

Cardiac Transplantation: Costs and Ethics

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DR. THOMPSON: The patient who will be the springboard for this conference is a 49-year-old man with a history of asthma, gout, coronary artery disease, and congestive heart failure. He was admitted to the University of Kentucky Albert B. Chandler Medical Center with heart block and in cardiogenic shock. A pacemaker was inserted and the intra-aortic balloon pump he had received before being transferred to the university medical center was replaced. About two months after admission, the patient underwent cardiac transplantation.

Before opening the discussion, I will provide a bit of background information. When cardiac transplantation was first performed in the mid-1960s, 22% of patients survived for one or more years. By 1980, one-year survival approached 70%; today at

some centers the one-year survival rate is 85% to 90%, and five-year survival is 70%. The overall one-year survival rate for all cardiac transplantation centers in the United States is about 80%, an achievement that is probably due to advances in immunotherapy.

Cardiac transplantation is now clinically approved by Medicare, Blue Cross/Blue Shield, and other health insurers. In the United States, 2,340 cardiac transplantations were performed in 1994—a total limited by the availability of donor hearts and by the cost of the procedure.

In short, cardiac transplantation has become a highly successful procedure that offers patients not only longer life but also improved quality of life. Moreover, continued research may result in lower costs and increased benefits.

Case Presentation

DR. SEKELA: The patient, who had had multiple previous hospital admissions, had a three-year history of congestive heart failure and known coronary artery disease. He was working some distance from his home as a truck driver when the latest heart attack occurred, and he was admitted to a local hospital. His condition was complicated by pump failure and by cardiogenic shock that required treatment with pressors and placement of an intra-aortic balloon pump. He subsequently had two more cardiac arrests, but he was successfully resuscitated and his condition was stabilized. Ten days after admission, he was transferred to the university medical center to undergo evalua-

tion as a candidate for a heart transplant.

On arrival, he was being treated with intravenous dobutamine and dopamine. His condition was stabilized in the intensive care unit (ICU) and he was weaned from some of the intravenous drips. On the third hospital day, he had an episode of asystole and cardiogenic shock that required

failure every year. In addition, there are three to four million people who at one time or another have had a diagnosis of heart failure. In 1990-1991, heart failure was the most common hospital admission diagnosis for persons over 60 years of age.

One reason for the increasing incidence and prevalence of heart failure is that our population is

The number of heart transplant candidates continues to increase, for two reasons: The population is aging, and new drugs for treating acute myocardial infarction are allowing many patients to survive with left ventricular dysfunction.

placement of a temporary pacemaker and replacement of the intra-aortic balloon pump.

The balloon pump was left in place and inotropic therapy was continued for about two weeks, until the patient's condition again appeared to have stabilized. But removal of the balloon pump resulted in cardiogenic shock and a thrombosed femoral artery. The balloon pump was replaced in the contralateral femoral artery and an emergency thrombectomy was performed. With the balloon pump in place, his condition remained stable, and four weeks later he underwent orthotopic cardiac transplantation. Postoperative bleeding occurred but resolved after a tear in the atrial suture line was repaired. The patient then recovered rapidly and was discharged from the hospital three weeks later, having spent 74 days in the hospital.

DR. BERK: For patients with heart failure, cardiac transplantation clearly is very effective therapy, with impressive and improving survival rates. More significant, however, is that only a small percentage of patients with heart failure and left ventricular dysfunction receive transplants. In the United States, there are 400,000 to 500,000 new cases of heart

aging. A second reason is that in the past 10 years, new drug therapies have been made available for the treatment of patients with acute myocardial infarction. Many of these patients who in the past would have died are now surviving—but they are surviving with left ventricular dysfunction, which eventually may present as heart failure. Studies indicate that these new medications (e.g., angiotensin-converting enzyme inhibitors) may prolong the lives of a wide range of patients—not only those with mild to moderate symptoms but also those who are very, very ill.

The patient discussed here clearly benefited from cardiac transplantation. He was being treated with an intra-aortic balloon pump and inotropic agents and would not have survived without a new heart. Selecting transplant recipients from among mildly symptomatic candidates is more difficult. Such patients are able to accomplish most of their daily tasks without fatigue or shortness of breath. Nevertheless, despite their mild symptoms, 40% of these patients die suddenly. It is impossible to judge from the severity of their symptoms or from their cardiac function which of them are at risk for sudden death.

Psychosocial Aspects

DR. GALLAGHER: I had three sources of information about this patient: the case records, the cardiac transplantation social worker, and the patient himself.

A patient's personal history and current lifestyle are relevant to his or her future prospects. This patient was single (having gotten a divorce 12 years earlier) and had three children from his only marriage. Following his divorce, he had been rather distant from his children. Now, however, after his illness, some closeness had developed and he was temporarily living in the household of a married son in western Kentucky.

Prior to the latest admission, the patient had worked as a long-distance driver for a trucking company. His usual work pattern was to carry materials between Georgia and two northeastern cities. He was on such an expedition when he had the heart attack in West Virginia.

During my interview with him, the patient said he was lucky that the problem occurred when and where it did. Several years ago, when he had begun having disabling periods of labored breathing and chest pain, he had had no health insurance—today he at least has a Social Security disability pension. He also said that he believed he would have died if his heart episode had occurred elsewhere—he has a high regard for medical resources in West Virginia and Kentucky.

The patient struck me as a free spirit, no great respecter of regulations and formalities. He seemed to be an easy-come, easy-go sort of person, neither out to please people nor dependent on them. He was able to converse easily and spontaneously during the interview and was on friendly terms with other cardiac patients who visited the clinic. He wryly observed that the same doctors who had arranged for his acquisition of a new heart were now taking it back piece by piece, in the form of monthly biopsy specimens.

The social worker told me that the patient had an erratic job history; his episodes of unemployment had been more frequent than is typical for

long-distance truck drivers, many of whom lead a nomadic, gypsy life. Every now and then, bored with driving, he would leave his job and move to Florida, where he would stay with friends and earn his living doing carpentry and house painting. The resulting lack of long-term steady employment with the trucking company explains his lack of health insurance and lack of savings for medical expenses.

Another indication of his free spirit is that despite earlier heart problems and, presumably, physicians' warnings, he continued to smoke. His medical records at the university medical center reported (curiously enough, under the heading "social history") that he was free of the habit. I decided to check on his current smoking status during the interview; he reported smoking "something like" a half-pack a day. His hedging on that point made me think that he probably smokes a pack a day or more.

Despite good recovery thus far, the patient can never return to truck driving (though he quickly resumed driving his own car). His monthly income

This case illustrates that it's easier to get inpatient dollars than outpatient dollars.

from truck driving fluctuated considerably but apparently averaged about \$1,200 a month. His base disability pension after surgery was \$407 a month; thus his income was drastically reduced. The patient felt, however, that he could manage. He said that he was on comfortable terms with his son and family and that he planned to buy a small house within close visiting range of the family.

The patient came to our center as a medical indigent with no financial resources or insurance coverage. Many patients like him are never able to re-

turn to gainful employment; how can they be expected to one day "repay society" for the value of the medical resources invested in them? Also, isn't it true that any one of us can be rendered indigent if we require enough medical intervention of sufficient technological complexity? That many patients will never be able to repay society for their care is a given.

DR. THOMPSON: It is interesting to note that vocational rehabilitation is often more successful for patients who have received a heart transplant than

Many programs do refuse high-risk patients . . . [but] . . . many patients who have the greatest potential to benefit from transplantation are those at highest risk.

for kidney recipients. Kidney patients often need to spend long periods on dialysis prior to transplantation. After this period of relative inactivity they are less able to resume a normally active life.

Financial Aspects

DR. BLOMQUIST: Costs culled from 100 pages of documents give an idea of the extraordinary nature of this case. There were hospital charges for 50 days in the coronary care unit, seven days in the surgical ICU, and 17 days in a medical/surgical semiprivate room. Then there were ancillary and one-time charges for blood gas analyses, dobutamine injections, temporary pacemaker, intra-aortic balloon catheter, operating room set-up and time, transfusion administration, open heart pack,

and other services. With physician fees added in, the total cost of this heart transplant was thus about \$200,000—considerably more than the current average cost of a heart transplant at this hospital (\$110,000).

Finally, the *sine qua non* of costs: The cost of acquiring a usable heart is \$15,600. Does this amount reflect the organ's value to the recipient? Or the value to society of the recipient's additional years as a productive citizen? Or the potential value of research experience gained with each procedure?

Dr. Thompson has cited the problem of the limited availability of organs for transplantation. This is a major factor in cost-benefit assessment and is a fertile area for economic as well as medical research. Related problems have been studied by researchers such as Nobel laureate Ronald H. Coase (see sidebar, page 133), an economist who asks such fundamental questions as, How do individuals organize to advance their economic interests? When should government intervene to coordinate the process?

Coasian analysis of "transaction cost" is relevant to the question of balancing society's demand or need for transplantable organs against the needs or wishes of the families of prospective donors. What Coase, perhaps, would suggest is that any public policy that reduced the transaction costs involved in the matching of potential recipients and donors would benefit both society and patients.

DR. GALLAGHER: Since any heart transplant case serves well for general discussion of social policy for the allocation of expensive medical resources, may I add some information at this point to make our discussion more inclusive? Postdischarge services and expenses were not included in Dr. Blomquist's inventory. It was a difficult feat of discharge planning and patient advocacy for the cardiac social worker to obtain housing outside the hospital for the patient during this period. Kentucky Medical Assistance (the state's version of Medicaid) covers postdischarge housing only

ECONOMICS AND THE SUPPLY OF ORGANS

At age 21, Ronald H. Coase already had developed the ideas which led 60 years later to his Nobel Prize in Economic Sciences in 1991. Coase's contribution to economic theory was to draw attention to "the importance for the working of the economic system of what may be termed the institutional structure of production." Two centuries earlier Adam Smith had explained the wealth of nations as arising from an "invisible hand" that guided individual decisions so as to increase the well-being of society. This invisible hand was said to act through the competitive pricing of commodities and services in an open market.

In his Nobel Prize acceptance speech, Coase said that he experienced a conceptual breakthrough when he realized that "What the prices are have to be discovered. There are negotiations to be undertaken, contracts have to be drawn up, inspections have to be made, arrangements have to be made to settle disputes, and so on. These costs have come to be known as transaction costs." Coase's discovery increased awareness of the role of the costs that are involved in making individual transactions, and it focused attention on constructing, through law and policy, commercial environments that make good (i.e., socially desirable) transactions easier and thus more efficient.

Can these insights be applied to the field of organ transplantation? The existing altruistic system for making donor-recipient matches seems inefficient. Coase's insight suggests that what may be needed is the creation, by means of public policy, of special institutions to facilitate matches between potential heart donors and recipients. Institutional frameworks would be designed to make mutually beneficial transactions as easy as possible.

Institutions of this kind could facilitate the compensation of potential donors. This could be done, say, by offering to give the committed donor priority if he or she needs blood or organs in the future or by offering to share funeral expenses when the donor dies. Such approaches would supplement the altruistic motives that now generate the supply of organs for transplantation. The growing acceptance of living wills—thoughtfully made in advance of the anxious moment of donation—indicates that such prearranged agreements may be socially acceptable.

We currently see in Eastern Europe the difficulties encountered when countries advised to rely more on markets and less on bureaucratic planning do not possess the Coasian institutions that would make markets work. The rapid development of modern medical innovations creates a similar situation and similarly requires that appropriate institutional infrastructures be created if the social system is to function efficiently. With current chronic shortages of hearts for transplantation, can a dose of Coase's economics mitigate the symptoms of the problem, or even provide a cure?

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reluctantly. By closely comparing what the federal Medicaid law requires of states with what Kentucky actually provides, the social worker was able to wrest from the state agency sufficient coverage for this patient's maintenance. Thus for a month after discharge, the patient was able to live within easy commuting distance of the hospital. He had to return there for frequent postoperative checkups and to learn to manage a medication regimen that included treatment for preexisting gout and asthma as well as immunosuppressive therapy. Although I do not have the precise figures, it appears that lodging, meals, and transportation for that month were obtained for an estimated \$1,500.

Returning to policy analysis: We like to consider abstractly the marginal utility of dollars spent on alternative treatments when the utility can be measured in various ways: by years of life saved, by whether the patient is free of disability or free of symptoms, or by quality-of-life indices. But another principle that we must incorporate into our analysis is that some dollars are scarcer than others. This case—and it is far from unique in this respect—illustrates that it's easier to get inpatient dollars than outpatient dollars, no matter what the range of utilities or benefits associated with each category.

It would be interesting to compare the decision making that went into the setting up and use of the operating room, at a cost of \$5,000, with the social work maneuvers that went into obtaining money to pay for a month of postdischarge maintenance at a cost of roughly \$1,500. The \$1,500 is a much smaller amount than the \$5,000, yet was much harder to obtain.

It might be argued that the transplant procedure was lifesaving and was thus easier to justify economically, and easier to finance, than postoperative housing and rehabilitation training. But do we really want to press that argument? Of course the surgery was critical, but without many other less immediately critical services, the whole transplantation undertaking would founder.

It is curious and unsound, from a medical and

social standpoint, for inpatient dollars to be more easily available than outpatient dollars. It also shows that our earnest cost-benefit analysis is, rather than simple in a conceptual sense, simplistic in an addled sense. I refer to it as simplistic because it takes into account only what the dollars buy (surgery versus housing) and not the professional effort or costs of acquiring the necessary dollars. Sociomedical policy would be much better served if third-party payers, whether governmental or private, could support *all* the components of necessary care in cardiac transplantation—low-cost residential accommodation during postoperative observation as well as direct medical-surgical care.

Discussion

COMMENT FROM AUDIENCE: Perhaps heart transplantation should be considered not in isolation, but in relation to other health care services. If this discussion were taking place in the federal Office of Management and Budget or in the Oregon State Legislature, Dr. Berk's observation regarding candidates for transplantation probably would not get a hearing. Eligibility for the Oregon indigent care program is based on maximum benefit per dollar spent. The number of heart transplants is limited not only by the number of available donor hearts but also by budgetary constraints.

Society needs objective criteria for securing the highest return on investment. Will the number of transplants allotted be governed by the average cost per diagnosis—in other words, the cost per 1,000 cases of coronary artery disease actuarially spread across a population? Allocation and rationing are issues not usually included in discussions of clinical economics. We need to consider them carefully because they will become a reality in the next few years.

DR. SEKELA: The political factors involved in organ transplantation have always been apparent. For example, the United Network for Organ Sharing

(UNOS) and the Health Care Financing Agency have tried to define solid criteria for recipients by mandating survival rates. Heart transplant programs are at risk if they fail to meet the UNOS standard of a one-year survival rate of at least 73%. Under these circumstances, physicians' attitudes can change from "I can get this patient through" to "This is a high-risk case, so I won't operate." I don't do that—I transplant and hope for the best. But many programs do refuse high-risk patients, which is an ethics issue beyond my realm of competence.

QUESTION FROM AUDIENCE: Isn't that ethics issue fundamental to the clinical selection process for you and Dr. Berk?

DR. SEKELA: Dr. Berk and I are doctors and we're taking care of our patients. What else can we do?

DR. BERK: I agree with Dr. Sekela. A major problem is that many of the patients who have the greatest potential to benefit from transplantation—the sickest patients—are those at highest risk. At the same time, patients who would have the best post-transplantation prognosis are, perhaps, patients to whom resources should not be allocated because they may do well without transplantation. However, whether you're talking about survival after heart transplantation or after open heart surgery, if your results are not good, your program is in jeopardy.

DR. BLOMQUIST: I'm reminded of Dr. Gallagher's comment that at certain level of medical technological intervention, the expense can be great enough to make anyone indigent. It is clear that costs reported for this case cover much more than the transplant. Should decisions be based on prognosis 1) with transplantation, 2) without transplantation, and 3) with alternative therapies? The result would be an analysis of various scenarios, reflecting differences in probabilities of survival. The \$200,000 cost of the transplant may be comparable to the cost of other high-technology alternatives

but large relative to the cost of less aggressive alternatives. As for the benefits derived from the \$200,000 investment in transplantation and care, prolonged life of probably very good quality is, of course, not the only possible outcome—there are gradations of quality of life, and some patients die. Thus the value of the benefits varies greatly.

DR. THOMPSON: It is easy to say that we need to budget our resources—that is, allocate treatment on the basis of universally applicable economic factors—and then allow only, say, 20 transplants a year. This happened in the early days of kidney transplantation. Initially, patients who had diabetes did not receive renal transplants because resources were being conserved. When a person had diabetic end-stage renal disease, we thoughtfully nodded, took the matter under consideration, and tried to find a way to tell the patient that he or she didn't have the right disease. For those of us who take care of patients and become involved with them, the "allocation of resources" becomes an almost impossible issue.

To expand the point beyond transplantation, suppose a patient with hepatic failure is treated in the ICU at an average cost of \$150,000 to gain one year of life. Contrast this with a 25-year-old patient who has attempted suicide, is treated in the ICU, and survives at a cost of less than \$1,000 for every year of life gained. Does it follow that we refuse to treat the patient with hepatic failure? The cheapest course is to let the patient die. But we have other goals.

COMMENT FROM AUDIENCE: Objective criteria could take the decision out of the hands of the physician.

DR. THOMPSON: Delegating hard decisions to "objective criteria" may be a way out, but I can't avoid looking at the other side. I'm not sure I want such decisions taken out of the hands of the individual physician. There are no easy answers here.

DR. BLOMQUIST: No one wants to make decisions on who lives and who doesn't. That's a fact of life.

AEROBID®/AEROBID®-M (flunisolide)

Inhaler system for oral inhalation only
Brief summary of prescribing information

CONTRAINDICATIONS

AEROBID Inhaler is contraindicated in the primary treatment of status asthmaticus or other acute episodes of asthma where intensive measures are required.
Hypersensitivity to any of the ingredients of this preparation contraindicates its use.

WARNINGS

Particular care is needed in patients who are transferred from systemically active corticosteroids to AEROBID Inhaler because deaths due to adrenal insufficiency have occurred in asthmatic patients during and after transfer from systemic corticosteroids to aerosol corticosteroids. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) function. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery or infections, particularly gastroenteritis. Although AEROBID Inhaler may provide control of asthmatic symptoms during these episodes, it does NOT provide the systemic steroid that is necessary for coping with these emergencies.

During periods of stress or a severe asthmatic attack, patients who have been withdrawn from systemic corticosteroids should be instructed to resume systemic steroids (in large doses) immediately and to contact their physician for further instruction. These patients should also be instructed to carry a warning card indicating that they may need supplementary systemic steroids during periods of stress or a severe asthma attack. To assess the risk of adrenal insufficiency in emergency situations, routine tests of adrenal cortical function, including measurement of early morning resting cortisol levels, should be performed periodically in all patients. An early morning resting cortisol level may be accepted as normal if it falls at or near the normal mean level.

Localized infections with *Candida albicans* or *Aspergillus niger* have occurred in the mouth and pharynx and occasionally in the larynx. Positive cultures for oral *Candida* may be present in up to 34% of patients. Although the frequency of clinically apparent infection is considerably lower, these infections may require treatment with appropriate antifungal therapy or discontinuance of treatment with AEROBID (flunisolide) Inhaler.

AEROBID Inhaler is not to be regarded as a bronchodilator and is not indicated for rapid relief of bronchospasm.

Patients should be instructed to contact their physician immediately when episodes of asthma that are not responsive to bronchodilators occur during the course of treatment. During such episodes, patients may require therapy with systemic corticosteroids.

There is no evidence that control of asthma can be achieved by administration of the drug in amounts greater than the recommended doses, which appear to be the therapeutic equivalent of approximately 10 mg/day of oral prednisone. Theoretically, the use of inhaled corticosteroids with alternate day prednisone systemic treatment should be accompanied by more HPA suppression than a therapeutically equivalent regimen of either alone.

Transfer of patients from systemic steroid therapy to AEROBID Inhaler may unmask allergic conditions previously suppressed by the systemic steroid therapy, e.g., rhinitis, conjunctivitis, and eczema.

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG), may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chicken pox develops, treatment with antiviral agents may be considered.

PRECAUTIONS

General: Because of the relatively high molar dose of flunisolide per activation in this preparation, and because of the evidence suggesting higher levels of systemic absorption with flunisolide than with other comparable inhaled corticosteroids (see CLINICAL PHARMACOLOGY section), patients treated with AEROBID (flunisolide) should be observed carefully for any evidence of systemic corticosteroid effect, including suppression of bone growth in children. Particular care should be taken in observing patients post-operatively or during periods of stress for evidence of a decrease in adrenal function. During withdrawal from oral steroids, some patients may experience symptoms of systemically active steroid withdrawal, e.g., joint and/or muscular pain, lassitude and depression, despite maintenance or even improvement of respiratory function (see DOSAGE AND ADMINISTRATION for details).

In responsive patients, flunisolide may permit control of asthmatic symptoms without suppression of HPA function. Since flunisolide is absorbed into the circulation and can be systemically active, the beneficial effects of AEROBID Inhaler in minimizing or preventing HPA dysfunction may be expected only when recommended dosages are not exceeded.

The long-term effects of the drug in human subjects are still unknown. In particular, the local effects of the agent on developmental or immunologic processes in the mouth, pharynx, trachea, and lung are unknown. There is also no information about the possible long-term systemic effects of the agent.

The potential effects of the drug on acute, recurrent, or chronic pulmonary infections, including active or quiescent tuberculosis, are not known. Similarly, the potential effects of long-term administration of the drug on lung or other tissues are unknown.

Pulmonary infiltrates with eosinophilia may occur in patients on AEROBID (flunisolide) Inhaler therapy. Although it is possible that in some patients this state may become manifest because of systemic steroid withdrawal when inhalational steroids are administered, a causative role for the drug and/or its vehicle cannot be ruled out.

Carcinogenesis: Long-term studies were conducted in mice and rats using oral administration to evaluate the carcinogenic potential of the drug. There was an increase in the incidence of pulmonary adenomas in mice, but not in rats.

Female rats receiving the highest oral dose had an increased incidence of mammary adenocarcinoma compared to control rats. An increased incidence of this tumor type has been reported for other corticosteroids.

Impairment of Fertility: Female rats receiving high doses of flunisolide (200 mcg/kg/day) showed some evidence of impaired fertility. Reproductive performance in the low (6 mcg/kg/day) and mid-dose (40 mcg/kg/day) groups was comparable to controls.

Pregnancy: Pregnancy Category C. As with other corticosteroids, flunisolide has been shown to be teratogenic in rabbits and rats at doses of 40 and 200 mcg/kg/day respectively. It was also fetotoxic in these animal reproductive studies. There are no adequate and well-controlled studies in pregnant women. Flunisolide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because other corticosteroids are excreted in human milk, caution should be exercised when flunisolide is administered to nursing women.

ADVERSE REACTIONS

Adverse events reported in controlled clinical trials and long-term open studies in 514 patients treated with AEROBID (flunisolide) are described below. Of those patients, 463 were treated for 3 months or longer, 407 for 6 months or longer, 287 for 1 year or longer, and 122 for 2 years or longer.

Musculoskeletal reactions were reported in 35% of steroid-dependent patients in whom the dose of oral steroid was being tapered. This is a well-known effect of steroid withdrawal.

Incidence 10% or greater

Gastrointestinal: diarrhea (10%), nausea and/or vomiting (25%), upset stomach (10%); **General:** flu (10%); **Mouth and Throat:** sore throat (20%); **Nervous System:** headache (25%); **Respiratory:** cold symptoms (15%), nasal congestion (15%), upper respiratory infection (25%); **Special Senses:** unpleasant taste (10%).

Incidence 3-9%

Cardiovascular: palpitations; **Gastrointestinal:** abdominal pain, heartburn; **General:** chest pain, decreased appetite, edema, fever; **Mouth and Throat:** candida infection; **Nervous System:** dizziness, irritability, nervousness, shakiness; **Reproductive:** menstrual disturbances; **Respiratory:** chest congestion, cough, hoarseness, rhinitis, runny nose, sinus congestion, sinus drainage, sinus infection, sinusitis, sneezing, sputum, wheezing; **Skin:** eczema, itching (pruritus), rash; **Special Senses:** ear infection, loss of smell or taste.

Incidence 1-3%

General: chills, increased appetite and weight gain, malaise, peripheral edema, sweating, weakness; **Cardiovascular:** hypertension, tachycardia; **Gastrointestinal:** constipation, dyspepsia, gas; **Hemic/Lymph:** capillary fragility, enlarged lymph nodes; **Mouth and Throat:** dry throat, glossitis, mouth irritation, pharyngitis, phlegm, throat irritation; **Nervous System:** anxiety, depression, faintness, fatigue, hyperactivity, hypoactivity, insomnia, moodiness, numbness, vertigo; **Respiratory:** bronchitis, chest tightness, dyspnea, epistaxis, head stiffness, laryngitis, nasal irritation, pleurisy, pneumonia, sinus discomfort; **Skin:** acne, hives, or urticaria; **Special Senses:** blurred vision, earache, eye discomfort, eye infection.

Incidence less than 1%, judged by investigators as possibly or probably drug-related: abdominal fullness, shortness of breath.

*The incidences as shown of cough, wheezing, and chest tightness were judged by investigators to be possibly or probably drug-related. In placebo-controlled trials, the overall incidences of these adverse events (regardless of investigators' judgment of drug relationship) were similar for drug and placebo-treated groups. They may be related to the vehicle or delivery system.

Caution: Federal Law prohibits dispensing without prescription.

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CARDIAC TRANSPLANTATION

DR. BERK: One alternative to transplantation for our patient would have been to keep him in the ICU for an even longer period, at a cost of \$2,000 to \$3,000 a day. On the other hand, if heart transplantation had not been available here, we would not have accepted this patient in transfer and he would probably have died in a primary or secondary care facility. Once we commit to high-tech medicine—and that is one of the ways I practice—we have to go all the way. Had cardiac transplantation not been possible, I'm not sure it would have been ethical to put him on an intra-aortic balloon pump. Without the transplant, he would have died slowly from kidney failure, pneumonia, thrombosed femoral arteries, and arrhythmias. He would have died at a tremendous cost to himself and to society. And he would have taken up a bed that would otherwise have been available for more viable patients.

In this era of high-tech medicine, we must offer something that is at least partially curative, such as cardiac transplantation, because practicing high-tech supportive intervention that is not curative often simply increases the cost and lengthens the suffering of patients and their families.

DR. SEKELA: It's a new and fascinating experience to hear your comments on cardiac transplantation. Since I run the program, I know its costs. However, I see each patient as an individual and I am committed to each individual. From this point of view, costs are irrelevant. □

Selected Reading

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For:

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