

whom transplantation of a single lung is contraindicated because the remaining contralateral lung would infect the newly transplanted lung. Transplantation of the heart and both lungs is effective therapy for patients with Eisenmenger's syndrome with complicated congenital heart defects which cannot be repaired (eg, truncus arteriosus, complete arteriovenous canal, transposition of the great arteries). Considerable experimental work suggests that living-related donor lung transplants will be offered soon for selected children with respiratory failure; this would involve removing the lower lobe from a parent and transplanting it into the chest of the child.

## RESULTS

These very debilitated patients often show dramatic improvement within 24 to 48 hours after transplantation. Patients are generally extubated 48 hours after the transplant and are completely off oxygen by the end of the first week. Most patients are hospitalized for 2 to 3 weeks following transplant.

Lung rejection and infection are most likely within the first 3 months. The differentiation of rejection from infection usually requires transbronchial lung biopsy with bronchial washings. The clinical diagnosis is substantiated by chest radiograph findings (pulmonary infiltrates and pleural effusion with rejection) and pulmonary function changes (hypoxemia, decreased FEV<sub>1</sub>).

At selected centers with the most experience, 1-year survival averages 75% for heart-lung, single-, and double-lung transplantation. Rehabilitation, in general, is excellent. Long-term complications, such as obliterative bronchiolitis, appear to be decreasing in frequency and severity with the use of triple drug immunosuppression (cyclosporine A, prednisone, and azathioprine).

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## GALLSTONE THERAPY: RETURN TO THE GOLD STANDARD

Despite the growing number of nonsurgical therapies for symptomatic gallstones, cholecystectomy remains the standard, accepted treatment. Enthusiasm has waned for some nonsurgical alternatives—particularly biliary lithotripsy. Clinical experience with others, such as bile acid therapy and contact dissolution, has shown them to be effective only for selected patients. The newest alternative, laparoscopic cholecystectomy, may prove to be a viable option, but the results to date are still preliminary.

## LIMITATIONS OF NONSURGICAL THERAPIES

### Bile acid therapy

The bile acids chenodiol (Chenix) and ursodiol (Actigall) work primarily by lowering the cholesterol:bile acid ratio in gallbladder bile, with gradual gallstone dissolution. These agents appear to have other, complementary mechanisms of action, including lowering hepatic cholesterol secretion.

Chenodiol never gained widespread acceptance, partly because of reports of limited efficacy and partly because of a significant incidence of unacceptable side effects, including diarrhea and hepatotoxicity. Ursodiol, which has been used in conjunction with biliary lithotripsy, is much less frequently associated with clinically significant side effects.

The gallstone dissolution rate with bile acid therapy is, on average, 1 mm per month. A patient with a single, 1-cm gallstone can expect to be on bile acid therapy for approximately 10 months. Compliance may be a problem. This duration may be acceptable if symptoms are minimal or colics are infrequent, but symptoms and complications may occur during therapy. Patients with frequent colic or a history of gallstone complications are not good candidates for dissolution therapy.

### Lithotripsy

The recent enthusiasm for biliary lithotripsy has diminished. Lithotripsy was envisioned as a noninvasive method of effective, ambulatory treatment of gallstones, with inherent cost savings. However, this technology is appropriate only for a limited subgroup of cholelithiasis patients. Furthermore, when the costs of the lithotripter, adjuvant bile acid therapy, and possible re-treatment of recurrent gallstones are factored in, there appears to be limited potential for cost savings when compared to standard cholecystectomy.

Currently available data suggest that patients with solitary gallstones are the best candidates for lithotripsy. The procedure can lead to rapid gallstone fragmentation but, in the Cleveland Clinic experience, gallstone fragments rarely clear from the gallbladder completely and spontaneously soon after fragmentation. In most cases, adjuvant fragment dissolution with bile acids is required. This is why biliary lithotripsy results are reported in terms of 6 or 12 months of gallbladder clearance. The gallstone fragments themselves can cause biliary colic or, rarely, lead to complications such as pancreatitis.

### Invasive nonsurgical treatment

Invasive nonsurgical therapies for gallstone disease have also emerged. These include the use of dissolution agents such as methyl tert-butyl ether (MTBE) and fragmentation of gallstones through direct contact with mechanical lithotripters or lasers. When it is successful, invasive contact dissolution therapy has the advantage of rapid elimination of gallstones from the gallbladder. If laparoscopic cholecystectomy proves to be effective and safe, with brief hospitalizations and limited time away from work, these other invasive therapies will likely apply only to patients at increased operative risk.

### Narrow indications

Only cholesterol gallstones can be treated effectively with bile acid therapy, lithotripsy, or contact solvents such as MTBE. It can be difficult to determine whether a gallstone is cholesterol in composition. Radiolucency on plain film or oral cholecystography is the most commonly used criterion. But many such radiolucent stones are not exclusively cholesterol in composition, which lowers the therapeutic success rate considerably. For contact dissolution with MTBE, a computed tomographic (CT) scan is used to further characterize gallstone composition and to guide catheter placement. The cost of CT scanning added to that of oral dissolution therapy or lithotripsy would further decrease the appeal of these procedures.

### Recurrence

A 7% to 10% per year recurrence rate of gallstones for the first 5 years after successful nonsurgical therapy can

be expected. This is not surprising, since the factors originally responsible for gallstone formation remain. Not all of these stones will become symptomatic or require re-treatment, however.

In our experience, the risk of recurrence does not deter patients from nonsurgical therapy. Nevertheless, recurrence is a significant problem to the patient because of the possible morbidity of recurrent symptomatic stones or re-treatment, and to the health care system because of the added cost of treating recurring stones.

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### CHOLECYSTECTOMY: COST-EFFECTIVE AND SAFE

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In many respects, cholecystectomy remains preferable to the newer, noninvasive, nonsurgical options. The operation removes the gallstones as well as the organ where gallstones form, and it eliminates the threat of further symptoms, complications, and recurrence. Laparoscopic cholecystectomy is said to have these advantages and to minimize length of hospitalization, length of time away from work, and size of surgical scar. However, laparoscopic cholecystectomy has proliferated without benefit of controlled clinical trials, and it will be some time before we know whether these claims will be fulfilled.

With appropriate patient selection, oral dissolution therapy, biliary lithotripsy, and contact dissolution therapy do work. We can expect treatment options for gallstones to continue to proliferate, and many will likely find niches in the treatment of selected patients with symptomatic cholelithiasis. Controlled clinical trials are needed, however, before we can identify optimal treatments for specific patients.

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