

Chapter 2

THE SAFETY AND EFFECTIVENESS OF HOME DRUG INFUSION THERAPY

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THE SAFETY AND EFFECTIVENESS OF HOME DRUG INFUSION THERAPY

Overview

Introduction

There is no well-established or formal definition of home drug infusion therapy (HDIT). In this report, HDIT describes treatment that consists of prolonged (or continuous) injections of drugs that are administered in the home, usually repeatedly.

Spurred by public- and private-sector policies that have encouraged alternatives to hospital inpatient care, HDIT has become a widespread mode of therapy affecting hundreds of thousands of people. Market analysts have estimated that between 1986 and 1990 alone, the number of patients treated outside the hospital with drug infusion therapy grew from approximately 39,000 to between 200,000 and 225,000 (275,289). These numbers may overestimate the number of patients actually treated at home, since they probably include some patients treated in outpatient clinics.

HDIT encompasses an increasingly wide variety of specific drugs and therapies, each with its own characteristics and considerations. Accordingly, this chapter describes how the drugs used in HDIT are delivered, the patients who use this therapy, the drugs they use, and the safety and effectiveness of those drugs when infused in the home.

Properly speaking, HDIT should include only drug therapy. In this report, however, it is often also used for the sake of simplicity to include some therapies other than drugs (e.g., hydration and blood transfusions) that are not usually covered by Medicare when administered in the home. Another related therapy, total parenteral nutrition (TPN), is currently covered; it is discussed in this report only as a separate form of infusion therapy and is not considered part of HDIT.

Summary of Conclusions

- Most prescriptions for HDIT are for anti-infective drugs. However, the number and variety of drugs that are being infused in the home are large and increasing.

- In general, HDIT can be provided safely and effectively if adequate precautions are taken against side effects of the therapy and potential adverse drug reactions. The safety and effectiveness in any given situation, however, depends critically on the particular drug and the condition of the patient receiving it. The safety and effectiveness of anti-infective drugs in individuals who are healthy in all respects except the infection being treated are well-established. Therapies used in patients with cancer and acquired immunodeficiency syndrome (AIDS) are also well-established, but their use in the home requires special caution because of the disabilities of the patients treated, the multitude of therapies these patients may require, and the potential toxicity of many of the drugs they receive.
- The ability to deliver infused drugs safely in the home HDIT has enabled the use of therapies in ways that might rarely have been tried if, instead, the patient had to be continually hospitalized. HDIT thus can sometimes make new, more powerfully effective drug protocols more attractive to try. However, it also may encourage the rapid transfer of new drugs and new protocols into the relatively unmonitored home setting without a thorough testing of their effectiveness in this setting or an appreciation of their costs. Dobutamine, for example, is being infused at home despite evidence suggesting that long-term therapy increases mortality rates in some patient groups. Immune globulin infusion is likewise a small but growing home technology whose effectiveness has been documented in a few cases but whose actual uses are expanding extremely rapidly and whose costs may be extremely high.
- Even among well-established home infusion therapies, questions exist that can probably only be answered by research and experience that involve home patients. For example, despite the fact that most HDIT in the United States involves drugs administered intravenously, recent studies from Europe and Britain

suggest that some therapies (e.g., pain management, heparin, immune globulin) may be administered more simply, safely, and effectively subcutaneously.

Drug Administration

Considerations in Oral v. Parenteral Administration

From both the patient's and the physician's perspective, the most desirable route of administration is the one that is easiest, most effective, and poses the lowest risk of side effects and potential complications. Oral administration often fulfills these criteria and is the route of choice for most drugs. Sometimes, however, oral administration is inadequate or inappropriate, necessitating *parenteral drugs* (i.e., drugs not administered into the digestive tract). Factors that can lead to a preference for parenteral over oral administration include the drug's absorption and metabolic characteristics, its side effects, its predictability, and the condition of the patient.

Drug Absorption

To perform their intended functions, drugs must be delivered to the relevant tissues of the body. Orally administered drugs are first absorbed from the digestive tract and then carried in the blood to the tissues. The absorption of drugs from the digestive tract is highly variable. Some drugs (e.g., aspirin) are almost completely absorbed into the blood. Others, such as the aminoglycosides (a class of antibiotic), pass through the entire digestive system with less than 1 percent absorption (129).

Drugs that are not adequately absorbed cannot attain blood levels sufficient to treat the particular condition and must, therefore, be administered parenterally. The factors that determine the absorption of a particular drug include its physical and chemical properties (e.g., its volatility), the presence of other substances in the digestive tract, the relative acidity of the digestive tract, and the time it takes the stomach to empty (11).

Even if a particular drug is eventually completely absorbed, the rate of absorption may be too slow to produce a therapeutic concentration in the blood (i.e., the concentration that is necessary to treat that condition). Or, the absorption rate may be so rapid

that high concentrations of the drug cause adverse reactions (11).

Drug Metabolism

The degree of metabolism that a drug undergoes—i.e., its biological decomposition—also influences the route of administration. While many drugs can be given orally with little loss of biologic activity, others are metabolized by digestive enzymes and their potency either reduced greatly or lost entirely.

Human immune globulin, for example, is a naturally occurring substance composed of antibodies produced by a particular kind of white blood cell. Immune globulin has been used to supplement the deficiency of normal antibodies in certain individuals with rare diseases (e.g., severe combined immunodeficiency syndrome) whose bodies are unable to manufacture their own (54). If given orally, immune globulin would be digested and biologically destroyed. Consequently, it must be administered parenterally in order to retain its function.

Side Effects

Many drugs can be administered effectively either orally or parenterally, but the side effects they produce may vary depending on the route of administration. Orally administered drugs often can cause nausea and vomiting, which limit the amount of that drug that can be given by mouth.

Methotrexate, for example, can be given either orally or intravenously—i.e., directly into a vein. When used in small doses to treat diseases such as psoriasis and rheumatoid arthritis, oral methotrexate is usually well-tolerated and has minimal side effects (216). When used as an antineoplastic agent to treat certain cancers, however, the dose of the drug that is required to be effective would produce severe digestive upset if administered orally. Thus, for this use it is usually administered intravenously.

Predictability of Parenteral Administration

Parenterally administered drugs are subject to far less variability of absorption than oral drugs, and the amount of delivered drug that reaches therapeutic concentration is far more predictable. Consequently, drugs that have a narrow 'therapeutic window,' the range in which a drug is effective but does not produce toxic effects, are often administered parenterally so that the amount absorbed can be better controlled. In addition, intravenously administered medication is essentially completely absorbed, be-

cause it goes directly into the blood. This characteristic usually leads not only to more predictable but to higher drug levels than those produced by any other route.

Erythromycin, for example, is a common antibiotic used to treat a variety of infections. After a single oral dose of 500 mg, peak concentration of active drug in the bloodstream ranges from 0.3 to 1.9 ug/ml, depending on the particular preparation used. The same 500-mg dose administered intravenously, however, results in a peak blood level of approximately 10 ug/ml, a level 5 to 30 times greater than that obtained by oral administration (129).

Patient Condition

The choice of oral v. parenteral administration depends not only on the characteristics of the drug but also on the condition for which it is being used. Urinary tract infections, for example, are usually susceptible to oral antibiotics, while bone infections are not. In the past, parenteral administration has been the only feasible way of administering sufficient antibiotic to achieve adequate concentrations of the drug in the bone. A recently developed class of antibiotic, however, the fluoroquinolones, can now be used orally to treat some bone infections (125).

A patient's physical condition can also affect the route of drug administration. A patient with oral cancer, for example, may be unable to swallow oral analgesics and may require parenteral narcotics even for mild to moderate pain (37).

Routes of Parenteral Drug Administration

Most commonly, drugs that cannot be administered orally and must be infused over a period of time are administered intravenously. For certain drugs, however, or for patients in whom access to the vein is for some reason compromised, drugs may be infused into the body through other routes. Some antineoplastic¹ drugs, for example, may be infused into an artery (*intraarterially*), which carries the drug directly to the site of the tumor. *Intraperitoneal drugs*, administered into the peritoneal (abdominal) cavity, are also occasionally used for certain cancers. Drugs used to manage pain in terminal cancer may be infused in the *epidural* or *intrathecal* spaces

surrounding the spinal cord, where they are absorbed directly into the central nervous system. Some drugs may be infused under the skin (*subcutaneously*) rather than by other routes, either because the drug is best absorbed that way, because of a reduced risk of serious infection, or because the patient's veins are not adequate to sustain venous infusion.

As with the choice of oral v. parenteral drugs, the choice of which parenteral route of drug administration to use depends heavily on the characteristics of the drugs and its limitations (table 2-1). For example, some drugs (e.g., many antibiotics) are effective when given either intravenously or *intramuscularly* (injected into the muscle). Intramuscular injection, however, can cause severe pain and discomfort if the drug must be administered gradually, frequently, or in large doses. In such cases, intravenous (IV) administration is usually preferred.

The preferred route of parenteral administration can change over time with new evidence. Two recent reports, for example, suggest that heparin—usually administered intravenously when used as extended therapy for deep-vein thrombosis²—can be safely and effectively administered subcutaneously as well (165,271). Furthermore, one of these reports suggests that subcutaneous administration reduces the need for continual laboratory monitoring and dose adjustment, enhancing the drug's attractiveness for home use (271).

Conditions Treated With HDIT

Individuals on HDIT may be treated for any of a wide variety of diverse medical conditions, ranging from high-risk pregnancy to congestive heart failure. The most common conditions treated with HDIT, however, fall into three general categories: infections, cancer, and AIDS. Each of these conditions and the home infusion therapies that may be used to treat it are described below.

Infections

The classic candidate for HDIT is the patient who has an infection requiring a long course of IV antibiotics, but who has no other complicating conditions. These patients are likely to have two of the characteristics that allow for home IV administration and make this form of drug delivery an

¹ Antineoplastic drugs act against cancerous tumors.

² Deep-vein thrombosis is the formation of a clot in a main vein of the trunk or extremities, inhibiting blood flow.

Table 2-I-Some Characteristics of Common Routes of Drug Administration^a

Route	Absorption pattern	Special utility	Limitations and precautions
Oral ingestion	• Variable, depends on many factors	<ul style="list-style-type: none"> • Most convenient and economical • Usually safer than other methods 	<ul style="list-style-type: none"> • Requires patient cooperation • Availability potentially erratic and incomplete for drugs that are poorly soluble, slowly absorbed, unstable, or extensively metabolized by the liver
Intravenous	<ul style="list-style-type: none"> • Absorption circumvented • Potentially immediate effects 	<ul style="list-style-type: none"> • Valuable for emergency use • Permits titration of dosage • Suitable for large volumes and for irritating substances, when diluted 	<ul style="list-style-type: none"> • Increased risk of adverse effects • Must inject solutions slowly, as a rule • Not suitable for oily solutions or insoluble substances
Subcutaneous	<ul style="list-style-type: none"> • Prompt (from aqueous solution) • Slow and sustained (from repository preparations) 	<ul style="list-style-type: none"> • Suitable for some insoluble suspensions and for implantation of solid pellets 	<ul style="list-style-type: none"> • Not suitable for large volumes • Possible pain or necrosis from irritating substances
Intramuscular	<ul style="list-style-type: none"> • Prompt (from aqueous solution) • Slow and sustained (from repository preparations) 	<ul style="list-style-type: none"> • Suitable for moderate volumes, oily vehicles, and some irritating substances 	<ul style="list-style-type: none"> • Precluded during anticoagulant medication • May interfere with interpretation of certain diagnostic tests (e.g., creatinine phosphokinase)

^aOther routes include topical, transdermal, otic, sublingual, buccal, intranasal, rectal, ocular, intraarterial, epidural, and intrathecal.

SOURCE: Adapted from A.G. Gilman, L.S. Goodman, R.W. Rail, et al., *Goodman and Gilman's The Pharmacological Basis of Therapeutics* (New York, NY: McMillan Publishing Co., 1985).

attractive alternative. First, many of these patients have stable medical conditions and require little additional medical attention besides their course of antibiotics. Second, as discussed later in this chapter, most IV antibiotics are relatively free from serious side effects and adverse reactions, making them less dangerous than other IV therapies. Consequently, antibiotics and other anti-infectives make up about two-thirds of the HDIT market (34).

Osteomyelitis (infection of the bone) was one of the earliest conditions to be treated at home with IV antibiotics (see, e.g., 16). This condition occurs when bacteria invade the bone, such as after a compound fracture that opens the broken bone to the outside environment. Long courses of therapy with high concentrations of antibiotics are often required to treat this condition; treatment of 4 or more weeks duration is common (106,148,325). In published studies of home and outpatient IV antibiotic use, high proportions of the patients studied-over half in some reports-had osteomyelitis (16,136,148,267). The condition remains a popular one for treating with outpatient or home antibiotics. A recent report of drug infusion therapy in one large outpatient practice found that 32 percent of the patients treated had osteomyelitis (340).

Cellulitis (infection of the skin and surrounding tissue) is another condition frequently treated with home IV antibiotics. This condition, often found in

persons with impaired immune systems, can result when bacteria enters a break in the skin and the body's immune system is unable to fend off the invading organisms. Persons with diabetes, for example, often have poorly functioning immune systems, and even a minor local infection can develop into a life-threatening problem. Other infections sometimes treated with home IV antibiotic therapy when oral drugs are insufficient include respiratory infections (e.g., pneumonia and bronchitis), urinary tract infections, pelvic inflammatory disease, and endocarditis (infection of the heart valves). Examples of the relative prevalence of these conditions in programs that treat patients with home or outpatient IV antibiotics are presented in table 2-2.

The relative prevalence of conditions treated varies considerably among providers. For example, in contrast to the two programs represented in the table 2-2, the National Alliance for Infusion Therapy reports that in a sample of its members, Lyme disease (which was not even separately listed in the reports of the programs represented in table 2-2) accounted for 13 percent of patients treated with antibiotics (256).

Sometimes, IV antibiotics are used to combat repeated infections in persons with underlying disorders that predispose them to these diseases. Persons with cystic fibrosis, for example, are espe-

Table 2-2—Relative Prevalence of Conditions Treated With Home or Outpatient Intravenous Antibiotic Therapy in Two Programs

Type of infection	Percent of patients with condition	
	Poretz, 1989	Tice, 1991
Bone and joint.....	38	41
Skin/skin structure.....	22	18
Respiratory.....	13	2
Urinary tract.....	8	1
Endocarditis.....	2	3
Gynecologic.....	3	19
Other.....	12	16
Total.....	100*	100

*Total may not add to exactly 100 due to rounding.

SOURCES: D.M.Poretz, "Home Management of Antibiotic Therapy," *Current Clinical Topics in Infectious Diseases* 10:27-42, 1989; A. D. Tice, "An Office Model of Outpatient Parenteral Antibiotic Therapy," *Reviews of Infectious Diseases* 13(Suppl2):S184-8, 1991.

cially susceptible to certain respiratory infections (64). Traditionally, these individuals required frequent hospitalizations to treat the infections. A number of studies published since the mid-1970s, however, have documented safe and effective home treatment of cystic fibrosis patients with IV antibiotics (128,290,328,400).

More recently, investigators have begun testing prophylactic (i.e., preventive) IV antibiotic regimens for persons with cystic fibrosis (88,102). The long-term effectiveness of these regimens in preventing infections, however, is still uncertain.

Cancer

Individuals with cancer make up another large group of patients utilizing HDIT. Many cancer treatment protocols require frequent administration of antineoplastics, toxic antitumor drugs that must be delivered directly into the bloodstream due to their inherently caustic properties. One of the therapeutic regimens for metastatic³ breast cancer, for example, involves the continuous infusion of vinblastine, an antineoplastic drug, every 3 weeks for a 5-day period (1 16). Rather than returning to the hospital for each successive round of treatment, some patients on this (and other) protocols are

receiving their treatment in the home. The particular antineoplastic that is used, more than the type of cancer being treated, determines the appropriateness of home IV use (35).

Unlike patients with simple infections, cancer patients may receive a number of different infusion therapies simultaneously. In addition to antineoplastics, persons with cancer may at sometime during the course of their disease receive:

- parenterally administered narcotic analgesics to relieve severe pain;
- TPN or hydration⁴ to help to minimize the anorexia and physical deterioration caused by the disease and by the drugs used to treat it;
- blood transfusions necessitated by the anemia that results from both the therapy and the underlying disease;⁵ and
- IV antibiotics to combat infection. (The suppression of bone marrow that results in anemia also makes cancer patients susceptible to infection).

All of these therapies are sometimes administered at home. In addition, the patient may receive other drugs, such as anti-nausea drugs, that are administered as periodic rapid injections (rather than as slow infusions).

AIDS

Like persons with cancer, those with AIDS often require a multitude of parenteral therapies to combat the disease and the secondary effects of some of the medications used to treat it. Characteristic infusion therapies that might be administered in the home include:

- . Anti-infective drugs such as gancyclovir (an antiviral agent) and amphotericin (an antifungal drug) to treat opportunistic infections;
- TPN to maintain in adequate weight and nutrition; and
- . Blood transfusions to treat the anemia that results from both the underlying disease and the

³Metastatic disease is the spread of a malignant cancer to distant parts Of the body.

⁴TPN (total parenteral nutrition) is the administration of nutrients directly into the bloodstream. Hydration is the administration of simple fluids (e.g., dextrose solutions).

⁵Antineoplastic drugs act by inhibiting the growth of rapidly dividing cells, such as those in the tumor. However, they also inhibit the division of normal cells that divide rapidly, such as the blood precursor cells in bone marrow, causing anemia (a lack of red blood cells). The cancer itself can also enter the bone marrow and inhibit normal growth in these cells.

drugs used to treat it.⁶ Azidothymidine, for example, was until very recently the only drug approved by the Food and Drug Administration (FDA) to treat the infection that causes AIDS. A major side effect of this drug, as with antineoplastic drugs, is its toxic effect on the blood precursor cells in bone marrow. Gancyclovir and amphotericin also produce anemia.

Pain medication and adjunct injectibles, such as antiemetic drugs, are also sometimes used by individuals with AIDS. (Aerosolized pentamidine, an inhaled drug sometimes prescribed for pneumonia in AIDS patients, is widely used in this population and is often also supplied by HDIT providers.)

The Safety of HDIT

Considerations and Risks Infusion Therapy

All medical therapies carry some degree of risk. Although drug infusion therapy has been a routine inpatient procedure for many years and is generally safe, adverse outcomes do occur, even in closely monitored hospital settings. Each year almost 1.5 million patients of the 17 to 24 million that receive IV therapy (mostly as inpatients) experience some form of complication (345). Of these, about 3,000 die from complications of IV therapy (93).

Complications of infusion therapy fall into two general categories: local and systemic (i.e., not confined to a specific area of the body). Table 2-3 summarizes some of these potential complications, the more common of which are described briefly below. Although the complications described are applicable to most types of infusion therapy, IV therapy is the most common, and complications are described in this context.

Local Complications

Phlebitis—Perhaps the most frequently encountered complication of any infusion therapy is phlebitis—inflammation at the site of the catheter insertion. (If there is also a blood clot at the IV site, the condition is termed thrombophlebitis.) Depending on the situation, this complication has been estimated to occur in 3.5 to 70 percent of *all* patients receiving IV medication (61). Phlebitis can result

Table 2-3-Potential Complications of Intravenous Therapy

Local complications
Phlebitis, thrombosis, thrombophlebitis (inflammation and/or blood clot of a vessel)
Suppurative thrombophlebitis (infected blood clot in a blood vessel)
Infiltration and extravasation (seepage of infusate into surrounding tissue)
Cellulitis (infection of the soft tissue)
Nerve, tendon, or ligament damage
Hematoma (accumulation of blood within tissues)
Collapsed blood vessel
Venous spasm
Pain
Systemic complications
Septicemia, bacteremia, pyrogenic reaction (diffuse, blood-borne infection)
Embolism (obstruction of a blood vessel)
Pneumothorax, hemothorax, hydrothorax (air, blood, or fluid in the chest cavity)
Hypersensitivity/allergic reaction

SOURCE: Adapted from C.W. Delaney and M.L. Lauer, *Intravenous Therapy: A Guide to Quality Care* (Philadelphia, PA: J.B. Lippincott Co., 1988).

from chemical (e.g., a highly irritating drug), mechanical (e.g., catheter-caused irritation), and biologic causes (e.g., contamination of the drug container). Careful attention to proper procedure can reduce the rate of infection (see ch. 3). If left untreated, infectious thrombophlebitis has the potential to cause more severe complications, including septicemia and death (see below).

Infiltration—Venous catheters that are improperly placed or have dislodged from the vein deliver the infused solution into the tissue around the vein rather than into the vein itself. This complication can be extremely painful, especially if the infusate (the infused solution) consists of some kind of irritant. In the case of antineoplastic therapy for cancer patients, an IV infusion that has infiltrated can be particularly devastating. Antineoplastic drugs are, by nature, very caustic, and infiltration of these agents into soft tissue can cause widespread tissue destruction, necessitating tissue debridement, skin grafting, and other surgical procedures (398).

⁶ The need for blood transfusions maybe reduced somewhat with the introduction on the market of the drug erythropoietin, recently approved by the FDA to treat anemia in AIDS patients.

⁷ Septicemia is the presence of disease-causing bacteria in the bloodstream.

Systemic Complications

Sepsis—One of the causes of phlebitis is infection at the site of IV catheter insertion. Untreated infectious thrombophlebitis can lead to severe consequences. If the patient's immune system is unable to destroy the invading organism, it can continue to multiply and infect virtually all recesses of the body. This condition, known as sepsis, can be fatal; each year 20,000 to 30,000 patients die from catheter-related sepsis (79). Careful attention to early signs of catheter infection or even early sepsis can mitigate the impact of this devastating condition.

Embolism—Particulate matter that is introduced into the venous system by an IV catheter (the embolus) becomes lodged in small vessels and stops circulation (embolism). If the tissue supplied by that blood vessel does not have adequate collateral circulation, it dies. The consequence of this complication depends on where the embolus lodges. Because of the dynamics of circulation, an embolus from a venous catheter usually ends up in the lung, causing a variable amount of destruction—and even death—depending on the size of the embolus.

Embolic material maybe of several sources. The most frequent form of catheter-associated embolism is a blood clot that has formed at the site of thrombophlebitis, then broken loose and lodged elsewhere in the bloodstream (93). Improperly inserted catheters can also break off or dislodge and form a source of embolic material. Air, if mistakenly introduced into the catheter, can also serve as an embolic source (93).

Allergic Reaction—Almost all IV drugs have the capacity to produce an allergic reaction. The manifestation of that reaction, however, can range from a mild skin eruption to circulatory shock and death. Unless there is a prior history of drug allergy in the particular patient, allergic reactions are not predictable. Safe administration of parenteral drugs thus requires prompt identification and early treatment of reactions.

Drug allergies are relatively common. For example, about 2 percent of the population is allergic to penicillin (387), and an estimated 400 to 800 deaths in this country are attributable to this cause (320). Elderly patients (who may have more exposure to a drug and, therefore, more chance to develop an allergy to it), patients with a history of other allergies, patients with a history of a prior drug

reaction, and patients with certain underlying conditions all represent groups at risk for drug allergy. Certain biological and chemical characteristics of the drug also affect the frequency with which it causes allergic reactions in those exposed to it.

Other Drug Reactions—Besides allergic reactions, drugs can cause a variety of other problems. Some of these are predictable occurrences and are frequent, recognized side effects of the drugs that are used. Other complications are less predictable and are termed *idiosyncratic*. For example, patients treated with the antibiotic chloramphenicol have a small but distinct chance of developing complete destruction of their bone marrow. Only about 1 out of 30,000 patients will develop this complication, but the mortality rate in those patients who do develop it is quite high (129). The consequences of many idiosyncratic drug reactions can be minimized if the reaction is identified early. Thus, prevention of serious complications from many drug reactions relies on prompt recognition and early intervention.

Factors Affecting Complication Rate and Severity

The frequency and severity of complications in patients receiving infusion therapy depends heavily on the clinical characteristics of the patient, the therapy given, and the clinical competence of the provider.

Of these factors, the patient's underlying condition is probably the most fundamentally important. Comorbid conditions that predispose individuals to complications significantly affect the outcome of patients treated with infusion therapy (131). An AIDS patient treated for bacterial pneumonia, for example, would be expected to be at a far greater risk for complications than would another pneumonia patient without the underlying problem of AIDS.

The specific diagnosis for which any particular drug infusion therapy is employed also influences its safety. For example, a patient treated for cellulitis with IV antibiotics can tolerate the complications associated with that therapy much better than a patient with meningitis treated with the same therapy; the patient with meningitis has an inherently less stable condition and is more at risk for poor outcome should any drug side effect occur. For this as well as many other reasons, the cellulitis patient might be treated at home, but the meningitis patient would remain in the hospital for therapy.

Some categories of therapeutics are inherently more risky than others. Antineoplastic drugs, for instance, are usually more toxic than are anti-infectives. Within each category, however, is a hierarchy of toxicities; some anti-infectives have the potential for more serious side effects than some antineoplastics. Amphotericin B, a drug used to treat severe fungal infections, for example, causes “potentially dangerous reactions in most patients” (11) and can be fatal if inadequately administered and monitored. In contrast, the side effects of leupride, a hormone used in the management of prostatic cancer, include bone pain, hot flashes, nausea, and impotence (11). Although these side effects are unquestionably unpleasant, they are far less potentially lethal than those seen with amphotericin B.

Similarly, the choice of vascular access device⁸ can affect the types and rates of complications that arise. Central venous catheters, which lie near major vessels, nerves, and organs, have the potential to cause more severe consequences if infiltrated or inserted improperly than a standard peripheral IV catheter, and the long-term implantation and direct vascular access of central catheters makes them more susceptible to potentially dangerous infections (see ch. 3).

The provider also plays a major factor in the outcome of patients treated with infusion therapy. Adherence to published guidelines for the proper care of infusions and infusion devices reduces the frequency and severity of complications (311). Strict aseptic technique, regular changing of the site where a peripheral catheter is inserted, and careful attention to any early sign or symptom of an infusion-related complication is required of any home care provider (312). (The role of quality review to ensure the competency of providers is explored in chapter 5.)

Relative Risks: Home v. Hospital Drug Infusion Therapy

None of the complications of infusion therapy described above is setting-specific. The consequence of these problems, however, may differ depending on whether the therapy is given in the home or in a medical setting.

The degree of monitoring that occurs in the standard inpatient setting is usually greater than can occur in the home, because of the use of electronic

monitoring in many patients and because nurses and physicians are on site. One tradeoff to home administration of infusion therapy, therefore, is a potentially higher frequency of unrecognized and/or untreated complications from the drugs themselves. Infection at the catheter site, for example, can potentially be recognized at an earlier stage by trained personnel in the hospital and be treated effectively by IV site rotation. The same catheter site infection may not be recognized as early at home and a more extensive infection may ensue.

Alternatively, there are certain complications that can actually be worse in the hospital setting than if they were encountered in the outpatient (or home) setting. Catheter site infections that occur in the outpatient setting, for example, are usually caused by organisms that are fairly susceptible to most antibiotics. Those acquired in the hospital, on the other hand, are usually caused by more aggressive, less sensitive organisms which can be more difficult to treat. In one survey of a hospital-based home infusion therapy program, nosocomial (hospital-acquired) infections were seen in approximately 14 percent of hospitalized patients compared with almost no infections in the patient group being treated as outpatients (15). Some of this difference is undoubtedly due to the presence of more stable patients in the outpatient group, but some is probably also due to the reduced exposure of outpatients to potentially significant nosocomial infections.

Any patient who is starting a new drug is at risk of experiencing an unpredictable allergic reaction or other drug-related complications. Thus, even when home infusion is otherwise feasible and safe, the first dose of any infused drug is usually administered under medical supervision, in the hospital, physician's office, or outpatient clinic, where personnel have access to needed resources should a dangerous reaction occur (15,131). Similarly, when the drug is changed during the course of home therapy (e.g., when a more sensitive antibiotic is substituted to achieve better therapeutic results), many providers believe the patient should return to a supervised setting for the initial dose (15).

Whether the elderly are, on average, at greater risk of infusion-related complications than younger patients is not entirely clear. On the one hand, elderly individuals are more likely to have other disabilities

⁸See chapter 3 for a discussion of venous access devices.

that may affect their health state, and they may be more likely to develop allergic reactions to a drug due to a greater chance of past exposure. On the other hand, there is no clear evidence that well-screened elderly patients on HDIT are at higher risk of complications. The single study in the literature on the topic found no difference in the therapeutic outcome of elderly and nonelderly patients treated with home IV antibiotic therapy when similar clinical and social inclusion criteria were used for both groups (65). It may be that fewer elderly than nonelderly patients would meet strict screening criteria, but that once those criteria are met the risks of HDIT in the two groups are comparable.

The Effectiveness and Use of HDIT

Reports on home use of a multitude of drug infusion therapies can be found in the literature. By far, the most common category of drugs is antibiotics and other anti-infectives. Based on estimates by market analysts and other sources, it appears that about two-thirds of current HDIT involve anti-infective drugs (34,193) (table 2-4). Approximately another 15 percent of HDIT drugs are antineoplastics or pain medications. The diverse remaining group of drugs makes up somewhere between 10 and 20 percent of HDIT at present. Although small and encompassing many unrelated drugs, this "other" group appears to be have grown rapidly (364).

Estimates based on drug orders and drug revenues may not reflect exactly the actual distribution of patients on different therapies. One investigator, for example, reports that antibiotics accounted for about two-thirds of drug orders but only about one-half of patients in his study (193a). A recent survey of the records of 35,000 patients served primarily by large infusion specialty companies likewise found that just over one-half (52 percent) of drug infusion patients were on antibiotics, another 21 percent were receiving either antineoplastics or pain medications, and over 5 percent were receiving more than one type of drug infusion therapy (256).

Antibiotics

Antibiotic and other anti-infective drugs constitute the bulk of HDIT for good reason. Their safety and efficacy when provided in nonhospital settings has been demonstrated in a number of studies (106,148,267,325). In virtually all of these studies, home patients achieved cure rates as good as or better than those attained in the inpatient setting.

Table 2-4-The Home Drug Infusion Market, 1989

Therapy	Total revenues	
	Millions of dollars	Percent of market
Antibiotic therapy	600.0	69.6
Pain management	91.1	10.6
Antineoplastic therapy	125.8	5.1
Other therapies	484.2	14.6
Total	1,301.1	100.0 ^a

^aNumbers do not add to exactly 100 due to rounding.

SOURCE: Adapted from Biomedical Business International, Santa Ana, CA, "Home Infusion Therapy Markets," 1989.

Table 2-5-Percentage of Intravenous Antibiotics Used in Home Treatment in Two States, 1989

Drug	North Carolina	Florida
Amphotericin	6.5	—
Cefazolin	3.2	16.7
Cefotetan	8.1	—
Ceftazidime	8.1	2.7
Ceftriaxone	25.8	11.1
Gentamicin	8.1	6.9
Tobramycin	3.2	8.3
Vancomycin	12.9	15.3
All other drugs	22.8	35.9

SOURCE: Adapted from C. Kozma and J. Glaze, "Impact of Home I.V. Benefits on Beneficiary Utilization of Services," interim paper prepared for Health Care Financing Administration, Baltimore, MD, Cooperative Agreement No. 17-C-9957/4-01, April 1990.

Home antibiotic therapy is reported to be effective in over 90 percent of cases (148,325).

The frequency with which a particular compound or class of compounds finds use in HDIT is related to the severity of associated complications. More aggressive and potentially complicated drugs are used less often.

Cefazolin and ceftriaxone, two members of a class of antibiotics known as cephalosporins, account for about half of all home IV antibiotics (table 2-5). Cephalosporins are relatively new antibiotics that share a number of characteristics that make them attractive for use in the home setting. In general, they are comparatively safe and act on a fairly broad spectrum of disease-causing organisms. Additionally, they require little monitoring and fairly infrequent administration. Ceftriaxone, for example, is usually administered only once or twice a day (11). Its infrequent administration makes it much more convenient for home use than penicillin, which has a similar spectrum of action but must be given much more frequently to be effective.

Unfortunately, ceftriaxone may not be particularly effective against *Staphylococcus aureus*, a

common organism that is frequently encountered in the kinds of infections seen in the home care setting (148,317). Other antibiotics, such as cefazolin and methicillin, appear to be more effective and can be used in the home to treat infections from this organism, although they require a more frequent dosing schedule (317).⁹

Another consideration in choosing a particular antibiotic for use in the home is the stability of the compound once the drug is mixed. Several antibiotics that are used extensively in hospitals, such as ampicillin and trimethoprim-sulfamethoxazole, have a very short period of stability when prepared for an IV infusion. Thus, they are rarely used in the home, where drugs and supplies are often delivered no more than once every week or two to minimize costs (3,317,364).

Complications

The incidence of complications arising from home IV antibiotic use is small. Although no drug is entirely safe, antibiotics, in general, are relatively safe and without significant adverse side effects when compared with other classes of drugs. Specific complication rates documented in published studies and in data provided to the Office of Technology Assessment (OTA) range from 6 to 20 percent (106,148,250,267). Almost none of the complications encountered were unique to the home setting but were inherent to IV therapy per se. A detailed record review performed by one HDIT provider found an IV-related complication rate of 10 percent (250) (table 2-6).

One complication unique to the home setting is an "antabuse" type of reaction¹⁰ seen with certain cephalosporins. When a patient treated with these drugs also consumes alcoholic beverages, the combination can produce symptoms that include severe flushing, nausea and vomiting, chest pain, marked uneasiness, weakness, and confusion. Hospitalized patients do not usually consume alcohol and are not prone to developing this side effect. Patients at home, on the other hand, have free access to alcohol and thus have the potential for developing this drug interaction (106). The severity of the reaction is

Table 2-6-Complications of Infusion Therapy Reported by One Home Infusion Provider

Complications presumed related to infusion therapy	
Catheter infection	
HIV ^a infection complication (resulting in immunosuppression)	
Diarrhea/dehydration	
Respiratory distress	
Increased wound infection symptoms	
Fever of unknown origin	
Central venous catheter replacement	
Sepsis	
Exacerbation of condition (possibly drug related)	
Bacteremia	
Proportion of all home infusion patients experiencing complication10.1%
^a HIV = human immunodeficiency virus.	

SOURCE: H. O'Keiff, Barnes Home Health Agency, Inc., St. Louis, MO, letter to the Office of Technology Assessment, Feb. 28, 1991.

roughly proportional to the amount of alcohol ingested (11).

Antineoplastic Therapy

The goal of antineoplastic therapy is to selectively inhibit or destroy the rapidly dividing cells of a malignant tumor, while leaving the patient's normal cells intact. Different classes of antineoplastic drugs accomplish this goal in a variety of ways, with no single therapy universally applicable to all forms of cancer. Often, multiple antineoplastic agents are combined in a regimen to take advantage of the different modes of action while minimizing the varied toxicities.

Several trials and pilot studies have demonstrated the efficacy and safety of home IV antineoplastic therapy (116,201,263,294). In practice, a wide variety of agents are employed. One home infusion provider, for example, supplied seven different antineoplastics and related services to home patients in 1989 (250).¹¹

Antineoplastic agents are frequently accompanied by serious side effects (table 2-7). The drugs find use despite these side effects because the underlying condition being treated has such a grim prognosis. Nonetheless, antineoplastic therapy presents a particular concern for safety in the home,

⁹ There is not complete agreement on the relative effectiveness of these drugs; some physicians maintain that ceftriaxone maybe nearly as effective as cefazolin against this organism (340a).

¹⁰ This reaction is identical to that seen in patients taking the drug disulfiram (Antabuse), a drug used as an adjunct to &W@ chronic alcoholism (129), and has, therefore, been termed the "antabuse reaction."

¹¹ The drugs were mitoxantrone, vinblastine, methotrexate, fluorouracil, doxorubicin, cyclophosphamide, and vincristine.

Table 2-7—Toxicity of Antineoplastic Drugs

Drug	Major acute toxicity				Major delayed toxicity		
	Chills/ fever	Diarrhea/ nausea/ vomiting	Local irritant/ local pain	Hypersensitivity reactions and anaphylaxis	Other ^a	Bone marrow depression	Other ^a
Asparaginase	X	X		X			X
Bleomycin	X	x		x			X
Carmustine		x	X			X	X
Cisplatin	X	x		x		x	x
Cytolosphamide		X				x	
Cytarabine, cytosine arabinoside . . . X				x		x	X
Dacarbazine		X	X			X	
Dactinomycin		X	x			X	X
Daunorubicin		X	X		X	X	X
Doxorubicin		x	X		X	x	X
Floxuridine (FUDR)		x				x	x
Fluorouracil (5-FU)		x				X	X
Mechlorethamine		X	X			X	
Methotrexate		X		X		X	X
Mitomycin		X	X			X	X
Plicamycin		x				x	x
Streptozocin/streptozotocin		x	x			X	X
Thioquanine		x				X	
Thiotepa		X	X			X	
Vinblastine		X	X			X	X
Vincristine		X	X			X	X

^a"Other" acute toxicities include red urine, electrocardiogram changes, and orthostatic hypotension. "Other" delayed toxicities include such side effects as hair loss, liver and kidney damage, oral ulcers, stomatitis, neurological defects, and thrombocytopenia.

SOURCE: Based on T.M. Speight (ed.), Avery's *Drug Treatment* (Auckland, New Zealand: ADIS Press Ltd., 1987).

where both the ability to deal with the side effects and the system to dispose of the toxic drugs themselves are less available.

Many antineoplastic agents are *vesicants* and can cause severe irritation to the vein. When administered through a peripheral catheter, the incidence of thrombophlebitis is much higher than for most antibiotics and other nonvesicant drugs. To minimize the damage done to the vein, antineoplastic agents are frequently administered directly into a large, central vein to dilute the drug and diminish its toxicity. Table 2-8 lists some examples of IV antineoplastic agents and the requirements for administration.

Depending on the particular kind and location of the cancer, some antineoplastic drugs can be given directly into the artery that supplies it with blood. By delivering a more concentrated dose of a drug to the tumor, the potential for side effects can be minimized. Thus, intraarterially delivered antineoplastics produce fewer systemic side effects than they would if given intravenously. The tradeoff, in this instance, is the potential problems associated with intraarterial drug administration.

The advent of continuous infusion therapy has expanded the number and kinds of antineoplastic agents that may be delivered in the home setting (201,297). To achieve effective concentrations when given intermittently, a drug may need to be given at such high dosage that it causes serious side effects. As a continuous infusion, however, the concentration required for efficacy is often not as great and some adverse consequences can be avoided. Thus, the toxic effects of certain antineoplastic agents can be reduced by utilizing a longer exposure to a lower dose without losing any of the clinical efficacy.

The appropriateness of home antineoplastic therapy for a particular patient depends heavily on the underlying condition of that patient. Cancer patients are often weakened or incapacitated by the devastating effects of the disease and the therapies used to treat it. Unless these patients have sufficient in-home help in the form of a family member or other caregiver, home IV antineoplastic therapy is often not possible. Patients who are unwilling to learn the techniques, have an inadequate support system, or are physically unable to master the skills required thus represent poor risks for home IV therapy (35). Even if help and support are available, the tremendous demands frequently presented by cancer pa-

Table 2-8-Examples of Special Considerations in Administering Intravenous (IV) Antineoplastics

Drug	Special considerations
Asparaginase	Life-threatening anaphylaxis can occur. Skin testing and desensitization recommended before administration. During administration, a physician/life support equipment and epinephrine, antihistamine, and corticosteroids should be available; monitor blood pressure.
Bleomycin sulfate.	Increased incidence of anaphylaxis in lymphoma patients; give test dose. Give acetaminophen and antihistamine 30 min. before chemotherapy to prevent fever and chills.
Carmustine	Pain, burning at IV site and facial flushing may occur secondary to alcohol diluent; if this occurs decrease rate, increase volume in which drug is diluted.
Cisplatin	Before and during treatment, hydration and raised urinary output are essential to prevent nephrotoxicity. Shorter infusion time may be associated with increased risk of kidney toxicity. Avoid the use of needles containing aluminum, as it reacts with Platinol to create a black precipitate and loss of potency. Anaphylactic reactions may be controlled by epinephrine and corticosteroids.
Cyclophosphamide	To prevent hemorrhagic cystitis, patient should drink 3 to 4 liters of fluid per day and void frequently. Dizziness, rhinorrhea, sneezing and diaphoresis have been reported with doses of greater than 500 mg when given quickly.
Etoposide	Hypotension and wheezing may occur if given too rapidly (in less than 30 min.). Stop infusion if wheezing occurs; antihistamines may be helpful.

SOURCE: Based on C.B. Hughes, "Giving Cancer Drugs IV: Some Guidelines," *American Journal of Nursing* 86:34-38, 1986.

tients can easily overwhelm the support system, requiring inpatient hospitalization.

Analgesics

Pain is a dominant feature of many disease conditions. Up to 70 percent of cancer patients suffer severe pain (401). Pain can usually be managed effectively with oral medication, but certain circumstances preclude this form of therapy. Patients with oral, esophageal, or other cancers which prevent normal swallowing, patients with breakthrough pain despite high doses of oral narcotics, and patients who suffer side effects related to the high doses of oral narcotics often required to control pain are candidates for parenteral analgesics (185).

Parenteral narcotic analgesics include meperidine, morphine, and hydromorphone. Their use in parenteral pain management varies widely; in one survey, the average duration of pain management therapy for different drugs ranged from 2 to 240 days (193). This variation probably reflects the relatively few patients on this therapy represented in the survey and the heterogeneous conditions for which pain control is used. IV narcotic pain relief has even been reported in a 2-year-old child being treated at home for advanced cancer of the brain (286).

While IV narcotic administration for pain control has been available for many years, the concept of home administration is fairly new. Two recent developments have been particularly important to enabling home parenteral pain control in many patients. First has been the development of infusion

pumps with a patient-controlled analgesia feature. This feature allows patients to optimize pain relief but minimize drug side effects, by combining a constant preprogrammed baseline level of relief with the option to self-administer larger boluses of medicine when pain is particularly severe (265). Second, subcutaneous administration of narcotics has become a more accepted alternative that avoids some of the potential complications of IV therapy. In fact, subcutaneous pain management is considered by some to be superior to IV administration because of its equivalent effectiveness in many patients and its technical advantages (227).

Additionally, intrathecal and epidural administration of narcotics have been used for several years and are being increasingly considered as options for the home. A number of reports of parenteral pain management through one of these routes have been published (316,326,327), and HDIT providers report having provided them (250). However, intraspinal administration of narcotics is associated with complications including urinary retention, nausea and vomiting, and respiratory depression (202). Narcotic-induced respiratory depression, which is especially dangerous, can be detected by using an apnea monitor and can be counteracted by infusing an antagonistic agent (e.g., for morphine, Narcan is the antagonist) (202). Because respiratory complications may not present for up to 22 hours after epidural narcotics administration (309), these patients require extended monitoring and therefore can pose additional challenges for home care.

One concern unique to home parenteral narcotics administration is the potential for abuse of the drugs on the part of patients or family caregivers.¹² Providers of this therapy report such measures as hospitalizing patients with a history of IV drug abuse, rather than treating them at home, to minimize the opportunity for abuse; and discontinuing home therapy when it became apparent that a family member was diverting drugs intended for the patient (364). Special measures, such as using infusion pumps that enable the drug cassette to be locked and replaced only by a visiting nurse, may be required for home parenteral narcotic administration to be a safe option.

*Other Therapies*¹³

Dobutamine

Patients with congestive heart failure (CHF) suffer from an inability of the heart to pump a sufficient amount of blood to the vital organs. Dobutamine, which acts by increasing the force of contraction of the heart, has been used conventionally as a temporary measure in patients with underlying CHF whose heart needs assistance to deal with additional stress (e.g., an acute viral infection) (198). Dobutamine can only be administered intravenously, and until recently it was only administered in the hospital. In 1977, however, researchers discovered that 72-hour intermittent infusions of dobutamine improved cardiac function for prolonged periods (196). Subsequent studies confirmed these findings and furthered the idea that periodic outpatient administration of IV dobutamine may add to the treatment options for patients with CHF (205,348,349).

While the hemodynamic benefits of outpatient dobutamine are encouraging, the unexpected finding of increased mortality in these patients is not. One controlled study of the treatment found that despite significant improvement in symptoms during the study, 15 of 37 dobutamine patients (40 percent) died, while only 5 of 23 placebo-treated patients (22 percent) did so (94). The increased mortality was subsequently attributed to cardiac arrhythmias (irregular heartbeats). A recent study of an oral drug

related to dobutamine likewise found that, despite the drug's predicted benefits, long-term therapy actually increased morbidity and mortality in patients with severe CHF (251).

Some researchers believe that many of the patients at risk of death during dobutamine treatment could be identified by means of pretreatment cardiac monitoring (322). The poor record of this and related drugs in existing studies, however, suggests that they do not merit long-term use in the home unless effectiveness in specific patient groups can be demonstrated.

One final argument favoring the use of IV dobutamine is that it may enable a patient with CHF who is a heart transplant candidate to survive until a suitable organ becomes available. Dobutamine is prescribed by some physicians for this purpose (73,365). Given the current evidence described above, this strategy may not really enhance a given individual's chance of receiving a transplant. Even if it does, it cannot increase the total number of people who ultimately can receive a new heart, because the number of heart transplants is limited by the supply of donor organs. The number of persons on the waiting list for heart transplants exceeds the number of transplants by about 30 percent (385a).

Immune Globulin

Human immune globulin was first used to treat patients whose bodies were naturally deficient in this substance in 1952 (52). Early administration consisted of periodic intramuscular injections (54). Intravenous preparations became available in the United States in 1981, and they are generally preferred for long-term therapy because they are less painful to receive and enable much larger doses to be given (54).

The clearest and most accepted indications for immune globulin therapy are for treating patients with severely impaired antibody-producing capacity (54). These patients may have any of a number of rare primary immunodeficiency diseases, such as severe combined immunodeficiency. Many of these conditions are chronic, and some individuals with

¹²“Family caregivers” are defined in this report as caregivers who are close friends or relatives of the patient and who generally receive no financial compensation for their services.

¹³ In addition to the therapies described here, the list of drugs sometimes infused at home includes tocolytic drugs to prevent preterm labor (e.g., terbutaline and ritodrine); anticoagulant drugs (e.g., heparin); certain antiulcer drugs; and chelating drugs to rid the body of toxic levels of metals (e.g., deferoxamine).

them conditions require IV immune globulin therapy for life.

IV immune globulin is also sometimes used to bolster the immune systems of persons whose immunodeficiencies are secondary to another condition (e.g., those who have received immunosuppressive drugs in connection with their cancer treatment) (54,235). Recently, immune globulin has been shown to be effective in reducing the incidence of infections in children with AIDS (234) and in patients with chronic lymphocytic leukemia (77). The therapy is also gaining acceptance in treating other disorders that involve the immune system in some way, such as immune thrombocytopenic purpura, Kawasaki syndrome, and steroid-dependent asthma (323). Some have suggested that it may be successful in treating intractable seizure disorders, but it has not been tested for this use in a controlled study (235).

As IV immune globulin therapy has become used to treat a wide variety of diseases, questions have been raised about its cost. The charge for a single infusion of immune globulin has been reported anecdotally to be \$125 to \$250, making the annual charge for therapy for a typical adult requiring regular infusions over \$25,000 for the drug alone (54). In some hospitals, immune globulin has become one of the top four drug expenditures (323). Some researchers have calculated the cost of prophylactic IV immune globulin for chronic lymphocytic leukemia to be \$6 million for every quality-adjusted year of life gained (394).

The high cost of IV immune globulin therapy in the hospital, the fact that many patients are on therapy indefinitely, and the fact that many of these patients are children make home therapy attractive. A number of studies have shown that IV immune globulin therapy can indeed be provided safely in the home, with an effectiveness comparable to hospital therapy (17,190,191,247). Home use, however, will not reduce the costs of the drug itself.

Immune globulin therapy is not entirely free from the possibility of adverse events associated with the infusion of this substance. Mild reactions include nausea, fatigue, and headache; more serious reactions include severe chest pain, abnormal heartbeat, and mental confusion (122,235). These reactions can

occur during or within minutes of treatment and may require immediate countermeasures (122). One recent study found that, of three methods of administering home immune globulin (intramuscular injection, IV infusion, or rapid subcutaneous infusion), rapid subcutaneous infusion resulted in the fewest adverse events while retaining its effectiveness (122). The results of this study, which was carried out in Sweden, suggest that more examination of subcutaneous administration in U.S. patients on long-term immune globulin therapy is warranted.

Blood Transfusions

The prototypical home transfusion patient is one who is anemic because of a chronic, debilitating condition, such as cancer or AIDS, and for whom transportation to a hospital or outpatient clinic would cause great difficulty (3,7,223,261). Anemia, by definition, is a reduction in the volume of red blood cells, and anemic patients usually have insufficient oxygen-carrying capacity in the blood (262). In addition to cancer- and AIDS-related anemias, certain other anemias (e.g., sickle-cell anemia) also may require transfusions of red blood cells¹⁴ and might occasionally be treated in the home.

Individuals with thrombocytopenia (platelet deficiency), which impairs blood clotting at the site where a blood vessel is injured, may be candidates for home platelet transfusions. Thrombocytopenia can be caused by many different mechanisms, such as a bacterial infection or secondary to certain types of liver disease and bone marrow disorders (184).

Transfusion therapy poses certain risks unique to this form of infusion. It requires strict patient selection criteria and rigid transfusion procedures due to the potential severity of the body's reaction to foreign blood components.

The most serious reactions result from an incompatibility between antigens of the transfused blood component and the patient's antibodies. The consequence of this incompatibility is hemolysis, the vast destruction of red blood cells (7,184). Hemolysis can be fatal. Clinical symptoms include fever, chills, back pain, and possible shock. Proper followup and good patient records are imperative to ensure that donor and recipient blood are appropriately

¹⁴ Home blind transfusions virtually always involve transfusions of only certain extracted blood components. patients in need Of whole blood transfusions usually are those in need of urgent and intensive care (e.g., trauma patients) who are therefore unsuitable for home therapy.

matched; all home acute hemolytic reactions are due to clerical errors.

Febrile, non-hemolytic reactions are usually due to antibodies that cause clumping of the white blood cells that poison or destroy cells. Such a reaction usually occurs within the first 1 or 2 hours of the transfusion. Characterized by chills and fever, non-hemolytic reactions usually can be treated successfully with aspirin or acetaminophen. However, a non-hemolytic reaction may signal a hemolytic reaction; symptoms must be considered potentially life-threatening until a hemolytic reaction can be ruled out (7,184).

Emerging Therapies

The broad acceptance of home drug infusion makes it likely that new and future drugs that must be given parenterally may find application in the home. Following are some examples of drugs that have recently begun to be used in this setting, or which might be provided in this setting in the future.

- *Granulocyte colony stimulating factor (G-CSF)*—A bioengineered version of a natural substance that regulates the growth and development of certain white blood cells, G-CSF has recently been approved by the FDA for use in cancer patients with low white blood cell counts and fever (151). Because it is a protein and subject to degradation by digestive enzymes, G-CSF must be administered parenterally (either IV or subcutaneously). It is administered as a daily injection for up to 2 weeks in conjunction with the patient's antineoplastic therapy cycle (14a). Because many patients are now receiving their antineoplastic therapy at home, G-CSF is also sometimes administered concomitantly at home (176).
- *Granulocyte macrophage-colony stimulating factor (GM-CSF)*—Closely related to G-CSF, GM-CSF plays a similar biological role in acting to raise the white blood cell count. It also has been recently approved by the FDA for use in patients with Hodgkin's disease, rOrl-Hodgkin's lymphoma, and acute lymphoblastic leukemia who undergo bone marrow transplant (151). GM-CSF must be administered parenterally and may be used in the home by post-transplant patients. In addition, it has possible uses in cancer and AIDS patients who are at risk of infections (302).
- *Post-transplant immunosuppressive drugs*—Transplant recipients must usually take drugs that suppress their immune systems, preventing the body from rejecting the grafted organ. Most drugs currently used for long-term post-transplant immunosuppression are oral drugs such as cyclosporine. One FDA-approved drug, however—Orthoclone OKT-3—is an IV drug. Although its prophylactic use thus far has taken place while the patient is still hospitalized after the transplant (91), this and any future parenteral immunosuppressives might move home as part of strategies to reduce the hospital stays of transplant patients.
- *Interleukin-2*—Still under development, interleukin-2 holds promise as a future treatment for kidney cancer (282). The drug is not yet approved by the FDA for use in the United States, but its mode of administration (subcutaneous or IV) and the long-term nature of the disease it treats make it a likely candidate for home therapy if it should receive marketing approval.