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Preventive Practices in the Critically Ill

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Chapter #3

INFECTION CONTROL IN THE ICU

Laymen always associate bacteria, microbes, and *germs with disease.*
John Postgate, Microbes and *Man*

Microbial organisms (microbes) make up about 90% of the living matter on this planet. They're all around us: in the air we breathe, the food we eat, and the water we drink. They're on our skin, under our fingernails, in our nose and mouth, and armies of them congregate in our intestinal tract. Are these organisms the nasty little "germs" that are eager to invade the human body to conquer and destroy, as they are so often portrayed, or are they peace-loving creatures that mean us no harm? More the latter, it seems. Most microbes have nothing to gain by invading the human body (I'll exclude viruses here), but they have much to lose because they can be killed by the inflammatory response. It seems then that survival would dictate that microorganisms avoid the interior of the human body, not invade it.

For more than a century, medicine has viewed the microbial world as an enemy that should be destroyed, and the practices described in this chapter are an expression of that belief. These practices are collectively known as "infection control," and they are designed to prevent the spread of microorganisms from one person to another, or from one site to another on the same person. Most of the information in this chapter is taken from clinical practice guidelines published by the Centers for Disease Control and Prevention (CDC) and other expert agencies, and these are listed in the bibliography at the end of the chapter (0-7). As you will see, some infection control practices are rational, and some are ritual, but all are an essential part of daily life in the ICU.

SKIN HYGIENE

The surface of the skin is home to several species of bacteria and fungi, some of them attached to the underlying squamous cells of the skin (resident flora), and some of them are unattached and easily removed (transient flora) (3,4,8). Because most microbes are aquatic in nature and thrive in a moist environment, the microflora on the skin tend to congregate in moist regions like the groin and axilla. Contact surfaces like the skin on the hands can also be densely populated with microorganisms, and this micro flora is a principal concern in infection control because it can be transmitted to others. An example of the organisms that populate the hands of ICU personnel is shown in Table 3.1. The most frequent isolate is *Staphylococcus epidermidis* (a coagulase-negative staphylococcus), followed by gram-negative enteric organisms and *Candida* species (3,4,8,9). Eradicating microbes on the hands of hospital personnel is one of the holy crusades of infection control.

Cleaning vs Decontamination

Plain soaps are detergents that can disperse particulate and organic matter, but they lack antimicrobial activity. Cleaning the skin with plain soap and water will remove dirt, soil, and organic matter from the skin, but will not eradicate the microbes on the skin. Scrubbing the skin with soap and water can remove transient (unattached) organisms, but the attached (resident) microorganisms are left in place. The removal of microbes from the skin, known as decontamination, requires the application of agents that have antimicrobial activity. Antimicrobial agents that are used to decontaminate the skin are called *antiseptics,* while those used to decontaminate inanimate objects are called *disinfectants*.

TABLE 3.1 Organisms Isolated from the Hands of leu Personnel

Organism	% Total Cultures
Gram-positive cocci	
Staph. epidermidis	100%
Staph. aureus (MSSA)	7%
Gram-negative Bacilli	21%
Acinetobacter spp.	
Klebsiella spp.	
Enterobacter spp.	
Pseudomonas spp.	
Serratia spp.	
Yeasts and fungi	16%
Candida spp.	

MSSA, methicillin-sensitive *Staph. aureus.*

From Larson EL, Rackoff WR, Weiman M, et al. Assessment of two handmens for intensive care unit personnel. crit Care Med, 2001

TABLE 3.2 Commonly Used Antiseptic Agents

Antiseptic Agent	Advantages	Disadvantages
Alcohols	Rapid onset of action	Little residual activity
	Broad spectrum of activity	Aqueous solutions can cause skin dryness.
Iodophors	Broad spectrum of activity	Slow onset of action
		Prolonged contact can irritate the skin
Chlorhexidine	Good residual activity	Relatively narrow spectrum of activity
		An ocular irritant

From References 3, 4, and 8.

Antiseptic Agents

The popular antiseptic agents in the United States are the alcohols (ethanol, propanol, and isopropyl alcohol), iodophors (slow-release iodine preparations), and chlorhexidine. (Hexachlorophene, once the most popular antiseptic agent in the U.S., is no longer recommended because of its limited spectrum of activity.) The relative advantages and disadvantages of each antiseptic agent are summarized in Table 3.2.

Alcohols

The alcohols have excellent germicidal activity against gram-positive and gram-negative bacteria (including multidrug-resistant bacteria), various fungi (including *Candida* spp.), and viruses such as human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) (3,4,8). Alcohol solutions containing 60% to 95% alcohol are most effective. Alcohols have a rapid onset of action but little persistent (residual) activity. They are less effective in the presence of dirt and organic matter, and are not recommended for use when the skin is visibly dirty or soiled with body fluids (e.g., blood) (4). Repeated use of aqueous (water-based) alcohol solutions can lead to drying and irritation of the skin, but these adverse effects are virtually eliminated when a waterless alcohol gel is used (4,8,9). Alcohol-impregnated towelettes are available but have limited amounts of alcohol and are no more effective in removing skin microbes than plain soap and water (4).

Iodophors

Iodine is germicidal and has a broad spectrum of activity similar to the alcohols, but it is irritating to the skin and soft tissues. Skin irritation is reduced when a carrier molecule is used to release iodine slowly. Preparations that contain iodine and a carrier molecule are called iodophors, and the most popular iodophor in the United States is povidoneiodine (Betadine). Since the active ingredient in iodophors (iodine) is released slowly, *iodophors must be left* in *contact with the skin for a few minutes to achieve maximal efficacy.* However, prolonged contact with

iodine can be irritating, so iodophors should be wiped from the skin after drying (3). Persistent (residual) activity is inconsistent after iodophors are wiped from the skin. Iodophors are neutralized by organic matter (3,4,9), so skin that is soiled with blood and body fluids should be cleaned before applying an iodophor. Povidone-iodine is usually provided as an aqueous solution, but alcohol-based solutions of povidoneiodine are available and may be more effective.

Chlorhexidine

Chlorhexidine gluconate is a germicidal agent that is equally effective against gram-positive bacteria as the alcohols and iodophors, but is less effective against gram-negative bacilli and fungi. Its onset of action is slower than the alcohols but faster than the iodophors. The major advantage of chlorhexidine over the other antiseptic agents is its prolonged activity, which can last for six hours or longer (4). This is demonstrated in Figure 3.1. The residual activity is reduced by soaps and hand creams (4). Chlorhexidine is available in aqueous solutions ranging in strength from 0.5% to 4.0%. The 4% solution is most effective, but repeated use can

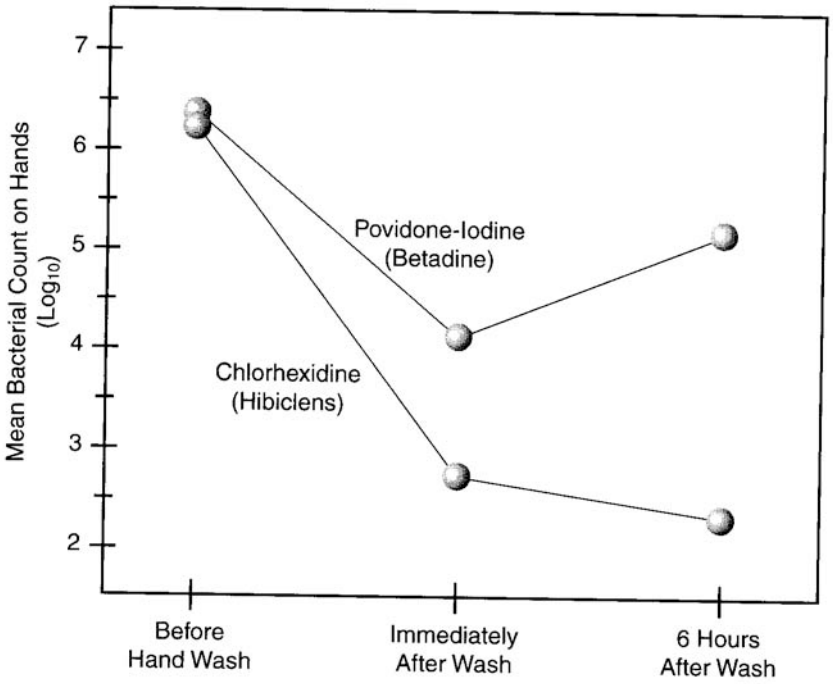

FIGURE 3.1 Comparative effects of a 6-minute hand scrub with 0.75% povidone-iodine (Betadine) and 4% chlorhexidine gluconate (Hibiclens) on microbial growth on the hands. Bacterial counts are expressed as log base 10 values. (From Peterson AF, Rosenberg A, Alatary SD, et al. Comparative evaluation of surgical scrub preparations. Surg Gynecol Obstet 1978;146:63*.)

cause skin irritation and dermatitis (4). Chlorhexidine is also an ocular irritant (4), and care should be taken to avoid contact with the eyes.

Spore-Forming Organisms
None of the antiseptic agents described here is an effective sporicidal agent that can prevent the spread of spore-forming bacteria like *Clostridium difficile* and *Bacillus anthracis* (4). Gloves are needed whenever contact with these organisms is possible.

Handwashing
Handwashing (a nebulous term that can include cleaning, antisepsis, or both) has been described as " ... the single most important measure to reduce the risks of transmitting organisms from one person to another or from one site to another on the same patient" (ref. 2, updated guidelines). The recommendations for handwashing issued by the Centers for Disease Control are shown in Table 3.3. Note that an antiseptic solution rather than plain soap and water is recommended for most instances of hand washing, and that a waterless alcohol gel is recommended if the hands are not visibly soiled (remember that alcohol is much less effective in the presence of organic matter). The preference for alcohol gel is based

TABLE 3.3 Recommendations for Hand Hygiene

I. Handwashing with soap (plain or antiseptic) and water is recommended:
1. When hands are visibly dirty or contaminated with proteinaceous material or are visibly soiled with blood or other body fluids
2. Before eating
3. After leaving a restroom
II. Handwashing with an antiseptic preparationa is recommended:
1. Before direct contact with patients
2. After contact with a patient's skin (intact or nonintact)
3. After contact with body fluids, secretions, excretions, mucous membranes, wound dressings, and contaminated items
4. Before donning sterile gloves to insert central intravascular catheters
5. Before inserting urinary catheters, peripheral venous catheters, or other invasive devices that do not require a surgical procedure
6. After removing gloves
7. When moving from a contaminated body site to a clean body site during patient care
8. After contact with inanimate objects in the immediate vicinity of the patient

on evidence that alcohol-containing products are superior to povidoneiodine or chlorhexidine solutions for reducing bacterial counts on the hands (4) and evidence that alcohol gels cause less skin irritation than antimicrobial soaps or aqueous antiseptic solutions (4,9).

Compliance
Despite the accolades showered on the practice of hand washing, surveys of ICU personnel reveal a consistent pattern of poor compliance with published guidelines for handwashing. Compliance rates are well below 50% in most surveys, and physicians are consistently the worst offenders (3,4,8,9). There are several reasons for this observation, and one of them is evident in Table 3.3: i.e., there are simply too many indications for hand-washing. Anyone who has taken care of patients in an ICU will realize that full compliance with the recommendations in Table 3.3, particularly the recommendation that handwashing be performed before and after every patient contact, is neither practical, affordable, nor achievable on a consistent basis.

Technique
Handwashing can be performed with plain soap or a variety of antiseptic preparations (soaps, aqueous solutions, or waterless gels). In general, alcohol-based products are more effective in reducing bacterial counts on the hands than are antiseptic soaps containing povidone-iodine or chlorhexidine (4). Whenever a soap (plain or antiseptic) is used, the wash should begin by wetting the hands with tap water. The soap should be applied to the palms of the hands and then rubbed over the entire surface of the hands for at least 30 seconds (4,8). Special attention should be given to the subungual areas under the fingernails, where microbes are usually most concentrated (3,4). The soap is then removed by rinsing with water, and the hands dried with a disposable towel. Hot water is not recommended for hand washing (4) because it is not more effective in removing organisms from the skin than warm or cold water (11) and can be irritating to the skin. Using a disposable towel to dry the hands is equivalent to forced air drying (2) but is favored because it is quicker and more convenient.
When a waterless alcohol gel is used, the hands should be cleaned first if necessary (remember that alcohol does not work well in the presence of organic matter), and the gel should be rubbed into the hands until they are dry. Repeated application of gels can leave the hands with a greasy feeling, and a periodic soap and water wash is sometimes preferred to remove any residual gel from the hands.

PROTECTIVE BARRIERS
Protective barriers like gloves, gowns, masks, and eye shields provide a physical impediment to the transmission of infectious agents. The principal role of these barriers is to protect hospital staff from infectious agents

TABLE 3.4 Recommendations for Glove Use in the leu

I. Sterile gloves
1. Recommended for the following procedures
A. Central venous catheterization
B. Peripherally inserted central catheters (PICC)
C. Artherial catheterization
D. Placement of drainage catheters in a closed space (pleural, pericardial, or peritoneal cavities)
E. Insertion of epidural catheters (for analgesia) or intraventricular catheters (for intracranial pressure monitoring
II. Nonsterile gloves
1. Should be used for contact with any moist body substance-blood, body fluids, secretions, excretions, nonintact skin, and mucous membranes. Clean (unsoiled) gloves should be used for contact with non intact skin and mucous membranes
2. Can be used for insertion of peripheral venous catheters as long as the gloved hands do not touch the catheter
III. General recommendations
1. Gloves should be changed between tasks and procedures on the same patient if there has been contact with material that may be infectious
2. Gloves should be removed immediately after use, before contact with noncontaminated objects in the environment, and before going to another patient

From References 2, 6, and 13.

that can be transmitted by blood and body fluids, such as the human immunodeficiency virus (HIV) and hepatitis Band C viruses.

Gloves

Rubber gloves were popularized in this country in the late nineteenth century by William Halstead, the first (and enigmatic) Chief of the Surgery at Johns Hopkins Hospital, who covered only his palms and three fingers with the gloves because they were heavy and impaired the sense of touch. Today, sterile rubber gloves are the second skin of the operating surgeon. In the ICU, sterile gloves are used primarily for placing catheters in the bloodstream (see Table 3.4).

In the 1980s (a century after the introduction of surgical gloves), the use of nonsterile gloves was popularized by the discovery that HIV is transmitted in blood and body fluids. This discovery prompted a policy known as Universal Precautions (1), which considered all patients as possible sources of HIY. An updated policy known as Standard Precautions (2,13) contains the current recommendations for nonsterile gloves, and these are shown in Table 3.4. Nonsterile gloves should be used for any contact with a moist body substance, which includes

blood, body fluids, secretions, excretions, nonintact skin, and mucous membranes. Note also in Table 3.4 that non sterile gloves are considered safe for insertion of peripheral venous catheters as long as a "no touch" technique is used (i.e., as long as the gloved hands are not permitted to touch the catheter) (6).

Handwashings and Gloves

As indicated in Table 3.3, handwashing is recommended before donning gloves and again after they are removed. This recommendation is based on two concerns. The first is the fear that gloves can leak or tear and thereby allow microbial transmission between the hands of the healthcare worker and the patient. The second concern is the potential for moisture buildup on the hands during prolonged glove use, which would favor microbial growth on the hands while the gloves are on. Both of these are valid concerns for invasive surgical procedures, where glove use is prolonged and soiling of gloves is prominent. However, the signifi· cance of these concerns in a nonsurgical setting like the ICU (where glove use is not prolonged and soiling of gloves is usually not prominent) is less certain. The graph in Figure 3.2 provides some interesting observations about the need for antiseptic hand washing when gloves are used. The data ir this graph is from a study involving two groups of ICU nurses: one group performed an antiseptic hand wash with 4% chlorhexidine before don· ning sterile gloves, while the other group did not wash their hands before donning gloves (4). Hand cultures were then obtained before, during and after short-term glove use. The two graphs in Figure 3.2 show thai microbial growth on the gloved hands was minimal in both groups indicating that the pre-glove antiseptic handwash did not influence the infectious risk to patients from the gloved hands. The graphs also show that microbial activity on the hands was reduced in both groups after the gloves were removed. Thus, microbial proliferation on the hands is not a concern during short-term glove use. These results suggest that hand washing before and after short-term glove use in a nonsurgical setting like the ICU may be unnecessary.

Latex Allergy

The dramatic increase in the use of rubber gloves over the last twc decades has created a problem with latex hypersensitivity in hospital workers. Latex is a natural rubber product that is used in over 40,000 household and medical products, including gloves, face masks, blood pressure cuffs, and catheters (5). Repeated exposure to latex can promote hypersensitivity reactions that can be evident clinically as either contact dermatitis (urticaria or eczema), anaphylaxis, rhinoconjunctivitis, or asthma 06,17). Latex hypersensitivity is reported in 10% to 20% of hospital workers, compared to 1 % of the general population (16), For unclear reasons, patients with spina bifida have the highest risk of latex allergy, with as many as 40% of the population having this

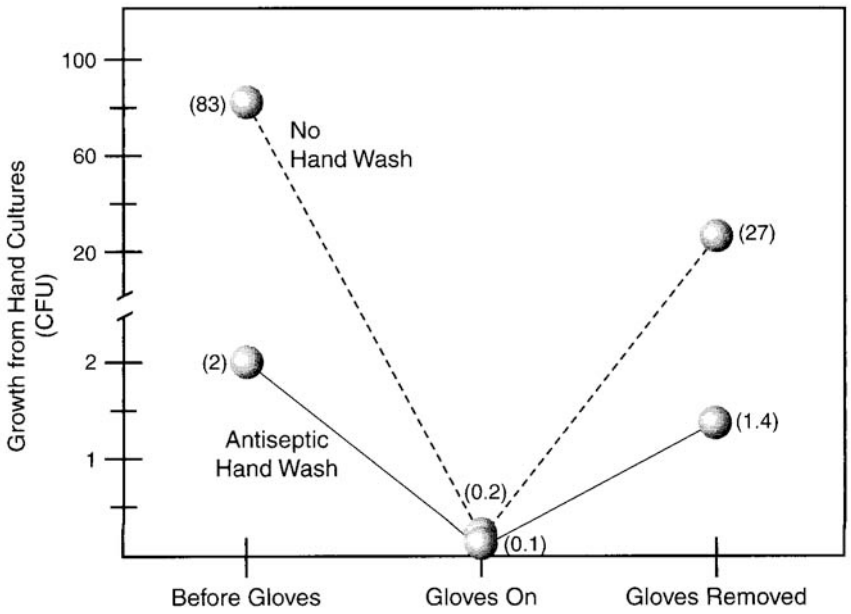

FIGURE 3.2 Influence of pre-glove handwashing with an antiseptic agent (4% chlorhexidine) on hand cultures obtained during and after the use of sterile gloves. CFU = Colony-forming units 48 hours after the fingers of both hands were pressed directly on culture plates. The numbers in parentheses correspond to the values on the vertical axis of the graph. Note the break in the vertical axis and the different scales above and below the break. (From Rossoff LJ, Borenstein M, Isenberg HD. Is hand washing really needed in an intensive care unit? Crit Care Med 1995;23:1211, with permission.)

DIAGNOSIS. The diagnosis of latex allergy can be elusive. One problem is the nonspecific manifestations of disease. Another problem is the fact that *symptoms of latex allergy can appear without direct physical contact with latex.* This is often the case with the rhino conjunctivitis and asthma, which are triggered by airborne latex particles. A history of symptoms confined to the workplace should create suspicion for latex allergy. The clinical manifestations of latex allergy often coincide with exposure to latex, so hospital workers with symptomatic latex allergy often display these symptoms while in the hospital and are symptom-free at home.

There are two tests for latex hypersensitivity (9). One is a skin test, and the other is an assay for latex-specific immunoglobulin E levels in the bloodstream. Both have shortcomings. There is no standardized extract for the skin test (allergists have to make their own extract by pulverizing latex gloves!), so results are operator-dependent. The assay for latexspecific IgE in blood is currently the favored test, but the sensitivity can be low (9). If confronted with a case of possible latex allergy, you should contact the clinical laboratory in your hospital and ask about the availability and reliability of these tests in your region.

TREATMENT. The treatment of latex allergy is symptom-driven and non-specific. Removing latex from the patient's immediate environment is the best strategy, but this may not be possible because latex is ubiquitous in the hospital environment (it is even found on tongue depressors!). The hospital should provide substitutes for latex products (e.g., vinyl gloves) when necessary.

Masks and Other Barriers

As was the case with nonsterile gloves, the use of other barriers like masks, eye shields, face shields, and gowns increased markedly after the discovery that HIV is transmitted in blood and body fluids. These barriers are currently recommended for all procedures or patient care activities that are likely to generate splashes of blood, body fluids, secretions, or excretions (2,14). Nonsterile gowns are adequate, and gowns coated with a plastic covering are the least impervious to blood and body fluids (20). Soiled gowns and other barriers should be removed and discarded as soon as possible, and before going to another patient **(4)**.

Types of Masks

There are two types of face masks: surgical masks and respirators. Surgical masks were introduced to prevent contamination of the operative field during surgical procedures. In the past 2 decades, they have been adopted as a means of protecting healthcare workers from inhalation of airborne infectious agents. There is no evidence that surgical masks are effective in preventing infection (23), yet they continue to be used without question.

Respirators are devices that protect the wearer from inhaling a dangerous substance (23). The different types of respirators include particulate respirators (block particulate matter), gas mask respirators (filter or clean chemical gases in the air), and the Self-Contained Breathing Apparatus (equipped with its own air tank), which is used by firefighters. Particulate respirators are used to block inhalation of airborne pathogens, particularly the tubercle bacillus that causes pulmonary tuberculosis. The respirator currently recommended for this purpose is called an N95 respirator (22,23). The "N" indicates that the mask will block non-oil-based or aqueous aerosols (the type that transmits the tubercle bacillus), and the "95" indicates the mask will block 95% of the intended particles (a requirement for a respirator mask to be judged effective) (23).

Types of Airborne Illness

Infectious organisms that are capable of airborne transmission are divided into two categories: those greater than 5 microns (>5μ) in diameter, and those that are 5 microns or less (<=5μ) in diameter. The organisms and airborne illnesses in each category are shown in Figure 3.3 (2). In each of these illnesses, airborne infectious particles are produced by coughing or sneezing (one cough or sneeze can produce 3,000 airborne

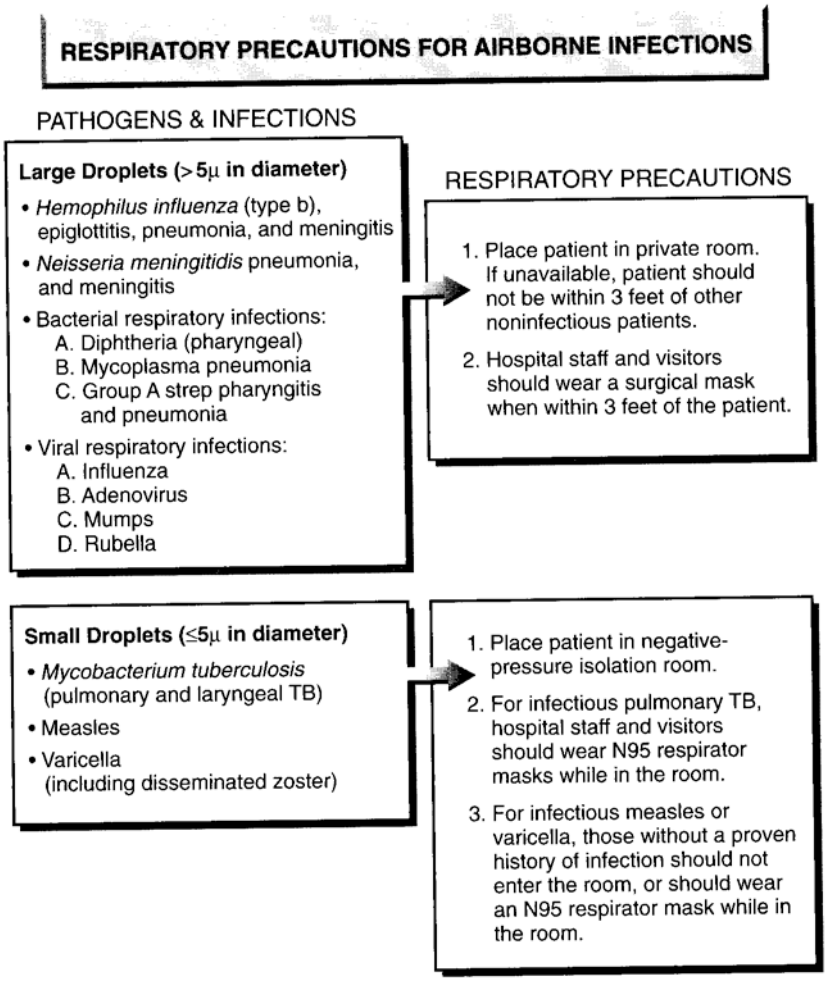

FIGURE 3.3 Infection control precautions for diseases that can spread via the airborne route. (From Reference 2.)

particles) or procedures such as airways suctioning and bronchoscopy. The airborne particles can be inhaled or can impact on nonintact skin, or on the mucosa in the nose or mouth.

Infectious particles >5μ in diameter usually travel no farther than 3 feet through the air, and to block transmission of these particles, a surgical mask is recommended (despite lack of proven efficacy!) when hospital staff or visitors are within 3 feet of the patient (2,21). The smaller (<=5μ in diameter) infectious particles can travel long distances in the air, and to prevent transmission of these particles, patients should be isolated in private rooms that are maintained at a negative pressure relative to the surrounding areas. For patients with infectious tuberculosis (pulmonary or laryngeal), all hospital staff and visitors should wear an N95 respirator

mask while in the room (2,22). For patients in the infectious stages of rubeola (measles) and varicella (chickenpox or herpes zoster), individuals with no prior history of these infections who are also pregnant, immunocompromised, or otherwise debilitated by disease should not be allowed in the patient's room. For other susceptible individuals who must enter the room (i.e., hospital workers), an N95 respirator mask should be worn at all times while in the room.

ATYPICAL PULMONARY TB. **It** is important to distinguish infections caused by *Mycobacterium tuberculosis* from those caused by atypical mycobacteria (e.g., *Mycobacterium avium* complex) when determining the need for respiratory protection. Unlike the behavior of M. z, there is no evidence for person-to-person transmission of atypical mycobacteria (22), so special respiratory precautions (isolation and masks) are not required for patients with atypical pulmonary tuberculosis (2).

BLOOD-BORNE PATHOGENS

The greatest infectious risk you face in the ICU is exposure to bloodborne pathogens like HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV). This section will describe the occupational risks associated with each of these pathogens and the preventive measures used to minimize these risks.

Needlestick Injuries

The transmission of blood-borne infections to hospital workers occurs primarily via needlestick injuries (i.e., accidental puncture wounds of the skin caused by hollow needles and suture needles). Each year, an estimated 10% of hospital workers sustain a needlestick injury (24). Most of these injuries occur in nurses, but the risk is also high in medical students, postgraduate trainees, and staff surgeons. As many as 70% of residents and medical students report a needles tick injury during their training (the incidence is highest in surgical residents) (25), and a survey in one hospital revealed that 60% of the staff surgeons experienced a needlestick injury at some time in their careers (26). The activities most often associated with needlestick injuries outside the operating room involve recapping and disposal of used needles (24).

Safety Devices

The problem of needles tick injuries came to the attention of the United States Congress in the year 2000, and as a result, Congress passed the Needlestick Safety and Prevention Act that mandates the use of "safety-engineered" needles in all American health care facilities. The illustration in Figure 3.4 shows a simple safety device designed to eliminate the risk of needlestick injuries. The needle is equipped with a rigid, plastic housing that is attached by a hinge joint to the hub of the needle. The protective housing is normally positioned away from the needle so it

does not interfere with needle use. When the needle is no longer needed, it is locked into the protective housing by holding the housing against a rigid structure and moving the needle about the hinge joint (like closing a door) until it snaps in place in the housing. The needle stays attached to the syringe during this procedure, and the hands never touch the needle. The protected needle and attached syringe are then placed in a punctureproof "sharps container" for eventual disposal.

One-Handed Recapping Technique

Once the needle is locked in its protective housing, it is not possible to remove it for further use. In situations where a needle has multiple uses (e.g., filling a syringe with a drug preparation and later injecting the drug

in several increments), the needle can be rendered harmless between uses by recapping it with the one-handed "scoop technique" shown in Figure 3.5. With the needle cap resting on a horizontal surface, the needle is advanced into the needle cap. Using the tip of the needle cap as a fulcrum, the needle and cap are then lifted vertically until they are perpendicular to the horizontal surface. The needle is then pushed into the cap until it locks in place. The hands are never in a position to permit an accidental needle puncture.

Human Immunodeficiency Virus (HIV)

The spread of HIV to hospital staff, although universally feared, is not a common event. As of June, 2000, there have been a total of 56 cases of HIV seroconversion in healthcare workers that can be definitely linked to HIV exposure in the workplace. Some of these cases involve laboratory

workers, and only 44 cases involve percutaneous injury from hollow needles (the mode of transmission expected in ICUs) (24). Since HIV statistics were monitored for 15 years up to the year 2000, the 44 pertinent cases represent an average of 3 cases per year of HIV transmission in a nonoperative hospital setting. If all these cases occurred in the 6,000 ICUs in this country, the average yearly occurrence of HIV transmission in the ICU is one case for every 2,000 ICUs. Not much of a risk.

Percutaneous Exposures
A needles tick puncture with a hollow needle will transfer an average of one microliter (10-6 L) of blood (27). During the viremic stages of HIV infection, there are as many as 5 infectious particles per microliter of blood (28). Therefore puncture of the skin with a hollow needle that contains blood from a patient with active HIV infection is expected to transfer at least a few infectious particles. Fortunately, this is not enough to establish HIV infection in the recipient in most cases. A single needlestick injury with blood from an HIV-infected patient carries an average 0.3% risk of **HIV** seroconversion (5,24). This means that for every 1,000 needles tick injuries with HIV-infected blood, there will be an average of 3 cases of effective HIV transmission. The likelihood of HIV transmission is greater than 0.3% in the following circumstances: a deep skin puncture, visible blood on the needle, and injury from a needle that was placed in an artery or vein of the source patient (29).

Mucous Membrane Exposures
Exposure of mucous membranes and nonintact skin to infectious body fluids carries much less risk of HIV transmission than needlestick injuries. A single exposure of broken skin or mucous membranes to blood from an HIV-infected patient carries an average 0.09% risk of **HIV** seroconversion (5,24). This means that for every 1,000 mucous membrane exposures to contaminated blood, there will be one (0.9) case of HIV transmission. (A one-in-a-thousand risk!)

Postexposure Management
When a member of the ICU staff experiences a possible exposure to HIV from a needlestick injury or blood splash to the face, the appropriate steps to take are determined by the presence or absence of HIV anti-bodies in the blood of the source patient. If the HIV antibody status of the source patient is unknown, you should (with permission) perform a rapid HIVantibody test on a blood sample from the source patient. This is done at the bedside (by an appropriately trained member of the staff), and the results are available in 10 to 15 minutes. The results of this test can be used to guide initial management decisions, but a positive result must be confirmed by another test such as a Western blot or immunofluorescent antibody assay. The recommendations for possible HIV exposure based on the HIV status of the source patient are outlined in Table 3.5 (5).
The major decision following possible HIV transmission is whether or not to begin prophylactic therapy with antiretroviral agents in the exposed individual. If HIV infection is proven or suspected in the

TABLE 3.5 Postexposure Prophylaxis for HIV Infection

Indications for Each Type of Postexposure Drug Regimen

No Drugs	Two Drugs·	Three *Drugsb*
1. When source is HIV-negative	1. When source is HIV-positive but asymptomatic	1. When source is HIV-positive and symptomatic
2. When HIV status of source is not **known** but HIV is unlikelyC	2. When HIV status of source is not known but HIV is likely.c	2. When source is HIV-positive and asymptomatic but exposure is severee
3. When source is not known but HIV is unlikelyd	3. When source is not known but HIV is likelyd	

From Reference 5.

aThe recommended two-drug regimen is zidovudine (200 mg TID) plus (150 mg BID) for 4 weeks. The two agents are available together as cOMBIVIR.

b Add one of the following drugs to the two-drug regimen: efavirenz (600 mg at indinavir (800 mg every 8 hr, between meals), or nelfinavir (2.5 g daily in 2 or 3 doses, with meals).

cWhen the HIV status of the source is unknown, the likelihood of HIV is based presence or absence of risk

dWhen the source is unknown, the likelihood of HIV is based on the prevalence the population served.

e Severe exposure is defined as deep injury, needle soiled with blood from and exposure from needle inserted into artery or vein of source patient.

source patient, prophylactic therapy with at least 2 antiretroviral agents is started and continued for 4 weeks (or until there is convincing evidence for the absence of HIV infection in the source patient). A popular two-drug regimen is the combination of zidovudine (200 mg TID) and lamovudine 050 mg daily). These two drugs are available in a combination tablet (COMBIVIR, GlaxoSmithKline), each containing 150 mg lamovudine and 300 mg zidovudine. A third antiretroviral agent is added if there is evidence for symptomatic or advanced HIV infection in the source patient, or if the HIV exposure is severe (i.e., deep needlestick injury, injury from a needle soiled with infectious blood, or injury from a needle that was placed in an artery or vein of an HIV-infected patient) (29). The agents that can be added to the two-drug regimen are included at the bottom of Table 3.5.

It is important to emphasize that the current recommendations for prophylaxis with antiretroviral agents are empiric, and not based on proven efficacy. Even if antiretroviral therapy is completely effective in preventing HIV transmission, an average of 330 patients who have been exposed to HIV-infected blood would have to be treated to prevent one case of HIV transmission. Considering that the prophylactic regimens of antiretroviral drug therapy are poorly tolerated (one of every three subjects given antiretroviral drugs for postexposure prophylaxis will stop taking the drugs because of troublesome side effects) (5), the risks of antiretroviral

drug prophylaxis may outweigh the overall benefit in many subjects, particularly when HIV infection in the source patient is not proven.
POSTEXPOSURE SURVEILLANCE. Antibody responses to acute or primary HIV infection can take 4 to 6 weeks to become evident. Therefore anyone with documented exposure to HIV infection should have serial tests for HIV antibodies at 6 weeks, 3 months, and 6 months after the exposure (5). More prolonged testing is not warranted unless the exposed person develops symptoms compatible with HIV infection.
POSTEXPOSURE HOTLINE. The National Clinicians' Postexposure Prophylaxis Hotline (PEP line) is a resource for anyone with questions about postexposure prophylaxis for HIV infection. The toll-free number is 888448-4911.

Hepatitis B Virus
The blood-borne hepatitis B virus (HBV) is much more transmission prone than HIV One microliter 00~6 L) of blood from a patient with HBV-induced acute hepatitis can have as many as one million infectious particles, whereas, as just mentioned, a similar volume of blood from a patient with active HIV infection will have only 5 or fewer infectious particles (28). Fortunately, there is a vaccine that can provide immunity against HBV infection.

Hepatitis B Vaccination
Vaccination against hepatitis B is recommended for anyone who has contact with blood, body fluids, and sharp instruments (5), which is virtually everyone who works in an ICU. The only contraindication to the vaccine is a prior history of anaphylaxis from baker's yeast (5). The vaccination involves 3 doses and should proceed as follows (5):
The first 2 doses (given by deep 1M injection) are given 4 weeks apart, and the third dose is administered 5 months after the second dose.
If the vaccination series is interrupted after the first dose, the whole sequence is not repeated. If the second dose was missed, it is given as soon as possible, and the third dose is administered at least 2 months later. If the third dose was missed, it is administered as soon as possible, and the vaccination series is considered completed.
The hepatitis B vaccine produces immunity by stimulating production of an antibody to the hepatitis B surface antigen (anti-HBs). The primary vaccination series is not always successful in providing immunity, so the following evaluation is recommended (5).
One to two months after the vaccination is completed, the serum anti-HBs level should be measured. Immunity is indicated by an anti-HBs level that is >=10 mIU /mL. If the anti-HBs is <10 mIU / mL, the 3-dose vaccination series should be repeated.

Nonresponders have a 30% to 50% chance of responding to the second vaccination series (5). If there is no response after the second vaccination (i.e., if the anti-HBs is still below 10 mIU/mL), then the subject is classified as a nonresponder and receives no further vaccination attempts. Nonresponders have the same risk for acquiring HBV as those who have never received the vaccine. Responders do not require a booster dose of the vaccine, even though antibody levels wane with time (5).

Postexposure Risks and Management

The risk of acquiring HBV is determined by the vaccination history of the individual at risk. For those who are vaccinated and have responded appropriately, there is virtually no risk of acquiring HBV infection. For unvaccinated (or nonresponsive) individuals who have been exposed to infectious blood via needlestick injuries, the risk of developing serologic evidence of HBV infection is as high as 60%, and the risk of developing clinical hepatitis is as high as 30% (5).

The management strategies following possible exposure to HBV are outlined in Table 3.6 (5). These strategies are guided by the vaccination status of the exposed individual and the presence or absence of the hepatitis B surface antigen (HBsAg) in the blood of the source patient. For exposed individuals who have completed the HBV vaccination and have documented evidence of immunity, no treatment is necessary following exposure. For all others (i.e., unvaccinated, vaccinated but not immune, and vaccinated with unknown immunity), the management is based on the likelihood of HBV infection in the source patient. If HBV infection in the source patient is proven (by the presence of HBsAg in the blood) or suspected (by the presence of risk factors for HBV or a high prevalence of HBV infection in the source population), the treatment usually involves an intramuscular dose of hepatitis B immune globulin (0.06 mL/kg) and initiation of the HBV vaccine series.

Hepatitis C Virus

Hepatitis C virus (HCV) is a blood-borne pathogen of some concern because HCV infection leads to chronic hepatitis in about 70% of cases (7). Fortunately, HCV transmission in the hospital setting is uncommon. The prevalence of anti-HCV antibodies in the blood of hospital personnel is only 1 % to 2% (7), which is no different than the general population. Following after needlestick injuries with HCV-infected blood, the average risk of acquiring HCV is only 1.8% (5). Transmission from mucous membrane exposure is rare, and there are no documented cases of HCV transmission through nonintact skin.

There is no effective prophylaxis for HCV following exposure to infected blood. Both immunoglobulin therapy and antiviral agents such as interferon have been ineffective in preventing HCV infection following exposure to blood (7). In addition, there is currently no vaccine for HCV. When hospital workers are exposed to HCV, they should be counseled about the risks associated with HCV infection, particularly the risk for chronic liver disease. For those with documented exposure

TABLE 3.6 Postexposure Management for Hepatitis B Virus (HBV)

Vaccination Status of Exposed Person	Management Based on HBsAg Status of Source Patient		
	HBsAg Positive	HBsAg Negative	HBsAg Unknown
Not vaccinated	HBIG x *1a* & start HBV vaccination	Start HBV vaccination	Start HBV vaccination
Vaccinated and Immuneb	No treatment	No treatment	No treatment
Not *immuneC*	HBIG x *1a* & start HBV revaccination or HBIG x *2d*	No treatment	If source is high risk for HBV, treat as if source is HBsAg positive
Immunity unknown	Measure anti-HBs level in exposed person 1. If immune,b no treatment 2. If not immune,c HBIG x *1c* and vaccine booster	No treatment	Measure anti-HBs level in exposed person 1. If immune, *b* no treatment. 2. If not *immune,c* vaccine booster & recheck titer in 1-2 mo

to HCV-infected blood via needlestick injuries, serial determinations of anti-HCV antibodies is recommended for 6 months (7).

Chapter #4

ALIMENTARY PROPHYLAXIS

We are told the most fantastic biological tales. For example, that it is *dangerous to have acid in your stomach.*
J.B.S. Haldane

The last chapter demonstrated that standard infection control practices are designed to prevent microbial invasion from the skin. However, the skin is not the only body surface that can be breached by microbes. The alimentary tract, which extends from the mouth to the rectum, is outside the body (like the hole in a donut), and the mucosa that lines the alimentary canal serves as a barrier to microbial invasion, just like the skin. However, unlike the skin, which is multilayered and covered with a keratinized surface, the mucosa of the alimentary tract is a single cell layer that is only 0.1 mm thick. Facing this thin barrier in most regions of the gastrointestinal (CI) tract is a population of microbes that far outnumbers the microflora on the skin. In fact, the number of bacteria in just one gram of stool (10 to 100 billion) is greater than the number of people on Earth (6.5 billion in 2005). Considering the thin mucosa and the hordes of microbes in the CI tract, it seems that the real threat of microbial invasion comes from the bowel, not the skin.
This chapter will introduce you to the importance of the oral cavity and the bowel as sources of infection in critically ill patients, and what can be done to prevent infections from these sites. A section is included on stress-related injury to the gastric mucosa (stress ulcers), and the preventive measures that limit troublesome bleeding from these lesions.

MICROBIAL INVASION FROM THE BOWEL

Microbial organisms are aquatic creatures that require a watery environment to thrive, and the moist environment in the mouth and CI tract is ideal for microbial proliferation. There are 400 to 500 different species of bacteria and fungi in the adult alimentary tract (1,2) with an estimated

TABLE 4.1	Microbial Density in the Alimentary Tract
Segment	**Population Density***
Oral cavity	105-106
Stomach	<103
Distal small bowel	107-109
Rectum	101°_1012
'Colony-forming units (CFUs) per gram or mL of luminal	
From Simon GL, Gorbach SL. Intestinal microflora. Med Clin North Am	

total mass of 2 kg (about 41/2 pounds) (3). The protective mechanisms that help to prevent this army of microbes from gaining access to the interior of the body are described next.

Protective Mechanisms

There are three levels of protection from microbial invasion in the alimentary tract. The first level of protection takes place in the lumen of the upper gastrointestinal (CI) tract, where the antimicrobial actions of gastric acid help to eradicate microorganisms that are swallowed in food and saliva. This is demonstrated in Table 4.1, which shows a marked decrease in microbial density in the stomach compared to the oral cavity. The second level of protection occurs at the bowel wall, where the mucosal lining of the CI tract acts as a physical barrier that blocks the movement of microbes across the bowel wall. The third level of protection takes place on the extraluminal side of the bowel wall, where the reticuloendothelial system traps and destroys microbes that breach the mucosal barrier. Roughly two-thirds of the reticuloendothelial system in the body is located in the abdomen (4), which suggests that microbial invasion across the bowel wall may be a frequent occurrence.

Gastric Acid

Castric acid is often misperceived as a digestive aid. An acid environment in the stomach can facilitate the absorption of iron and calcium, but patients with achlorhydria (inability to acidify gastric secretions) are not troubled by malabsorption (5). So what is the function of gastric acid? It seems to be an antimicrobial defense mechanism, as described next.

ANTISEPTIC ACTIONS. Most microorganisms do not survive in an acid environment, as demonstrated in Figure 4.1. In this case, the common enteric organism *Escherichia colli* is completely eradicated in one hour when the pH of the growth medium is reduced from 5 to 3 pH units. The antimicrobial effects of an acid environment was appreciated by Sir Joseph Lister, the father of antiseptic practices in medicine, who used carbolic acid as the first antiseptic agent for the skin. Another use of acid as a microbe killer is the method of food preservation known as *pickling,* which used vinegar, a weak acid, to preserve food.

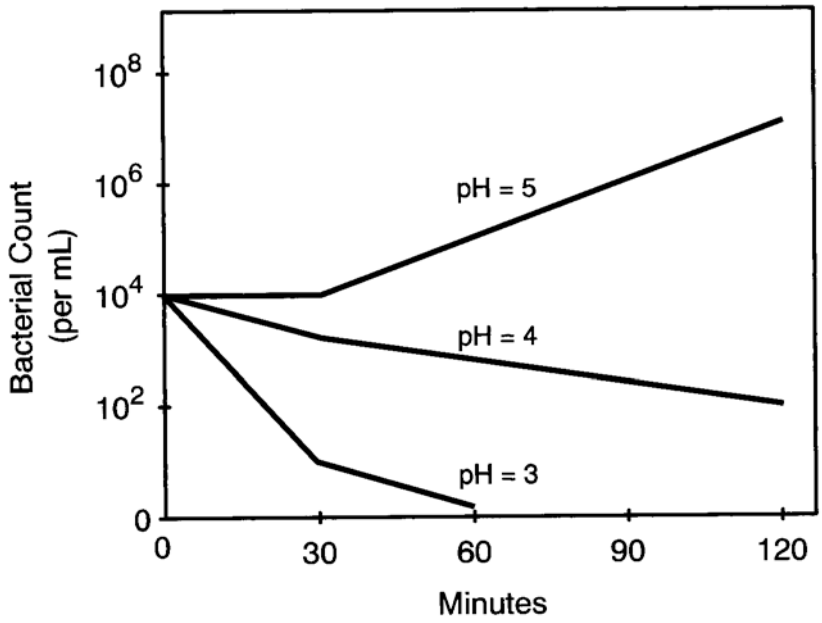

FIGURE 4.1 The influence of pH on the growth of *Escherichia coli*. (From Gianella RA, Broitman SA, Zarncheck N. Gastric acid barrier to ingested microorganisms in man: studies in vivo and in vitro. Gut 1972;13:251.)

In light of the antimicrobial activity of acid, it is likely that gastric acid serves as an endogenous antiseptic agent that eradicates microorganisms swallowed in saliva and food. The eradication of microbes swallowed in saliva would explain why gastric acid secretion is a continuous process that does not require food ingestion. However, the importance of this function is unclear because the microbes that populate the mouth are mostly harmless saprophytes. The eradication of microbes in ingested food may be a more important role for gastric acid. This would explain why drug-induced inhibition of gastric acid production is associated with recurrent *Salmonella* enteritis (6) and why achlorhydria is associated with an increased risk of bacterial gastroenteritis (5-7). Food processing techniques might not completely eradicate microbes, and gastric acid could then serve as our own built-in method of disinfecting the food we eat.

The Acid Phobia

Gastric acid has a long-standing reputation of being a corrosive agent that can eat through an unprotected stomach wall and "burn a hole in your stomach." However, as stated in the introductory quote by J.B.S. Haldane (a popular science writer in the early twentieth century), the perceived dangers of gastric acid are more fantasy than fact. An acid environment can be corrosive for certain inorganic compounds like

metals and enamel, but acid is not destructive for organic matter. If you have ever spilled orange juice (pH=3) or lime juice (pH=2) on your hands, you have experienced the non-destructive nature of acidity in the organic world. In fact, as mentioned in the last section, the pickling process uses an acid (vinegar) to *preserve* organic matter (food).

The perception of gastric acid as a destructive force is a direct result of the traditional notion that gastric acid is the principal cause of peptic ulcer disease. However, recent evidence indicates that local infection with *Helicobacter pylori* is responsible for most cases of peptic ulcer disease.

Predisposing Conditions

A defect in any of the protective mechanisms just described will promote the movement of organisms across the bowel wall and into the systemic circulation. This process is called *translocation* (8), and it is considered an important source of septicemia in critically ill patients (see Chapter 42). The illustration in Figure 4.2 shows three conditions that will promote translocation: microbial overgrowth in the bowel lumen, disruption of the mucosal barrier, and defective clearance by the lymphatic system.

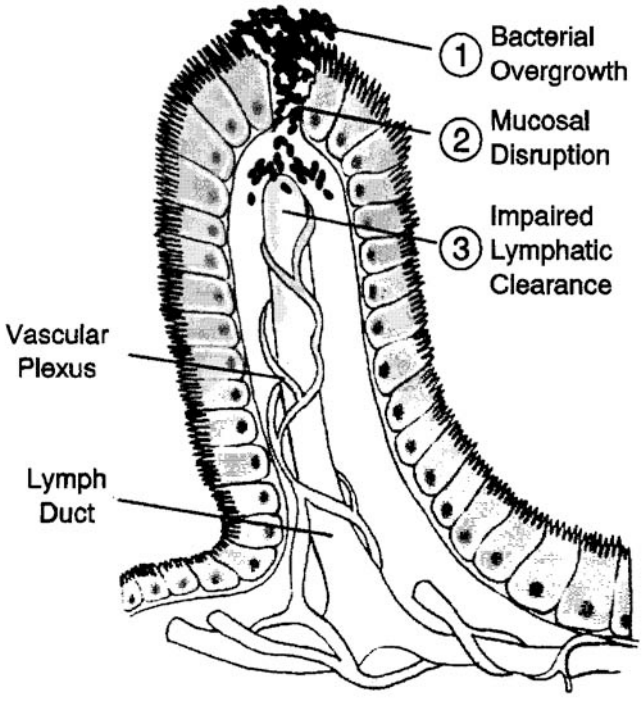

FIGURE 4.2 The triple threat of translocation. This diagram of an intestinal microvillus shows three conditions that predispose to bloodstream invasion by enteric microorganisms.

Reduced Gastric Acidity

Loss of the normal antiseptic actions of gastric acid will result in bacterial overgrowth in the stomach, and this can be a prelude to several types of infections, including infectious gastroenteritis (as described previously), pneumonia from aspiration of infectious gastric contents into the lungs (9,10), and septicemia from bacterial translocation across the bowel wall (11). The risk of bacterial overgrowth and its consequences is reason to avoid the use of drugs that inhibit gastric acid secretion, if possible.

STRESS-RELATED MUCOSAL INJURY

Stress-related mucosal injury is a term used to describe erosions in the gastric mucosa that occur in almost all patients with acute, lifethreatening illness (12,13). These erosions can be superficial and confined to the mucosa, or they can bore deeper and extend into the submucosa (see Figure 4.3). The deeper lesions are called *stress ulcers.*

Pathogenesis

The mucosal lining of the GI tract is normally shed and replaced every 2 to 3 days. When nutrient blood flow is inadequate to support the replacement process, the surface of the bowel becomes denuded, creating superficial erosions. The actions of gastric acid may serve to aggravate this condition, but the principal cause of stress-related mucosal injury is impaired blood flow, not gastric acidity (13). This is an important distinction when considering a rational approach to preventing this condition, as described later.

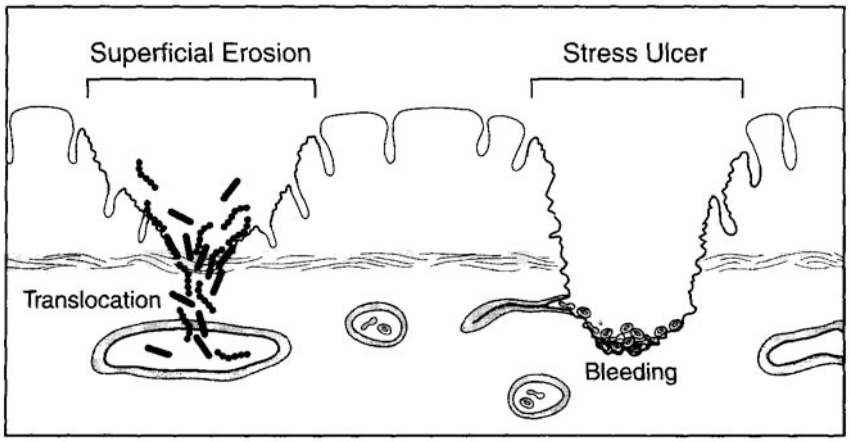

FIGURE 4.3 The different types of gastric erosions that develop in critically ill patients.

Clinical Consequences

Erosions in the gastric mucosa can be demonstrated in as many as 75% to 100% of patients within 24 hours of admission to the ICU (14). Fortunately, these lesions are often clinically silent. The disruption of the gastric mucosa can, however, promote bleeding from surface vessels, and can also promote microbial translocation across the gastric mucosa. Clinical studies of gastric erosions have focused exclusively on the risk of GI bleeding. Without prophylactic measures to prevent bleeding (see later), clinically apparent GI bleeding can occur in as many as 25% of ICU patients (14), while clinically significant bleeding (i.e., causes a significant drop in blood pressure or requires transfusion) occurs in only 1 % to 5% of ICU patients (14,15). The low incidence of clinically significant bleeding is explained by the superficial location of most gastric erosions, which disrupts only small capillaries.

High-Risk Conditions

Since most patients have gastric erosions after just one day in the ICU, the concern in the individual patient is the risk of developing complications from these lesions. The conditions listed below are associated with an increased risk of clinically significant bleeding from gastric erosions (12,15).

Mechanical ventilation for longer than 48 hours
Coagulopathy (i.e., platelets <50,000, INR >1.5, or PTT >2 X control)
Hypotension
Severe sepsis
Multisystem trauma
Severe head injury
Burns involving >30% of body surface area
Renal failure or hepatic failure

Only two of these conditions have proven to be independent risk factors for significant bleeding: mechanical ventilation for longer than 48 hours, and coagulopathy (15). For the other conditions, at least two must be present to consider the patient high-risk for bleeding. These high-risk conditions also serve as indicators for prophylactic therapy to prevent CI bleeding from gastric erosions.

Preventive Strategies

This section describes the interventions that are used to limit the risk of significant bleeding from gastric erosions. Each is presented in order of (my personal) preference.

Preserving Gastric Blood Flow

Because impaired blood flow is the culprit in most cases of stressrelated mucosal injury, preserving gastric blood flow should be the best preventive measure. Unfortunately, there are no readily-available

methods for monitoring gastric blood flow in the clinical setting. Sublingual capnometry, which is a technique that measures the PC02 in the tissue on the underside of the tongue, is a promising method for detecting significant decreases in gastric blood flow at the bedside (16), but the experience with this methodology is currently limited. The best strategy for now is to maintain systemic blood flow and oxygen transport using standard markers (e.g., blood lactate levels) or invasive parameters (e.g., oxygen delivery, oxygen uptake) if available. The bedside methods for monitoring the adequacy of tissue perfusion (including sublingual capnometry) are described in Chapter 11.

Enteral Nutrition

Enteral tube feedings exert a trophic effect on the bowel mucosa that helps to maintain the structural and functional integrity of the bowel mucosa (17). Both of these effects should provide protection against the development of stress-related gastric erosions. Clinical studies in burn patients (18) and patients receiving mechanical ventilation (19) have shown that enteral tube feedings are effective in preventing overt bleeding from the GI tract. Although more clinical studies are needed, enteral tube feedings can be considered adequate prophylaxis for stress-related gastric hemorrhage unless there is some other condition that raises special concern for GI bleeding, such as a coagulopathy, a prior history of bleeding from gastritis or peptic ulcer disease, or active peptic ulcer disease.

Pharmacologic Strategies

There are two pharmacologic approaches to prevent bleeding from gastric erosions. One approach uses an agent that provides local protection to the gastric mucosa (cytoprotection), and the other approach uses drugs that block the production of gastric acid (reduced acidity). The drugs involved in both of these approaches are shown in Table 4.2 (antacids have fallen out of favor and are not included here). There has been a

TABLE 4.2	Drugs Used for Prophylaxis of Stress Ulcer Bleeding		
Agent	Type	Route	Dose Recommendations
Sucralfate	Cytoprotective agent	NG tube	1. 1 g every 6 hr
			2. Watch for drug interactions
Famotidine	H_2 Blocker	IV	1.20 mg every 12 hr
			2. Adjust dose in renal
			insufficiency
Ranitidine	H_2 Blocker	IV	1 . 50 mg every 8 hr
			2. Adjust dose in renal
			insufficiency
Pantoprazol	Proton-pump inhibitor	IV	1. 40 mg daily as a single
			dose

long-standing debate over which pharmacologic approach is the best, and much of this debate concerns the role of gastric acid as a defense against infections of bowel origin (see later).

Sucralfate

Sucralfate is an aluminum salt of sucrose sulfate that forms a protective covering on the gastric mucosa and helps to preserve the structural and functional integrity of the mucosa (20). Part of this effect may be due to local stimulation of prostaglandin production, which helps to preserve gastric blood flow. The pH of gastric secretions is not altered by sucralfate. The drug is given orally or via nasogastric tube in the dosage shown in Table 4.2, and it is the least expensive of the prophylactic drug regimens.

Sucralfate is effective in reducing overt bleeding from gastric erosions in critically ill patients (21). Its efficacy in preventing clinically significant bleeding is not well studied. Several studies have compared sucralfate with drugs that reduce gastric acidity, and these will be described later.

INTERACTIONS. Sucralfate can bind to a number of drugs in the bowel lumen and reduce their absorption. The most important of these are listed below (22).

Warfarin (Coumadin)	Ranitidine
Digoxin	Quinidine
Fluoroquinolones	Thyroxine
Ketoconazole	Tetracycline
Phenytoin	Theophylline

To avoid potential interactions in the bowel, these drugs should be given at least 2 hours before sucralfate. The aluminum in sucralfate can also bind phosphate in the bowel, but hypophosphatemia is only rarely reported in association with sucralfate therapy (23). Nevertheless, sucralfate is not advised for patients with persistent or severe hypophosphatemia. Despite its aluminum content, sucralfate does not elevate plasma aluminum levels with prolonged use (24).

Histamine Type-2 Receptor Antaeonists

Inhibition of gastric acid secretion with histamine type-2 receptor antagonists (H2 blockers) is currently the most popular method of stress ulcer prophylaxis (25). Cimetidine, the original drug in this class, has fallen out of favor because of frequent drug interactions, and has been replaced in popularity by famotidine (Pepcid) and ranitidine (Zantac). Both these drugs are given intravenously in the dosing regimens shown in Table 4.2. Continuous infusion of H_2 blockers is the most effective method of maintaining gastric acid inhibition (26); however, intermittent dosing is currently the favored regimen for stress ulcer prophylaxis. Famotidine is longer lasting than ranitidine [i.e., a single 20 mg intravenous dose of famotidine will inhibit gastric acid for 10-12 hours (27), while a single 50 mg intravenous dose of ranitidine inhibits gastric acid for 6-8 hrs (28)].

DOSE ADJUSTMENTS. Intravenous doses of famotidine and ranitidine are largely excreted unchanged in the urine, and accumulation of these drugs in renal insufficiency can produce a neurotoxic condition characterized by confusion, agitation, and even seizures (27,28). Therefore, the dose of these drugs should be reduced in renal insufficiency. (See the Appendix at the end of the book for drug dosing guidelines in renal insufficiency.)

BENEFITS VERSUS RISKS. Clinical studies have shown that H2 blockers can reduce the incidence of clinically significant bleeding from gastric erosions (21). However, as expected from gastric acid inhibition, H_2 blocker therapy has been associated with an increased risk of infection (6,7,9-11), most notably pneumonia in ICU patients (10). Therefore, the benefits of H_2 blockers in preventing bleeding must be weighed against the risks associated with bacterial overgrowth in the stomach. More on this in the next section.

Sulcrafate versus H 2 *Receptor Antagonists*
Several clinical trials have evaluated the relative effects of sucralfate (cytoprotection) and H_2 blockers (reduced acidity) in critically ill patients (29,30). The results of the most recent clinical trial are shown in Figure 4.4 (29). This study involved 1,200 ventilator-dependent patients in 16 ICUs who were randomized to receive sucralfate (1 gram every 6 hours) or

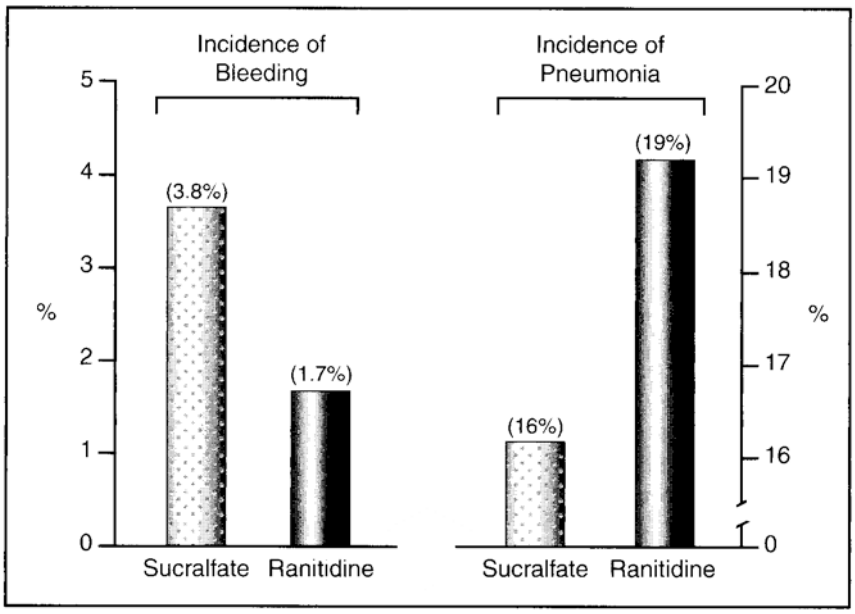

FIGURE 4.4 A comparison of the effects of stress ulcer prophylaxis with sucralfate and ranitidine on the incidence of clinically significant bleeding and hospital-acquired pneumonia in ventilator-dependent patients. (From Cook D, Laine LA, Guyatt GH, et al. A comparison of sucralfate and ranitidine for the prevention of upper gastrointestinal bleeding in patients requiring mechanical ventilation. N Engl J Med 1998;338:791.)

ranitidine (50 mg every 6 hours, adjusted for renal insufficiency). The results show that clinically significant bleeding occurred more frequently in the patients receiving sucralfate (the absolute difference was 2,1 %), while hospital-acquired pneumonia occurred more frequently in the patients receiving ranitidine (the absolute difference was 2.9%). Although the pneumonia difference was not statistically significant in this study, a combined analysis of 8 other studies comparing sucralfate and ranitidine shows a significantly greater incidence of pneumonia with ranitidine (30). The results in Figure 4.4 show that ranitidine is superior too sucralfate for the prevention of bleeding from gastric erosions, while sucralfate is superior to ranitidine for the prevention of pneumonia. So which is preferred: fewer bleeding episodes or fewer pneumonias? The answer can't be based on survival benefit because the mortality in sucralfate- and ranitidine-treated patients is the same (30). One consideration that may be important is the relative incidence of GI bleeding versus pneumonia in ICU patients. As indicated in Figure 4.3, pneumonia occurs much more frequently than GI bleeding, which means that fewer patients would have to be treated with sucralfate to see a benefit (i.e., fewer pneumonias) as compared to ranitidine. Therefore sucralfate may offer an advantage over ranitidine simply because it reduces the risk of the disorder with the greatest risk. Which approach is preferred by critical cafe specialists? A recent survey showed that H2 blockers are used much more frequently than sucralfate for stress ulcer prophylaxis in the ICU (25). However, the major reason for this preference was drug availability rather than clinical efficacy (25).

Proton Pump Inhibitors

Proton Pump Inhibitors (PPIs) block gastric acid secretion by binding to the membrane pump responsible for hydrogen ion secretion by gastric parietal cells (31). These drugs are actually prodrugs, and must be converted to the active form within gastric parietal cells (31). Once activated, PPIs bind irreversibly to the membrane pump and produce complete inhibition of gastric acid secretion. These drugs are much more effective in reducing gastric acidity than H2 blockers, and unlike H2 blockers, they do not produce tolerance with prolonged use (31).

PPIs have replaced H2 blockers as the agents of choice for the treatment of gastroesophageal reflux and peptic ulcer disease. They have also been recommended to prevent stress ulcer bleeding in ICU patients, and the lack of tolerance to PPIs has been proposed as an advantage over H2 blockers (31). Intragastric administration of PPIs can be problematic because these agents are inactivated by acid. Enteric coated granules of omeprazole (Prilosec) and lansoprazole (Prevacid) have been mixed in 8.4% sodium bicarbonate solutions and given via nasogastric tube (32), but this regimen is time consuming to prepare, and the bioavailability may be inconsistent (31). Pantoprazole (Protonix) is available for intravenous use (31,33), but there is no experience with this formulation in stress ulcer prophylaxis.

Given the low frequency of bleeding from gastric erosions and the effectiveness of other prophylactic measures, the use of PPIs for stress ulcer prophylaxis seems unnecessary. Furthermore, the potency of PPIs in raising gastric pH will create even greater risks from bacterial overgrowth in the bowel than the H2 blockers.

Occult Blood Testing

Testing for occult blood in gastric aspirates is not necessary for evaluating the efficacy of stress ulcer prophylaxis. Nasogastric aspirates almost always contain occult blood in the presence of gastric erosions (34), and because few of these cases progress to clinically significant bleeding, the presence of occult blood in nasogastric aspirates has no predictive value for assessing the risk of significant bleeding. For those who insist on monitoring occult blood in gastric aspirates, guaiac and Hemoccult tests are not appropriate because they give false-positive and false-negative results when the test fluid has a pH less than 4 (35). The Castroccult test (Smith, Kline Laboratories) is not influenced by pH (35) and is the more appropriate test for occult blood in gastric aspirates.

DECONTAMINATION OFTHE ALIMENTARY TRACT

The microorganisms that normally inhabit the oral cavity and CI tract seem to live in peaceful coexistence with us. However, in the presence of severe or chronic illness, the alimentary tract becomes populated by more pathogenic organisms capable of causing invasive infections. This section describes two methods for combating this pathogenic colonization. Both methods haven proven effective in reducing the incidence of hospital-acquired infections in the ICU.

Oral Decontamination

The aspiration of mouth secretions into the upper airways is believed to be the inciting event in most cases of hospital-acquired pneumonia. An average of 1 billion (109) microorganisms are present in each milliliter of saliva (36), so aspiration of one microliter (10-3 mL) of saliva will introduce about one million (106) microbes into the airways. Fortunately, the microbes that normally inhabit the mouth are harmless saprophytes (e.g., lactobacillus and alpha--hemolytic streptococci) that show little tendency to produce invasive infection. Critically ill patients are not as fortunate, as described next.

Colonization of the Oral Cavity

The oral cavity in hospitalized patients is often colonized with pathogenic organisms, most notably aerobic gram-negative bacilli like *Pseudomonas aeruginosa* (37). The change in microflora is not environmentally driven, but is directly related to the severity of illness in each patient. This is demonstrated in Figure 4.5. Note that healthy subjects were not colonized

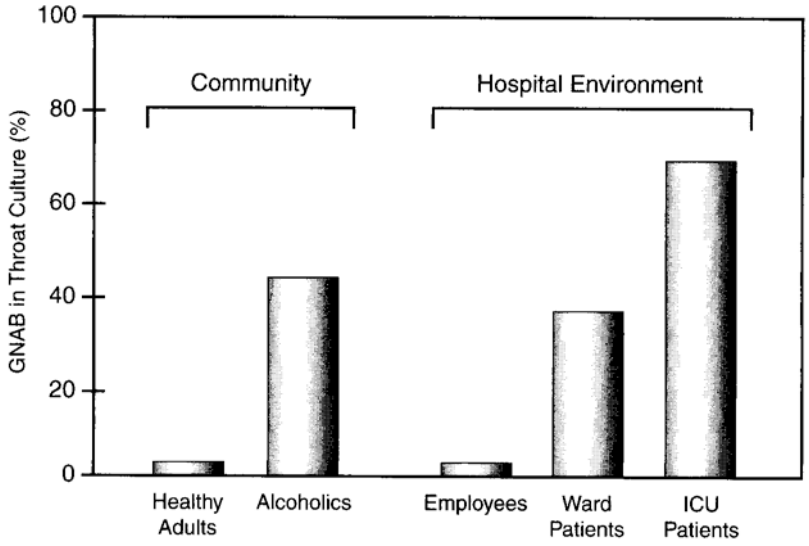

FIGURE 4.5 Colonization of the oral cavity with gram-negative aerobic bacilli (*GNAB*) in different groups of subjects. (From Johanson WG, Pierce AK, Sanford JP. Changing pharyngeal bacterial flora of hospitalized patients. N Engl J Med 1969;281:1137.)

with aerobic gram-negative bacilli, regardless of the time spent in the hospital environment. This highlights the importance of host-specific factors in the microbial colonization of body surfaces.

BACTERIAL ADHERENCE. The host-specific factor in colonization of body surfaces is the tendency for bacteria to adhere to underlying cells, Colonization is not merely a result of microbial proliferation; it requires that microbes adhere to the underlying surface. Epithelial cells on body surfaces have specialized receptor proteins that can bind to adhesion proteins (called *adhesins)* on the surface of bacteria. In healthy subjects, epithelial cells in the mouth express receptors that bind harmless organisms (e.g., lactobacillus), but in seriously ill patients, the epithelial cells bind organisms that are more pathogenic. This change in bacterial adherence is a prelude to hospital-acquired infections. Bacterial adherence is an exciting field of study because manipulation of epithelial cell receptors could be used to prevent (colonization and) infection in seriously **ill** patients (38).

Oral Decontamination Regimen

Colonization of the oral mucosa with aerobic gram-negative bacilli can be viewed as a prelude to pneumonia because gram-negative aerobic organisms are the most common isolates in nosocomial pneumonia (see Chapter 41). This is the basis for a decontamination regimen that uses nonabsorbable antibiotics applied locally in the mouth. One regimen that has proven successful in ICU patients is shown on the next page (39,40):

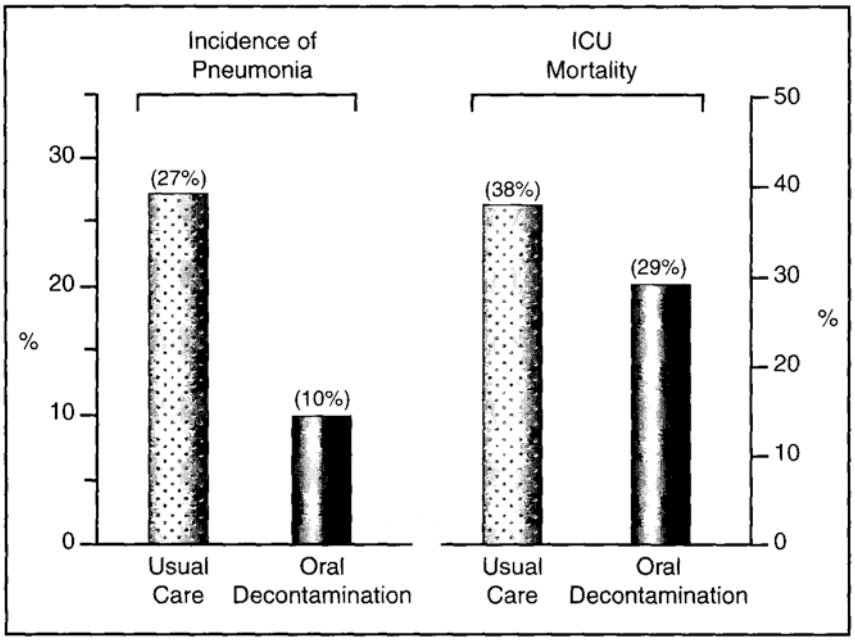

FIGURE 4.6 The effects of oral decontamination on the incidence of pneumonia and the mortality rate in a group of ventilator-dependent ICU patients. (From Bergmans C, Bonten M, Gaillard C, et al. Prevention of ventilator-associated pneumonia by oral decontamination. Am J Respir Crit Care Med 2001;164:382–388.)

Preparation: Have the pharmacy prepare a mixture of 2% gentamicin, 2% colistin, and 2% vancomycin as a paste.
Regimen: Apply paste to the buccal mucosa with a gloved finger every 6 hours until the patient is extubated.

This regimen will eradicate most aerobic bacteria and *Candida* species from the mouth in about one week. The clinical impact of this regimen on the incidence of pneumonia in the ICU is demonstrated in Figure 4.6. This data is from a study of ventilator-dependent patients (39), and oral decontamination reduced the incidence of pneumonia (from 27% to 10%) and the mortality rate (from 38% to 29%) in these patients. This represents a 60% reduction in acquired pneumonias and a 23% reduction in death rate that can be attributed to oral decontamination. A more recent study using the same decontamination regimen showed similar reductions in the incidence of pneumonia (40). Prolonged use of this locally applied antibiotic regimen has not resulted in the emergence of antibiotic resistant organisms (39,40).
INDICATIONS. The success of oral decontamination in reducing the incidence of nosocomial pneumonia has prompted the Centers for Disease Control (CDC) to include a recommendation for oral decontamination in their updated guidelines on preventing pneumonia in health-care

TABLE 4.3	Conditions in the ICU that Might Benefit from Decontamination of the Alimentary Tract	
Oral Decontamination		**Selective Digestive Decontamination**
1 . Ventilator dependence for longer than 1 wk		1. After liver transplantation
2. Severely impaired lung function from any condition		2. Severe burn injuries
3. Increased risk of pulmonary aspiration from any condition		3. Recurrent septicemia of unknown origin
4. Recurrent pneumonia in the ICU		4. Neutropenia in the ICU that lasts 1 wk
		5. Postgastrectomy patients with a prolonged ICU stay

settings (41), Table 4.3 lists the conditions in the leu that might benefit from oral decontamination. The patients who are best suited for this intervention are ventilator-dependent patients with severe respiratory impairment, because the chances of developing a pneumonia in the ICU is highest in these patients, and they are the least likely to tolerate the added insult of a lung infection.

Selective Digestive Decontamination

Selective digestive decontamination (SDD) is a more extensive version of oral decontamination that includes the entire alimentary tract. An example of a successful SDD regimen is shown below (42):

Oral cavity: A paste containing 2% polymyxin, 2% tobramycin, and 2% amphotericin is applied to the inside of the mouth with a gloved finger every 6 hours.

GI tract: A 10 mL solution containing 100 mg polymyxin E, 80 mg tobramycin, and 500 mg amphotericin is given via a nasogastric tube every 6 hours.

Systemic: Intravenous cefuroxime, 1.5 grams every 8 hours, for the first four days of therapy.

This regimen uses nonabsorbable antibiotics in the mouth and GI tract, and it will eradicate most gram-negative aerobic bacteria and yeasts after one week. The intravenous antibiotic provides systemic protection until the bowel regimen is fully effective at one week. Some SDD regimens do not include an intravenous antibiotic, but they are less successful (see later). The oral and CI components of SDD are continued until the patient is well enough to be discharged from the ICU. SDD is selective because it does not eliminate the normal inhabitants of the bowel. Preserving the normal microflora in the bowel is considered an important factor in preventing colonization with opportunistic pathogens.

The influence of SDD on the incidence of ICU-acquired infections is shown in Figure 4.7 (42). In this study, all three infections (pneumonia, urinary tract infections, and septicemia from vascular catheters) were

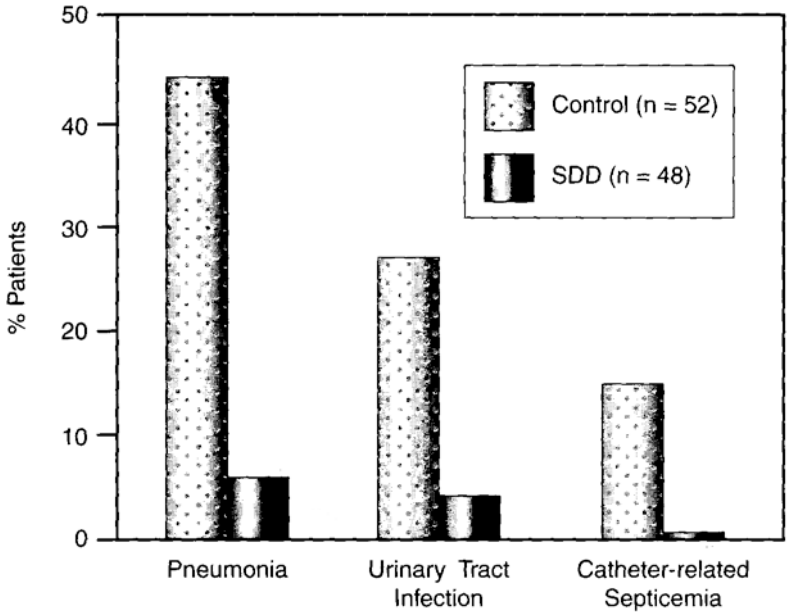

FIGURE 4.7 The effects of selective digestive decontamination (SDD) on the incidence of hospital-acquired infections in ICU patients. (From Ulrich C, Harinck-de Weerd JE, Bakker NC, et al. Intensive Care Med 1989;15:424.)

significantly less frequent in patients who received SDD. Similar results were reported in 10 other clinical trials of SDD, which showed a combined 40% relative reduction in the frequency of acquired infections in the ICU (43).

The Never-Ending Debate

Despite over 20 years of experience with SDD and numerous reports of its efficacy as an infection control measure, there is a continuing debate over the merits of this practice. Two concerns fuel this debate: the impact of SDD on mortality, and the possible emergence of antibiotic-resistant organisms. As for mortality, most of the early studies of SDD showed no reduction in mortality despite the decreased rate of infections. However, a recent large-scale study involving almost 1,000 ICU patients showed a relative 35% reduction in mortality in patients who received SDD (44). The recent study used an intravenous antibiotic for the first few days of treatment, while many of the early SDD regimens did not include an intravenous antibiotic, and this may explain the improved results of the most recent study.

As for the fear of antibiotic resistance, there is no evidence to support this fear (45). The debate over the merits of SDD seems to overlook one simple fact: the goal of SDD is to reduce hospital-acquired infections, and it achieves this goal consistently. Therefore, SDD must be considered an effective method of infection control in the ICU. The observation that

lower incidences of hospital-acquired infections are not accompanied by a lower mortality is a separate issue and should not detract from the success of SDD in reducing acquired infections in the ICU. In fact, the notion that every therapy in the ICU has to save lives to be considered worthwhile is both unfocused and unreasonable.

Indications for SDD
The conditions that are most likely to benefit from SDD are listed in Table 4.3. SDD seems best suited for burn patients (because the incidence of translocation is particularly high in these patients) and following liver transplantation (because SDD reduces the risk of translocation and this can counteract the diminished ability of the newly transplanted liver to clear organisms that have escaped the bowel lumen and entered the venous outflow from the bowel).
REFERENCES

Chapter 5

VENOUS THROMBOEMBOLISM

Two words best characterize the mortality and morbidity due to venous thromboembolism in [he United States: substantial and unacceptable.
Kenneth M. Moser, MD

The threat of venous thrombosis and acute pulmonary embolism (i.e., venous thromboembolism) is a daily concern in the ICU. Several conditions promote venous thrombosis in ICU patients (1-4). These thrombi usually form in proximal leg veins and are often clinically silent, becoming evident only when a portion of the thrombus breaks loose and travels to the lungs to become a pulmonary embolus. This progression from silent thrombosis in the legs to acute pulmonary embolism is believed to be responsible for 10% of all hospital deaths (5) and, because it is possible to prevent thrombus formation in the legs (3,5-7), deaths from pulmonary emboli are considered preventable. **In** fact, pulmonary embolism is one of the leading causes of preventable deaths in hospitalized patients (5).
The principal goal in the approach to venous thromboembolism is to prevent unnecessary deaths from pulmonary embolism. This is best accomplished by preventing thrombus formation (thromboprophylaxis) in proximal leg veins. The importance of thromboprophylaxis in preventing unnecessary hospital deaths has been emphasized by the Agency for Healthcare Research and Quality, who issued a report stating that **prophylaxis for venous thromboembolism is the single most important measure for ensuring patient safety in hospitalized patients** (8).
This chapter presents the current practices for preventing venous thromboembolism in hospitalized patients. Sections also are included on the diagnostic and therapeutic approaches to suspected or documented thromboembolism. Some useful clinical practice guidelines (5-7) are included in the bibliography at the end of the chapter.

PATIENTS AT RISK
There are several factors that promote venous thromboembolism (VTE) in hospitalized patients, and the major ones are listed in Table 5.1 (1-3). These risk factors are responsible for the prevalence of VTE in the clinical groupings shown in Figure 5.1. (The high prevalence of VTE in this figure is an exaggeration of the problem because these rates include asymptomatic cases of VTE that may have no clinical consequence). VTE is most prevalent in three clinical conditions: major surgery (particularly if it is cancer-related or involves the hip or knee), acute stroke, and major trauma (especially spinal cord injury).
Major Surgery
Autopsy studies of surgery patients who die in the hospital reveal pulmonary emboli in up to 30% of cases, and about 30% of these emboli are the direct cause of death (9). There are several factors that predispose to VTE after major surgery, but the most important are vascular injury (in orthopedic procedures) and a

generalized hypercoagulable state caused by thromboplastin release during surgery. Patient-specific factors (e,g" increasing age over 40, prior history of VTE) add further to the risk of postoperative VTE.

TABLE 5.1 Risk Factors for Venous Thromboembolism in Hospitalized Patients

Surgery
Major surgery: abdominal, gynecologic, urologic, orthopedic, neurosurgery, cancer-related surgery
Trauma
Multisystem trauma, spinal cord injury, spinal fracture, fractures of the hip and pelvis
Malignancy
Any malgnancy, overt or covert, local or metastatic. Risk higher during chemotherapy and radiotherapy
Acute medical illness
Stroke, acute myocardial infarction, heart failure, neuromuscular weakness syndromes (e.g., Guillain-Barre)
Patient-specific factors
History of thromboembolism, obesity, increasing age older than 40, hypercoagulable state (e.g" estrogen therapy)
leU-related factors
Prolonged mechanical ventilation, neuromuscular paralysis (drug-induced), central venous catheters, severe sepsis, consumptive coagulopathy, induced thrombocytopenia

From References 2, 3 and 5.

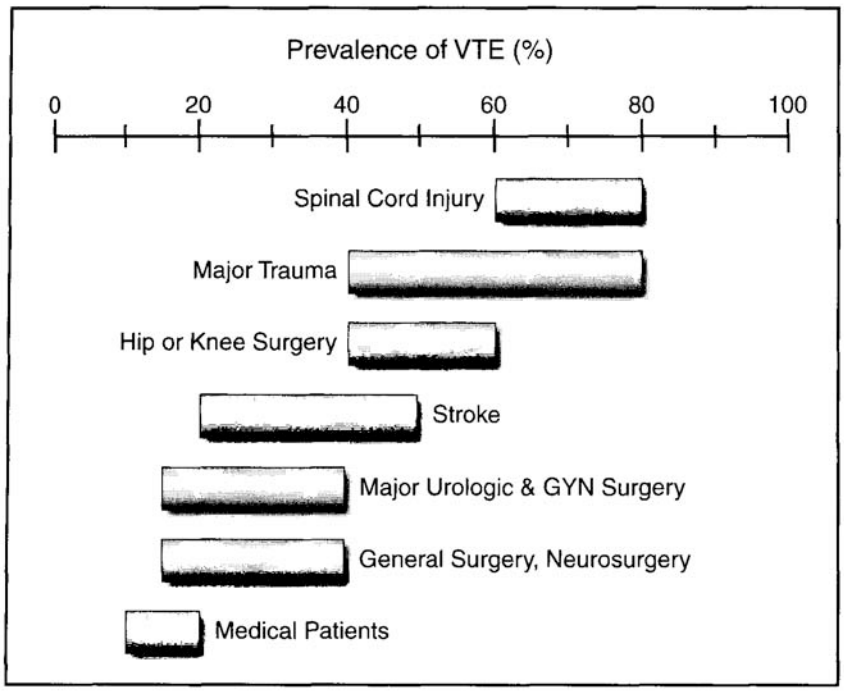

FIGURE 5.1 The prevalence of thromboembolism in different groups of hospitalized patients. From Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest 2004;126:338S.

The risk of VTE after general surgery is determined by 3 factors: the type of procedure (e.g" major vs. minor procedure, cancer-related surgery), the age of the patient, and the presence of other patient-specific risk factors (e.g., malignancy, obesity, prior history of VTE) (3,5). These factors are combined in the risk stratification system shown in Table 5.2, The lowest risk of VTE occurs after minor procedures performed on young patients «40 years of age) who have no other risk factors for VTE. No special preventive measures are required in these patients (5). The highest risk of VTE occurs after major surgery in older patients (>40 years of age) who have one or more risk factors for VTE. The effective methods of thromboprophylaxis for these patients are shown in Table 5.2 and will be described later in the chapter.

Orthopedic Suraery

The highest incidence of postoperative VTE (40 to 60%) occurs after major orthopedic procedures involving the hip and knee. Table 5.3 shows the high-risk procedures and the recommended methods of

TABLE 5.2 Thromboprophylaxis for General Surgery

Risk Categories*	Recommended Prophylaxis†
I. *Low risk*	
Minor surgery + age <40 yr and no other risk factors	Early mobilization only
II. *Moderate risk*	
Major surgery + age <40 yr and no other risk factors	$LDUH_1$ or LMWH,: First dose 2 hr before surgery
III. *High risk*	
Major surgery + age >40 yr or other risk factors	$LDUH_2$ or $LMWH_2$: First dose 2 hr before surgery
IV. *Highest risk*	
Major surgery + age >40 yr and other risk factors	$LDUH_2$ or $LMWH_2$ as above plus mechanical aid
Prophylaxis Regimens	
$LDUH_1$: Unfractionated heparin, 5,000 units SC every 12 hr	
$LDUH_2$: Unfractionated heparin, 5,000 units SC every 8 hr	
LMWH,: Enoxaparin, 40 mg SC once daily, or dalteparin, 2,500 units SC once daily	
$LMWH_2$: Enoxaparin, 30 mg SC every 12 hr, or dalteparin, 5,000 units SC once daily	
Mechanical aid: graded compression stockings or intermittent pneumatic compression	

tMinor surgery: performed under local or spinal anesthesia and lasts <30 min;
gery: performed under general anesthesia and lasts >30 min; other risk factors: obesity, history of thromboembolism, estrogen Rx or other hypercoagulable
LDUH: low-dose unfractionated heparin; LMWH: low-molecular-weight heparin; ed compression stockings; IPC: intermittent pneumatic compression, SC:
tAdapted from Reference 5.

thromboprophylaxis. Arthroscopy alone does not carry a high risk of VTE and does not require thromboprophylaxis (5).

Other Surgeries

The other types of major surgery that have a moderate-to-high risk of VTE are listed in Table 5.4. Missing from this list are laparoscopy, vascular surgery, and closed urologic procedures (e.g., transurethral prostatectomy), These procedures have a low risk of VTE, and thromboprophylaxis is not required unless the patient has one or more of the risk factors for VTE in Table 5.1 (5).

Major Trauma

Major trauma shares the same predisposing factors for VTE as major surgery (which is a form of controlled trauma) (2,3,5). Victims of major

TABLE 5.3 Thromboprophylaxis for Hip and Knee Surgery

Procedures
Elective hip and knee arthroplasty, hip fracture surgery
Drug regimens
Use any of the following:
1. LMWH: Enoxaparin, 30 mg SC every 12 hr, or dalteparin, 2,500 units SC as first dose, then 5,000 units SC once daily. Give first dose 12-24 hr before surgery or 6 hr after surgery.
2. Fondaparinux, 2.5 mg SC once daily. First dose 6-8 hr after surgery (may be the preferred regimen for hip fracture surgery).
3. Adjusted-dose warfarin to achieve INR of 2.0 to 3.0. Give first dose the evening before surgery.
Duration
A. For elective hip and knee surgery, prophylaxis should continue for 10 days after surgery.
B. For hip fracture surgery, prophylaxis should continue for 28 to 35 days after surgery.

LMWH: low-molecular-weight heparin; SC: subcutaneous.
Adapted from Reference 5.

trauma have a greater than 50% chance of developing VTE while hospitalized, and pulmonary embolism is the leading cause of death in those who survive the first week (5). The trauma conditions with the highest risk of VTE are spinal cord injuries, spinal fractures, and fractures of the pelvis (3,5).

Acute Medical Illness

Patients with acute medical illnesses (other than stroke) have a much lower risk of developing VTE than their comrades in the surgery and trauma wards (see Figure 5,1). Despite the relatively low incidence of VTE in medical patients, autopsy studies show that a majority of deaths due to pulmonary embolism occur in medical patients *(10).* This tendency for VTE to be life threatening in medical patients is reason not to overlook the importance of thromboprophylaxis in this patient population.

The ICU Patient

The typical ICU patient has several risk factors for VIE. Some are present on admission (e.g., advanced age, malignancy, major surgery, and major trauma), and some are acquired while in the ICU (e.g., prolonged mechanical ventilation, central venous catheters). Because of this multitude of risk factors, most patients who stay in the ICU more than a few days are considered candidates for thromboprophylaxis. Unfortunately, as many as one of every four ICU patients will continue to have evidence

TABLE 5.4 Thromboprophylaxis for Other Clinical Conditions

Clinical Situation	Recommended Prophylaxis
1 . Major trauma	1. $LMWH_2$ or leg compression (IPC)
2. Spinal cord injury	2. $LMWH_2$ plus leg compression
3. Intracranial surgery	3. Leg compression (I PC}
4. Gynecologic surgery	
a. Benign disease	4a. $LDUH_1$
b. Malignancy	4b. $LDUH_2$ or $LMWH_2$
5. Urologic surgery	
a. Closed procedures	5a. Early mobilization only
b. Open procedures	5b. LDUH, or leg compression
6. High-risk medical illness	6. LDUH, or LMWH,

Prophylaxis Regimens

LDUH,: Unfractionated heparin, 5,000 units SC every 12 hr

$LDUH_2$: Unfractionated heparin, 5,000 units SC every 8 hr

LMWH,: Enoxaparin, 40 mg SC once daily, or dalteparin, 2,500 units SC once daily

$LMWH_2$: Enoxaparin, 30 mg SC every 12 hr, or dalteparin, 5,000 units SC once daily

Leg-compression methods: graded compression stockings (GCS) or intermittent pneumatic compression (IPC)

LDUH: low-dose unfractionated heparin; LMWH: low-molecular-weight heparin; SC: subcutaneous.
From Reference 5.

of deep vein thrombosis (usually asymptomatic) despite appropriate thromboprophylaxis (11,12).

METHODS OF THROMBOPROPHYLAXIS

A number of interventions have proven effective in reducing the incidence of thromboembolism in hospitalized patients (3-6). These include both mechanical and pharmacologic methods of thromboprophylaxis.

External Leg Compression

There are two external compression devices for the legs: graded compression stockings and intermittent pneumatic compression pumps. These devices can be used as an adjunct to anticoagulant prophylaxis or as a replacement for anticoagulant prophylaxis in patients who are bleeding or have a high risk of bleeding.

Graded Compression Stockings

Graded compression stockings (also known as thromboembolism deterrent or TED stockings) are designed to create 18 mm Hg external pressure at the ankles and 8 mm Hg external pressure in the thigh (13). The resulting 10 mm Hg pressure gradient acts as a driving force for venous outflow from the legs. These stockings have been shown to reduce the incidence of VTE when used alone after abdominal surgery and neurosurgery (14,15). However, this is considered the least effective method of thromboprophylaxis, and it is almost never used alone in patients with a moderate or high risk of VTE.

Intermittent Pneumatic Compression

Intermittent pneumatic compression (IPC) pumps are inflatable bladders that are wrapped around the lower leg. When inflated, they create 35 mm Hg external compression at the ankle and 20 mm Hg external compression at the thigh (13). These devices also create a pumping action by inflating and deflating at regular intervals, and this acts to further augment venous flow. Intermittent pneumatic compression is considered more effective than graded compression stockings for thromboprophylaxis (5), and this method can be used alone for selected patients who are not suitable for anticoagulant prophylaxis because of bleeding. This method is particularly popular after intracranial surgery (Table 5.4) and in trauma victims who are at risk for bleeding.

Low-Dose Unfractionated Heparin

The standard heparin preparation is a heterogeneous collection of mucopolysaccharide molecules that can vary in size by a factor of 10 or more. The anticoagulant activity is dependent on the size of the heparin molecule (smaller molecules have greater anticoagulant activity), so the variable size of the molecules in the standard or unfractionated heparin (UFH) preparation means that these preparations will have variable anticoagulant activity. **In** general, only one third or fewer of the molecules have anticoagulant activity (6,7).

Rationale for Low-Dose Heparin

Heparin is an indirect-acting drug that must bind to a cofactor (antithrombin III or AT) to produce its effect. The heparin-AT complex is capable of inactivating several coagulation factors, including factors IIa (thrombin), IXa, Xa, XIa, and XIIa (6). The inactivation of factor IIa (antithrombin effect) is a sensitive reaction and occurs at heparin doses far below those needed to inactivate the other coagulation factors (6). This means that **small doses of heparin can inhibit thrombus formation** (antithrombin effect), **without producing full anticoagulation** (because the other coagulation factors are unaffected). This is the basis for the effect of low-dose heparin in preventing venous thrombosis in high-risk hospitalized patients.

The heparin-AT complex also binds to platelet factor 4, and some patients develop a heparin-induced antibody that can cross-react with

this platelet binding site to produce platelet clumping and subsequent thrombocytopenia. This is the mechanism for heparin-induced thrombocytopenia, and it can be triggered by low-dose heparin as well as therapeutic-dose heparin (4,6). (See Chapter 37 for more information on heparin-induced thrombocytopenia.)

Dosing Regimen

The regimen for low-dose unfractionated heparin (LDUH) is 5,000 Units given by subcutaneous injection twice or three times daily. More frequent (3 times daily) dosing is recommended for higher risk conditions (see the $LDUH_2$ regimen in Tables 5.2 and 5.4). When LDUH is used for surgical prophylaxis, the first dose should be given 2 hours before the procedure. Pre-surgical dosing is recommended because thrombosis can begin during the procedure, and allowing time for the thrombus to grow will reduce the anticoagulant effect of heparin. Postoperative prophylaxis is continued for 7 to 10 days, or until the patient is fully ambulatory. Monitoring laboratory tests of coagulation is not necessary.

Who Beniflts

Low-dose unfractionated heparin (LDUH) provides effective thromboprophylaxis for high-risk medical conditions and most non-orthopedic surgical procedures (see Tables 5.2 and 5.4) (3,5). **It** does not provide optimal prophylaxis for major trauma (including spinal cord injury) and for orthopedic surgery involving the hip and knee. These conditions benefit more from a special preparation of heparin described next.

Low-Molecular- Weight Heparin

The variable-sized heparin molecules in unfractionated heparin can be cleaved enzymatically to produce smaller molecules of more uniform size. Because smaller heparin molecules have more anticoagulant activity, the resultant low-molecular-weight heparin (LMWH) is more potent and has more uniform anticoagulant activity than UFH. LMWH has several potential advantages over unfractionated heparin, including less frequent dosing, a lower risk of both bleeding and heparin-induced thrombocytopenia, and no need for routine anticoagulant monitoring with full anticoagulant dosing (this is described later in the chapter) (4,6). The disadvantage of LMWH is the cost: LMWH can be 10 times more costly (per day) than unfractionated heparin (16-18).

Who Benefits

LMWH is more effective than unfractionated heparin for orthopedic procedures involving the hip and knee, and for major trauma, including spinal cord injury (5).

Low-Dose Regimens

There are currently seven LMWH preparations available for clinical use, but only two have been studied extensively for thromboprophylaxis:

enoxaparin (Lovenox) and dalteparin (Fragmin). Enoxaparin was the first LMWH approved for use in the United States (in 1993), and the clinical experience with this drug is the most extensive.

The recommended doses of enoxaparin and dalteparin for thromboprophylaxis are shown in Tables 5.2-5.4 (see $LMWH_1$ and $LMWH_2$). Both drugs are given by subcutaneous injection. Enoxaparin is given once daily (40 mg) for moderate-risk conditions, and twice daily (30 mg in each dose) for high-risk conditions (3-6,17). Dalteparin is given once daily in a dose of 2,500 units for moderate-risk conditions and 5,000 units for high-risk conditions (3-6,18).

TIMING. For non-orthopedic surgery, the first dose of each drug (30 mg for enoxaparin, 2,500 U for dalteparin) should be given 2 hrs before surgery (5). For orthopedic procedures, the first dose of each drug has traditionally been given 12-24 hours before surgery. However, preoperative drug administration can increase bleeding in orthopedic procedures and may offer no added protection, so preoperative dosing may be abandoned in favor of starting prophylaxis 6 hours after surgery (waiting longer reduces efficacy) (19).

SPINAL ANESTHESIA. The use of LMWH in conjunction with spinal anesthesia for orthopedic surgery can result in a spinal hematoma and paralysis (17-19). When spinal anesthesia is used for an orthopedic procedure, the first dose of LMWH should be delayed until 12 to 24 hours after surgery (19), or adjusted-dose warfarin should be used for thromboprophylaxis.

RENAL FAILURE. LMWHs are excreted primarily by the kidneys, although the extent of renal clearance differs for individual agents. For patients with renal failure, the prophylactic dose of enoxaparin should be decreased from 30 mg twice daily to 40 mg once daily for high-risk patients (5). No dose adjustment is recommended for dalteparin (18).

Adjusted-Dose Warfarin

Systemic anticoagulation with warfarin (Coumadin; Bristol-Meyers Squibb) is a popular method of prophylaxis for major orthopedic surgery. There are two benefits with warfarin: the preoperative dose does not create a bleeding tendency during surgery because of the delayed onset of action with vitamin K antagonists, and warfarin can be continued after discharge if prolonged prophylaxis is required (see later). The disadvantages of warfarin prophylaxis include a multitude of drug interactions (20), the need to monitor laboratory tests of coagulation, and difficulty adjusting doses to the desired effect because of the delayed onset of action.

Dosing Regimen

The initial dose of warfarin is 10 mg orally, given the evening before surgery. This is followed by a daily dose of 2.5 mg, starting the evening after surgery. The dosage is then adjusted to achieve a prothrombin time with an international normalized ratio (INR) of 2 to 3 (5), This is usually not reached until at least the third postoperative day.

Who Benefits
Adjusted-dose warfarin is one of three effective regimens for major orthopedic procedures involving the hip and knee (see Table 5.3) (5). It is the most popular prophylactic regimen for hip replacement surgery in North America, despite evidence that LMWH is more effective (5). Warfarin may be preferred in patients who require prolonged prophylaxis after hospital discharge (see later) because of the convenience of oral dosing.

Fondaparinux
Fondaparinux (Arixtra; GlaxoSmithKline) is a synthetic anticoagulant that selectively inhibits coagulation factor Xa. Like heparin, it must bind to antithrombin III to exert its anticoagulant effect but, unlike heparin, it only inhibits the activity of factor Xa. The benefits of fondaparinux are a predictable anticoagulant effect (thus obviating the need for laboratory monitoring) and the absence of a heparin-like, immune-mediated thrombocytopenia (4,21).

Dosing Regimen
The prophylactic dose of fondaparinux is 2.5 mg given once daily as a subcutaneous injection. When used for surgical prophylaxis, the first dose should be given 6 to 8 hours after surgery (if given sooner, there's an increased risk of bleeding) (5). The drug is cleared by the kidney, and, when creatinine clearance is <30 mL/min, drug accumulation and bleeding can occur (21). Therefore the drug is contraindicated in patients with severe renal impairment (creatinine clearance <30 *mL/min) (22).* It also is contraindicated in patients who weigh <50 kg because of a marked increase in bleeding in these patients (22).
Who Beniflts
Fondaparinux is as effective as LMWH for thromboprophylaxis after major orthopedic surgery involving the hip and knee (5). The only advantage of fondaparinux over LMWH is the absent risk of heparin induced thrombocytopenia.

Duration of Prophylaxis
Following major orthopedic procedures involving the hip and knee, there is an increase in symptomatic VTE after prophylaxis is terminated and patients are discharged from the hospital, and symptomatic VTE is the most common cause of readmission after hip replacement surgery (5). These observations prompted the following recommendations: 1) thromboprophylaxis should be continued for at least 10 days following major orthopedic surgery, even if patients are discharged before this time (5), and 2) following hip surgery, patients with additional risk factors for VTE (e.g., malignancy, advanced age, prior history of VTE), should receive prophylaxis for a total of 28 to 35 days (5). Post-discharge

thromboprophylaxis can be achieved with usual prophylactic doses of warfarin, LMWH, or fondaparinux (the latter two agents require subcutaneous injections, which may be a problem in some outpatients),

DIAGNOSTIC APPROACH TO THROMBOEMBOLISM

As mentioned earlier, thrombosis in the deep veins of the legs is often clinically silent, and becomes evident only when a pulmonary embolus occurs. Therefore, the diagnostic evaluation of symptomatic thromboembolism usually involves cases of suspected acute pulmonary embolism.

The Clinical Evaluation

The clinical presentation of acute pulmonary embolism is non-specific, and there are no clinical or laboratory findings that will confirm or exclude the diagnosis of pulmonary embolism (23). The predictive value of clinical and laboratory findings in acute pulmonary embolism is shown in Table 5.5. Note that none of the findings provides more than a 50% chance of identifying pulmonary embolism when present, and none is able to absolutely exclude the presence of pulmonary embolism when absent (a normal test must have a predictive value of 98% or greater to reliably exclude the diagnosis). Note also that hypoxemia has a negative predictive value of 70%, which means that 30% of patients with acute pulmonary embolism are not hypoxemic. Although not included in

TABLE 5.5 Clinical and Laboratory Findings in Patients with Suspected Pulmonary Embolism

Findings	Positive Predictive Value	Negative Predictive Value
Dyspnea	37%	75%
Tachycardia	47%	86%
Tachypnea	48%	75%
Pleuritic chest pain	39%	71%
Hemoptysis	32%	67%
Hypoxemia	34%	70%
Elevated plasma D-dimer[8]	27%	92%
Increased dead-space ventilation[b]	36%	92%

Positive predictive value: the percentage of patients with the findings who had a nary embolus. It expresses the likelihood that a pulmonary embolus is present finding is present; negative predictive value: the percentage of patients without ing who did not have a pulmonary embolus. It expresses the likelihood that a embolus is not present when the finding is also not present.

Table 5.5, a normal alveolar-arterial $P0_2$ gradient likewise does not exclude the presence of acute pulmonary embolism (24).

Plasma D-Dimer Levels

Cross-linked fibrin monomers, also called *fibrin D-dimers* or simply *D-dimers,* are products of clot lysis and are expected to be elevated in the setting of active thrombosis. Although popular in the emergency department, plasma D-dimer assays have little value in the evaluation of thromboembolism in the ICU. The problem is the multitude of other conditions that can elevate plasma D-dimer levels, including sepsis, malignancy, pregnancy, heart failure, renal failure, and advanced age (25). As a result, a majority (up to 80%) of ICU patients have elevated plasma D-dimer levels in the absence of venous thromboembolism (26). This is reflected in the poor positive predictive value shown in Table 5.5.

Plasma D-dimer levels may be more valuable for excluding the diagnosis of venous thromboembolism. In ICU patients, the negative predictive value of a normal plasma D-dimer level is 92% (see Table 5.5), which means that when the plasma D-dimer level is not elevated, 92% of the patients will not have venous thromboembolism. However, since only a small percentage of ICU patients have normal plasma D-dimer levels, the value of a normal test result is limited.

Alveolar Dead Space

The cardiopulmonary consequences of pulmonary emboli include a decrease in pulmonary blood flow leading to an increase in alveolar dead space ventilation (see Chapter 19 for a description of dead space ventilation). In patients who present to the emergency room with suspected pulmonary embolism, a normal dead space measurement (i.e., < 15% of total ventilation) has a high predictive value for excluding the diagnosis of pulmonary embolism (see the negative predictive value of 92% in Table 5.5) (27). Adding a normal plasma D-dimer level to a normal dead space measurement adds further to the predictive power for excluding pulmonary embolism (27).

The value of the dead space measurement has not been studied in ICU patients, Most patients in the ICU are expected to have elevated dead space ventilation (from cardiopulmonary disease), so a normal measurement might be too infrequent to be useful. Monitoring for *changes* in dead space ventilation (which is easily done in ventilator-dependent patients) might be more useful for evaluating patients who develop respiratory distress while in the ICU.

Venous Ultrasound

Because the clinical evaluation of suspected pulmonary embolism will not confirm or exclude the diagnosis, specialized tests are required. These tests are included in the flow diagram in Figure 5.2.

Since most pulmonary emboli originate from thrombosis in proximal leg veins (28), the evaluation of suspected pulmonary embolism

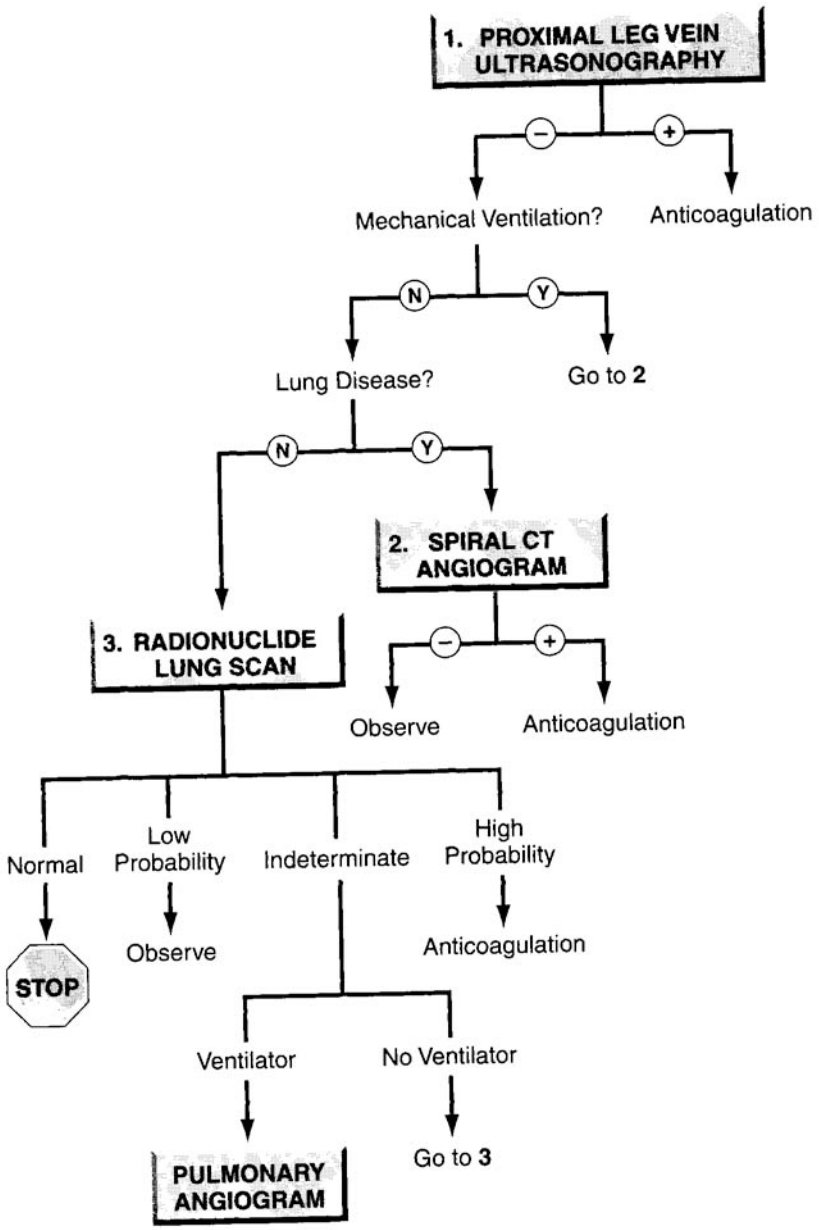

FIGURE 5.2 Flow diagram for the evaluation of suspected pulmonary embolism.

often begins with an ultrasound evaluation of the femoral veins. Two complementary techniques are combined for the ultrasound detection of venous thrombosis. One of these techniques is *compression ultrasound.* This method uses two-dimensional brightness modulation (B-mode) ultrasound to obtain a cross-sectional view of the femoral artery and

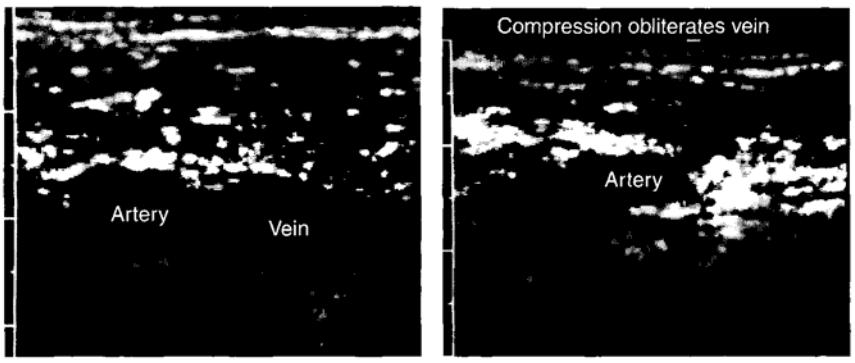

FIGURE 5.3 Ultrasound images showing a transverse view of the femoral artery and vein (image on the left) and obliteration of the femoral vein by compression of the overlying skin (image on the right). (From Cronan J, Murphy T. A comprehensive review of vascular ultrasound for intensivists. J Intensive Care Med 1993;8:188, with permission.) Images digitally retouched.

vein, as shown in the image on the left in Figure 5.3. External compression is then applied by pushing down on the ultrasound probe to indent the skin. This will normally compress the underlying vein and obliterate its lumen, as shown in the image on the right in Figure 5.3. When a vein is filled with blood clots (which are usually not visualized by ultrasound), external compression does not compress the vein. Therefore an incompressible vein is used as indirect evidence of venous thrombosis (29).

The other technique is *Doppler ultrasound*, which relies on the wellknown Doppler shift to detect the velocity of blood flow in vessels. Flow velocity can be recorded audibly (the faster the flow, the higher the frequency of the Doppler signal) or by color changes (faster flows cause a shift from the blue to the red spectrum of light). Doppler ultrasound is valuable for distinguishing arteries from veins and can also detect sluggish flow in veins (a possible sign of partial occlusion by thrombi). The combination of compression and Doppler ultrasound is known as *duplex ultrasound.*

Accuracy

For the detection of deep vein thrombosis (DVT) in the thigh (proximal DVT), duplex ultrasound has a sensitivity of 95% to 100% a specificity of 97 to 100%, a positive predictive value as high as 97%, and a negative predictive value as high as 98% (29). These numbers show that duplex ultrasound is highly accurate and reliable for the detection of proximal DVT in the legs.

Unlike its performance for proximal DVT, duplex ultrasound does not perform well for the detection of venous thrombosis below the knee (calf DVT). For the detection of calf DVT, ultrasound has a sensitivity of only 33% to 70% (2). This means that as many as two-thirds of cases of

DVT below the knees can be missed by ultrasonography. If calf DVT is suspected because of symptoms (pain, swelling, etc.) and ultrasound is unrevealing, one option is to follow with serial ultrasound examinations (as long as the thrombus does not propagate to above the knee, there is little risk of pulmonary embolism), and the other is to perform contrast venography.

Leg DVT and Pulmonary Embolism
Despite the consensus view that most pulmonary emboli originate from proximal DVT in the legs, as many as 30% of patients with acute pulmonary embolism show no evidence of venous thrombosis in the legs (30). As a result, a negative evaluation for proximal DVT in the legs does not exclude the diagnosis of acute pulmonary embolus. When the search for leg vein thrombosis is unrevealing and the clinical suspicion of pulmonary embolism is high, the next step in the evaluation is either spiral computed tomography (CT) or a radionuclide lung scan. As shown in Figure 5.2, the procedure that is most appropriate is determined by the presence of mechanical ventilation and the presence of lung disease.

Radionuclide Lung Scan
Ventilation-perfusion lung scans are widely used in the evaluation of suspected pulmonary embolism, but they secure the diagnosis in only about 25% to 30% of cases (31). The problem is that the presence of lung disease (particularly infiltrative disease) will produce an abnormal scan in about 90% of cases (31). Lung scans are most helpful in patients with no underlying lung disease (which, unfortunately, excludes most ICC patients). If the decision is made to proceed with a lung scan, the results can be used as follows (31):

A *normal lung* scan excludes the presence of a (clinically important) pulmonary embolus, whereas a high-probability lung scan carries a 90% probability that a pulmonary embolus is present.

A *low-probability* lung scan does not reliably exclude the presence of a pulmonary embolism. However, when combined with a negative ultrasound evaluation of the legs, a low-probability scan is sufficient reason to stop the diagnostic workup and observe the patient.

An *intermediate-probability* or *indeterminate* lung scan has no value in predicting the presence or absence of a pulmonary embolus. In this situation, the options include spiral CT angiography (see next) or conventional pulmonary angiography.

Spiral CT Angiography
Spiral (helical) computed tomography (spiral CT) is a technique where the detector is rotated around the patient to produce a volumetric two-dimensional view of the lungs (32). (This differs from conventional CT,

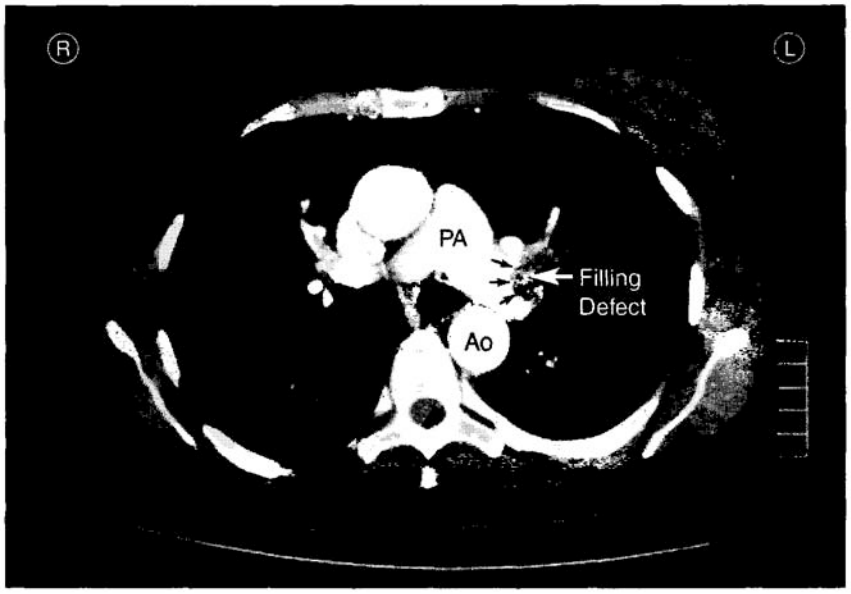

FIGURE 5.4 Spiral CT angiogram showing a pulmonary embolus (filling defect) in the left main pulmonary artery. PA = pulmonary artery; AO = aorta. Image digitally retouched.

where the detector is moved in increments along the thorax to create two-dimensional "slices" of the lungs.) This procedure is completed in about 30 seconds, There must be no lung motion during the procedure, which means that patients must be able to breath-hold for 30 seconds to perform a spiral CT scan (32). This excludes patients who are ventilatordependent or are unable to follow commands. Spiral CT has been performed on a few ventilator-dependent patients using continuous positive airways pressure (CPAP) combined with heavy sedation to inhibit chest wall movements (33), but the safety and reliability of this approach has not been validated in large numbers of patients.

When spiral CT is combined with peripheral injection of a contrast agent, the central pulmonary arteries can be visualized. A pulmonary embolus appears as a filling defect, as shown in Figure 5.4. Spiral CT angiography is best suited for detecting clots in the main pulmonary arteries, where the sensitivity and specificity are 93% and 97%, respectively (34). Unfortunately, as many as 70% of emboli in smaller, subsegmental vessels can be missed with this technique (34). However, the importance of detecting smaller, sub segmental emboli is questionable because withholding anticoagulant therapy based on a negative CT scan does not seem to adversely affect clinical outcomes (35).

Spiral CT is gaining popularity in the evaluation of suspected pulmonary embolism. It is most valuable in patients who have lung disease (see Figure 5.2), because lung scans are often non-diagnostic in these

patients. Its value in the ICU is limited by the difficulty of performing the procedure in ventilator-dependent patients.

Pulmonary Angiography

Pulmonary angiography, still considered the most accurate method for detecting pulmonary emboli, is performed in fewer than 15% of cases of suspected pulmonary embolism (36). Considering the array of other diagnostic modalities, the low rate of pulmonary angiography seems justified.

ANTITHROMBOTIC THERAPY

Anticoagulation

The initial treatment of thromboembolism that is not life-threatening is anticoagulation with heparin.

Unfractionated Heparin

The standard treatment of both deep vein thrombosis and acute pulmonary embolism is unfractionated heparin (UFH) given by continuous intravenous infusion using weight-based dosing, as shown in Table 5.6. These guidelines have been derived from patients weighing less than 130 kg (37). For body weights in excess of 130 kg, the guidelines in Table 5.6 can result in excessive anticoagulation (38), so it is important to monitor anticoagulation carefully in these patients.

TABLE 5.6 Weight-based Heparin Dosing Regimen

1. Prepare heparin infusion by adding 20,000 IU heparin to 500 mL diluent (40IU/mL).
2. Give initial bolus dose of 80 IU/kg and follow with continuous infusion of 18 IU/kg/hr. (Use actual body weight.)
3. Check PIT 6 hr after start of infusion, and adjust heparin dose as indicated below.

PTI (sec)	PTI Ratio	Bolus Dose	Continuous Infusion
<35	<1.2	801U/kg	Increase by 4 IU/kg/hr
35-45	1.2-1.5	401U/kg	Increase by 2 IU/kg/hr
46-70	1.5-2.3	–	–
71-90	2.3-3.0	–	Decrease by 2 IU/kg/hr
>90	>3	–	Stop infusion for 1 hr then decrease by 3 IU/kg/hr

4. Check PIT 6 hr after each dose adjustment. When in the desired range (46-70 sec), monitor daily,

From Raschke RA, Reilly BM, Guidoy JR, et al. The weight-based heparin gram compared with the "standard care" nomogram. Ann Intern Med

Low-Molecular- Weight Heparin
Low-molecular-weight heparin (LMWH) is an effective alternative to UFH for treatment of deep vein thrombosis and acute pulmonary embolism (7). The therapeutic dose of a standard LMWH preparation is:

Enoxaparin 1 mg/kg by subcutaneous injection every 12 h

As mentioned earlier, LMWH is cleared by the kidneys, and dose adjustments are necessary in patients with renal impairment (see Chapter 17 for these dose adjustments). In patients with renal failure and thromboembolism who require heparin, UFH is recommended over LMWH (7).
LMWH offers several advantages over UFH, including simplified dosing, no need to monitor anticoagulant activity (see below), and the ability to treat outpatients (which could help to reduce hospital admissions for deep vein thrombosis). For these reasons, LMWH is slowly replacing UFH for the initial management of thromboembolism.

Monitoring Anticoagulation
As mentioned earlier in the chapter, the anticoagulation produced by a given dose of UFH can vary, primarily because of the variable size of the heparin molecules in UFH. As a result, laboratory tests of anticoagulant activity must be monitored to determine the anticoagulant response to UFH. The activated partial thromboplastin time (aPTT) can be used for this purpose because it is a reflection of coagulation factor IIa activity, and one of the prominent effects of UFH is inhibition of factor IIa (antithrombin effect). The aPTT cannot be used to monitor anticoagulation with LMWH because LMWH acts primarily to inhibit factor Xa, and the aPTT is not a reflection of factor Xa activity. Since LMWH produces a more predictable level of anticoagulation than heparin, monitoring laboratory tests of anticoagulation is usually not necessary with LMWH. If needed, the anticoagulant response to LMWH can be assessed by measuring factor Xa activity (7).

Warfarin Anticoaaulation
For patients with a reversible cause of venous thromboembolism (e.g., major surgery), oral anticoagulation with warfarin (Coumadin) can be started on the first day of heparin therapy. When the prothrombin time reaches an international normalized ratio (INR) of 2 to 3, the heparin can be discontinued. (See reference 39 for a description of the INR.) Oral anticoagulation with coumadin is continued for at least 3 months (7). Patients with cancer-related or recurrent VTE require longer periods of anticoagulation (see reference 7 for more information on long-term anticoagulant therapy).

Thrombolytic Therapy
Thrombolytic therapy is usually reserved for life-threatening cases of pulmonary embolism accompanied by hemodynamic instability (7,40).

Some also recommend thrombolytic therapy for hemodynamically stable patients with right ventricular dysfunction (41) and for cardiac arrest (42), although the benefits of lytic therapy in these situations is unclear (7,42). The major problem with thrombolytic therapy is bleeding: there is a 12% incidence of major hemorrhage (40) and a 1 % incidence of intracranial hemorrhage (7,40). Although the presence of risk factors for bleeding is usually a contraindication to thrombolytic therapy, in the setting of a life-threatening condition, the risk of withholding lytic therapy (i.e., death) can sometimes outweigh the risk of bleeding.
All thrombolytic agents are considered equally effective (7,40), and systemic drug administration is favored over local infusion into the pulmonary arteries because of bleeding at the catheter insertion site (7). The two drug regimens shown below are designed to achieve rapid clot lysis.

Alteplase: 0.6 mg/kg over 15 minutes.
Reteplase: 10 Units by bolus injection, and repeat in 30 minutes.

The usual alteplase dose is 100 mg infused over 2 hours, but the alteplase regimen shown here achieves the same degree of clot lysis in a shorter period of time (43). Reteplase is not currently approved for treatment of thromboembolism in this country, but the bolus administration of this drug is well-suited for rapid clot dissolution (44), For more information on the use of thrombolytic agents, see Chapter 17.

Inferior Vena Cava Filters
Meshlike filter devices can be placed in the inferior vena cava to trap thrombi that break loose from leg veins and prevent them from traveling to the lungs. These devices can be used in any of the conditions listed below.
Indications
Patient has proximal deep vein thrombosis in the legs and has one of the following conditions:
A contraindication to anticoagulation
Pulmonary embolization during full anticoagulation
A free-floating thrombus (i.e" the leading edge of the thrombus is not adherent to the vessel wall).
Poor cardiopulmonary reserve and unlikely to tolerate a pulmonary embolus.
Patient does NOT have proximal deep vein thrombosis in the legs but has one of the following conditions:
Requires long-term prophylaxis of pulmonary embolism (e.g., patients with a history of recurrent pulmonary embolism)
Has a high risk of thromboembolism and a high risk of hemorrhage from anticoagulant drugs (e.g., trauma victims)

About 80% of inferior vena cava (IVe) filters are placed in patients who have deep vein thrombosis in the legs combined with one of the conditions listed in section A (45).

The Greenfield Filter

The most widely used IVC filter in the United States is the Greenfield filter (Boston Scientific, Glen Allen, VA), shown in Figure 5.5. The major advantage of this filter is its elongated, conical shape, which allows the basket to fill with thrombi to 75% of its capacity without compromising the cross-sectional area of the vena cava. This limits the risk for vena cava obstruction and troublesome leg edema, which plagued earlier models of IVC filters.

Insertion

IVC filters are inserted percutaneously, usually through the internal jugular vein or femoral vein, and are placed below the renal veins, if possible. Suprarenal placement is occasionally necessary when the thrombus extends to the level of the renal veins, but this does not impair venous drainage from the kidneys. Although usually inserted in the radiology department, IVC filters can be placed at the bedside, thereby eliminating the risks and manpower involved in patient transport (46).

IVC filters have proven both safe and effective, which explains why their use has increased 25-fold over the last two decades (45). The incidence of post-insertion pulmonary embolism is about 5% (47), and major complications (e.g., migration of the filter) are reported in less than 1 % of patients (47). Despite their intravascular location, IVC filters rarely become infected in the face of septicemia (for unclear reasons).

References