Appendix C

Future Developments in Life-Sustaining Technologies

Introduction

Future developments in life-sustaining technologies will improve existing technologies and create new therapies and devices to treat currently untreatable conditions. Technological improvements should make treatments more effective, more comfortable, more portable, cheaper, less invasive, or some combination of these factors. These improvements may change how often and under what circumstances certain life-sustaining technologies are used, and they may contribute to changing attitudes about appropriate care. However, fundamental questions of access to and quality of care, cost, quality of life, and decisionmaking will remain even as the technologies change.

This appendix describes the general directions of current research and development, both in the public and the private sectors, that are pertinent to the use of life-sustaining technologies for elderly patients. Areas in which basic research is crucial to further progress are highlighted.

Factors Affecting the Demand for Life-Sustaining Technologies

The demand for new life-sustaining technologies will depend on a variety of factors, including the degree to which preventive strategies are implemented, the size of the potential patient population, reimbursement policies, and attitudes about the extension of life. Numerical projections of the groups at risk for the five life-sustaining technologies discussed in this report are not attempted, because of the lack of data on current use of the technologies and because the size and composition of future patient groups will be determined in large part by the availability and use of various new preventive, diagnostic, and therapeutic technologies. The effects of those treatments yet to be developed are impossible to gauge. Nevertheless, given both the growth and the aging of the elderly population, an increase in demand is likely.

The future social context in which technological development will occur and health care decisions will be made is also uncertain. The Institute for the Future, a private research and consulting firm in Menlo Park, CA, recently developed two possible scenarios to show the wide range of possibilities. These are not predictions of what the sociopolitical environment will be, but rather indicators of the wide range of factors that might influence health care decisionmaking and the development of new life-sustaining technologies (47).

One scenario, entitled "Cost Containment," envisions the development of societal consensus to contain health care costs. The consensus is sustained by the relatively young, college-educated, baby-boom group whose needs center more on housing, education, and child care than on health; the competitive climate for business; the concern over government deficits; and the public's sharp eye on the public purse and the family budget. In this scenario, total health care expenditures as a percentage of gross national product (GNP) remain at their 1983 level in the year 2000 (47).

In the other scenario, entitled "People Want More," the historic pattern of growth in the health care system continues despite efforts to contain costs. The demographic, attitudinal, technological, political, and economic forces assumed in this scenario create pressures to provide a wider range of health care services to an aging population. Progress is made in treating a variety of diseases. People accept the value of these interventions and demand that they be made available. The result is widespread support for an expanding range of chronic care, acute care, and rehabilitation services. Somewhat paradoxically, say the authors of this scenario, the hospice movement will continue to grow because there will still be many illnesses for which the limits of medical science are obvious to the public (47).

The burden of chronic illness in the years to come is also impossible to foresee. One major theory holds that although the incidence of chronic disease may increase, the average age at onset and the disabling effects of these diseases will increase faster than will life expectancy. This would produce a "compression of morbidity" in which the average period of chronic disease and disability in old age will be less than current levels. Another scenario foresees longer average periods of disability and chronic illness in the future, based on the assumption that recent lifesaving and other health care technologies have lengthened lives more than they have reduced the incidence of chronic diseases (87).
Factors Affecting the Availability of Life-Sustaining Technologies

A spectrum of individuals and organizations plays a role in the development of medical technologies. Patients and clinicians identify and define specific medical problems that may be controlled, cured, or compensated for technologically. Biomedical engineers and others apply their expertise to identified clinical problems. Some technologies are not so much a result of physiological understanding as they are a triumph in solving a vexing technical problem. Other developments require better understanding of physiology. Once a useful drug or device has been developed, a manufacturing company must assess a variety of factors and make a decision about whether to produce and market the technology.

Research and Development

Biomedical research and development (R&D) is focused on understanding physiological processes and developing cures or prostheses to use when these processes are pathological. Some R&D is specific to a particular technology, while some will affect several technologies. Computerization and new biocompatible materials will have applications in most if not all of the technologies described in this report. The “skin button,” for example, can be used in dialysis, nutritional support, intravenous (IV) antibiotic therapy, and other treatments that require vascular access. (See box c-1.)
Biocompatible materials are required in almost all of the technologies discussed in this report. New materials could be used for a variety of purposes, such as smaller, more comfortable feeding tubes or dialysis membranes that more closely mimic the action of the kidney. Biocompatible materials can be made from a variety of substances, including ceramics, polymers, cellulosics, and metals (17,43,51).

Computers also have increasing applications. Computers are being applied to infusion pumps to assure proper delivery of antibiotics and nutritional formulas, to defibrillator to automatically provide the appropriate electric shock, and to blood gas monitors, important in mechanical ventilation. Metabolic monitoring systems can measure oxygen consumption and carbon dioxide production, using computers for data storage and graphics (12).

In addition to treatment technologies, computers will have applications in prognosis and decisionmaking. As-similating the immense amount of information pertinent to clinical decisions and selecting from many potential treatments is becoming increasingly difficult as the knowledge base grows. New techniques referred to as “decision analysis,” “medical decisionmaking,” or “clinical decisionmaking” are being developed to systematize decisionmaking and objectify uncertainty (see ch. 10). “Expert systems,” computer systems that are programmed to approximate human thought processes, will increasingly aid physicians in making diagnoses and prescribing treatments. Computer networks and databases are evolving to link physicians with information about treatment modalities and outcomes. Computers can store and sort the constantly increasing amount of medical information (2), allowing physicians to keep up with and add to the expanding knowledge base.

An example of a computer application relevant to the technologies discussed in this report is the computer surveillance of hospital-acquired infections and antibiotic use. One study showed that computer screening to identify patients most likely to have infections can find more infections faster than traditional methods (31). Timely control measures are believed to be important for interrupting the spread of hospital-acquired infections (31).

Eventually, home health monitors might incorporate a microprocessor with reservoirs of drugs and electronic probes. Several prognosticators envision a “hospital on the wrist,” a wearable, miniature health monitoring device that could sense changes in the body and administer drugs or therapeutic electrical charges automatically (8,59).

New power sources are also an important area of research. Power sources are currently an important issue for pacemakers, defibrillator, and cardiac pros-

thesis and assist devices. Compact power sources will be needed for implantable or portable devices.

Production, Diffusion, and Use of New Medical Technologies

Development of a new technology does not always result in its availability. A drug or device that has been determined to be technologically feasible (from an engineering and production standpoint) must still pass through a complex and lengthy approval process to become commercially available. Once new drugs, devices, or procedures are available, health care providers must make decisions about adopting or investing in them. Those decisions are influenced by a variety of factors, including the general climate of the health care industry.

Several analyses foresee longer development times for new technologies in the coming years, due at least in part to increasing emphasis on cost containment. Industry’s willingness to support equipment-related R&D is expected to decline as more hospitals forgo expensive equipment purchases whose cost-effectiveness has not been clearly demonstrated (11,63).

Economic influences sometimes prevent the development of socially desired drugs and medical devices. For instance, the potential profitability of a drug that treats only one disease of low incidence may not provide pharmaceutical companies with adequate incentive to bear the expense of development.

In addition, once a drug or device enters the testing and approval-seeking stage, various Federal agencies influence its ultimate availability. The National Institutes of Health (NIH) may support randomized clinical trials; the Food and Drug Administration (FDA) evaluates safety and efficacy prior to commercial distribution; the Health Care Financing Administration (HCFA) determines Medicare coverage and reimbursement.

As technologies are marketed, the role of third-party payers in determining the fate of drugs and devices should not be underestimated. In some situations, reimbursement policies have contributed to the overuse of certain medical technologies. Other factors that sometimes encourage overuse of medical technologies include competition among hospitals to attract patients and physicians, public demand for sophisticated technologies, increasing specialization within medicine, physicians’ desire to do as much as possible for their patients, and uncertainties related to what constitutes appropriate use. The threat of malpractice suits can also encourage the overuse of medical tests and procedures (85). In addition, the promise of new technol-
ologies has at times lured providers into creative financing and partnership arrangements so they can gain access to a major new technology in spite of certificate-of-need limitations or other regulatory obstacles (77).

**Alternative Treatment Settings**

Many providers and manufacturers are investigating alternate-site care, to replace or supplement traditional inpatient hospital care. They hope to develop more cost-effective ways of providing health care and to identify new markets. As competition and cost-containment efforts in the health care industry intensify, technologies useful in alternate-site treatment will become increasingly important. The health care industry has recognized these opportunities, as reflected in a series of reports analyzing nonhospital providers (40) and the increased production of devices intended for home use (e.g., larger IV bags to last through the night). Reduced size and increased portability of medical equipment will facilitate the use of various technologies in nonhospital settings.

Among the settings receiving increased attention are nursing homes, patients’ homes, and ambulatory care centers, including pain management centers and diagnostic imaging centers. Each of these sites provides opportunities for technological innovation and increased involvement of lay personnel and less trained health professionals. However, the adoption and use of technologies suitable for either home or outpatient use is often limited by reimbursement policies. For example, lack of Medicare coverage for IV antibiotics at home may limit the use of this technology for elderly patients (see ch. 9).

**Future of Resuscitation**

In spite of the proven value of cardiopulmonary resuscitation (CPR) as a life-saving procedure, resuscitation remains fraught with potentially severe problems and complications, and it is often unsuccessful. As discussed in chapter 5, resuscitation involves two stages: basic and advanced life support.

**Basic Life Support**

Current research in the area of basic life support focuses on developing techniques to improve ventilation and blood flow in the event of cardiac arrest, reduce the number of CPR-related injuries, and improve survival across all diagnostic classes of resuscitation patients. Another area of research is the development of techniques to correct certain types of arrhythmias (e.g., asystole or bradycardia) that are difficult to treat with current CPR methods.

Efforts to improve basic life support are focused on modifying current techniques, rather than developing equipment. The most obvious areas of research are the duration of chest compression and the rate and timing of ventilation during CPR. Methods to improve blood flow during CPR, especially to the brain, are also under investigation. The risk of brain damage during CPR is very high because inadequate circulation of blood deprives the brain of needed oxygen.

New CPR is an experimental process that requires specialized equipment and endotracheal incubation. This more complex version of CPR combines chest compression and lung inflation with abdominal binding to increase pressure inside the chest. This pressure is transmitted up the carotid arteries to increase the flow of blood to the brain, thus minimizing the risk of brain damage. This model has proven successful in dogs and is being investigated in humans. Some success has also been reported with the use of pneumatic anti-shock trousers (as a means of abdominal binding) in increasing survival rates. The initial data showed slightly higher resuscitation and discharge rates with the use of pneumatic trousers but were statistically significant in only one group of patients (57).

Other variations on standard CPR under investigation include asynchronous ventilation; simultaneous ventilation and compression; intermittent abdominal counterpulsation; and high-frequency, high-momentum chest compression. All are designed to take maximum advantage of the mechanisms of blood flow. All of these approaches represent the broader and increasingly prevalent view of CPR as cardiocerebropulmonary resuscitation, a term that recognizes the goal of increased blood flow to the brain and the prevention of neurological deterioration from global ischemia (lack of blood flow) (74).

Open-Chest cardiac massage is receiving renewed interest, although it was virtually abandoned following the introduction of closed-chest massage (standard CPR) in 1960. Some studies have demonstrated successful open-chest CPR following failure of closed-chest massage. In addition, some authors have noted that closed-chest massage was introduced and accepted because of its clinical usefulness and efficacy, but without any controlled studies to compare its efficacy with that of open-chest massage, or to determine the appropriate use of either procedure (74). Thus, additional studies of open-chest CPR may be warranted. Some clinicians, however, believe that the trauma of open-chest CPR is so great that the technique should be used only as a last resort. These clinicians warn that renewed interest in open-chest CPR may lead to its overuse (52).
Defibrillation, Antitachycardial Pacing, and Cardioversion

Since early defibrillation has been shown to be one of the most important factors in the favorable outcome of out-of-hospital cardiac arrests (84), many efforts in the last 20 years to improve CPR survival have been directed at shortening the time to defibrillation. Physicians and paramedics are the professionals most likely to be trained to defibrillate patients at the scene of the arrest. Programs are now being developed to train Emergency Medical Technicians (EMTs) and lay people in the use of automatic external defibrillator (13). These devices sense cardiac rhythms, generally through adhesive chest electrodes, and determine whether ventricular fibrillation is present. Some models automatically shock a patient in ventricular fibrillation; others allow the user to decide whether or not to deliver a shock. All operators must be trained in basic CPR, since proper resuscitation with such a defibrillator depends on the integration of both CPR and defibrillation.

The implantable defibrillator, a relatively new device, substantially improves the survival rates of patients who experience ventricular fibrillation. These devices are surgically implanted in patients known to be at risk of arrhythmias; they monitor and respond automatically to aberrations in heart rhythms. The first implantable defibrillator to receive FDA approval is described in box C-2.

Two other implantable devices are useful for the automatic termination of ventricular tachycardia and fibrillation: antitachycardia pacemakers and low energy cardioverters. The pacemakers have been tested in clinical trials, and several models are available. Because of their lower energy requirements, low energy cardioverters are smaller than implantable defibrillator, but they have not been widely tested. Currently, both devices require the use of a defibrillator as a backup system, although the high energy produced by a defibrillator is not always necessary to terminate arrhythmia. Therefore, an ideal automatic electronic arrhythmia-terminating device should combine antitachycardia pacemaking, low energy cardioversion, and higher energy defibrillation. The ideal device would be fully programmable between these three modes of arrhythmia termination and incorporate automatic arrhythmia detection algorithms. Clinical trials of an implantable defibrillator with antitachycardia and regular pacing functions are expected in 1987 (10).
Drugs and Drug Delivery

Drugs play a significant role in resuscitation, and new methods of drug delivery are being developed. For instance, some observers suggest that the use of endotracheal administration of drugs during resuscitation deserves more attention (32). In cases where adequate intravenous routes cannot be located quickly, endotracheal administration may provide an important alternative for the delivery of epinephrine, atropine, lidocaine, and certain other drugs. (Drugs that require a large volume of fluid to achieve an effective dose—e.g., sodium bicarbonate—are unsuitable for endotracheal administration.) One advantage of the endotracheal route is its extended duration of action (two to five times that of intravenous administration). Also, it can be used by paramedics (or others) or when conditions preclude efficient intravenous access (32).

Another promising development in drug delivery is a new device to administer lidocaine. The device is about the size of a lipstick tube, costs approximately $15, and automatically injects lidocaine into a muscle when a safety cap is removed. This technique could prevent up to 30 percent of pre-hospital deaths from heart attack, depending on how quickly the lidocaine was administered, according to the director of one randomized controlled study (65). FDA has approved the device for emergency use by physicians and paramedics, or by certain heart patients who are undergoing remote monitoring (53,65). Oral analogs to lidocaine have also been developed (71).

Tissue-type plasminogen activator (t-PA) may also be administered by an automatic intramuscular injection device. Two companies are collaborating to develop such a device to permit patients to self-inject themselves with t-PA, a drug expected to gain FDA approval for dissolving blood clots associated with myocardial infarction (13).

Other new drugs may help reduce the risk of cardiac death for certain patients. One drug, flecainide acetate, received FDA approval in November 1985 for the treatment of life-threatening ventricular arrhythmias and for patients with symptomatic ventricular arrhythmias (3). FDA also approved the drug amiodarone hydrochloride for use in patients who would otherwise die from uncontrolled ventricular arrhythmias. This drug has very serious side effects and is described as “a drug of last resort, to be used by experts very familiar with the treatment of severe heart rhythm disorders and only after attempts to use alternative agents have failed” (4).

Heart Replacement and Assist Technologies

The use and success of heart transplants have greatly increased in recent years, largely due to the introduction of the drug cyclosporine, which helps prevent rejection of the new organ. Human heart transplantation has become so routinely successful that it is virtually perceived as a standard medical practice. Data from about 1,200 heart transplants worldwide indicate that 90 percent of patients revert from “severely compromised function” to “uncompromised function” after a successful transplant (26). Artificial heart implantation, however, is currently experimental and very controversial. Judging from the complications associated with the current generation of artificial hearts, it seems unlikely that artificial hearts will become widely available in the near future (27). Knowledge gained from artificial heart research may, however, be used to develop various forms of cardiac-assist technologies. In addition, cardiac-assist technologies may be useful in some patients for temporary cardiac support until a failing natural heart recovers, or until a suitable donor heart is available for transplantation. A variety of heart replacement and assist devices are under development or in clinical trials (table C-1).

Artificial Hearts. As of November 1986, a total of 20 American patients had received artificial hearts. Four models have been used: the Jarvik-7; the Jarvik-70, a smaller model; the Penn State heart; and the Phoenix heart. The Jarvik-7 artificial heart has been tested in five patients as a permanent replacement. All four models of artificial heart have been used as a temporary prosthesis, until a suitable human heart was available (27).

The Jarvik-7 artificial heart is a pneumatically driven, plastic “pump” with a smooth, nonthrombogenic polyurethane interior surface to reduce the risk of blood clotting. Nonetheless, despite careful administration of anticoagulants, the patients who have received the Jarvik-7 have suffered complications resulting from blood clotting.

Attempting to overcome problems with the Jarvik-7, investigators have developed other approaches to a permanent artificial heart. In May 1985, FDA granted approval for the implantation of the “Penn State heart” in six patients—the second artificial heart approved for human implantation. The Penn State heart differs from the Jarvik-7 in that it is intended to be used as a temporary “bridge” to “eventual and timely [human] cardiac transplantation” (26).
Table C-1.—Heart Replacement and Assist Devices

<table>
<thead>
<tr>
<th>Type</th>
<th>Status</th>
<th>Major Developers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-Aortic Balloon Pump</td>
<td>FDA approved for clinical use</td>
<td>Datascpe, Kontron, SMEC, Aries</td>
</tr>
<tr>
<td>Percutaneous Left Ventricular Assist Device</td>
<td>Pre-clinical trials</td>
<td>Abiomed, Electro-Catheter</td>
</tr>
<tr>
<td>Emergency Left Ventricular Assist Device</td>
<td>Clinical trials</td>
<td>Electro-Catheter, Biomedicus, 3M, Novacor, Thermedics, Thoratec, Abiomed, Nimbus</td>
</tr>
<tr>
<td>External Left Ventricular Assist Device</td>
<td>Pre-clinical trials</td>
<td>Abiomed, Novacor, Thermedics, 3M, Symbion</td>
</tr>
<tr>
<td>Implantable Ventricular Assist System</td>
<td>Pre-clinical trials</td>
<td>Abiomed, Symbion, Thermedics, 3M, Symbion, Thoratec, Cambridge Medical Technology</td>
</tr>
<tr>
<td>Externally Driven Total Artificial Heart</td>
<td>Clinical trials</td>
<td>Symbion, Thoratec, Abiomed, Symbion, Thoratec, Cambridge</td>
</tr>
<tr>
<td>Implantable Total Artificial Heart</td>
<td>R&amp;D</td>
<td>Symbion, Thoratec, Cambridge Medical Technology</td>
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*Electro-Catheter*—5 pulsatile pump major component of the CardiacAssist device, has been used in clinical trials

SOURCE Biomedical Business International, Inc., Cardiovascular Therapy Products, Report #7027 (Tustin, CA March 1987)

Major goals for the next generation of artificial hearts derive from the problems that have resulted during the first few implantations in humans. These goals include:

- development of an implantable power source useful for an extended period of time;
- construction from all nonthrombogenic materials;
- identification (or development) of effective and long-lasting valves; and
- elimination of infection and rejection problems.

At this time, it appears that the next generation of artificial hearts will have electrically powered motors, probably with the power delivered transcutaneously, to preclude the need for leads exiting from the body and providing more mobility for heart recipients (26,55). An early model of such a heart kept a calf alive for 222 days, until an electric component failed. Human trials are not expected until the 1990s (48,55).

Cardiac-Assist Technologies.—Many researchers are concentrating their efforts on options other than complete artificial heart implantation—although some of these technologies go hand in hand with artificial heart research—e.g., the left ventricular assist device (LVAD). Other technologies for cardiac assist include the biventricular bypass device, the intra-aortic balloon pump, and cardiopulmonary bypass surgery.

The left ventricle does about 80 percent of the heart’s work. The LVAD is a potentially implantable pump that assists, rather than replaces, the heart left ventricle. The natural left ventricle pumps the blood into the LVAD, which then pumps the blood back into the patient’s circulatory system. A major advantage of the LVAD is that the natural heart is left in place and may be able to sustain circulation if the LVAD should fail. As of mid-1985, four makers of electric LVADs had received funding from the National Heart, Lung, and Blood Institute to begin preclinical testing of their devices; makers also received stipulations about minimum reliability requirements. Researchers have estimated that experimental LVAD implants in humans could begin as early as 1987 or 1988 (55); experimental implants of LVADs in animals have succeeded for up to 7 months (48).

Power sources have been a major obstacle to the development of LVADs and artificial hearts. Early models used an external battery pack that was connected to an implanted pump by a wire piercing the skin. Current models use electric coils (one implanted below the skin and one worn on the surface of the skin) to transmit electrical current inductively. The third generation of devices is expected to use thermal engines that are powered by energy provided by high-temperature, encapsulated salts. Animal experiments are underway (16,48,55).

Other technical issues include the optimal material for implantable pumps, optimal location in the body for implantation of an artificial pump, the type of electrical system to use, and the means to regulate pulse rate.

Future of Mechanical Ventilation

Developments important for long-term mechanical ventilation include improved reliability, portability, ease of use, and comfort. Some research is geared toward simulating natural respiratory functions and, ultimately, toward developing a completely implantable artificial lung. The technologies likely to change the capabilities of acute ventilator therapy range from variations on standard types of mechanical ventilation (e.g., high-frequency ventilation) to hybrids of new and old methods (e.g., extracorporeal membrane oxygenation, with low-frequency, positive-pressure ventilation).

Mechanical ventilation involves considerable deviation from the normal dynamics of spontaneous breathing and may be accompanied by dangerous side effects and complications. These include potentially harmful cardiovascular effects, damage to the lungs,
uneven ventilation, disturbances of acid-base balance, constriction of cerebral blood vessels, and side effects to the kidneys or liver (48) (see ch. 6). To improve mechanical ventilation, these harmful effects must be minimized.

**High-Frequency Ventilation**

High-frequency ventilation (HFV) is a form of mechanical ventilator support that differs from conventional modes of ventilation in both relative tidal volume (i.e., volume of gas exhaled in one breath) and respiratory rate (29). Recently, HFV has gained support based on the concept that oscillatory flow can accelerate diffusion and is adequate for gas transport (23). Although there is no uniform definition, HFV is usually characterized by tidal volumes less than or equal to anatomic dead space and frequencies at least twice the resting respiratory rate (1). HFV may be useful for elderly patients because of their likelihood of decreased regional lung compliance. HFV renders lung compliance relatively unimportant (29). However, despite the theories as to why HFV should work, the technique has shown surprisingly little success so far (38).

There are basically three kinds of HFV systems: open, closed, and pleural surface systems (29). In an open HFV system, a port is open to the atmosphere at all times to allow the escape of exhaled gases. This system requires no pneumatic seal at the airway opening; however, gas pressures and flows in the airway may still be adjusted (29). The airway in a closed HFV system is isolated from the atmosphere during the inspiratory phase of the ventilator cycle, thus assuring that the total tidal volume generated by the ventilator enters the respiratory system (29).

Recently, a new type of closed ventilator has been developed. The system is completely sealed and thus has the advantage that oscillatory pressure cannot leak from it. A portable HFV system using a miniature motor has been developed at NU-TECH Industries, Inc., with the assistance of a grant from the National Institutes of Health. The unit will provide 5 to 10 liters per minute of extra ventilation to elderly patients with chronic obstructive pulmonary disease, for example, without increasing the work of breathing by the patient. An improved system with a portable configuration, high reliability, and simple control features would greatly enhance long-term home treatment (48).

Pleural surface I-WV systems employ oscillations at the chest wall rather than at the airway. This has the advantage of not requiring airway access but has the disadvantage that the transfer of oscillatory energy to the lung may be technically difficult. This technique may ultimately prove valuable in giving mechanical assistance to patients with incipient respiratory failure (48).

Experiments on laboratory animals showed that normal gas exchange can be maintained with this system for extended periods when the animals are anesthetized and paralyzed to prevent spontaneous breathing. A vest-like device for HFV by vibration of the chest wall is being tested on patients with respiratory failure (5).

**Extracorporeal Membrane Oxygenation**

Extracorporeal membrane oxygenation (ECMO) is a complex treatment for patients in acute respiratory failure. ECMO involves threading a tube into the heart to carry blood outside the body to an artificial lung machine, where the blood is oxygenated and then returned to the body. Oxygenation and removal of carbon dioxide are achieved using passive diffusion across a membrane similar to that used in hemodialysis. ECMO avoids the drawbacks of mechanical ventilation—high airway pressure and high oxygen concentration—while allowing the lungs to rest. In the early years of its development in the 1970s, available data suggested that ECMO increased the likelihood of survival for patients with certain types of acute lung injury (89). However, the use of ECMO in adults decreased rapidly as evidence began to suggest that although the technology can support respiratory gas exchange, it does not increase the probability of long-term survival in patients with severe acute respiratory failure (38, 89).

There are fundamental limitations to this therapy, particularly for elderly patients. The best candidates for ECMO are patients in reversible acute respiratory failure; it has little therapeutic value for patients with chronic progressively deteriorating respiratory insufficiency, which may be more typical among elderly patients (48). In addition, acute respiratory distress is often a manifestation of multiple organ failures (70); thus, the primary therapy may be more appropriately directed to other organs or organ systems. Finally, a major study found no improvement in survival rates with ECMO except in very special circumstances (79). However, experience with ECMO could ultimately lead to a portable artificial lung for long-term use (48).

**Ventilation Supplemented by Extracorporeal Technologies**

A relatively new approach for treating acute respiratory failure dissociates the two main respiratory functions, i.e., transport of oxygen and removal of carbon dioxide. Oxygenation is accomplished by low-frequency, positive-pressure ventilation (LFPPV), to cause diffusion through the diseased lungs and to preserve...
pulmonary mechanics and volumes. The carbon dioxide is extracted by use of an extracorporeal membrane through a low-flow bypass, thus preserving pulmonary blood flow. The goals of this technique (referred to as LFPPV-ECCO,R) are to keep the lungs statically inflated to allow optimal oxygenation of blood, avoid the local and systemic complications of continuous positive pressure ventilation, and enable lung healing (37).

Another possible treatment method would use high-frequency ventilation (HFV) along with a new (as yet undeveloped) extracorporeal membrane. Gas exchange would occur through the lungs with HFV but would be supplemented by a low-flow gas exchange system using a variation on a dialyzing membrane. Hemodialyzers have been found quite effective for the removal of up to 50 percent of the carbon dioxide, but available membranes have a functional life of under 30 hours. The following improvements in oxygenation membranes will be necessary if such a system is to become a reality:

- gas exchange capacity should last at least 1 week, and the membrane should be easily replaceable at the end of its functional life;
- the membrane should have a small surface area and be constructed of highly biocompatible material;
- a simple, small, atraumatic pump that can function for at least 1 month must be developed; and
- a simple and small priming volume system is needed.

Development of a system meeting these criteria would allow the reduction (or elimination) of anticoagulant administration and enhance the likelihood of home treatment (48).

peritoneal Oxygenation and Carbon Dioxide Removal

Another theory holds that peritoneal gas exchange of oxygen and carbon dioxide is possible through a method similar to peritoneal dialysis (see ch. 7). Although the oxygen transport capacity of the peritoneal membrane is small, it maybe possible to augment this by using a red blood cell substitute with a high oxygen-carrying capacity. The red blood cell substitute would be saturated with oxygen and pumped into the peritoneal cavity. Oxygen then would diffuse down a concentration gradient into the tissues and blood supply of the peritoneum (7). Also, the use of a red blood cell substitute for peritoneal oxygenation may facilitate the removal of carbon dioxide, since some such substitutes have a relatively high carbon dioxide affinity (75). This method could also help wean some patients from mechanical ventilation and free other patients from tracheal incubation.

Future of Renal Dialysis

Research to prevent and reverse renal failure holds potential to reduce chronic renal failure and deaths from acute renal failure, both of which are prevalent among elderly people.4

As discussed in chapter 7, dialysis is an empirical therapy, meaning that treatment is determined by observing results in the individual patient rather than based on an understanding of the basic physiological mechanisms. Improvements in dialysis (or the development of an implantable artificial kidney) require basic physiological research. Researchers will be severely limited in devising new technologies until they identify specific parameters of ideal renal clearance. For example, the ideal clearance of urea is not known. Whether urea clearance is even an appropriate marker for adequate removal of other toxic substances is a subject of debate. Some experts believe the “middle molecules” are the substances responsible for the symptoms of the uremic state and should be the focus of filtration efforts, although the identification and toxicology of these substances have not been established (77).

Improvements in conventional dialysis treatment will most likely be in these areas:

- devices and parts of the dialysis apparatus (e.g., dialyzers and catheters) to improve efficacy or reduce complications;
- supplemental or adjunct therapies (e.g., absorbents or anticoagulants), also to improve efficacy and reduce complications; and
- the use of designs and techniques to enhance patient independence and mobility (e.g., CAPD, home dialysis, and miniaturization of apparatus).

Related technologies, such as plasma exchange and hemoperfusion, hold promise for arresting the progression of renal disease as well as for treating other diseases. Plasma exchange has been cited for use in a range of conditions, but proof of its efficacy is still needed (48). For instance, the majority of references on plasma exchange treatment are case reports, without any systematic or convincing evidence such as data from controlled studies or clinical trials.

4Mortality from acute renal failure in patients over age 70 currently approaches 50 percent (28).

5While hemodialysis is effective in removing small molecules, substances of higher molecular weight will not pass easily through the dialysis membrane. These so-called “middle molecules” are thought to be uremic toxins and causes of dialysis complications.
A spectrum of technologies exists for the detoxification of blood, most of which are variations of hemodialysis. Approaches to blood detoxification fall into two categories: extracorporeal and intracorporeal. Extracorporeal approaches, including hemodialysis, hemofiltration, hemoperfusion, and other techniques, are characterized by the circulation of blood outside the patient’s body. The intracorporeal approaches, such as peritoneal dialysis, are characterized by action within the body; the blood does not leave the body, although wastes must be disposed outside the body.

**Hemodialysis**

New hemodialysis products are regularly introduced. Efforts have been directed toward developing supplemental and adjunct therapies used in dialysis, scaled down dialysis equipment for patient convenience, and, ultimately, a wearable artificial kidney.

Adsorbents.—Adsorbents are used to regenerate and permit the reuse of dialysate and hemofiltrate. This controversial practice would not be possible without absorbents. They are also an important supplemental therapy for dialysis and are especially important for the development of a compact artificial kidney system.

One example, the Redy adsorbent system, operates by enzymatic decomposition of urea by urease and adsorption of ammonium by zirconium phosphate. Creatinine, uric acid, and middle molecules are removed by activated charcoal (48). The Redy system can also be used for hemoperfusion, therapeutic hemapheresis, and as a dialysis monitor (14).

The oral administration of absorbents is also used as a supplemental therapy for dialysis patients. A new combination of oxystarch (dialdehyde starch) and activated charcoal administered orally has proven effective as a supplemental therapy to dialysis (48). The oxystarch combines with urea or ammonium and the activated charcoal can adsorb creatinine, uric acid, and certain other middle molecules. Oral absorbents must be coated to prevent damage to the patient’s intestinal mucosa and decreased efficiency due to competitive adsorption of substances in the bowel tract. Because the major problems accompanying dialysis in elderly patients are poor blood access and an unstable cardiovascular condition caused by the strain of extracorporeal circulation, oral administration of absorbents could be particularly beneficial because they could reduce or even eliminate the need for hemodialysis.

Membranes.—Semipermeable membranes are the surfaces across which the diffusion of dialysis occurs. One goal in the development of new membranes is improved biocompatibility. The majority of membranes developed since the early 1970s have been modified cellulosics or other synthetic materials. The older cellulosic membranes have been associated with complement activation, and may be responsible for the high incidence and prevalence of infection in hemodialysis patients. Newer membranes show improved biocompatibility, i.e., less reduction of blood cell counts (especially white blood cells), and lower complement activation. Also, dialysis with a new synthetic membrane can be performed without anticoagulants (61). Most recently, a membrane (polysulfone) with a high protein permeability has been found to lessen the complications of chronic dialysis (62). Despite the numerous studies in this field, exact parameters of overall biocompatibility in blood purification systems are not well established.

Anticoagulants.—The use of an anticoagulant, usually heparin, is necessary during dialysis to prevent blood clots. However, chronic dialysis patients who use heparin regularly may suffer adverse effects on complement activation (81), platelet function change (82), lipid metabolism (22), and bone metabolism (48). Recently, new anticoagulants have been used to replace heparin, and dialysis has even been attempted without any anticoagulant. Although these alternatives are still experimental and have disadvantages (e.g., chemical instability, vasodilatory side effects), new drugs may make it possible to minimize or eliminate the use of heparin.

Dialysate.—Repeated exposure of the blood to dialysate is a problem because of chronic toxicity and unproven biocompatibility. Strategies to reduce dialysate-associated side effects include using a new buffer, quality control of dialysate to eliminate trace elements, and the reduction of the volume of dialysate per administration. For instance, a bicarbonate buffer results in less hemodynamic instability and other metabolic changes (49). Since dialysis systems are incapable of preventing the toxicity caused by trace elements combining with serum proteins, other means must be devised, such as agents capable of combining with and removing trace elements like aluminum, magnesium, and zinc, to prevent chronic toxicity (25,44,46). Also, dimethyl nitrosamine, a known carcinogen, has been reported in dialysate water; this may play a role in the increased incidence of malignant tumors in the dialysis population (50). Finally, a reduction in the volume of dialysate used per treatment would result in less cumulative exposure and could minimize the complications of such use.

**Complement** is a constituent of normal (nonimmune) serum that is required in addition to a specific antibody to cause the immune destruction of red blood cells and of certain bacteria. Complement consists of at least 17 proteins, which form a membrane attack complex. Complement activation plays a role in the induction of inflammation, various aspects of immunological defense, and in the pathogenesis of various immunologically mediated diseases (68).
Portable or Wearable Dialysis Systems.—Several methods to make dialysis more compact, and thus improve mobility and facilitate travel, are under investigation. For instance, some portable dialysis systems have been developed. One is a wearable artificial kidney, the WAK-III, consisting of a pumping section and an 18-liter reservoir, that was developed by investigators at Junken Co. (Japan) and the University of Utah. The large reservoir is, however, a problem for portability. Investigators at the University of Tokyo have been working on a more compact version, made possible by incorporating an adsorbent system to recycle the dialysate. Combined with pump sections, battery, and reservoir, this system weighs approximately 20 pounds. Another, lighter (10 pound) variation on the same system has been developed at the University of Tokyo. This simplified system, which is still in the preclinical stages, includes urea adsorbent, charcoal, ion-exchanger, and pump sections (48).

Another wearable continuous dialysis system is being developed by Research Development Systems of Pasadena, CA. Although animal trials have not yet begun, most of the components for the system exist. The proposed system would use 120 inches of dialysate tubing, holding 90 milliliters of blood outside the body at any given time. The system would weigh about 5 pounds and would be held by a holster under one arm. By continuously dialyzing blood, the system should avoid the discomfort associated with the more rapid cleansing of blood that occurs in traditional hemodialysis (39).

Continuous Arteriovenous Hemofiltration

Continuous arteriovenous hemofiltration (CAVH) utilizes water permeable membranes to remove excess fluids in acute renal failure. A hemofilter with a small surface area, small volume, and minimum circuit length are required to prevent straining the heart. Hemofiltration may be performed using the patient’s own blood pressure without a blood pump. This allows for hemodynamically stable withdrawal of excess fluid without the use of elaborate extracorporeal circuits (66). (This method may also be used to provide nutritional support (58).) It may be especially appropriate for elderly patients, who are at added risk of developing multiorgan failure and often suffer nutritional, metabolic, acid-base, electrolyte, or hemodynamic abnormalities.

Continuous Ambulatory Peritoneal Dialysis

The most important complication associated with continuous ambulatory peritoneal dialysis (CAPD) is peritonitis (see ch. 7). Two relatively new products demonstrate the innovative approaches being investigated to control CAPD complications. DuPont’s Sterile Connection Device (SCD) automatically makes a sterile splice between an air-filled extension tube of the dialysate bag and the patient administration set—thus eliminating the need to aseptically spike into the port of the bag and reducing the risk of infection (9). Another device to control infection irradiates with ultraviolet light the critical connection between the solution container and transfer set immediately before spiking. It does not, however, eliminate the need for aseptic practice (85).

Anemia Treatments

Practically all chronic dialysis patients eventually suffer from red blood cell anemias, requiring frequent blood or red blood cell transfusions. The anemias stem from the kidneys’ inability to make erythropoietin, a hormone that controls the production of red blood cells by the bone marrow (21). Erythropoietin can now be mass-produced by genetic engineering. Patients receiving regular injections of the hormone need fewer blood transfusions and have more energy (6).

Future of Nutritional Support

Nutritional support is used to provide necessary nutrients and fluids to patients who are unable for a variety of reasons to take in, digest, or absorb adequate amounts of food or fluids (see ch. 8). Receiving nutritional support, however, can be an uncomfortable experience for patients. Research on technology for enteral nutrition focuses on new materials to make feeding tubes more pliable, durable, and compatible with the body’s own tissues and the composition of nutritional support formulas. Innovations for parenteral nutrition are devices designed to minimize patient discomfort and complications, especially the so-called “tunnel” infections associated with the use of catheters in long-term care.

Parenteral Nutrition

Even patients receiving meticulous care may develop complications associated with catheters, including thrombus formation, structural failure, and infection. Research efforts are focused on reducing complications associated with the catheters used for parenteral administration. For example, the standard polyethylene or silicone catheters in widespread use

\textsuperscript{7}Thrombus is essentially a blood clot, but is differentiated by the fact that a thrombus frequently causes vascular obstruction at the point of its formation, while a blood clot is more likely to be carried through the circulatory system.
for total parenteral nutrition (TPN) have been associated with a 33 percent incidence of thrombus formation (34,56). To alleviate such complications, researchers hope to identify better biocompatible materials for the catheters. Preliminary evidence from clinical investigation shows that the incidence of thrombophlebitis is lower with a polyurethane catheter than with a silicone catheter (56). Another trial of polyurethane catheters showed no evidence of venous thrombosis (up to 820 days) without the administration of any heparin (33). Another strategy maybe to coat catheters with antimicrobial agents (35).

Vascular Access Devices.—Other attempts to minimize complications associated with TPN have focused on developing implanted vascular access devices, which consist of a self-sealing silicone rubber septum encased in a port made of metal or plastic attached to a silicone catheter. Fluids, drugs, and blood can be administered into this port system by a simple needle puncture through the skin into the port. These systems could lessen the potential for infection and be more esthetically acceptable to patients. Also, the need for dressing changes is eliminated (48).

Infusion Pumps. -Computerized infusion pumps represent a dramatic improvement over gravity-flow procedures in the accuracy of infusion volume (see ch. 8), but could be improved. Some factors that may require additional attention include: range and accuracy, flow rate continuity, operation during transport, resistance to tampering and accidents, memory functions, alarm disable, battery life, electrical safety, electromagnetic interference, quiet operation, ease of use, and servicing (48).

Enteral Nutrition

Research on equipment for enteral feeding includes two main areas. Some work is focused on the actual tubes used to deliver formula. Using the smallest tube that will allow for passage of the formula maximizes patient comfort and tolerance. Other research focuses on the electronic enteral pumps now being used to maintain an accurate infusion rate and facilitate delivery of the viscous solution by applying continuous positive pressure.

Enteral formulas specific to the nutritional needs of elderly people are not available. Nutritional support specialists and industry representatives differ in their views about whether such formulas could or should be developed. The numerous commercially available premixed enteral formulas differ in osmolarity, digestibility, caloric density, lactose content, viscosity, residue, fat content, taste, and cost (48). Customization of enteral formulas according to individual needs would be ideal; however, the capability of many long-term care facilities to accurately assess an individual’s nutritional needs and provide the appropriate formula lags far behind this ideal, primarily because they lack trained personnel (see ch. 8).

Some research is looking at nutritional support as a way to treat diseases, not simply to correct malnutrition. For instance, evidence shows that dietary manipulation can substantially slow the loss of renal function at early and late stages of chronic renal disease (60). Adjustment of fat intake can reduce the retention of carbon dioxide, a problem for some ventilation patients. Rheumatoid arthritis, diabetes, chronic obesity, and heart disease may be ameliorated by nutritional therapy (45).

Extracorporeal Blood Treatment

Some extracorporeal blood treatment technologies may have applications for improving the nutritional status of very ill elderly patients by means of immunometabolic support. For instance, therapeutic hemapheresis, especially on-line plasma treatment with the return of essential nutrients, is an approach to preserving nutritional and immunological homeostasis. The treatment may be used to filter off the pathological macromolecules associated with certain diseases and then to add essential nutrients to the plasma being returned to the patient. Certain plasma treatment technologies result in the discarding of a portion of the plasma, which may result in further nutritional depletion in patients whose nutritional status may already be compromised; therefore, use of extracorporeal technologies must be considered carefully (48).

Future of Antibiotic Therapy

New strategies to cope with life-threatening infections span a variety of research areas, including new drugs and techniques for developing drugs, the metabolism of drugs in elderly patients, drug delivery systems, and manipulation of the immune system.

Antibiotic Development

More than three dozen new antibacterial will be approved by the FDA by 1991, according to one industry report (80). The development of new drugs takes advantage of new manufacturing opportunities, such as genetic engineering, computer-assisted design of pharmaceuticals, and, potentially, pharmaceutical manufacturing in space. Ongoing antibiotic development will quicken as the pharmaceutical industry masters new biotechnology techniques. New or next-generation antibiotics could significantly improve antibiotic therapy, but early information on the develop-
ment of new antibiotics is not easy to obtain because of the proprietary nature of most pharmaceutical research and development.

Antibiotics are developed by screening compounds from natural sources, often soil molds, and often chemically modifying these substances. Such modification can broaden or narrow the antibiotic's range of activity (80). The most significant contribution of new antibiotics may be in conquering bacteria that are resistant to the usual drug of choice (e.g., penicillin, tetracycline).

Two recently developed antibiotics can act against a wide spectrum of bacteria, including many infections that are resistant to other antibiotics. Primaxin, developed by Merck, is especially useful against multorganism infections and infections caused by bacteria that are resistant to other antibiotics (19). Aztreonam, recently approved by the FDA, acts against gram-negative bacteria, the cause of about half of all nosocomial infections. Because Aztreonam does not induce bacterial synthesis of a particular enzyme, bacteria should be slow in developing resistance to this drug (24).

Along with new drugs, better application of existing drugs can be expected in the coming years. Recent medical literature highlights the lack of complete information on the pharmacological effects of drugs in elderly people. Research to identify proper geriatric dosages and to eliminate, or at least reduce, adverse effects and toxicity is crucial to safe and effective treatment of infection in the elderly, particularly since compromised immune systems and polypharmacy are more likely in elderly patients (see ch. 9). Some progress may be made toward these problems with the development of computer programs to perform tasks such as checking new prescriptions for compatibility with other prescriptions or issuing prescription guidelines with age-adjusted dosages. One computer system under development, for example, constantly monitors indications for antibiotic therapy and reports its medical decisions to physicians, thus bringing potentially life-saving information to their attention (31).

Drug Delivery Systems

Traditional methods of introducing drugs into the body include oral, topical, nasal, intravenous, intramuscular, subcutaneous, and intrathecal (into the spinal column) administration. Certain drugs are only suitable for particular delivery methods. In recent years, considerable effort has been devoted to developing new technologies for drug delivery. Among the innovations that may be particularly important for elderly patients are sustained or timed-release drugs, targeted antibiotics (high local but low general levels), and monitoring systems that assure proper therapeutic levels of the drug in the bloodstream. More precise control over dose maintenance can reduce the toxicity and side effects associated with serial administration (very high immediately after introduction, decreasing over time). Sustained- or automatic-release drugs may also protect against forgotten medication and dosage mistakes. Directed delivery systems are especially important for treating localized infections and controlling the administration of toxic drugs.

The emphasis on alternate-site care will fuel demand for alternate drug delivery systems. Oral and other self-administered drugs and timed-release drugs often reduce the need for conventional nursing and physician services, thus lowering personnel costs and increasing opportunities for nonhospital care. Since drugs have differing characteristics and patients have differing medication needs, personal preferences, treatment sites, degrees of independence, and other needs, alternatives to traditional drug delivery systems will affect quality of care.

Some drug delivery systems under development will provide feedback, such as information on the location and level of drugs in the body, so that treatment may be modified as necessary. Other feedback systems automatically regulate the release of a drug by responding to environmental stimuli. Some delivery systems are described in table C-2. It is not yet clear which systems may come to play a useful role in the treatment of life-threatening infections in elderly people.

Intravenous Antibiotic Administration.—Intravenous (IV) administration of antibiotics allows either continuous or intermittent delivery of antibiotics directly into the bloodstream. Although electrically powered and electronically controlled infusion pumps have allowed better control over the rate of delivery, other improvements are needed to reduce the complications of intravenous administration. The most frequent complication of IV therapy is infection as a direct result of the surgical insertion of a catheter, because the opening through the skin provides easy access for bacteria. The most imminent improvements are modified vascular access devices designed to eliminate infection.

“Microscopic” Delivery Systems.-Other drug delivery systems operate on a microscopic level–i.e., drugs are delivered by grouping or repackaging drug molecules. One theoretical approach is to develop polymeric forms of individual drugs, which are more stable, less toxic, and capable of slow release of active units. However, research to synthesize useful polymeric drugs (including antibiotics) has been unsuccessful so far (48).

A more feasible approach to drug delivery on the molecular level is encapsulation, a process in which pharmaceuticals are packaged inside a biodegradable
<table>
<thead>
<tr>
<th>Type of system</th>
<th>Primary advantages</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantable intum pump</td>
<td>Sustained constant release</td>
<td>One model utilizes a Chemical pump—a fluorocarbon inside the device vaporizes and exerts pressure on a “tiny bellows” that drives the drug out</td>
<td>Single-use pumps; require surgical implantation and removal; unresponsive to changes in environment; not yet used for antibiotic delivery</td>
</tr>
<tr>
<td>Oral osmotic “pill” pump</td>
<td>Sustained release; passes naturally through body in about 24 hours</td>
<td>Consists of a drug-filled core, surrounded by a semipermeable polymer membrane which lets gastric juice in. As the fluid enters, the pressure inside the membrane builds, and the drug is pumped out evenly through a tiny laser-drilled hole in the membrane</td>
<td>Successfully tested in clinical trials; not yet used for antibiotic delivery, although tested on several other drugs</td>
</tr>
<tr>
<td>Implantable osmotic pump</td>
<td>Sustained, local release</td>
<td>Relies on membrane-controlled osmosis for drug delivery</td>
<td>Successfully tested in animals for antibiotic delivery; requires surgical implantation and removal; significant technical questions remain unanswered</td>
</tr>
<tr>
<td>Biodegradable implant</td>
<td>Sustained, local release</td>
<td>One type of implant utilizes a biocompatible plastic, called Polyhydroxybutyrate (PHB), which is created by bacteria</td>
<td>Some capable of drug release for over 60 days; does not require removal; obstacle often cost-effective production of implant materials</td>
</tr>
<tr>
<td>Ferrofluids</td>
<td>Directed delivery</td>
<td>Biocompatible magnetic shavings could be suspended in drugs, then the drugs could be injected and then directed to and retained at specific treatment sites by an externally applied magnetic field</td>
<td>Still in early research stages; originally developed by NASA; not yet applied to drug (or antibiotic) delivery</td>
</tr>
<tr>
<td>Self-regulated, chemically modulated systems</td>
<td>Automatic regulation of rate of release</td>
<td>Releases drugs in response to a particular environmental stimulus</td>
<td>Experimental systems have little therapeutic relevance so far; a practical application might be one which released penicillin in response to the bacteria in the bloodstream</td>
</tr>
</tbody>
</table>

**SOURCES:**
microcapsule, either for sustained-release or for local concentration of the drug. The process also protects unstable molecules from the immediate environment, protects body tissue from certain drugs, inhibits toxicity and anaphylaxis by avoiding large doses, and masks unpleasant tastes and odors. However, scaling up production methods for industrial volumes can present a variety of problems. Such difficulties can result from sensitive environmental requirements for production or prohibitively expensive reagents (64). Three of the materials being investigated for drug encapsulation are described in box C-3.

A critical factor in the treatment of infection in elderly people is the natural change in the immune system associated with aging. In addition, the immune response in ill elderly people may differ considerably from that of healthy elderly people. Therefore, optimal treatment would require a good understanding of both normal, age-associated changes and abnormal, disease-related changes, and the ability to compensate for them. Infusion of fresh leukocytes or lymphocytes has been attempted, as well as the use of sophisticated sorting technologies to separate and infuse only certain subsets of cells (e.g., T-cells or B-cells) (48). Immunoactivation refers to the intentional manipulation of processes of the immune system to stimulate a specific immune response, such as complement activation or interferon therapy. Immunoadsorption refers to extracorporeal plasma treatment with absorbents to remove abnormal immunocomplexes. Although these techniques are still experimental, investigators hope that their use will someday enhance the effectiveness of treatment for infection in immunocompromised patients.

Technologies To Diagnose Infection

Treatment decisions for infections in elderly people are often complicated by compromised immune function, the presence of comorbidities, and multiple infections. In all cases, good treatment depends on rapid and accurate diagnosis. New biotechnologies, such as monoclonal antibodies and DNA probes, present a major opportunity to improve diagnostic methods because of their ability to recognize infectious agents with a high degree of specificity. If biotechnology is successfully merged with sophisticated computer scanners, rapid diagnoses should be possible through the analysis of blood or other body fluids, thereby allowing earlier selection of therapy (30).

In certain infections, identifying the pathogenic organism is the easy part. More difficult is locating the site of the infection to determine the appropriate course of treatment. But physicians do not yet have the means of locating all infections. The example of single-dose antibiotic treatment for urinary tract infections described in box C-4 demonstrates the nature of the diagnostic problem and efforts toward its resolution.
Uns certain years ago, the diagnosis of urinary tract infections (UTIs) was based on the presence of symptoms such as fever, chills, and cloudy urine. However, current tests used to diagnose UTIs are incapable of differentiating between deep tissue and superficial mucosal infections because the test is only capable of identifying the organism. Further, the disposition of UTIs is very different in men and women. In women, UTIs are very common and the great majority of infections (about 80 percent) are superficial mucosal infections; only a small group are deep tissue infections (i.e., bacterial infection of the kidney). In contrast, the vast majority of UTIs in men are deep tissue infections (e.g., prostate) (73).

The significance of this diagnostic insufficiency is that the great majority of superficial mucosal infections respond to a single dose of antibiotics, but deep tissue infections require an extended course (4 to 6 weeks) of antibiotic treatment. Thus, “diagnosis” of deep tissue infections is really the use of an algorithmic approach that divides patients according to their response to a single-dose of antibiotics. The goal of current research is to devise an assay that can stratify patients into treatment groups (single-dose or extended course) at the time of their initial diagnosis. Such a test would prevent the expense and risk associated with long-term antibiotic treatment. One specific approach to the development of such a test involves examining bacterial virulence factors; it is believed that there are identifiable markers that are correlated with the likelihood of deep tissue infections (73).

Little research has been done specifically on elderly patients. UTSs are frequently asymptomatic in elderly patients. Some physicians contend that it is not necessary, and possibly even improper, to treat asymptomatic UTIs in elderly patients. It has been demonstrated that if asymptomatic UTIs are treated, and the infection fails to respond to the antibiotic, the patient in relapse may experience painful or uncomfortable symptoms, which previously were not exhibited. Thus, some question the wisdom of altering what seems to be a natural symbiosis (73).

**Box C-4—Single-Dose Antibiotics**

Urinary tract infections (UTIs) are easily identified by a positive urine culture. However, current tests used to diagnose UTIs are incapable of differentiating between deep tissue and superficial mucosal infections because the test is only capable of identifying the organism. Further, the disposition of UTIs is very different in men and women. In women, UTIs are very common and the great majority of infections (about 80 percent) are superficial mucosal infections; only a small group are deep tissue infections (i.e., bacterial infection of the kidney). In contrast, the vast majority of UTIs in men are deep tissue infections (e.g., prostate) (73).

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**Conclusion**

Current research and development holds promise for improving both the quality of medical care and the quality of life for many patients dependent on life-sustaining technologies. Future developments could make treatments more effective, more comfortable, more portable, cheaper, and less invasive. These changes will occur as existing technologies are improved and new technologies are created. For some patients, however, improvements in the technologies may only serve to extend the period of pain and suffering caused by their underlying disease. The technologies themselves will not resolve the difficult dilemmas created by the advances of modern medical science. Thus, improvements in prognostic tools and decision-making are also needed.

Prevention of life-threatening diseases maybe more effective at reducing the incidence of illness and premature death than incremental improvements in life-sustaining technologies. But prevention, even if broadly and successfully implemented, will not obviate life-sustaining technologies. If preventive measures for heart disease were widely implemented, for example, other life-threatening illnesses would become more common.

Widespread implementation of preventive strategies is always difficult. The strategies discussed for preventing heart disease, for instance, are inconsistent and confusing. Even more significant is the low level of motivation that many people have for preventive health behavior before they become ill. Strategies for secondary prevention, at the time of symptom onset, may thus be more feasible. As preventive strategies are developed, policymakers may need to make more explicit decisions about the relative commitment of resources to preventive programs.

The technologies described in this appendix are only examples of a wide range of R&D efforts that are underway. Many other technologies could have been included. Some potential technologies will never be clinically used, while others will soon become standard procedures. Each technology may eventually find different applications from those described here, and new developments will make possible technologies not yet imagined. Decisions made in the next few years by researchers, manufacturers, providers, patients, and policymakers will determine which technological developments become available in the next decade and how they are used.

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