

Intestinal Transplantation

The Normal Intestinal Tract

The intestinal tract, also called the digestive tract, breaks food down into small pieces so that the body can absorb nutrients such as vitamins and protein. The intestinal tract is divided into four parts—the esophagus, the stomach, the small intestine, and the large intestine—each of which has a special purpose.

The esophagus moves food from the mouth into the stomach, where food is stored before it enters the small intestine. The small intestine is where most food is broken down and absorbed into the body. It is about 7 to 8 feet long in newborn babies and grows to about 20 feet by the time a child becomes an adult.

The small intestine has three parts: the duodenum, the jejunum, and the ileum. The duodenum, which is about 12 inches long in adults, connects to the stomach; fluids from the pancreas and liver (bile) drain into the duodenum to aid in digestion. At its lower end the duodenum connects to the middle section of the small intestine, known as the jejunum. Food and digestive fluids move through the duodenum and into the jejunum, and from the jejunum into the lower section of the small intestine, known as the ileum. The ileum is connected to the large intestine by a valve known as the ileocecal valve.

After food has been digested in the jejunum and ileum, it passes into the large intestine (also called the colon), which absorbs water from the digested food and forms solid stools that are then passed out of the body through the rectum. [Insert drawing of normal digestive system]

Intestinal Failure

Intestinal failure occurs when the intestinal tract does not digest food properly. There are two primary causes of intestinal failure: short-bowel syndrome and abnormal intestinal function.

Short-bowel syndrome

Short-bowel syndrome occurs when the small intestine is too short to digest food correctly. In short-bowel syndrome a person may have a lot of bowel movements, may not get enough nutrients, and may lose too much fluid. The causes of short-bowel syndrome are different for infants than for older children and adults.

The two primary causes of short-bowel syndrome in infants are:

- Birth defects that require removal of abnormal intestine, usually soon after birth.

- Acute inflammation that leads to tissue death in both the small and large intestines, known as necrotizing enterocolitis (NEC). NEC can affect premature infants.

Older children and adults may experience short-bowel syndrome for different reasons:

- The intestinal tract may be damaged by radiation treatment for cancers in the stomach or pelvis.
- Disorders that cause excess blood clotting or hardening of the arteries may limit or prevent blood circulation in the intestine.
- Crohn's disease, which can cause inflammation and scarring in the intestine, may result in one or more surgeries to remove the damaged sections of the small intestine.
- Sometimes part of the intestinal tract must be removed when certain stomach tumors, especially benign fibroid tumors known as desmoids, have to be removed.

Abnormal intestinal function

There are two types of abnormal intestinal function that can lead to intestinal failure. The first type is usually inherited and is generally seen in infants shortly after birth. In this type the inner lining of the intestine, where nutrients are digested and absorbed, is abnormal and causes severe diarrhea that does not improve when the infant is given baby formula or medication.

The second type of abnormal intestinal function is known as pseudo-obstruction. In this condition the intestine acts as if there is a blockage, even though there isn't one. Sometimes pseudo-obstruction is inherited, but it can also develop in young children or during adulthood. Patients with pseudo-obstruction have problems with bowel movements and experience severe nausea and vomiting, particularly when they try to eat. Many patients, both men and women, develop swelling of the abdomen that makes them appear pregnant.

Treatment of intestinal failure

Because most food is broken down and absorbed in the small intestine, the small intestine is the most important part of the digestive system. Most people can live without a stomach or large intestine, but it is harder to live without a small intestine. When all or most of the small intestine has to be removed or stops working (intestinal failure), most or all of a person's food must be placed directly into the bloodstream in liquid form (intravenously). This is called total parenteral nutrition, or TPN. TPN is a life-saving therapy that has been available to patients with intestinal failure for over 30 years. People who experience intestinal failure will need TPN for the rest of their lives, because the digestive tract will not get better over time. Currently at least 40,000 people in the United States receive TPN for intestinal failure.

Sometimes, however, complications occur with TPN, and some of these complications can be life-threatening. Examples of serious complications include TPN-associated liver disease, loss of

venous catheter access, and frequent life-threatening infections. When any of these life-threatening complications occurs, intestinal transplantation is considered as a treatment option.

TPN-Associated Liver Disease. TPN-associated liver disease may occur in up to half of all people with intestinal failure. It is uncertain what causes liver disease in people with intestinal failure, and not everyone on TPN develops liver disease. Patients who have had most of their intestine removed and are not able to eat much food are at the greatest risk of developing severe liver damage, which can be fatal. In infants, severe liver disease can appear after as little as 2 years of TPN therapy, and sometimes less; in adults, it can appear after about 6 years of TPN. Transplanting only the intestine will often allow patients to end TPN before liver damage has become severe and permanent, but over half of all patients who need an intestinal transplant also need a liver transplant because of permanent liver damage.

The primary symptom of severe liver disease is jaundice, in which the skin and whites of the eyes appear yellow. In older children and adults, jaundice may develop after many months or years of TPN. In infants, jaundice is common for several weeks after birth, but jaundice that fails to go away by 4 to 6 months of age indicates liver disease.

Loss of Venous Catheter Access. TPN must be given through an intravenous (IV) line that is inserted in a central vein, a large vessel that lies close to the heart. (Insert diagram of person with subclavian line) Over time, scar tissue can form and block the vein, especially if the catheter has had to be removed one or more times because of infection. Once a vein is blocked, it may not be possible to use it again for TPN. There are only six central vein sites in the body that can be used for TPN. Because people with intestinal failure must receive all or most of their food through TPN, blockage of these central veins can be life-threatening. If blockages occur in three or more veins, intestinal transplantation is recommended.

Frequent Life-Threatening Infections While Receiving TPN. The use of catheters can lead to infections of the bloodstream. These infections occur more often in patients with intestinal failure than in patients who are using catheters for other reasons. Patients with intestinal failure who have repeated bloodstream infections may need intestinal transplantation.

What is an Intestinal Transplant?

An intestinal transplant is a section of small intestine from a donor that is transplanted into a patient (the transplant recipient). Other organs, such as the liver, stomach, part of the large intestine, the pancreas, or in some cases the kidneys, may be transplanted along with the small intestine. When the stomach and the entire pancreas are transplanted along with the small intestine, it is called a multi-visceral transplant.

The first intestinal transplants in humans were done in the early 1960s. These transplants were not very successful, because patients' immune systems rejected the transplanted organs. After TPN was developed, there was less interest in intestinal transplants. However, by the late 1980s, interest in intestinal transplantation had once again increased, partly because drugs to suppress the immune system had become available, and also because some patients had developed serious problems with long-term TPN.

Who Should Receive an Intestinal Transplant?

Intestinal transplantation is recommended for any patient who may benefit from stopping TPN, particularly those with life-threatening complications from TPN therapy. However, not every patient will benefit from an intestinal transplant. Patients who are **not** likely to benefit from an intestinal transplant include the following:

- Patients who are unlikely to survive the stress of the transplantation because of serious heart, lung, or neurological problems.
- Patients who have tumors that cannot be completely removed before or during the transplant operation.
- Patients who have serious infections at the time of surgery.
- Patients who have serious defects of the immune system, including autoimmune diseases and autoimmune deficiency syndrome (AIDS).

Patients who need intestinal transplantation are evaluated on an individual, case-by-case basis. When patients are evaluated for a transplant, they should discuss the benefits and risks of the procedure with their doctor.

How an Intestinal Transplant is Performed

Selection of donor organs

Organs used in transplantation are called grafts. Intestinal grafts often come from someone who has died. The supply of intestinal grafts is small compared to the supply of other transplanted organs because:

- The intestine is often damaged at the time of death.
- The transplanted organ often must come from a small donor. Only small grafts will fit inside an intestinal transplant recipient because the recipient has usually had only part of his or her intestine removed.
- Donation by a living person is much less common than in liver or kidney transplantation.

The transplant operation

Because of the difficulty involved, intestinal transplants are performed at only a few Transplant Centers. Two factors make an intestinal transplant difficult:

- Scar tissue from previous surgery may interfere with removing some of the intestine and replacing it with the graft.
- Excessive bleeding may occur during the operation, particularly if the surgeon is also performing a liver transplant.

During the surgery the surgeon usually attaches the upper end of the graft to what remains of the original intestine. Less often, the upper end of the graft is connected directly to the stomach. In multi-visceral graft surgery, in which both the stomach and pancreas are transplanted along with the small intestine, the transplanted stomach is connected to the esophagus, and the lower end of the intestinal graft is attached to the large intestine; this allows the patient to have normal bowel movements after recovery. However, most patients who undergo an intestinal transplant receive a stoma, an opening created in the abdomen for stool to pass through into a bag. The stoma is formed using part of the intestinal wall and is attached to the stomach lining. It is usually removed during a second operation several months after the transplant. [Insert drawing of a stoma.]

Post-operative care

In many ways, care after an intestinal transplant is the same as after any complicated operation. Patients receive intravenous fluids, high-quality nutrition to promote healing, and antibiotics and antiviral drugs to reduce the chance of infection. However, because the immune system tends to attack a transplanted organ as if it were a dangerous virus or bacteria, drugs must be used to suppress the immune system and prevent rejection.

It is important to carefully follow medication instructions in order to maintain normal transplant function and avoid infections and other complications.

Immunosuppression and Prevention of Rejection. Organ rejection is most common within the first 3 to 6 months after transplantation. In the early days of intestinal transplantation, rejection occurred in almost all patients and was often fatal. Today medications are given to prevent rejection and suppress the immune system after intestinal transplantation. Each Transplant Center has its own preferred drug combinations and doses, but generally the following medications are used:

- **Prograf®, also known as tacrolimus.** This is the main immunosuppressive drug used. The dose of tacrolimus is determined by a blood test that is done just before each dose. After an intestinal transplant, the desired level of tacrolimus in the

blood is quite high, perhaps up to 20–25 ng/mL. This level is necessary because the immune system tends to easily reject an intestinal transplant.

- **Corticosteroids.** Right after the transplant, corticosteroids are generally given intravenously in the form of methylprednisolone, also called Solu-Medrol®. Later, they are given by mouth in the form of prednisone or prednisolone.
- **Antibodies.** Antibodies directed against various parts of the immune system are usually given right after surgery. They include anti-thymocyte globulin (Thymoglobulin®), basiliximab (Simulect®), daclizumab (Zenapax®), and alemtuzumab (Campath®).
- **Mycophenolate mofetil (Cellcept®) and sirolimus, also known as rapamycin (Rapamune®).** These medications, like tacrolimus, are used to prevent rejection.

Because of the wide variety of immune-suppressing drugs used today, rejection occurs in less than half of transplant patients; when rejection does occur, it can usually be stopped before it causes permanent damage to the graft.

Nutrition. Each Transplant Center has its own preferred methods for giving nutrition after an intestinal transplant. After surgery, liquids are usually given either by mouth or feeding tube, and often TPN is resumed. If all goes well, normal eating is then started within a few days to 1 or 2 weeks after surgery. As normal eating increases, TPN is decreased. Transplant Centers generally try to have all food and nutrition given through the mouth and intestinal tract within 4 to 6 weeks after the intestinal transplant. Sometimes fluids may have to be given intravenously for several more months.

Infants who have never eaten solid food before the transplant often will not eat well after the transplant and may need to be fed a liquid diet through a feeding tube. Low-allergy formulas are used at first, because immunosuppressive therapy may promote food allergies, particularly to cow's milk. Solid foods may be added later.

Most food items are easy to digest. Patients may experience increased stools after drinking sweet liquids like juice or eating fried foods. Eventually most patients, even infants and children, can eat or drink milk products.

Assessment of the Graft. No blood test can diagnose rejection of the intestinal transplant, and symptoms may not be present when rejection is just beginning. To check for signs of rejection, an instrument called an endoscope is often used to take biopsy samples of the transplanted intestine soon after the operation. The endoscope is passed into the intestine through the stoma. Biopsies may be done weekly or monthly in the beginning, when the risk of rejection is highest, and then once every year or so after the first year. If the patient has also had a liver transplant, blood tests will be used to check for liver damage and to see if a liver biopsy is needed. A biopsy is also done if symptoms of intestinal rejection develop. These symptoms include bloody stool

output (or an increase in stool) through the stoma, nausea and vomiting, swelling and pain in the abdomen, and fever. During rejection, the stoma can also swell and turn red.

Treatment of Rejection. If a biopsy does indicate rejection, treatment is started in the hospital, and may include high doses of methylprednisolone (Solu-Medrol®) and increased amounts of tacrolimus. More biopsies may be done to see whether the condition has improved or other medications are needed. In a few cases of severe rejection, the graft may have to be removed and another transplant performed, but this is rare.

Prevention of Infection. The risk of bacterial and fungal infection is high after an intestinal transplant because the graft cannot be sterilized before it is placed into the patient. In addition, the central vein catheter that was used for TPN before surgery must be left in place so that TPN can be given after surgery as well, and infection can occur at this site. Finally, the immunosuppressive therapy used to prevent infection makes common viruses dangerous to transplant recipients. These viruses include cytomegalovirus (CMV), also known as herpes virus; Epstein-Barr virus (EBV), which causes mononucleosis ("mono"); and adenovirus.

For these reasons, antibiotics are typically given after surgery. Most Transplant Centers also give antiviral drugs such as ganciclovir (Cytovene®) and CMV immune globulin (Cytogam®) for several weeks or months after transplant. Periodic blood tests are also performed after transplant to check for CMV and EBV.

What to Expect After Discharge

Monitoring the transplant graft

Intestinal transplantation is difficult, and complications can occur often. For that reason, many Transplant Centers require patients to live near the Transplant Center for several months after surgery. Once patients have returned home, they must continue to monitor the transplant graft to make sure the graft continues to function well. This often includes keeping track of certain body functions, such as:

- Vital signs (temperature, heart rate, and blood pressure). A rising temperature or heart rate may be an early sign of infection or dehydration (that is, not enough fluids).
- Body weight.
- Fluid and solid food intake.
- Stool output. A change in bowel movements may be a sign of a serious problem that needs immediate medical attention.

After the patient returns home, the local doctor who gave the transplant referral typically resumes most care, such as managing diet, blood pressure, and fluids. However, most Transplant

Centers prefer to monitor the patient's immunosuppressive therapy; they may also ask a gastrointestinal specialist to do an endoscopy if there are problems with the graft. Most Transplant Centers also want to be told of any major change in the patient's condition, any hospitalization, or any visit to an Emergency Department, regardless of the reason.

Frequent blood tests are an important part of post-operative care. Before returning home, the patient must choose a local lab for blood testing. In the beginning, blood tests are done once a week, and sometimes more often. After a while, testing is done once every 1 or two months. Test results are sent to the Transplant Center.

Monitoring symptoms

After returning home, patients should be careful to check for any symptoms that might indicate infection or graft rejection. These include the following:

- Increased output of stools
- Loss of appetite or weight loss
- Nausea and vomiting
- Blood in stoma fluid or stool
- Change in color or appearance of the stoma
- Fever without an obvious cause, such as flu

An endoscopic biopsy is generally recommended when symptoms develop. This test is the single best way to identify rejection or other conditions that can cause similar symptoms, particularly viral infections.

Taking medications properly

To maintain a healthy transplant graft, patients may have to take some or all of the following drugs:

- Immunosuppressant drugs to prevent rejection of the transplant.
- Drugs to prevent infections that are common with a suppressed immune system.
- Nutritional supplements and related medicines, which are often needed even if the intestinal transplant is working well.
- Blood thinners to prevent blood clots.
- Drugs for high blood pressure.

Some medications, particularly immunosuppressant drugs, are taken forever; others are required for only a short period of time after the transplant. Regardless of the type of medication, all drugs must be taken at the correct time in order to be effective.

Some Precautions About Immunosuppressant Drugs. Immunosuppressive drugs have many side effects and must be taken exactly as prescribed to be effective. Too little medication allows the immune system to destroy the newly transplanted intestine. Too much medication interferes with the body's ability to fight infection and causes other side effects. Taking doses at the wrong time can reduce the drug's effectiveness. The number of immunosuppressive drugs a patient must take usually decreases over time if rejection does not occur. However, rejection can still happen even though medications are taken properly; in such cases more drug therapy will be needed.

Preventing Infection at Home

Drugs used to prevent rejection decrease the body's ability to fight serious infections. After leaving the hospital, transplant recipients can protect themselves in several ways:

Be Aware and Keep Healthcare Providers Informed of Any Changes. Patients should take their temperature whenever they feel warm. Fever, swollen lymph glands, coughing, nighttime sweats, and new snoring can all indicate infection.

Get Blood Tests as Instructed to Detect Infection. These tests are especially important in the first year after surgery.

Take Medications Exactly as Instructed to Prevent Infection. These may include trimethoprim-sulfamethoxazole (Bactrim[®]), valganciclovir (Valcyte[®]), and nystatin (Mycostatin[®]). Patients who have had their spleen removed during the transplant may also need to take an antibiotic such as amoxicillin.

Avoid High-Risk Situations for Infection. The following common-sense practices are often recommended to reduce the chance of infection while taking immunosuppressant medications:

- Avoid people who have infections—especially anyone with chickenpox, a cold or flu, mononucleosis, or tuberculosis. Transplant recipients who have been exposed to any of these infections should tell their Transplant Center right away.
- Take antibiotics before and after dental work or other procedures, if recommended.
- Wash hands really well, especially before eating; after touching objects that carry germs (money, doorknobs, and public telephones); and after using the bathroom, especially in public facilities.
- Avoid compost piles; construction sites; damp hay; and decaying plants, fruits, and vegetables.
- Wear gloves during activities such as gardening.
- Wear shoes when outdoors.
- Cover the entire body, including arms and legs, when hiking.
- Do not get live vaccinations, and avoid people who have recently had one.

- Get tetanus shots as needed (in case of an animal bite or a dirty cut, for example).
- Get a flu shot every year.
- Do not share razors, toothbrushes, or eating and drinking utensils.
- Practice safe sex.
- Drink only treated city or bottled water. Questions about water quality can be directed to local water authorities (telephone numbers are generally listed on water bills) or the Environmental Protection Agency Safe Water Hotline at (800) 426-4791.

Special Considerations Regarding Animals and Pets

- Avoid contact with animal urine, vomit, or feces, especially bird droppings.
- Wash hands well after touching pets.
- Do not allow house pets to roam freely outside, especially cats.

Getting Back into a Normal Routine

Certain things are important in recovery, and patients will feel better if they can establish a normal routine.

Sleep. Transplant recipients sometimes develop the urge to sleep during the day and stay awake at night. Avoid long daytime naps; that will make it easier to sleep at night.

Regaining Strength. Transplant recipients are often weak right after transplantation. Exercise rather than rest is usually the best way to regain strength. If possible, exercise under the care of a physical therapist. Swimming in a chlorinated pool is usually okay after drainage and feeding tubes have been removed and all wounds and tube sites have healed. Most patients should be able to go back to work or school after an intestinal transplant.

Driving. Adult intestinal transplant patients are usually able to drive after surgery, but patients should first check with the Transplant Center. Some medications affect reflexes, judgment, and vision. If the doctor says it is okay to drive, a fastened seatbelt will not injure the intestinal transplant.

Alcohol. Most Transplant Centers advise against drinking alcohol after an intestinal transplant.

Medical Alert Identification. Many Transplant Centers suggest wearing medical alert identification, such as a pendant or bracelet sold under the brand name MedicAlert® (Tel: 1-800-830-0546, or e-mail: service@medical-id.com). This kind of ID will alert others to a transplant recipient's medical status if he or she cannot communicate. An intestinal transplant patient's ID should name the transplanted organs (for example, "Intestine Transplant" or

"Intestine and Liver Transplant") and indicate that the patient is "On Immunosuppressants," along with any other important medical information.

What to Expect Over the Long Term

Survival rates for patients after intestinal transplantation have improved greatly in recent years. Overall 5-year survival rates vary with the number of organs transplanted; single-graft transplants (for example, small intestine only) have a higher rate of survival. More than 75% of patients can expect to be free of TPN and tolerate oral nutrition after an intestinal transplant.