Chapter

Li Sustainin Antibiotic Therapy

CONTENTS

Figure

Tables

Chapter 9

Life-Sustaining Antibiotic Therapy

INTRODUCTION

The discovery of antibiotics has been described as the greatest life-saving technological development in the history of medicine. Prior to the development of antibiotics, infectious diseases accounted for over half of all hospitalizations and were responsible for most fatalities in this country. Sulfanilamide was the first antibiotic to be discovered, and physician-author Lewis Thomas has recalled the powerful impression this drug made during his intern years following its introduction in the late 1930s:

> . . . For most of the infectious diseases on the wards of the Boston City Hospital in 1937, there was nothing to be done beyond bed rest and good nursing care. Then came the explosive news of sulfanilamide, and the start of the real revolution in medicine.
>
> I remember the astonishment when the first cases of pneumococcal and streptococcal septicemia were treated in Boston in 1937. The phenomenon was almost beyond belief. Here were moribund patients, who would most surely have died without treatment, improving in their appearance within a few hours of being given the medicine and feeling entirely well within the next day or SO **(69).**

Antibiotics are now widely used to treat a variety of infections caused by viruses, fungi, bacteria, and other protists and are credited with a 10-year extension in average life expectancy at birth. By way of contrast, it is estimated that the successful elimination of cancer would result in only a 2-year extension of life expectancy at birth (31).

Antibiotics are currently prescribed more often than any other class of drugs in the United States and account for more than 25 percent of the $3 billion in annual hospital drug expenditures (52). Some antibiotics can destroy or prevent the growth of only one or a few different kinds of harmful agents, while newer derivatives act against a broader range of pathogens. Antibiotics are used most often to treat mild infections or to prevent infection. This chapter focuses, however, on the use of antibiotics to treat life-threatening infections that, without treatment, would result in death within a few days of onset of the infection.

Antibiotic treatment is generally effective. In addition, it is usually safe, readily available, and relatively inexpensive and painless. For these reasons, and because most people consider antibiotics noninvasive, many health care providers believe that antibiotic treatment is always appropriate when an active infection is present.

Despite this strong presumption in favor of using antibiotic therapy, some health care providers and others believe that there are circumstances in which it is justifiable to withhold life-sustaining antibiotic treatment (18,43,55,78). For example, one physician told about his 96-year-old mother who experienced two strokes a week apart and developed pneumonia following the second. The woman's children asked the hospital staff not to treat the pneumonia, but the hospital staff insisted that they could not "do nothing," and she was given intravenous antibiotics. She survived and was discharged to a nursing home. Her son wrote:

> She can still recognize her family visitors, say their names, and engage in trivial conversation, but her mind is substantially destroyed . . . She is no longer aware of her plight, and expresses no suggestion of despair, but everything she wanted to avoid has happened. In a semiivgetating state, she has lost her functional and mental independence. I, the physician son of this woman, weep for my mother and for what has happened to my profession (24).

Although antibiotics are usually effective in the treatment of infections in people of all ages, these drugs cannot cure underlying diseases or disabling conditions that are common among elderly patients. In some patients, a life-threatening infection is superimposed on a terminal illness or an incurable, severely debilitating, chronic disease. Some health care providers and other people believe that in such cases the use of antibiotics to treat the infection sometimes prolongs the dying

process or prolongs the patient's suffering unnecessarily.

The few available reports on decisions about antibiotic treatment for terminally ill and severely debilitated elderly people suggest that antibiotic treatment is sometimes withheld from such patients (8,14,33,50,65). Yet these treatment decisions have received much less attention and analysis than decisions about withholding or withdrawing other life-sustaining treatments. This chapter discusses the use of antibiotic therapy for elderly people with life-threatening conditions, the outcomes of such treatment, and what is known about the factors associated with nontreatment.

DESCRIPTION OF LIFE-SUSTAINING ANTIBIOTIC THERAPY

Life- Threatening Infections in Elderly People: The Need for Life-Sustaining Antibiotic Therapy

Despite the frequent success of antibiotics in reversing life-threatening infections, infectious diseases remain a serious problem for elderly people. At a time when medical technologies can support body functions almost indefinitely, severe infection is still one of the few challenges to such interventions. It has been estimated that infections account for approximately 30 percent of all deaths in the elderly population (48). One study based on autopsies found that infection was the second most frequent identifiable cause of death in persons over age 85 (following atherosclerosis) (39).

Some of the life-threatening infections that commonly affect elderly people—bacterial pneumonia, urinary tract infections, infected decubitus ulcers (bed or pressure sores), and iatrogenic infections that sometimes result from the use of medical devices—are described in table 9-1. Any local infection in a seriously ill older person, however, can rapidly spread and become life-threatening.

Various risk factors make people vulnerable to infection, and some risk factors are more prevalent among older people than younger people. One factor that increases the risk of infection is hospitalization. People in hospitals are exposed to a large number of agents that can cause infections. Elderly people are more likely to be hospitalized than younger people, and because of diminished immune function and other factors discussed below, hospitalized elderly patients are two to five times more likely to develop nosocomial (hospital-acquired) infections than hospitalized younger patients (30). Nosocomial infections are often fatal, in part because they are frequently caused by agents that are resistant to antibiotics (79).

A second risk factor for infection—also much more likely for older than younger people—is residence in a nursing home. Communal living, use of urinary catheters, and other factors often associated with nursing home care foster infections. Research indicates that, on average, 15 to 20 percent of nursing home residents have an active infection at any given time (17,26,44).

A third factor that makes many elderly people vulnerable to infections is the presence of multiple illnesses, or comorbidities. The proportion of people with such conditions rises rapidly with age, and it is estimated that 80 to 90 percent of elderly patients with infections also have other diseases including cancer, diabetes, Alzheimer's disease, chronic congestive heart failure, and chronic obstructive pulmonary disease (23).

Other important factors that increase the risk of infections are diminished immune function, diminished physiological function, and reduced physical activity. Immune function declines with age, with various diseases, with some medical treatments (e.g., cancer chemotherapy) (19,29,53), and with inadequate intake of food and fluids that may result from poverty, depression, forgetfulness, mobility impairments, illness, or medical treatments that decrease appetite. Diminished physiological function–for example, a diminished cough reflex-increases susceptibility to infections (8). Reduced physical activity often associated with chronic illness and impaired mobility increases the risk of respiratory infections and decubitus ulcers (19).

A final factor that increases the risk of infection is the use of life-sustaining medical devices

Table 9-1.—Life-Threatening Infections That Commonly Affect Elderly People[a]

Pneumonia is the leading cause of death due to infectious diseases and it ranks sixth as a cause of death for people of all ages in the United States (31). Bacterial pneumonia, along with infiuenza, is the fourth most common cause of death in elderly people, accounting for 185 deaths per 100,000 persons (40). Mortality rates range from 10 to 80 percent, depending on the bacteria involved and the degree of lung destruction (8). **Nosocomial (hospital-acquired) pneumonias are the most deadly and account for approximately 15 percent of hospital-acquired infections (75). Recent studies suggest that the risk is comparable in nursing homes. Several diseases or condition-associated factors that predispose people to pneumonia are more frequent in the elderly population or affect the elderly more severely—e.g., chronic bronchitis, congestive heart failure, stroke, and dementia (8).**	**infected decubitus ulcera (bed or pressure sores) are associated with immobility, malnutrition, and diabetes, all of which result in poor circulation and skin breakdown. One study found decubiti were the leading source of infection among 532 patients in nursing homes, with a prevalence rate of 6 percent (26). Despite appropriate medical and surgical care, elderly patients with pressure sores associated with bacteremia have a very poor prognosis. The overall mortality associated with sepsis (spread of the infection to the bloodstream) due to pressure sores is approximately 40 percent, and the highest rates (78 percent) have been documented in elderly patients (16).**
Urinary tract infections are common bacterial infections in older persons, especially women (37). They are the most common infections in hospitalized patients, affecting 1 million patients per year (31). The prevalence of urinary tract infections increases with age, level of care, and decreasing functional capacity. The reasons that urinary tract infections are so frequent in eider persons are unknown, but may include prostate problems in men; loss of pelvic support, fecal incontinence, and loss of local bladder mucosal defense mechanisms in women; and use of urinary catheters in both sexes (86).	**Iatrogenic Infections (infections resulting as a complication of medical treatment) are often related to the use of medical devices. in the late 1970s, for example, an estimated 850,000 infections were related to medical devices, accounting for approximately 45 percent of ail hospital-acquired infections in the United States. infections resulting from the use of life-sustaining technologies such as mechanical ventilators, dialysis machines, and nutritional support equipment constitute a substantial portion of the Iatrogenic complications due to medical devices (8,64). During infusion therapy for total parenteral nutrition (TPN) (see ch. 8), for example, infection can be caused by contamination. infectious bacteria gain access most frequently at the site where the device penetrates the skin (32).**

[a]OTA selected these four infections foremphasis in this chapter because of their Prevalence andImportance for critically, chronically, and terminally ill. andseverelv debilitated elderly people.

SOURCE: Office of Technology Assessment, 1987.

such as mechanical ventilators (see ch. 6), dialysis equipment (see ch. 7), and devices used to provide total parenteral nutrition (TPN) (see ch. 8). Elderly people constitute a large proportion of the patients who use these technologies.

In addition to increasing the risk of infection, three factors—reduced immunological function, reduced physiological function, and age-associated illnesses such as heart disease, respiratory disease, or cancer—may lower a patient's ability to withstand an infection. Half of the elderly people who die of an infection do so because of the added stress the infection places on their already weakened organs (62). An infection in an individual whose physiological status is already compromised can result in a series of escalating problems, as one woman's experience illustrates:

Mrs. W was a 67-year-old widow who lived with her sister in a senior high-rise apartment complex. She underwent a mastectomy about a year ago. At that time, the cancer had spread beyond the breast. After discussion with her doctor, Mrs. W agreed to chemotherapy and radiation despite the poor prognosis. But she did not tolerate the treatments well and suffered much nausea, vomiting, and pain.

When Mrs. W developed shortness of breath and difficulty breathing, her sister became very anxious, phoned the ambulance, and demanded that Mrs. W be admitted to the hospital. On admission, Mrs. W was found to have an elevated temperature with an increased pulse and breathing rate. X-rays confirmed pneumonia and numerous cancerous lesions in both lungs. Mrs. W became comatose, was intubated, treated with antibiotics for the pneumonia and admitted to the intensive care unit. Her fever gradually resolved and the pneumonia symptoms improved. Several attempts to wean her from the ventilator, however, proved unsuccessful. The pneumonia, effects of cancer, and her general weakened condition had precipitated complete respiratory failure (8).

Because of their exposure to a combination of several risk factors, certain elderly people are more vulnerable than younger people or other elderly people to life-threatening infections. Elderly people at greatest risk include:

- critically and terminally ill elderly people who are likely to be hospitalized and to have compromised immunological and physiological status;
- chronically ill, though often clinically stable, elderly people, especially those who may require mechanical ventilation, dialysis, or nutritional support; and
- severely debilitated elderly people with multiple comorbidities, especially those who reside in nursing homes and those who are immobile.

For any of these people, antibiotics are potentially life-sustaining.

Diagnosis of Infection

Infections in elderly people are sometimes difficult to recognize because some elderly patients do not manifest the symptoms of infection that are familiar in younger people. An elderly patient with pneumonia, for example, instead of exhibiting cough, fever, or chills, may instead present nonspecific symptoms such as confusion, anorexia, weakness, or falls. An elderly patient with a urinary tract infection may have no apparent symptoms (19,25,79).

To recognize the presence of infections in elderly patients, caregivers must first be aware that such infections may present differently than the same infections in younger people. They must then be attentive to nonspecific changes in an elderly patient's general physical condition and functioning that may indicate infection. This observation holds especially true for elderly patients with dementia, who are often unable to define or report their own symptoms (19,79).

The identification of the specific bacterial or other agent causing a suspected infection is accomplished via laboratory tests. Many tests used in diagnosis-e.g., the chest X-ray and a culture of secretions coughed up from the lower respiratory tract that are ordinarily used to diagnose pneumonia—are noninvasive.

obtaining uncontaminated secretions from a patient's lower respiratory tract without using invasive procedures is often difficult, however, because the secretions have to come through the patient's mouth. For this and other reasons, some physicians will treat suspected pneumonia without a culture. If the patient does not respond to the treatment in a few days, a culture maybe essential and invasive procedures may be needed to obtain uncontaminated secretions. One procedure, transtracheal aspiration, involves inserting a needle through the patient's neck and trachea and into the lung to withdraw fluid. Some physicians consider such procedures too dangerous to be used in older people (58). Others believe the procedures are safe and useful in diagnosing bacterial pneumonia, especially in severely ill and hospitalized elderly patients (8,11).

Even simple diagnostic procedures that require drawing blood, obtaining a urine specimen, or having a patient cough up sputum may be difficult with elderly patients who are confused as a result of dementia, severe infection, or other illnesses. Severely confused patients may have to be physically restrained during diagnostic procedures, and some patients may have to undergo more invasive diagnostic procedures because of their inability to cooperate with simple procedures.

All types of diagnostic tests are readily available to patients being treated in hospitals, but some tests may not be available or easily accessible for nursing home residents (8,60). Moreover, anecdotal evidence and research findings indicate that in many cases even relatively simple laboratory tests are not used for nursing home residents, and that antibiotic treatment is frequently provided without a diagnostic workup. Three studies of antibiotic use in nursing homes show, for example, that only 11 to 38 percent of residents for whom antibiotics were prescribed had any pretreatment diagnostic tests related to their infections (14,34, 80). Some observers believe that these figures reflect seriously inadequate diagnostic practices (8,80).

Choice of Antibiotic

The choice of a particular antibiotic to treat a life-threatening or other infection depends primarily on the infectious agent (or agents). Other factors that a physician may consider are the nature of the patient's underlying illnesses, his or

her history of drug allergies or intolerance, the risk of drug toxicity, and, in some cases, cost (28, 79)!

Currently, over 50 antibiotics are licensed for clinical use in the United States (table 9-2). Broad spectrum antibiotics are active against several types of infectious agents, and narrow spectrum antibiotics are active against one or only a few types (56). All antibiotics are fairly specific in their activity, but various antibiotics overlap in their spectrum of activity. Because of this overlap, more than one antibiotic may potentially be effective against a specific infection.

Given the wide range of options for antibiotic therapy and the rapid rate at which new antibiotic derivatives are synthesized, it is difficult to establish a consensus about how best to treat many infections. Clinical guidelines for treating elderly patients with infections do exist (see, for example, app. G), but many physicians base their selection of antibiotics on their own prior experience. The prevalence of any particular strain of bacteria or other infectious agent varies among hospitals, nursing homes, and community settings, so the antibiotic selected for use against a suspected infectious agent may also depend on the

Table 9.2.—Generic Antibiotic and Other Antimicrobial Agents Classified by Family

Penicillins
Natural penicillins
Penicillin G
Penicillin V
Penicillinase-resistant
Antistaphylococcal penicillins
Methicillin
Nafcillin
Oxacillin
Cloxacillin
Dicioxacillin
Floxacillin
Aminopenicillins
Amoxicillin
Ampicillin
Bacampicillin
Cyclacillin
Hetacillin
Epicillin
Pivampicillin
Talampicillin
Antipseudomonal penicillins
Carbenicillin
Carbenicillin indanyl
Ticarcillin
Azlocillin
Extended spectrum penicillins
Mezlocillin
Piperacillin
Amidino penicillins
Amdinocillin
Amdinocillin pivoxil

Amphenicols
Chloramphenicol
Thiamphenicol

Aminoglycosides
Tobramycin
Gentamicin
Amikacin
Kanamycin

Cephalosporins
First-generation
Cephalothin
Cefazolin
Cephapirin
Cephradine
Cephalexin
Cefadroxil
Second-generation
Cefamandole
Cefoxitin
Cefuroxime
Cefaclor
Third-generation
Cefotaxime
Moxalactam
Cefoperazone
Ceftizoxime
Ceftriaxone
Ceftazidime
Cefsulodin
Cefmenoxime

Tetracycline
Short-acting
Oxytetracycline
Tetracycline
Intermediate-acting
Methacycline
Demeclocycline
Long-acting
Doxycycline
Minocycline

Macrolides and lincosamides
Macro/ides
Erythromycin
Troleandomycin
Lincosamides
Lincomycin
Clindamycin

Sulfonamides and trimethoprim[a]
Sulfonamides and trimethoprim in combination
Sulfadiazine
Sulfamerazine
Sulfamethazine
Sulfamethoxazole
Sulfisoxazole
Trimethoprim
Other
Sulfacytine
Sulfadiazine
Sulfameter
Selfamethizole
Sulfamethoxazole
Sulfapyridine
Sulfasalazine
Sulfisoxazole
Trimethoprim

Miscellaneous antimicrobial
Urinary tract antiseptics
Cinoxacin
Methenamine
Nalidixic acid
Nitrofurantoin
Other[a]
Aminosalicylic acid
Amphotericin B
Colistin
Dapsone
Ethambutol
Isoniazid
Metronidazole
Polymyxin B
Polymyxin E
Potassium iodide
Pyrazinamide
Rifampin
Spectinomycin
Streptomycin
Sulfoxone
Vancomycin

[a]These items were adapted from the National Ambulatory Medical Care Survey 1980-81 classification scheme (8)

SOURCE American Medical Association, *AMA Drug* Evacuations, 5th ed. (Chicago, IL April 1983).

setting in which an infection is acquired (8,9,21,77). Thus, the choice of an antibiotic may vary from patient to patient, from one physician to another, and from one setting to the next.

To minimize the risk of death from life-threatening infections, antibiotic therapy is frequently initiated before a diagnosis can be obtained. In such cases, empirical treatment is administered—treatment employing antibiotics active against several probable causative agents. When or if the infection is subsequently diagnosed, antibiotics specifically targeted against the ”identified agent may be used.

Duration of Treatment

In the treatment of life-threatening infections, it is vital to continue antibiotic therapy for an adequate length of time. If the course of treatment is incomplete, some virulent infectious agents may remain, reproduce, and cause a potentially fatal relapse. However, there is no standard duration of antibiotic treatment for life-threatening infections. The appropriate length of antibiotic therapy depends on the type of infection, the specific infectious agent, and the rate of the individual patient's response to treatment (8).

Route of Administration

Antibiotics can be administered three ways: topically, enterally, or parenterally.

1. Topicall administered antibiotics are applied to the skin in cream form. Such antibiotics are seldom used to treat life-threatening infections.
2. Enteral antibiotic therapy is administered orally (in tablet, capsule, or liquid form), rectally, or by nasogastric or gastrostomy tubes (see ch. 8). Oral agents are used to treat serious infections only in special circumstances (e.g., when administering parenteral agents is difficult). Ordinarily, oral agents are used to treat infections on an outpatient basis and to complete a full course of therapy in uncomplicated infections.
3. Parenteral antibiotic therapy is therapy administered by intramuscular injection or intravenous infusion. Parenteral therapy is often needed in serious infections to achieve adequate levels of the antibiotic in the patient's blood. Many drugs cannot be tolerated when given by intramuscular injection if more than a few doses are needed per day. For that reason, long-term antibiotic therapy is usually administered by intravenous infusion. Intravenous therapy may also be used when high blood levels of an antibiotic are important, or when the patient has diabetes (56), a common condition among elderly people.

Treatment Setting

For a patient who acquires an infection but remains clinically stable, antibiotic treatment can usually be administered in a nonhospital setting. For a patient whose condition worsens or whose infection is life-threatening, however, admission to a hospital maybe necessary, In hospitals, equipment and personnel are available to identify specific infectious agents and to administer antibiotics by any route.

The need for intravenous antibiotic treatment is one of the primary reasons that nursing home residents are transferred to hospitals (8,71). Most nursing homes cannot administer antibiotics intravenously because they do not have an onsite pharmacist to mix the sterile antibiotic with dilutent solution, Furthermore, the number of nursing home personnel authorized to administer intravenous antibiotics is often limited.

According to the 1977 National Nursing Home Survey, there were 340,000 hospitalizations from 1,402,400 nursing home beds in the United States—an annual rate of about 250 hospitalizations per 1,000 nursing home beds (74). That survey does not indicate what percentage of hospitalizations was associated with infections. Findings from other smaller studies (27,35,49)71) indicate, however, that infection is responsible for an average of about 30 percent of hospitalizations of nursing home residents (range: 17 to 56 percent) (8).

In some cases, intravenous antibiotic therapy for life-threatening infections is administered at home. Home intravenous antibiotic therapy is administered to a variety of patients, including patients who acquire a life-threatening infection

while dependent on a mechanical ventilator, dialysis, or nutritional support at home and who wish to avoid admission to a hospital. Since patients who are severely ill usually cannot administer their own intravenous therapy, home intravenous antibiotic therapy generally requires the availability of family members or other caregivers who have been trained to provide it.

In hospices, where antibiotics are used primarily to improve patients' comfort, if at all, the use of parenteral antibiotic therapy is discouraged (4). oral antibiotics are much preferred because they avoid the added discomfort of intramuscular injections or intravenous infusions (8).

UTILIZATION AND COST OF ANTIBIOTIC THERAPY

Utilization of Antibiotics

The information available on utilization of antibiotics is not restricted to their use in treating life-threatening infections. Rather, the data cover all uses of antibiotics, including the more common use of antibiotics to treat mild to moderate infections and prevent infections. The extent of antibiotic use for life-sustaining purposes cannot be determined from available data.

Perhaps not surprisingly, the greatest use of antibiotics occurs in hospitals. Individual hospital surveys consistently report that 25 to 35 percent of all patients receive antibiotics during their hospital stay (70). For up to half of the patients who receive antibiotics in hospitals, the intent is to prevent an infection rather than to treat one (56).

One study of 28 hospitals in Pennsylvania found that the percentage of patients receiving antibiotics increased with patient age, ranging from a low of 22 percent in pediatric patients to a high of 49 percent in patients over age 85 (60). Elderly patients (over age 65) represented 20 percent of all patients in the study but accounted for nearly 40 percent of the patients receiving antibiotics.

In general, elderly nursing home residents receive antibiotics less frequently than hospitalized elderly people, although antibiotics are often used to treat urinary tract infections in nursing home residents (13,80). The percentage of nursing home residents receiving antibiotics at any one time ranges from 8 to 16 percent (26,73, 74,80). It is not known why this variability exists, but it may reflect differences among nursing homes in the proportion of patients who are very old, seriously ill, catheterized, or immobile.

One large-scale study, the 1976 Long-Term Care Facility Improvement Campaign, examined physicians' prescribing patterns in skilled nursing facilities nationwide (73). Most of the facilities were served by community pharmacies. Of more than 1.7 million prescriptions for approximately 284,000 residents in these facilities, 3 percent were for oral or injectable antibiotics. Sixteen percent of the residents were receiving an antibiotic (including preventive antibiotics) at any one time.

Another study, of nursing homes in New York State, found that about 8 percent of residents were receiving antibiotics on the day of the survey. Of these residents, 58 percent had urinary tract infections, 19 percent had lower respiratory tract infections, and 5 percent had skin or subcutaneous tissue infections, including pressure sores (80).

Noninstitutionalized elderly people are not major consumers of antibiotics. The 1980 National Ambulatory Medical Care Survey, a survey of office-based physicians, found that noninstitutionalized patients over age 65 were prescribed drugs to treat arthritis, diabetes, and especially cardiovascular problems more frequently than antibiotics (75). The 1980 National Medical Care Utilization and Expenditure Survey found that antibiotics accounted for only 5 percent of all drugs prescribed for noninstitutionalized elderly people (41).

In 1984, an estimated 14,000 persons were on home intravenous antibiotic therapy (12). It is not known how many of these persons were over age 65, however. Industry sources predict major growth (in excess of 30 percent annually) in the home intravenous antibiotic market.

People with ***life-threatening*** infections are usually treated in hospitals and are rarely treated at

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home (8). Thus, although the information presented here applies to antibiotic use in general, one pattern—the variation in use of antibiotics by setting—holds true for life-sustaining as well as general antibiotic use. Use of life-sustaining antibiotic therapy, like use of antibiotic therapy in general, is greatest in hospital settings and least in noninstitutional settings.

Cost of Antibiotic Therapy

The cost of life-sustaining antibiotic treatment is difficult to determine for several reasons. First, utilization data seldom specify the types of infections treated. Another reason is that studies of the costs of antibiotic therapy do not consistently measure the same costs. For instance, some studies calculate the costs of antibiotic therapy to the supplier, while others focus on the costs to the patient (i.e., what the hospital charges the patient).

In 1982, drug store expenditures for antibiotics totaled almost $0.9 billion. Hospital expenditures for antibiotics that year were over $1 billion, accounting for more than one-fourth of total hospital expenditures for prescription drugs (6).

The cost of antibiotic therapy depends on:

- the type of antibiotic used;
- the amount of antibiotic used (e.g., the daily dosage and duration of treatment);
- the method of delivery; and
- the setting where therapy is administered.

Antibiotic therapy for treatment of life-threatening pneumonia, for example, can cost from less than $30 a day for a relatively simple antibiotic regimen to over $2000 a day for a more sophisticated one (8,36).

Some antibiotics that are recommended to treat life-threatening infections are far more expensive than others. Third-generation cephalosporins for the treatment of pneumonia are among the most expensive antibiotics available. Cephalosporins alone account for approximately 1 percent of hospitals' total budgets (38,45).

Recommended antibiotic regimens for elderly patients with bacterial pneumonia, urinary tract infections, infected decubitus ulcers, and TPN-associated septicemia and an example of one hospital pharmacy's charges for the recommended antibiotics are presented in appendix G. Although the figures for charges are illustrative, it is not possible to determine whether they are typical for hospitals in the Nation.

Hospital charges for antibiotic therapy are influenced by the method of delivery. One study of 71 hospitals found that charges added for intravenous administration of antibiotics averaged over $9 per dose (46). In fact, expenses to prepare and administer antibiotics can sometimes exceed the purchase price for the antibiotics themselves (22,66).

The total cost of treating a life-threatening infection in a hospital includes far more than the costs or charges for antibiotic therapy. In a hospital, the total cost also includes diagnostic tests, supportive care, and hospital stay. These additional expenses are substantial (38).

Reimbursement for Antibiotics

Reimbursement for antibiotics by Medicare varies by treatment setting. Under Medicare's Part A prospective payment system (PPS) based on diagnostic related groups (DRGs), hospitals are paid a fixed amount per patient that depends on the patient's diagnosis (see ch. 2). Payment for antibiotics and other drugs provided for hospitalized patients is assumed to be included in the fixed payment for each DRG; there is no separate payment for antibiotics,

In nursing homes, Medicare Part A pays for prescription drugs, including antibiotics, for residents whose nursing home care is paid for by Medicare, provided that the drugs are administered by a health professional. Since Medicare pays for only about 2 percent of all nursing home care, however, only a small proportion of nursing home residents are eligible for Part A reimbursement for antibiotic therapy.

In a physician's office, the patient's home, or any other outpatient setting, antibiotics administered by intramuscular injection are reimbursed by Medicare Part B (Supplementary Medical Insurance). Drugs that are self-administered by the patient or administered by someone other than a licensed health care provider are not covered

by Medicare. Intravenously administered drugs, including antibiotics, are not covered by Medicare in any outpatient setting.

Medicaid, the Federal/State reimbursement program for the indigent, pays for most prescription drugs for eligible individuals, although intravenous antibiotics usually require prior approval in States where they are covered (5). A survey of the Medicaid programs in eight States found that seven programs covered home intravenous antibiotic therapy but required prior approval by the Medicaid program office (54). To be eligible, however, patients must have income and assets that do not exceed Medicaid financial eligibility standards, which are low in all States and extremely low in some States.

Little information about private insurance coverage of antibiotics is available. One study found, however, that 15 of 17 Blue Cross/Blue Shield plans in 8 States and 12 other large commercial insurance plans covered home intravenous antibiotics (54).

It is not known how Medicare policies (and the policies of other third-party insurers) that are intended to contain hospital costs) are affecting the use of antibiotics in hospitals. On the one hand, PPS could increase the use of antibiotics in hospitals because the system creates a financial incentive for shorter length of stay, and antibiotics, by treating complications often associated with certain diseases and treatments, can effectively shorten length of stay (8). On the other hand, PPS may discourage hospitals from treating Medicare patients who require long and expensive courses of antibiotics (e.g., after hip surgery or for an infection of the heart lining called endocarditis). For some infections, the level of DRG payment covers only about half the number of hospital days needed for the generally accepted antibiotic regimen (47).

Although home intravenous antibiotic therapy may yield cost-savings for hospitals, the lack of Medicare reimbursement for home intravenous antibiotic therapy probably limits its use with elderly patients. Patients who expect substantially lower-out-of-pocket costs for inpatient care than for outpatient care are unlikely to select outpatient care, regardless of their desire to avoid hospitalization (36)38).

OUTCOMES OF LIFE-SUSTAINING ANTIBIOTIC THERAPY

Antibiotics generally are successful in combatting most types of infections, with patients showing improvement within a few hours or days, and complete cure within a few days or weeks. In the heterogeneous older population, however, the outcomes of antibiotic treatment for life-threatening infections are often unpredictable. Many of the same factors that predispose certain elderly people to life-threatening infections, especially age-related physiological changes and the presence of multiple illnesses, also place them at higher risk of complications from treatment. These factors converge to create a wide range of possible treatment outcomes.

Cure of Infection

The cure of an infection by successful antibiotic treatment usually restores a patient's prior health status. If an elderly patient has been functioning independently before contracting a life-threatening infection, the cure of that infection may mean a return to independence and a personally satisfying quality of life, as illustrated by the following case:

> Mr. B, a 73-year-old man, had been living independently in the community with the help of his daughter, who brought groceries and helped with chores and cleaning. Following his wife's death from cancer some years earlier, he had discussed with his daughter his desire for a "natural" death and had made out a living will.
>
> For some years, he had had cataracts, congestive heart failure, and chronic obstructive pulmonary disease. With medication and medical supervision, however, his condition had remained stable. When Mr. B began to cough up thick sputum and noticed increased shortness of breath and swelling in his ankles, he saw his physician and antibiotics were prescribed.
>
> After 5 days, Mr. B's symptoms worsened. His daughter became alarmed and phoned the physician, who recommended immediate admission to

the local hospital for further diagnostic tests and treatment with intravenous antibiotics. Mr. B protested and despite his weakened condition made it clear that he felt very near death and that he wished no further efforts or heroics to be made on his behalf.

His daughter and physician reassured him that his chance for complete recovery was good, and he was admitted to the hospital, where he underwent X-rays, blood tests, and other diagnostic procedures and received oxygen therapy and intravenous antibiotics. After 7 days of treatment, Mr. B began to improve and to look forward to discharge from the hospital and return to his home. He thanked his daughter and his physician for undertaking aggressive treatment on his behalf, despite his objections (8).

Antibiotic therapy is especially important fo chronically ill people receiving long-term mechar ical ventilation, dialysis, or nutritional suppor Without antibiotic treatment of the iatrogenic ir fections often associated with these technologie it would be impossible to restore these patien to a clinically stable condition. Indeed, antibioti enable these other technologies to sustain live

For elderly or other patients who are terminal ill or severely debilitated, cure of an acute infe tion at best can only restore them to their prei fection health status. When terminally ill patien recover from an infection, their terminal illness remain, as do any accompanying pain and suffe ing. The situation is similar for severely debilitat patients with multiple comorbidities.

Death

When infection is superimposed on terminal ness or severely debilitating chronic disease, t patient's condition may worsen in spite of ant otic treatment, and death may result. In su cases, the antibiotic treatment may be complica by the patient's very weakened physiological c dition, as illustrated in the following case:

Mrs. G was a 92-year-old widow who had bee in a nursing home for 15 years. She had Alzhe mer's disease, was blind, and was confined to be In addition, she was fed by a nasogastric tub incontinent of urine and feces, and contracted in a fetal position. Occasionally, her movements suggested to the nurses that she was aware of the activities around her.

Mrs. G's stay in the nursing home had been complicated by repeated urinary tract infections. Her increasing incontinence had led to the insertion of an indwelling bladder catheter. With the catheter in place, antibiotics no longer cleared the urinary tract infections, and the bacteria in the urine were resistant to all but a few of the most powerful and toxic drugs.

One evening while turning Mrs. G, the nurses noticed that her temperature was high, and she was having difficulty breathing due to thick secretions accumulating in her throat. They notified her physician, and Mrs. G was transferred to the hospital. Her first 6 hours there consisted of two complete physical examinations by the intern and resident, chest X-rays, and multiple laboratory studies. Mrs. G was restrained during the vein punctures for these studies. In addition, because she was unable to cough up sputum, a small plastic tube was inserted through her nose into her throat, which caused her to gag, vomit, and choke, aspirating some vomit into her lungs.

The tests revealed pneumonia and an active urinary tract infection. Mrs. G was treated with three intravenous antibiotics. Although she initially improved, fluid in her lungs rapidly developed as a result of all the intravenous fluids that were required to deliver the antibiotics. This condition was aggressively treated with intravenous diuretics and digitalis, which seemed to increase her restlessness. During the night, her restraints became loosened and she fell out of bed, fracturing her hip. Since she had been confined to bed previously, it was decided not to repair the hip surgically.

On the seventh day, the fever returned, and Mrs. G became more short of breath and very restless. Another chest X-ray demonstrated a rapidly progressing pneumonia in her right lung. Because her kidney function was deteriorating, probably from the combination of antibiotics administered, it was decided not to treat the pneumonia with further antibiotics. Mrs. G died 3 days later with progressive pneumonia and kidney failure (8).

Even with antibiotic treatment, older people are more likely to die from infectious diseases than are younger people (8). Pneumonia is perhaps the most notable example. When penicillin was first developed, the mortality due to one form of bacterial pneumonia fell 32 percentage points (from 40 to 8 percent) in the population under age 50.

Although mortality fell 36 percentage points (from 64 to 28 percent) in the population over age 50, it remained at a considerably higher level (23).

Higher mortality in elderly people treated with antibiotics is due primarily to the general decline in physiological and immunological function associated with aging and to complicating comorbidities and disabilities, rather than to age per se (8). Because elderly people vary greatly in their physiological and immunological status, individual elderly patients may respond just as well to antibiotic treatment as younger ones.

Recurring Infection

Another outcome that can result from antibiotic treatment is a less than full cure. Recurring infections can be either relapses caused by the same infection or infection by a different organism. Elderly women in particular tend to have chronic, recurring urinary tract infections despite antibiotic therapy (57). About 80 percent of all patients treated for urinary tract infections develop a recurring infection within 18 months (3). Recurring urinary tract infections in older people often do not present clear symptoms (7). Such infections can occur infrequently, so that they seem to be unrelated, *or* they can occur *very* frequently. Broad spectrum antibiotics, in particular, encourage recurrence by fostering the proliferation of strains of bacteria that are resistant to antibiotics.

Superinfection

The human body normally houses many different types of microorganisms, both on the skin and internally. The surface of a normal tooth, for example, harbors approximately 70 different species of bacteria (31). Most of the microorganisms in the body are harmless, and some are quite beneficial, helping with digestion and liberating essential nutrients, Some prevent colonization by other, more virulent, microorganisms by competing for essential nutrients and producing natural antibiotics.

Antibiotics that destroy harmful microorganisms can also destroy microorganisms that are beneficial. When growth of beneficial microorganisms stops as a result of antibiotic therapy, other microorganisms that are not sensitive to the antibiotics may flourish and produce a ***superinfection,*** a new infection that appears during treatment of a primary infection. The broader the antibiotic that is used, the greater the alteration in the natural flora and the greater the possibility that a single type of microorganisms will predominate, invade, and produce infection. This new infection may be quite difficult to eradicate with the drugs currently available.

Adverse Reactions

Antibiotics are generally safe, and the adverse reactions that do occur are usually mild and cause no permanent damage. Mild diarrhea and nausea are common side effects of many antibiotics. Allergic reactions to antibiotics include skin rashes, hives, itching, wheezing, or difficulty breathing. Nearly all antibiotics, like many other drugs, can cause fever (31).

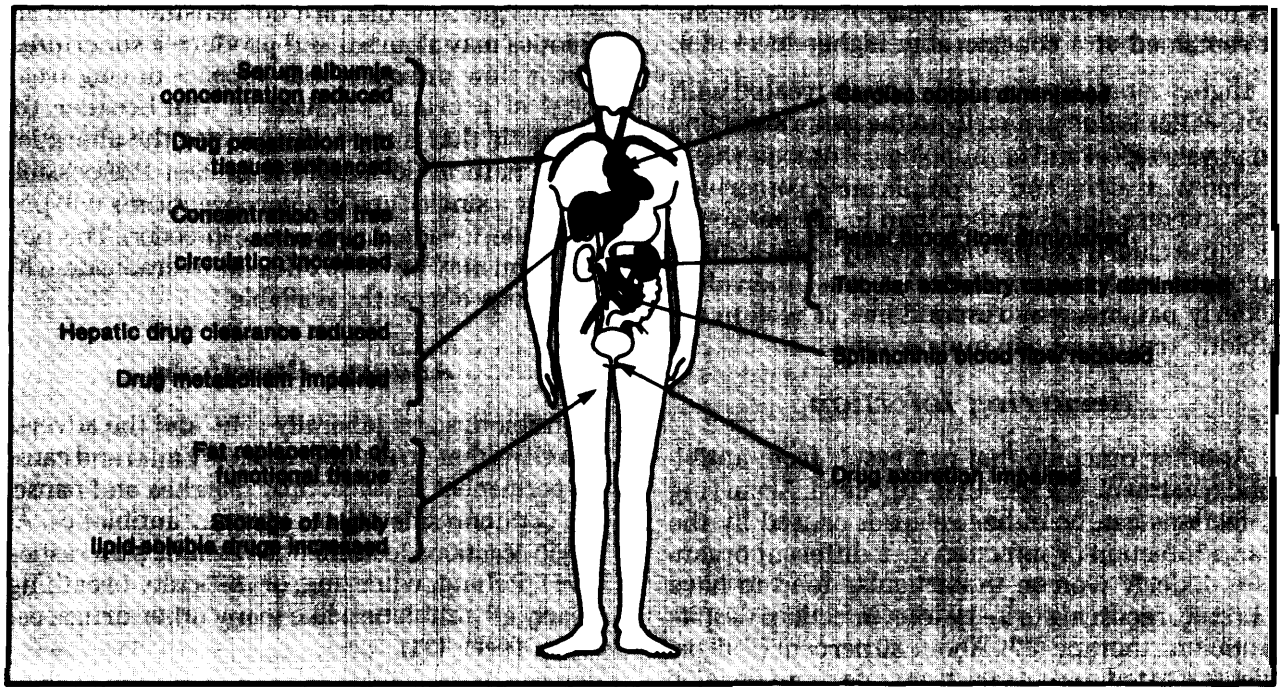
Other, less common, potential side effects of antibiotics include dizziness, hearing loss, seizures, convulsions, hallucinations, coma, and blood clotting problems. Kidney and liver damage in elderly patients are more likely when high doses of antibiotics are used than when low doses are used (2,10)20).

In general, elderly patients are more susceptible and sensitive than younger patients to the toxic effects of drugs. The adverse drug reaction rate is two to seven times higher in older patients than in younger patients (37). A study of patients at Johns Hopkins University Hospital, for example, found that 24 percent of patients over age 80 had adverse drug reactions, compared with only 12 percent of patients aged 41 to 50 (62).

The greater risk of adverse reactions older patients face is explained in part by age-related physiological changes. These changes illustrated in figure 9-1 affect the absorption, distribution, metabolism, and excretion of many medications, including antibiotics in the following ways:

- Reduced liver and kidney function in older patients interferes with the clearance and elimination of some antibiotics from the body.

Figure 9-1 .—Age-Associated Physiological Factors That Affect Drug Distribution in Elderly People



SOURCE" Adapted from I.M. Smith, "Infections in the Elderly;'Hospital Practice, 17(7):69-85, 1982.

- Fat gradually replaces muscle tissue in older people, so drugs that dissolve in fat are stored in the body for a longer period.
- Changes in body size that occur with aging alter the concentration of drugs in the body.
- Gastrointestinal function decreases with advancing age, reducing the volubility of drugs in the stomach and affecting absorption.
- Older people have a decreased amount of the protein albumin in their bloodstream. Since many medications bind to this protein, a decreased amount of albumin may result in a smaller percentage of drug being protein bound, and therefore inactive, and a larger percentage of drug being unbound, or active. This enhances the penetration of certain medications into tissues, while increasing the concentration of free active drug circulating in the bloodstream (62).

As with all physiological changes associated with aging, the timing, extent, and impact of each of these changes differ among individuals.

Patients in whom age-related physiological changes allow the accumulation of toxic concentrations of drugs such as antibiotics will experience adverse reactions. These complications may be especially dangerous when treating life-threatening infections because relatively toxic antibiotic regimens are often used to treat such infections, and elderly patients at high risk of such infections are likely to have compromised physiological and immunological status.

Combinations of various medications ("polypharmacy") also can heighten sensitivity and cause adverse reactions. Many elderly people take a variety of different medications at the same time (61,72). Polypharmacy can influence drug concentrations, decreasing antibiotic binding by enabling other substances to occupy the binding sites of the protein albumin.

The physiological and other factors just mentioned may influence the effect of medications in some elderly patients and alter the dosage required (20). In practice, however, the dose and dose interval are relatively standard for each antibiotic (42). "Usual" or '(average" doses of many medications are based on clinical trials that generally involve only young and middle-aged adults.

The altered physiology of many elderly persons is not accounted for in the standards. Thus, it is common for patients to receive identical or similar medication doses regardless of age (61,72).

The Food and Drug Administration recently recommended that dose information in product labeling include instructions for adjusting the dosage for varying degrees of renal impairment. The agency also recommended that a formula for estimating renal clearance, which includes an age factor, be incorporated in the labeling for renally excreted drugs (67,68).

MAKING DECISIONS ABOUT LIFE-SUSTAINING ANTIBIOTIC THERAPY

Decisions about whether to administer antibiotic therapy, unlike those about mechanical ventilation, dialysis, and nutritional support, affect the majority of seriously ill elderly persons and their caregivers (8). Relatively few studies, however, examine the specific factors, aside from clinical considerations, that may be involved in such decisions.

In general, there is very strong support for administering antibiotic therapy to any person with a treatable infection. Many physicians and other health care providers think of antibiotic therapy as ordinary or standard care and, therefore, would not consider withholding it. Antibiotics are generally safe, free of serious adverse effects, and effective. Their administration is usually pain-free and does not drastically alter the patient lifestyle, and the costs are generally minor.

Because of some or all of these factors, physicians are predisposed toward the use of antibiotics to treat life-threatening infections. This predisposition is strengthened by the fact that they cannot always predict the outcome of withholding antibiotics, since not treating a life-threatening infection may either hasten and ease death or prolong and increase suffering. Thus, the pressures are probably greater to use antibiotics than to use most of the other life-sustaining technologies discussed in this report. One observer has commented, in fact, that the "existence of antibiotics provides the pressure to find an infection to treat—even if infection, while perhaps present, is not the patient's problem" (15).

Since many physicians and other health care providers consider antibiotic therapy ordinary or standard care, they may fear that withholding it will expose them to legal risks. Moreover, some State living will statutes contain wording that is difficult to interpret with respect to antibiotics. The California Natural Death Act, for example, excludes from its definition of procedures that people may refuse with a living will, "the administration of medication or the performance of any medical procedure deemed necessary to alleviate pain" (1976 Cal. Stat. chapter 1439, Code and Health and §7187). The wording of this statute could be interpreted to mean that medications, including antibiotics, are not among procedures that people can refuse with a living will. There is insufficient experience at present to know how California's statute and others like it will be interpreted (63). Even the perception of ambiguity, however, may discourage caregivers from deciding to withhold treatment.

Factors Associated With Decisions Not To Treat

Despite the strong presumption in favor of antibiotic treatment, untreated infections may actually be a frequent cause of death among elderly people in some settings, and some observers suggest that nontreatment of severely debilitated and terminally ill elderly people may be intentional. Only one published study to date has specifically examined factors involved in the withholding of antibiotics (14). Results of that study, based on a review of the medical records of 1,256 residents admitted to 9 Seattle nursing homes in 1973, showed that 190 had one or more episodes of fever associated with infection: 109 of these residents (57 percent) were treated with antibiotics, whereas 81 residents (43 percent) were not. Of the residents treated with antibiotics, 9 percent died. In contrast, 59 percent of those who were

not treated with antibiotics died without resolution of their infections.

The factors associated with nontreatment of infections included the resident's diagnosis, physical condition, and mental status. Nontreatment was highest among residents with cancer. Many of these residents died of multisystem failure, and their infection was only a minor contributor to their death, although antibiotic treatment might sometimes have prolonged their lives. Residents who required more nursing care, who were bedridden, in pain, or receiving narcotics were less likely to be treated with antibiotic than residents who required less care. Confused residents were significantly less likely than cognitively normal residents to be treated with antibiotics (14).

Another factor associated with treatment decisions was the resident's marital status. Unmarried residents were least likely to be treated. Widowed residents were treated more frequently, and married residents were treated most. A resident's age was not significantly related to the decision not to treat (14).

Differences in antibiotic treatment decisions also can be related to physicians' familiarity with the nursing home resident. In the study of withholding antibiotics, physicians other than the patient primary physician were less likely to be aware of the patient's total condition and of any previous plans for nontreatment and were more likely to actively treat an infection. A patient's personal physician, surgeon, or oncologist was less likely to treat a fever. Nurses often determined the degree of treatment a resident would receive. In 20 of the 190 cases (11 percent), nurses did not contact a physician after noticing a patient's fever; this inaction was interpreted by the researchers as a decision not to treat (14).

Data provided to OTA from an unpublished 1984 study of three New York State nursing homes (65) show that 81 percent of residents with potentially life-threatening infections received antibiotic treatment while 19 percent did not. The study found no significant differences between these two patient groups in age, level of education, functional abilities, or marital status and no significant differences in a variety of psychological characteristics, including emotional health and life satisfaction, and in several measures of social support, including the availability of family and friends and the frequency of their visits to the patient. Interestingly, there was also no significant difference in mortality between the group that received antibiotic therapy and the group that did not. In fact, the only significant difference between the two groups was the frequency of the diagnosis of dementia. Residents with a diagnosis of dementia were significantly less likely to receive antibiotic treatment than residents with other diagnoses.

Another unpublished study of nursing home residents cared for by a group of physicians over a 7-year period suggests that both terminal illness and a diagnosis of dementia are correlated with a decision not to use antibiotics for elderly patients (50). As a part of routine treatment planning, the physicians assigned residents to one of four categories to show what treatment they should receive in the event of a life-threatening acute illness:

1. full, unrestricted medical intervention;
2. intermediate—probably full—medical intervention;
3. comfort care/intermediate-primarily restricted to comfort and supportive care, possibly including aggressive medical intervention for a life-threatening episode; and
4. comfort care, and attention to basic medical needs only (50).

Over the years, residents were reassigned to different categories as their condition changed.

Analysis of the characteristics of residents assigned to each category shows that residents in categories 3 and 4 were significantly more likely than those in categories 1 and 2 to have diagnoses of terminal cancer or dementia; about two-thirds of those in category 4 were diagnosed as having dementia. The percentage of residents who were treated with antibiotics also varied significantly among the four categories. For example, half the residents in category 1 who contracted an acute pulmonary infection were transferred to the hospital for treatment of the infection, compared to only 13 percent of residents in category 4 who contracted such infections. Of residents with acute pulmonary infections who remained in the nursing home, 99 percent of those in cate-

gory 1 received antibiotic therapy, compared to only 50 percent of those in category 4 (50).

Similar findings were obtained for urinary tract infections and infected decubitus ulcers (pressure sores). Forty percent of residents in category 1 who got urinary tract infections were transferred to the hospital for antibiotic treatment, compared to 28 percent of those in category 2 and none of those in categories 3 and 4. Among residents with urinary tract infections who were not hospitalized, 100 percent of those in categories 1, 2, and 3 were treated with antibiotics, compared to 62 percent of those in category 4. Likewise, 100 percent of residents with infected decubitus ulcers in categories 1, 2, and 3 received antibiotics, compared to only 57 percent of those in category 4 (50).

overall mortality due to acute pulmonary infections was only slightly higher among persons in categories 3 and 4 (29 and 22 percent respectively) than among persons in categories 1 and 2 (19 and 15 percent respectively). This was true despite the fact that a much higher percentage of residents in categories 1 and 2 received antibiotic therapy. The researchers concluded that a certain percentage (roughly 20 to 25 percent) of all pulmonary infections among nursing home residents will be fatal, with or without antibiotic therapy. They hypothesized that most of the fatal pulmonary infections occurred at times when the affected residents were particularly vulnerable because of their underlying diseases (50).

Anecdotal evidence suggests that settings of care may influence decisions about antibiotic therapy and that physicians are likely to implement more aggressive treatment in a hospital than in a nursing home (8). In an interview for OTA, one physician stated:

> [In the hospital,] the house staff and nursing staff are all geared primarily to use all methods possible to help patients, who may have already been started on antibiotics at the time they reach the hospital. Things can go fast and it is hard to stop something once you have started. I suppose there are psychological pressures on all of us to use the weapons that are readily available in the hospital. In the nursing home, those weapons are not immediately available and there may be just a little less pressure to do everything . . . It is easier in some ways to withhold treatment in a nursing home because you don't have to involve as many people in the decisionmaking and convince them if they are not convinced. You can make the decision on your own (8).

The type of infection a patient has may also influence treatment decisions. In general, it is recommended that pneumonia, urinary tract infections, and decubitus ulcers be treated with antibiotics when the symptoms are distressing to the patient (8,55). Untreated decubitus ulcers are frequently very painful. In contrast, untreated pneumonia may cause only mild discomfort due to shortness of breath. Some observers have even suggested that death from pneumonia ma-y be preferable to continuation of a life with severe disabilities:

> Pneumonia may well be called the friend of the aged. Taken off by it in acute, short, often painless illness, the old escape those "cold degradations of decay" that make the last state of all so distressing (5 I).

The Decisionmaking Process

Very little information is available about the decisionmaking process with regard to life-sustaining antibiotic therapy. Anecdotal evidence suggests that the physician often acts alone in making a decision about whether or not to treat a life-threatening infection. He or she may consider the opinions of nurses, the patient and/or family, and other caregivers. There are no data, however, to determine how often any of these individuals are consulted about such decisions.

Explicit written consent from the patient or surrogate usually is not obtained for the administration of antibiotics. The primary reason for this is that antibiotic therapy does not involve surgery and is generally considered noninvasive. As a result, hospitals, nursing homes, and other health care facilities usually do not require physicians to obtain a patient's or surrogate's written consent for it. In addition, obtaining written consent can be time-consuming and may interfere with prompt initiation of treatment that is frequently needed to ensure efficacy.

Anecdotal evidence indicates that in some cases, even verbal consent of the patient or surrogate is not obtained before antibiotic therapy is admin -

istered. This may occur because physicians and other health care providers assume, perhaps rightly, that patients with treatable infections want to receive antibiotic therapy. It is also sometimes said that a patient's consent for treatment of an infection is implied by his or her admission to a hospital.

It is not known how often life-sustaining antibiotic therapy is withheld without either written or verbal consent of the patient or surrogate. The three studies cited earlier on factors associated with nontreatment do not discuss this question (14,50,65). It is also not known whether physicians and other health care providers who believe that the administration of antibiotics does not require explicit consent also believe that life-sustaining antibiotic therapy may be withheld without explicit written or verbal consent of the patient or surrogate.

One very difficult aspect of decisionmaking with regard to life-sustaining antibiotic therapy is that some severely debilitated elderly people for whom antibiotic treatment might be used are incapable of participating in the decisionmaking process because of varying degrees of cognitive impairment. Such people are more likely to be kept alive by nutritional support and antibiotic treatment for intermittent infections than to need or receive more dramatic life-sustaining treatments like resuscitation and dialysis (59). Decisionmaking aids, such as the living will and durable power of attorney (see ch. 3), are often of little use with these patients because the patients often have been cognitively impaired for a long time and are unlikely to have given specific advance directives about their care while they were still able. It is frequently with these patients that physicians must wrestle with the decision of when or whether to "switch gears" from cure to supportive care and withhold life-sustaining antibiotic therapy.

One physician's description of his isolation in reaching these decisions generated numerous letters in response and seemed to touch an exposed nerve in the medical community:

> . . . Elsa Toivonen, 83 years old. Confined to the nursing home ever since her stroke 3 years ago. Bedridden. Aphasic [not able to verbally communicate]. I remember admitting her to the hospital after her stroke, . . . and those first few hospital days in which I aggressively treated the pneumonia that developed as a complication, giving her intravenous antibiotics despite her apparent desire to die. "Depressed," I had thought. "She'll get over it. Besides, she may improve substantially in the next few weeks. She recovered from the pneumonia, but she remained paralyzed and aphasic. For the past 3 years she has lain curled in her nursing home bed, a grim reminder of the "power" of modern medicine . . .
>
> . . . Wasted away to 89 pounds, decubitus ulcers on her back and hip, peering at me from behind her blank face—I'm used to all that from my monthly rounds. But this morning there is no movement of her eyes, no resistance to my examination, nothing to indicate that she's really there. There is little more to the history of Mrs. Toivonen's fever than what I gathered [from the nurse] over the phone, and Mrs. Toivonen's aphasia precludes much of an interview. My examination is brief, directed pointedly towards the usual causes of fever in elderly people . . .
>
> Essentially alone, foggy from tiredness in the middle of the night, I will make decisions that will essentially mean life or death for this poor old woman . . . There in the middle of the night I consider doing "everything possible" for Mrs. Toivonen: transfer to the hospital, intravenous lines for hydration and antibiotics, and even thorough laboratory and X-ray evaluation, twice-daily rounds to be sure she is recovering, more toxic antibiotics, and even transfer to our regional hospital for evaluation and care by a specialist. None of it is unreasonable, and another night I might choose just such a course. But tonight my human sympathies lie with Mrs. Toivonen and what I perceive as her desire to die . . .
>
> But I can't just do nothing, either. My training and background are too strong. I do not allow myself to be consistent and just go home. Compromising (and ultimately making a decision that makes no ethical sense at all), I write orders instructing the nursing staff to administer liquid penicillin, to encourage fluid intake, and to make an appointment with my office so I can reexamine Mrs. Toivonen in 36 hours . . . Driving home, I wonder why practicing medicine is so often dissatisfying . . .
>
> . . . The problem is simply too difficult for me as a single human being to face in a conscious way . . .

> For my part, the underlying irrationality of my decision has gnawed at me; the life-and-death importance of my actions has kept me awake at night; the guilt and depression of never really knowing whether I have acted properly have been overwhelming (33).

Very few guidelines have been proposed for when, if ever, it is appropriate not to treat infections. The President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research found "no particular treatments—including such 'ordinary' hospital interventions as antibiotics—to be universally warranted and thus obligatory for a patient to accept" (55).

Wanzer and associates (78), in their classification of levels of care for "hopelessly ill patients" determined that antibiotic treatment should generally be provided for all patients except those in their 4th category, general medical care. According to the classification system, patients in that category "are usually those clearly in the terminal phase of an irreversible illness" (78). With regard to patients who are in a "persistent vegetative state" (i.e., "the neocortex is largely and irreversibly destroyed, although some brain-stem functions persist"), the authors state:

> When this necrologic condition has been established with a high degree of medical certainty and has been carefully documented, it is morally justifiable to withhold antibiotics ... , as well as other forms of life-sustaining treatment, allowing the patient to die. This obviously requires careful efforts to obtain knowledge of the patient's prior wishes and the understanding and agreement of the family (78).

with regard to patients who are severely and irreversibly demented, they conclude:

> It is ethically appropriate not to treat intercurrent illness except with measures required for comfort (e.g., antibiotics for pneumonia can be withheld) (78).

With the exception of these guidelines, however, the medical literature rarely discusses when, if ever, it is appropriate not to treat infections. This may be due in part to the elusive nature of "quality of life ." Subjects like "how to treat pneumonias," "appropriate care for decubitus ulcers)" or "recommended antibiotic therapy for urinary tract infections, " are discussed at length in infectious disease journals and texts and are fairly straightforward. It is much more difficult to grapple with the question of whether or not to treat a patient who is terminally ill or severely debilitated. Since there has been so little discussion of this question in the clinical literature there are few criteria or guidelines for making these decisions.

FINDINGS AND IMPLICATIONS

Antibiotics are used most often to treat mild infections or to prevent infections, and no data are available to determine how many people of any age receive antibiotics for life-threatening infections. Antibiotic use for all purposes is greatest in hospitals and lowest in outpatient settings. Hospital surveys report that 25 to 35 percent of patients in the United States receive antibiotics during their hospitalization (70). The percentage of patients receiving antibiotics in the hospital increases with age; in one study, persons over 65 years of age represented 20 percent of the total patients but accounted for nearly 40 percent of patients receiving antibiotics (60).

Research in nursing homes shows that 8 to 16 percent of the residents are receiving antibiotics at any one time (26,73,74,80). A smaller percentage of persons receive antibiotics at home (41).

Life-sustaining antibiotic therapy is usually administered intravenously and may necessitate admitting a patient to a hospital, where a full range of support personnel and medical services are available. Such therapy must be initiated promptly if it is to be effective. Thus, empirical treatment with an antibiotic active against many different infectious agents is often initiated before a definitive diagnosis can be made.

Although life-sustaining antibiotic therapy often must be initiated before a definitive diagnosis is made, the usual and recommended medical practice is to perform laboratory tests to identify the

cause of the infection as quickly as possible. When the infectious agent is identified, antibiotics specifically targeted to it may be used. Research indicates that such tests are usually performed for hospitalized patients but are frequently omitted in the management of suspected infections in nursing home residents (80). Some observers believe that this constitutes inadequate medical care for these residents, and they have proposed guidelines for diagnosing infection and selecting antibiotics for patients in nursing homes (8,80).

The use of life-sustaining antibiotic therapy with elderly people involves special considerations. Infections sometimes present different symptoms in elderly people than in younger people. Caregivers must be aware of this possibility and attentive to nonspecific symptoms, such as confusion, weakness, or falls, that may indicate the presence of an infection. At the same time, more research is needed on the presentation of infection in elderly people.

The outcomes of life-sustaining antibiotic treatment of elderly patients range from complete cure to death. Antibiotics are usually effective in curing infections, However, they can neither eliminate nor alleviate preexisting illnesses in chronically, critically, or terminally ill or severely debilitated elderly people.

Elderly patients as a group are at higher risk of developing adverse reactions to antibiotic therapy than are younger patients. Age-related physiological changes affect the way drugs concentrate in the body and can allow accumulations to toxic levels. Most drug dosages are standardized and do not account for the higher blood levels of a drug that may result from an elderly person's altered metabolism. At present, the Food and Drug Administration does not require specialized dosages for elderly persons, although it has recommended that a formula for estimating renal clearance, which includes an age factor, be incorporated in the labelling for renally excreted drugs. More research is needed on the effects of physiological changes associated with aging on absorption, distribution, metabolism, and excretion of antibiotics and the implications of these effects for appropriate antibiotic therapy.

Despite these considerations, antibiotics remain among the least complex and least expensive life-sustaining technologies. Because many physicians consider antibiotics ordinary or standard treatment, their decisions to use them in the treatment of life-threatening infections are often automatic. Clinical criteria, rather than patient's or surrogate's wishes, are often their primary considerations. In most cases, the patient's or surrogate's explicit written consent is not obtained prior to the administration of antibiotic treatment. It is not known how often verbal consent is obtained.

Some people believe that requiring explicit informed consent (written or verbal) for antibiotics would help ensure that the patient's or surrogate's wishes are respected in the decisionmaking process. Others believe that requiring explicit informed consent, especially written consent, would create a time-consuming obstacle to prompt treatment and that explicit informed consent is not necessary in most cases of life-sustaining antibiotic therapy.

Many of the elderly patients being considered for life-sustaining antibiotic treatment are severely debilitated and incapable of making treatment decisions. Decisionmaking aids like the living will are rarely of use to these people, who often have been incapacitated for a long time and are unlikely to have given specific prior directives regarding their care. For these patients in particular, antibiotic treatment decisions may be strongly influenced by the setting of care. Infections are often aggressively treated in hospitals, where there are pressures to use all of the measures that are readily available. In nursing homes, where medical resources are less readily available, there may be less pressure to use antibiotic therapy.

Living will statutes in some States contain wording that may be perceived to exclude antibiotics from the life-sustaining treatments that people may refuse with a living will. The ambiguous wording in these statutes could be revised to clarify their intent. This might reduce caregivers' uncertainties about legal risks, thus encouraging them to rely on advance directives in making treatment decisions.

Current Medicare policies favor management of life-threatening infections in hospitals and may

discourage some patients from receiving therapy at home. A consequence maybe higher antibiotic use and expenditures in hospitals. Although Medicare reimbursement for antibiotic therapy administered at home could encourage use in that setting, no estimates are available of the number of elderly patients now treated in hospitals who could receive antibiotic therapy at home.

Few guidelines or criteria have been developed to help physicians decide when, if ever, nontreatment of a life-threatening infection is appropriate. Likewise, few hospitals or nursing homes have policies about the procedures to be followed in making such decisions. Some observers have expressed concern that these factors place overwhelming responsibility on the shoulders of the individual physician (33). Others have noted that the lack of guidelines and policies allows wide variability and individuality in decisionmaking (8). One OTA contractor concluded that guidelines or criteria for decisionmaking could have both good and bad consequences (8):

> Good consequences will result from providing a structure for physicians to consider carefully the goals for starting antibiotic therapy and to discuss with the patient and family all aspects of the decision to treat or not treat with antibiotics. Bad consequences will result because rigid guidelines (especially if enacted in statutes or codes) will severely limit the individual capabilities of the best physicians, already sensitive advocates for their patient's wishes, to practice the art of medicine (8).

professional associations could develop guidelines for decisionmaking to encourage communication among physicians and other professional caregivers about factors that should be considered in such decisions. Process-oriented guidelines in hospitals, nursing homes, and other health care facilities could delineate more clearly the role of the patient or surrogate in the decisionmaking process and the circumstances in which explicit consent, either written or verbal, should be obtained before antibiotic therapy is initiated or withheld.

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