfaces, such as skin. It eliminates both pathogenic microbes and reduces the amount of normal flora. The goal of antisepsis is to minimize the risk of contamination and infection.
- **Asepsis** is an ideal situation in a medical procedure where the skin and all instruments to be used are completely free of microbes.

The chemicals used to remove and destroy microbes must likewise be differentiated:

- **Germicides** are chemical agents which can destroy microorganisms and include both disinfectants and antiseptics.
- **Antiseptics** are chemicals which can kill or slow the growth of microbes on living tissue, such as skin and mucous membranes (the moist inner lining of body cavities).
- **Disinfectants** are chemicals used to kill microbes on inanimate surfaces and instruments. They are classified based on the type and concentration of the chemical ingredient. Disinfectant preparations have stronger antimicrobial action than antiseptics, but also are more toxic and corrosive. For this reason they are not considered safe for use on skin.

Antiseptics Commonly Used in Venipuncture

The goal of skin antisepsis in venipuncture is to adequately cleanse the patient's skin to the point of preventing contamination and infectious complications. It is not possible for all microbial life to be eliminated from the draw site since roughly 20% of skin bacteria are found within the deeper layers and structures which antiseptics cannot reach. (Calfee and Farr) Therefore, total sterilization of the skin is not required for routine venipuncture, only a reduction in the number of both normal skin flora and pathogenic microbes. For collection procedures where microbial contamination is especially undesirable (such as blood culture collection), more rigorous skin cleansing and adherence to aseptic techniques are necessary.

There are several types of commercially available antiseptic preparations which have been approved by the FDA. Listed below are some commonly used antiseptics in venipuncture. They are included in the FDA's list of *health care antiseptics*, defined as "drug products intended for use by health care professionals in a hospital setting or other health care situations outside the hospital". The FDA further describes their use as patient *preoperative skin preparations*, "products that are used for preparation of the skin prior to an injection". These preparations can be used individually or in combination to achieve the desired level of skin antisepsis suitable for a procedure.

Alcohol

Alcohol is considered to have multiple toxic effects on the structure and metabolism of microorganisms, including bacteria, viruses, and fungi. Alcohol evaporates easily after being applied, with no significant antiseptic residue left on the skin. Antiseptics used in the healthcare setting contain at least 60 percent alcohol, a concentration at which bacteria are unable to grow. It is also difficult for microbes to develop resistance to alcohol due to its speed of action and multiple, nonspecific toxic effects. (FDA) Alcohol solutions such as 70% isopropyl alcohol (isopropanol) and 70% ethyl alcohol (ethanol) are the most commonly used antiseptics used for venipuncture and are applied using sterile prep pads or towelettes. (Insert pictures of alcohol prep pads)

The following guidelines are set by the Clinical Laboratory and Standards Institute (CLSI) for cleansing the venipuncture site with alcohol:

- The site chosen for blood draw is cleansed with friction using a commercially prepared alcohol pad or a clean gauze pad containing 70% isopropyl alcohol
- Cleansing the skin using back-and-forth friction is more superior than using concentric circular motion (Insert diagrams of skin cleansing using back-and-forth and circular motions)
- For optimal decontamination, let the alcohol completely air dry after being applied to the skin

- If alcohol is still wet when the needle is inserted, it can cause patient discomfort (i.e., burning sensation)
- If the venipuncture site is touched after being cleansed, it must be re-cleansed
- When collecting blood cultures, use 70% isopropyl alcohol for initial skin cleansing (and allow to air dry) and follow with a secondary cleanse using another antiseptic as prescribed by the facility

Although achieving skin antisepsis remains the common purpose of applying alcohol before venipuncture, the implementation of specific guidelines regarding alcohol and other antiseptics may vary among institutions. This is due in part to the lack of consensus on best practices, whether it be in published guidelines or manuals.

For example, the most common reasons for allowing alcohol to air dry is to achieve optimal disinfection and to avoid patient discomfort. Other reasons include the possibility of the antiseptic causing chemical phlebitis, if it enters the vein, (Rosenthal) or causing hemolysis (rupture of the red blood cells) should alcohol enter the needle and specimen tube. However, the recommendations stated for wait times sufficient for alcohol to fully dry can range from 15-60 seconds.

In an effort to provide evidenced-based data and promote best practices, investigators have tested the validity of long-held concepts of antisepsis. Certain studies have affirmed then current beliefs on alcohol use, while others have refuted them. For example, a 2016 study found that leaving alcohol-based antiseptic on the skin during venipuncture did not lead to hemolysis upon visual inspection. (Sarmah, et. al.)

Also, CLSI guidelines recommend that alcohol-based antiseptics be avoided when collecting specimens for blood alcohol testing, as it is believed the alcohol used to cleanse the skin may end up contaminating the specimen. Questionable specimen integrity can have serious implications, especially when blood alcohol testing is being used in workplace injury cases, insurance programs, employee drug screening, as well as law enforcement. (McCall) However, a 2017 study observed that alcohol-based antiseptic on the skin did not have any significant effect on results of plasma alcohol testing. (Lippi, et. al.)

Iodine

Elemental Iodine is the active antimicrobial component in iodine-containing antiseptics. Being a small molecule, iodine can easily infiltrate microorganisms and cause oxidizing damage to their key structures. It has a wide range of antimicrobial activity against bacteria, viruses, and fungi, as well as some bacterial spores. (Lepelletier, et. al.) Iodine-containing antiseptics must be given sufficient contact time with the skin to effectively kill microbes. Similar to alcohol, if venipuncture is performed before iodine has dried on the skin it can contaminate the blood specimen. Iodine contamination has been found to cause falsely increased levels of certain chemical components (i.e., potassium, phosphorus, or uric acid) in specimens. (Lippi, et. al.)

Iodine is only slightly soluble in water. When used as an antiseptic it is frequently dissolved in an organic solvent (such as a tincture) or chemically bound to a carrier substance (such as povidone) which serves as a reservoir that slowly releases iodine:

- Tincture of iodine is composed of 2% iodine and 2% potassium iodide in 47% ethyl alcohol. It must be left on skin for a minimum of 30 seconds to achieve optimal skin antisepsis. (CLSI) Tincture of iodine is commonly used to cleanse the skin prior to collecting blood cultures.
- Povidone-iodine is a stable water-soluble complex of 9-12% elemental iodine and povidone (a polymer substance which is composed of very large molecules). Povidone-iodine must be left on the skin for 1.5 to 2 minutes to achieve sufficient antisepsis. (CLSI) Its antimicrobial activity has been found to be superior to other iodine formulations. (PubChem) (Insert pictures of iodine-containing antiseptics) As Povidone is a water-based antiseptic, it is preferred for use in cleansing skin when blood alcohol testing is performed.

Since iodine can cause chemical irritation of the skin, as well as pass through the skin and be absorbed by the bloodstream, it must be sufficiently removed from the skin's surface following a procedure. Skin reactions to iodine are rare but can include blistering, crusting, irritation, itching, or reddening of the skin. (Mayo Clinic) Iodine is commonly contraindicated in patients who have shellfish allergies, although there has never been a valid explanation for this practice. Studies have shown no correlation between shellfish allergies and reactions to iodine. (Hinkle, et. al.)

Iodine antiseptics can stain both the skin and clothing. Upon completion of the procedure, skin stains can be removed with alcohol, while stains on clothing can be removed with diluted ammonia. (Mayo Clinic)

Chlorhexidine

Chlorhexidine gluconate is a chemical which carries a positive charge. This property allows it to kill microbes by damaging their (negatively charged) cell membrane; the subsequent leakage of intracellular components leads to microbial destruction. (PubChem)

Chlorhexidine has been found to be nearly twice as effective in preventing post-surgical infection as iodine. (Wade, et. al.) ChloraPrep, which is 2% chlorhexidine gluconate combined with 70% isopropyl alcohol, has been found to have significantly more persistent antimicrobial activity than either chlorhexidine or isopropanol used individually. (Hibbard, et. al.) Similar to tincture of iodine, ChloraPrep is commonly used for skin antisepsis prior to collecting blood cultures.

Chlorhexidine is administered using an applicator which is rubbed on the skin in a back-and-forth motion for 30 seconds, then allowed to air dry for 30 seconds. It is the recommended antiseptic for blood culture collection in older infants, children, and adults. Unlike iodine-containing preparations, it is not associated with allergic reactions and does not need to be cleaned off the skin after a blood draw. (CLSI) (Insert picture of chlorhexidine being applied) However, it is not recommended for use in children less than 2 months of age due to its potential for causing excessive skin irritation and the risk of increased skin absorption. (Mayo Clinic) Chlorhexidine is flammable and must be applied in a well-ventilated area.

Benzalkonium

Benzalkonium chloride is classified as a quaternary ammonium compound. This family of chemicals provide antimicrobial activity against bacteria, viruses, and fungi, primarily from their disruptive effect on the microbial cell membrane. Benzalkonium has many domestic, agricultural, and industrial applications as a preservative and disinfectant. As a topical antimicrobial, it is commercially available in the form of alcohol-free antiseptic wipes, towelettes, and adhesive bandages.

Since benzalkonium chloride is an aqueous preparation, it is considered alcohol-free. Along with povidone iodine, benzalkonium is a preferred antiseptic for skin cleansing prior to blood alcohol testing. Soaps and detergents can inactivate benzalkonium, so if such agents were used on the site beforehand, they must be adequately rinsed prior to the application of this antiseptic. (Sanofi)

There have been conflicting reports on the safety of benzalkonium use in humans. It has been found to cause skin irritation and, in rare cases, lead to skin allergy. The manufacturer for the product Zephiran cautions that when used for antisepsis, it should not be allowed to have prolonged contact with the patient's skin. Possibly due to benzalkonium's widespread commercial and domestic use, several pathogens (including MRSA) have been shown to develop resistance to it. Furthermore, benzalkonium's toxic effects on aquatic animals and their environment have been thoroughly documented. (Pereira and Tagkopoulos)

Conclusion

Venipuncture is one of the most common clinical procedures worldwide. Every year, over 1.4 billion venipunctures are performed in the U.S. alone. (Leipheimer, et. al.) Thanks to the development of aseptic techniques, along with the use of safe and effective topical antiseptics, the potential for infection from venipuncture is greatly reduced making it a relatively safe procedure.

Still, the pervasive nature of microorganisms poses a constant threat for infection, and healthcare practitioners must consistently follow antisepsis protocols. Sadly, the CDC has noted that in many countries, there is a "documented lack of compliance with established guidelines for disinfection and sterilization," and that “failure to comply with scientifically based guidelines has led to numerous outbreaks.” The ongoing lack of consensus regarding best practices in skin antisepsis may also be playing a role in such compliance issues. Special collection procedures, such as blood culture collection, have even more stringent antisepsis requirements, yet current recommendations on the type of antiseptic to use for secondary skin cleansing prior to drawing a blood culture vary by facility. Blood culture contamination is a common occurrence among patients suspected of having bloodstream infections and carries both the health-related and economic cost implications. Establishing the most optimum means of antisepsis would therefore be highly advantageous. Further study and the development of evidence-based guidelines will play a large role in standardizing antiseptic techniques and achieving the goals of infection control.

Quiz

Choose the best answer.

1. In the 1840s, Ignaz Semmelweis was able to reduce transmission of infection by

    a. proving that microorganisms cause fermentation

    b. using carbolic acid as an antiseptic barrier

    c. demonstrating that dry heat and steam could kill microbes

    d. asking medical staff to wash their hands between patients

2. Which of the following is the most common normal skin flora?

    a. Staphylococcus aureus

    b. Staphylococcus epidermidis

    c. Clostridium difficile

    d. None of the above

3. Phlebitis and cellulitis are

a. possible infectious complications of phlebotomy

b. preventable adequately cleansing the skin before venipuncture

c. both A and B

d. None of the above

4. The highest level of decontamination is

a. Sterilization

b. Disinfection

c. Cleaning

d. Sanitizing

5. What is the goal of skin antisepsis in venipuncture?

a. complete removal of all microbes from the skin's surface

b. reduction in the number of both normal skin flora and pathogenic microbes

c. removal of pathogenic microbes but leaving normal flora on the skin

d. none of the above

6. Which of the following statements is false?

a. Staphylococcus aureus is found on the skin and in the nose of about 30 percent of individuals

b. Staphylococcus aureus can cause serious infections if it gets into the bloodstream

c. Antibiotic-resistant Staphylococcus aureus is harder to treat and can lead to prolonged hospital stay

d. None of the above

7. Which of the following statements is false?

a. Germicides are chemicals which can destroy microorganisms

b. Germicides include both antiseptics and disinfectants

c. Disinfectants are chemicals used to kill microbes on skin

d. Antisepsis is the removal of microbes from living surfaces such as skin

8. Which antiseptic is commonly preferred for skin cleansing prior to venipuncture when blood alcohol testing has been ordered?

a. isopropyl alcohol

b. benzalkonium chloride

c. chlorhexidine gluconate

d. tincture of iodine

9. Povidone iodine is

a. a water-soluble complex

b. superior in antimicrobial activity to other forms of iodine

c. allowed to remain on skin for 1.5 to 2 minutes to maximize its antimicrobial action

d. all of the above

10. In venipuncture, it is common practice not to use _____ on patients who are allergic to shellfish.

a. Chlorhexidine

b. Povidone iodine

c. Isopropyl alcohol

d. Ethyl alcohol

11. Which of the following antiseptics is classified as a quaternary ammonium compound?

a. Chlorhexidine

b. Benzalkonium

c. Povidone iodine

d. Isopropyl alcohol

12. CLSI guidelines regarding skin antisepsis in venipuncture include:

a. Cleanse the skin with 70% isopropyl alcohol using a circular motion

b. Insert the needle immediately after cleansing the skin with alcohol

c. If the puncture site is touched after cleansing, it does not need to be re-cleansed

d. Allow alcohol on the skin to air dry in order to prevent patient discomfort

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