

INTRODUCTION TO THE DUMONT-UCLA INTESTINAL TRANSPLANT PROGRAM IN THE DUMONT-UCLA TRANSPLANT CENTER

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INTESTINAL TRANSPLANTATION AT THE DUMONT-UCLA TRANSPLANT CENTER

Transplantation of the intestine is a procedure performed regularly at a few specialized transplant centers in the world. As one of the world's leaders in solid organ transplantation, the **University of California, Los Angeles (UCLA)** was one of the first centers to establish a program of intestinal transplantation. This program grew from the already established, successful, and busy liver transplant program in an effort to meet the needs of a unique set of patients with **short bowel syndrome (SBS or short gut syndrome (SGS))**, dependence on **total parenteral nutrition (TPN)**, and advanced liver disease. Established in 1991, this program has grown steadily over the past decade under the guidance of Drs **Douglas G. Farmer**, Ronald W. Busuttil, and Suzanne V. McDiarmid. Today, the Dumont-UCLA Intestinal Transplant Program is one of the largest of its kind in the world offering transplantation of the **intestine alone, liver and intestine**, and **multivisceral/intestinal** combination to appropriate **adult and pediatric** candidates.

One of the true strengths of the program is the multidisciplinary approach taken for each patient referred for evaluation. An experienced team consisting of specialists in transplantation surgery, gastroenterology, hepatology, cardiology, pulmonology, nephrology, nutrition, social work, and psychiatry routinely evaluate the unique needs of this patient population. Intestinal function is carefully assessed based on length, location, and function of remnant intestine. For patients with **intestinal failure**, the appropriate transplant involving the intestine is recommended. However, intestinal transplantation is not appropriate for all patients and any of a number of medical and/or surgical treatment options can be offered and administered as indicated. When appropriate, patients benefit from a long-term, careful follow-up by the multidisciplinary team resulting in optimal care and incorporating changes in the condition of the patient over time.

This approach has resulted in continued success over the past decade. Recipients of intestinal transplants at UCLA enjoy one of the highest survival rates in the world. Furthermore, clinical experience, preemptive and prophylaxis therapies have led to reduced rates of rejection and viral infections after transplantation. Successful transplantation leads to independence from TPN and reliance solely on enteral/oral nutrition to meet caloric needs.

Consults are available for intestinal transplant evaluation as well as to assist with the medical and surgical management of patients with difficult gastrointestinal conditions, short bowel syndrome,

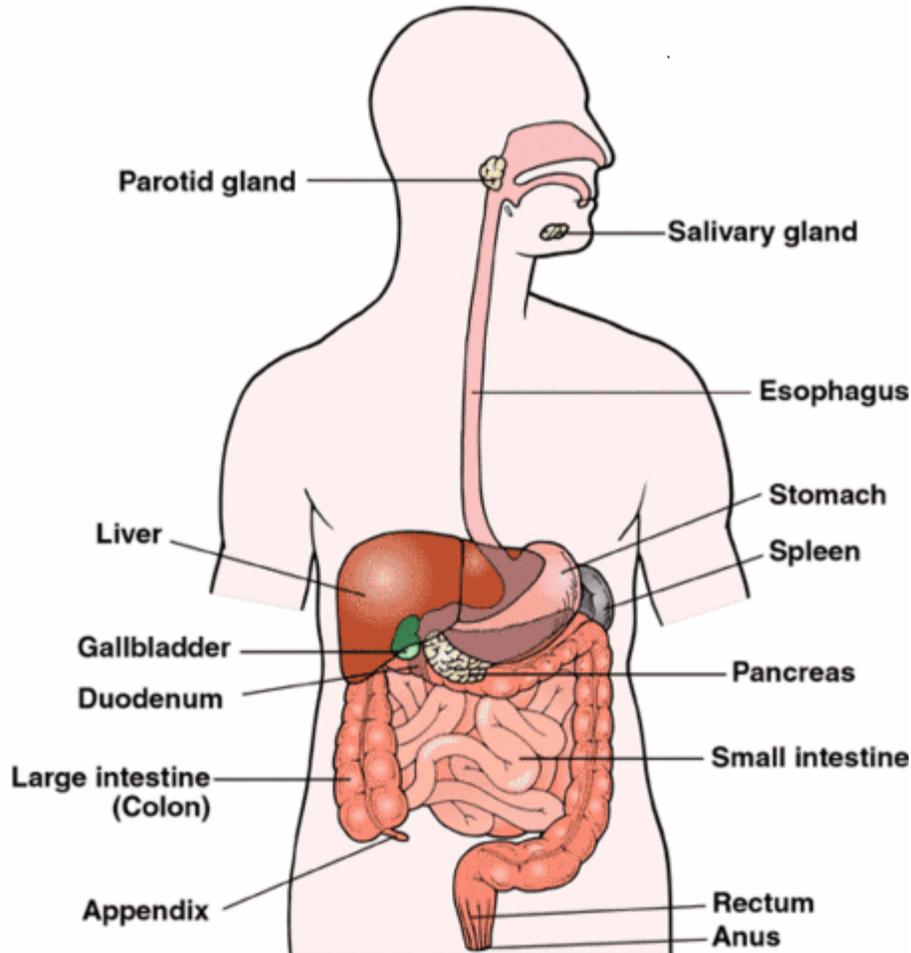
TPN-dependence, and liver disease. Information concerning the Intestinal Transplant Program at the Dumont-UCLA Transplant Center or concerning intestinal transplantation in general, can be obtained by writing or calling the central offices.

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What is the GI tract?

The **gastrointestinal (GI) tract** is the tube from the mouth to the rectum. The GI tract includes the esophagus, stomach, duodenum, liver, pancreas, small intestine (also known as jejunum and ileum), large intestine (also known as the colon) and rectum.

Digestive System



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When we chew and swallow food, it travels from the mouth to the stomach by moving through the esophagus. Once the food is in the stomach, the food is partially digested by the stomach acids and the movement in the stomach. The stomach empties the partially digested food into the duodenum. In the duodenum, the food is mixed with other digestive juices from the pancreas and liver. The liver provides the digestive juice, bile and the pancreas provides digestive pancreatic enzymes. Together, these digestive juices complete the breakdown of the foods we eat.

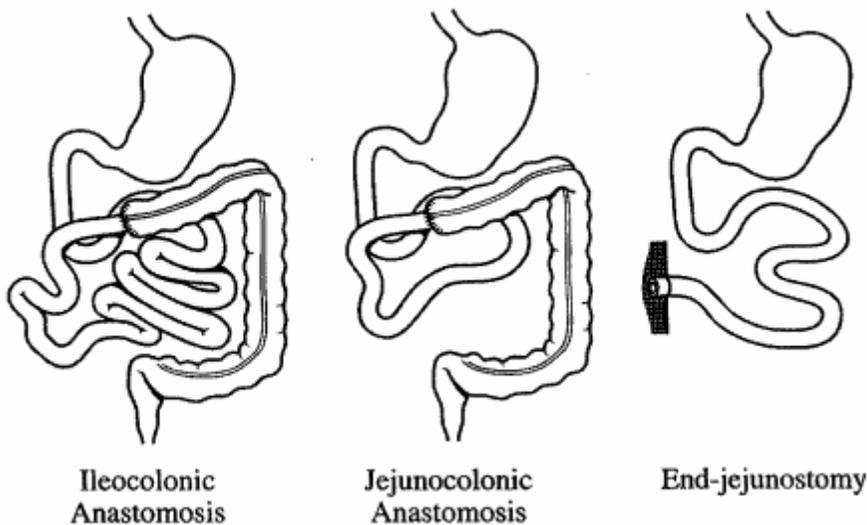
From the duodenum, the digested food moves into the small intestine for more digestion and absorption. The major role of the small intestine is to absorb nutrients from the food. Once the nutrients are absorbed, the remaining liquid is passed into the large intestine. The major role of the large intestine is to remove the extra water and to form stool. The large intestine moves the stool to the rectum where it is eliminated.

The gastrointestinal tract is a very long muscular tube. It works together with the other organs to complete the digestive process. The small intestine is a very long, coiled tube. It is measured to be approximately 10-12 feet in children and 20-25 feet in adults. The large intestine is also a long tube which measures approximately 3 feet in children and 6-9 feet in adults.

What is Short Bowel Syndrome?

Short bowel syndrome is a general term referring to the loss of absorptive function of the intestinal tract. This results in malabsorption, diarrhea, and malnutrition. So basically, the small intestine and large intestine do not work properly. The **small intestine** is the most important GI tract organ related to the development of this condition.

There are a variety of causes of short bowel syndrome. The causes can be placed into two broad categories; Surgical/Mechanical causes and Functional disorders. Surgical or mechanical causes are the most common. It often occurs because a doctor has to operate and remove segments of the intestine.



From Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease; 7th Edition; Figure 92-1, page 1808; 2002, Elsevier

The second category is functional disorders. Functional disorders are problems that arise with the intestines that prevent it from digesting, absorbing and moving food through the intestinal tract. In some cases, patients can have both surgical/mechanical and functional disorders causing short bowel syndrome.

In some cases, short bowel syndrome is temporary. Somehow, the remaining intestine has the ability to adapt to the short bowel syndrome. The remaining small bowel does more work than before and is able to make up for the shorter length of small bowel. Successful adaptation is when a patient can once again digest and absorb all nutrients through their gastrointestinal tract. Adaptation starts very soon after the onset of short bowel syndrome can take several years before it is complete. The potential to adapt depends on a number of factors such as health of patient, age of patient, length of remaining intestine, presence or length of colon, and presence or

absence of disease in remaining intestine. Your doctor will advise you on the potential of your intestine to adapt.

Unfortunately, there will be patients who do not adapt from short bowel syndrome. Those patients will require total parenteral nutrition (TPN) for the remainder of their lives to prevent malnutrition and death. When a patient's intestine does not adapt, it is labeled as intestinal failure.

Total Parenteral Nutrition (TPN)

Total parenteral nutrition (TPN) is a liquid form of calories and nutrients given into a large vein. TPN has been a life-saving option for patients who developed short bowel syndrome and intestinal failure. TPN was invented in the late 1960's and prior to the invention, all patients with short bowel syndrome died of malnutrition. After years of formulation and experience, TPN is a safe and effective way to provide life-sustaining nutrients to patients who cannot absorb these calories and nutrients from the gastrointestinal tract. Specialized teams of medical professionals including doctors, nurses and pharmacists work closely with patients on TPN to ensure all caloric, fluid, and electrolyte needs are met in the safest manner.

There are limitations associated with TPN. First, the patient must have long-term central venous access. Most often, this is provided through a surgically placed catheter also known as a central venous catheter (CVC). The catheter is placed into one of the large veins in the chest. These catheters require special care to prevent problems. Secondly, the patient needs to have special equipment and supplies for administration of the TPN. Thirdly, specialized medical care and monitoring is required to make sure the TPN administration is safe.

There are also risks associated with TPN. The risks of complications vary from patient to patient and cannot be predicted. Some of these complications can be life-threatening and require immediate medical attention. The major complications are liver disease, central venous catheter (CVC) infections, loss of CVC sites and major fluid and electrolyte imbalances. Even with the limitations and risks, 80% or more of all patients on TPN do well with few or no complications.

The risks of liver disease, CVC infections and fluid & electrolyte imbalances are explained in detail below:

1. Liver disease can be associated with the administration of TPN. The cause of liver disease is unknown. Some patients, particularly the very young patient appears to be more likely to develop liver disease. It can occur any time after the start of TPN therapy. While the causes are unknown, there are several theories as to why patients may develop liver disease. One theory is that the nutrients are delivered to the body first and not to the intestine and liver. This in some way alters the liver reaction to the nutrients leading to disease. A few other theories include a loss of beneficial hormones given to the liver when nutrients are delivered through the gastrointestinal tract, possibly there are increases in bacteria that reach the liver when nutrients are delivered through TPN, or that there is altered blood flow to the liver related to the short bowel syndrome. In truth, the cause may be unique to each patient and may represent a combination of event. If

patients develop progressive liver disease on TPN and cannot come off of TPN (that is, their intestine does not adapt), then they may develop end-stage liver disease or **cirrhosis**. This condition is very severe and will result in death without transplantation.

2. Vascular access complications are the next most common complication associated with TPN therapy. Multiple, recurrent **infections** of the central venous catheter can result in removal of the central venous catheter and can lead to severe, life-threatening infections. Doctors become very concerned when patients must have several central venous catheters removed due to infection, have infections with germs that are resistant to antibiotics, have infections with yeast, or have infections that are life-threatening. For unknown reasons, some patients appear more susceptible to these infections than others. In addition, a huge concern is the **loss of central venous access sites**. Adults generally have 6-8 standard venous access sites and children have 4-6 standard central venous access sites. When patient clot veins so that a catheter cannot be replaced in that vein, it is considered permanently lost. If a patient has more than half of their potential access sites removed, the medical team will become concerned over the long-term ability to maintain catheters to deliver TPN.

There are other significant complications that can be associated with TPN therapy. Patients can become dehydrated or develop renal failure. Patients may require a lot of medical care and frequent hospitalizations. Furthermore, the risk of death is slightly higher for patients on TPN than that of the general populations. The outcomes for an individual patient cannot be predicted.

Indications for Intestinal Transplantation

Patients with intestinal disease or injury who are doing well on TPN are NOT candidates for intestinal transplantation at this time. To be a candidate for an intestinal transplantation:

1. Patients must have intestinal failure whereby their remaining intestine is not expected to adapt

AND

2. Patients must have developed one or more life-threatening complications related to TPN as outlined above.

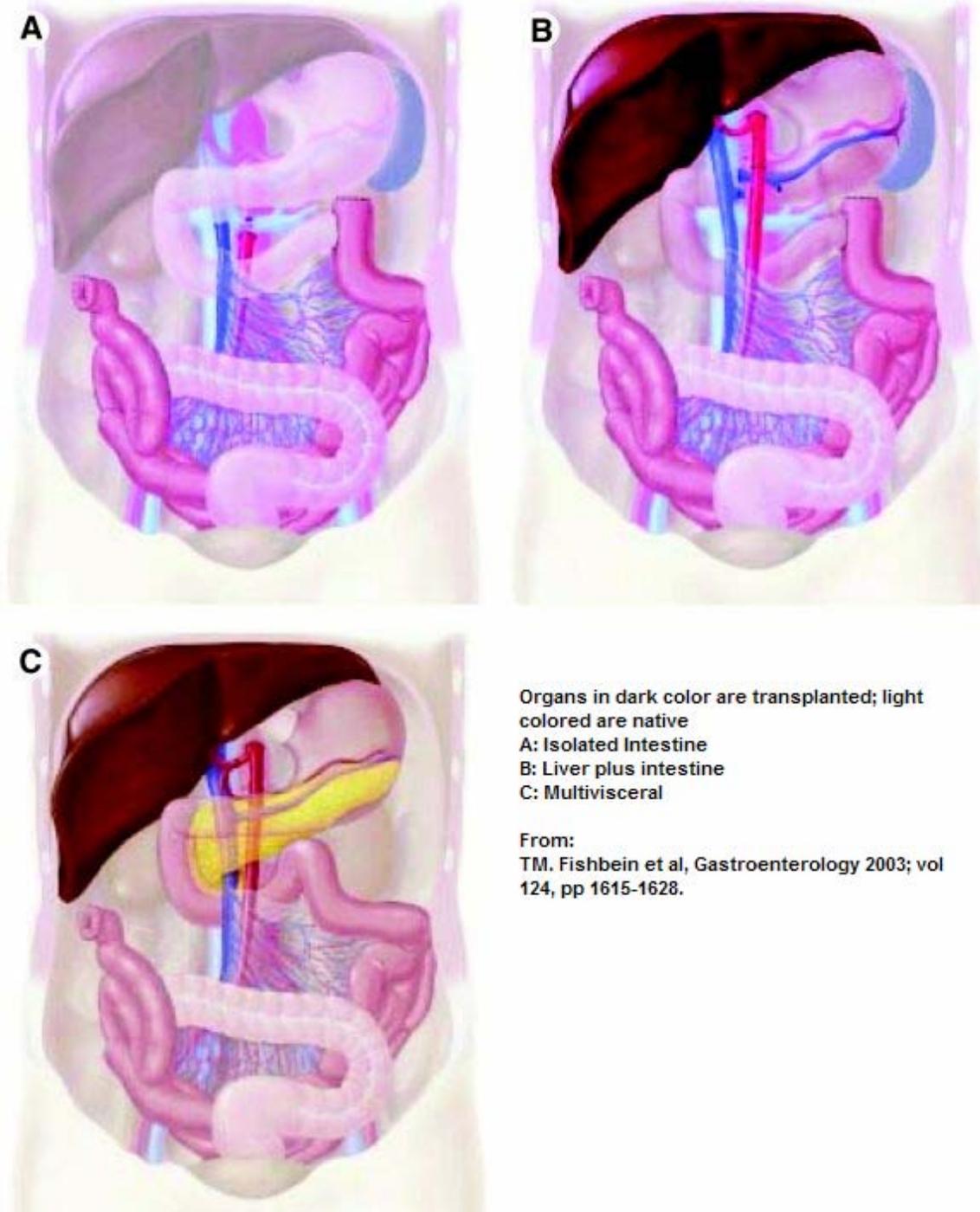
It is only when the risks from TPN exceed those of transplantation, is intestinal transplantation considered.

Types of Intestinal Transplants

The type of intestinal transplant offered to a patient depends on the individual patient needs. There are essentially 4 types of transplants involving the intestine.

1. The first is the **isolated intestinal transplant**. This type of transplant consists of the small bowel (jejunum and ileum) and is given to patients who have normal liver function or a liver with early/reversible liver disease and meet the criteria for intestinal transplantation.

2. The second type of transplant is the **combined liver and intestinal transplant**. This consists of two organs – the liver plus the entire small intestine together as one group. It is given to patients with irreversible liver disease and intestinal failure.
3. The third type of transplant is the **multivisceral transplant**. This transplant includes the liver, stomach, duodenum, pancreas, and small bowel. It is reserved for patients who have organ failure involving the liver, pancreas, and intestine or for patients with diffuse diseases of their intestines (such as Gardner’s Syndrome, intestinal polyposis, or motility disorders such as pseudo-obstruction) associated with liver disease.
4. The fourth option is a modification of the multivisceral transplant called the **modified multivisceral transplant** in which the liver is not included and the stomach may or may not be included. Again, the organs transplanted are tailored to the patients needs.



Referral Process for Intestinal Transplantation

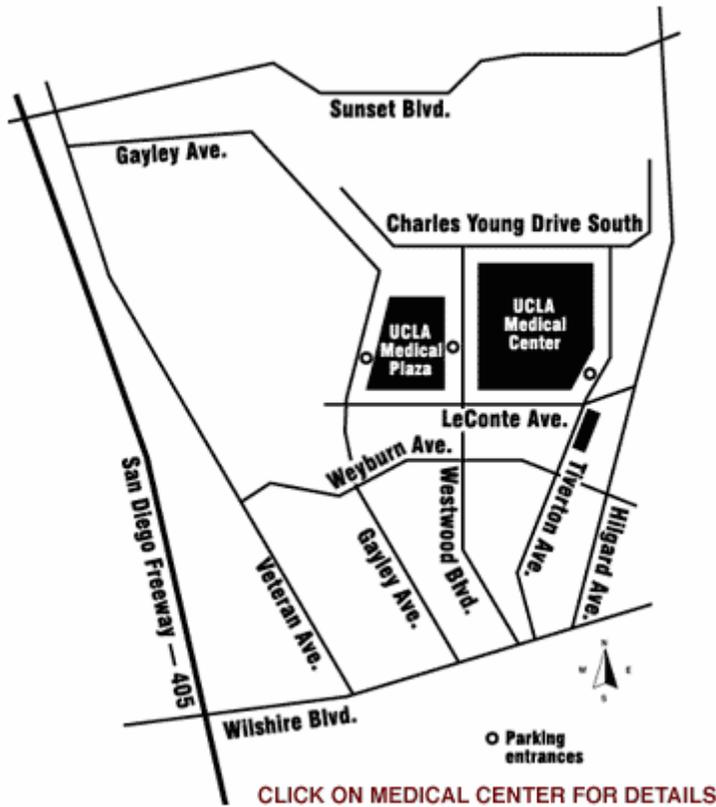
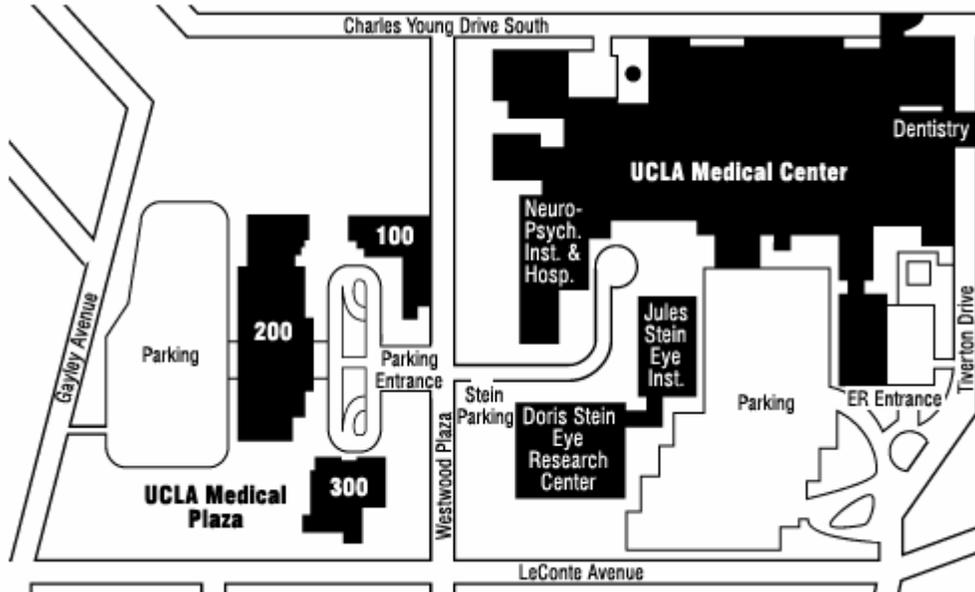
The process of deciding if intestinal transplantation is a treatment option for a patient starts with the referral to a transplant team that specializes in these types of transplants. Usually, a patient's primary physician, gastroenterologist, or surgeon will contact the transplant center directly and provide access to the patient's medical records and history. Patients can refer themselves directly

without going through their primary physician however, as an important aspect of the assessment is the patient's past medical history, contact with the referring physicians is recommended. Referrals should be directed to:

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INTESTINAL TRANSPLANT PROGRAM AT THE DUMONT-UCLA TRANSPLANT CENTER

The Intestinal Transplant Program at UCLA is one of the oldest and largest of its kind in the world. Initiated in 1991 by **Drs Ronald W. Busuttil** and **Douglas G. Farmer**, it has developed through the expertise and experience of the liver transplant program into one of the most experienced intestinal transplant programs in the county. The program meets the needs of adults and children with intestinal and liver diseases by providing all types of transplants involving the intestine as well as specialized medical care in the fields of short bowel syndrome, intestinal rehabilitation, gastrointestinal surgery, and total parenteral nutrition. The program is the only one of its kind specializing in intestinal transplantation in the Western USA. The evaluation and transplant volume is one of the largest in the world. UCLA is the fifth program in the USA to be certified by the **Centers for Medicare and Medicaid Services** (CMS; www.cms.hhs.gov) in the Department of Health and Human Services (DHHS). UCLA is an active participant in the **Intestinal Transplant Registry** (www.intestinaltransplant.org). The transplant center is located within the UCLA Medical Center in Westwood, California just off the 405 Freeway and Wilshire Boulevard. Please see [map](#) for directions.



EVALUATION FOR INTESTINAL TRANSPLANTATION

Once the referral process is complete, the patient will undergo a comprehensive, multidisciplinary evaluation for transplantation. This process usually requires 3 to 5 days in the hospital but can take place over several weeks as an outpatient. The evaluation provides a comprehensive assessment of a patient's medical condition using a multidisciplinary approach

that includes surgeons, gastroenterologist, hepatologist, nutritionist, TPN specialists, transplant nurse coordinators as well as many other sub-specialists. During the evaluation, patients will be assessed for the degree of intestinal failure and liver disease. A complete assessment as to the potential for bowel adaptation will be made as well as the current nutritional status of the patient. A detailed analysis of the TPN formulation and feeding regimen will be made. Radiographic examination of the abdomen and vascular access sites will be completed. Educational sessions will be arranged with the patient and family to review many aspects of their medical condition. A final session will be arranged to review the specific results of the evaluation.

RESULTS OF EVALUATION FOR INTESTINAL TRANSPLANTATION

The results of the evaluation will be discussed with the patient, family, and referring physicians. Medical records will be made available upon request. The final decision regarding the candidacy for intestinal transplantation is made by a multidisciplinary patient selection committee that meets 1-2 times per month. If intestinal transplantation is recommended, the exact types and special issues will be addressed. Otherwise, further intestinal rehabilitation attempts may be recommended or other non-transplant surgical options may be recommended. Sometimes, the recommendation is to follow a patient closely to determine if further TPN related complications can be prevented. In some instances, patients fail the non-transplant approach and require an abbreviated re-evaluation assessment for transplantation. A conservative approach is taken with the patient's best interest in mind.

LISTING AND WAITING FOR INTESTINAL TRANSPLANTATION

For those patients accepted for intestinal transplantation, the process of financial clearance and listing is undertaken. At UCLA, we accept most major government and third party insurance carriers. Approval through the patient's insurance plan must be obtained prior to listing for transplantation. Once this is obtained, the patient is listed for the appropriate organs through the United Network for Organ Sharing (UNOS, www.unos.org). Each organ requires a separate listing and status. For a patient requiring a new liver, pancreas, and intestine, he will be listed for each organ separately with UNOS. The listing status is based upon how diseased an organ is and organs are distributed based upon the scoring systems in place.

Waiting times vary depending on the UNOS score for each patient, the organs required, the size of the patient, the blood type of the patient, and the degree of illness of the patient. In general, most patients wait from 3 months to 1 year for organs. This can vary from shorter to longer times depending on the individual. Listing for transplant does not guarantee that the appropriate organs can be found in a timely manner. During the wait for organs, patients must have a rapid and reliable system in place for being contacted and traveling to UCLA to prepare for transplantation. In general, patients will have 1 to 4 hours to arrive at the medical center once contacted that an organ has been offered to them. Families of those patients already in the hospital at the time of organ offered will be notified immediately

THE TRANSPLANT HOSPITALIZATION

When an organ offer is obtained, the patient will undergo a rapid medical assessment to ensure that there are no major changes in the patient's medical condition that might temporarily prevent transplantation. Once completed, the surgical team will assess the donor organ quality in an operation. If the donor organs are not deemed suitable, the transplant will be cancelled. If the organs are suitable, then the patient will proceed to the operating room at UCLA to be put to sleep under anesthesia and prepared for the transplant procedure.

Transplantation involving the intestine requires at least 6 hours and can last as long as 12 hours. During the procedure, diseased organ or organs are often removed. The exact operative plan will be outlined by your surgeon. The diseased intestine (and other organs) will be replaced by new organs. The blood flow in and out of the organ must be re-established. Once completed and blood flow restored, the intestine of the donor must be connected to the patient's gastrointestinal tract. If a patient does not have a large bowel (colon), then a permanent ileostomy will be required. If a patient does have functional large bowel then the transplanted small intestine will be connected to this and a temporary ileostomy created. The presence of an ileostomy is important for assessing the function of the new intestine after surgery. Lastly, feeding tubes are placed into the patient's stomach and small intestine in the postoperative period to provide medications and feedings.

The postoperative care will vary from patient to patient depending on their medical condition at the time of transplantation. Obviously the exact course for each patient cannot be predicted nor can outcomes be guaranteed. Every effort will be made to expedite the recovery process but patient safety is the biggest concern. In general, patients stay in the intensive care unit from 3 days to 4 weeks after the transplant. They may require support on a breathing machine (ventilator) during this interval. The length of hospitalization depends on a number of factors and can range from 4 weeks to 3 months. While in the hospital frequent exams and blood draws will be performed. Patients will be monitored according to their medical condition. Biopsies of the transplanted intestine will be obtained at regular intervals after the transplant. A specialized formula will be used to start feeding nutrients into the new intestine and the TPN will be weaned off as the intestine recovers function after the transplant procedure. Monitors, lines, and tubes will be removed as indicated.

Drugs will be given to prevent infections and rejections. Most of the drugs are given through a central venous catheter. Patients will be monitored closely for the presence of infections and treated appropriately and aggressively should these occur. The combination of drugs used to suppress the immune system to prevent organ transplant rejection is important. Your doctor will review these drugs with you. All drugs have potential benefits and side-effects. They are dosed to achieve the greatest benefit with minimal side effects. Please do not hesitate to contact your doctor with questions regarding your medications. The patient will not be discharged until teaching is completed and the parents feel comfortable. Support groups are available for transplant recipients should the patient or his family want to attend.

OUTCOMES AFTER INTESTINAL TRANSPLANTATION

The results of intestinal transplantation have dramatically improved over the years. One of the most important indicators of outcome is related to the experience of the transplant center. The Intestinal Transplant Program at UCLA is one of the most experienced programs and has some of the best outcomes in the world. The severity of the patients illness at the time of transplant is also an important indicator of outcome – the sicker the patient, the more difficult the recovery. However, outcomes for any patient cannot be predicted nor guaranteed.

Successful intestinal transplantation is associated with freedom from TPN. All of our patients with successful intestinal transplants no longer require TPN and the TPN is weaned off prior to discharge from the hospital. Some, depending on their desire to eat, require formula feeding into the stomach via a tube. This mode of nutrition is proven to be much safer and require less care than that of TPN. Your doctor will advise you as to the expectation for nutrition. Complications can occur after intestinal transplantation. Many are common and can be predicted. Others are uncommon and cannot be foreseen, predicted, or prevented. The list of possible complications is too long to cover, especially those that can be encountered after any major surgical procedure. These would include heart attack, stroke, kidney failure, death, etc. There are some complications more pertinent to the intestinal transplant procedure. These include but are not limited to:

1. **Bleeding** can occur in any part of the body including the brain, lungs, kidneys, and incision. Most commonly it occurs in the abdomen after the surgery.
2. **Infections** of the blood, abdomen, incision, lung/pneumonia, urine, or intestine. The types of infection can be bacterial, viral, fungal, or parasites. Many infecting organisms have antibiotics that can be used to treat them. Some do not. Treatment is given to prevent some of the more common bacterial and viral infections. Examples include but are not limited to cytomegalovirus (CMV), Epstein Barr virus (EBV), and pneumocystis pneumonia. Infections are by far the most common cause of problems including death after intestinal transplantation.
3. **Reoperation** may be required to correct certain complications or complete surgical procedures. Most patients require reoperations after intestinal transplantation. Operations are reserved for conditions that require urgent attention and cannot be corrected by medical means.
4. **Rejection** is common after intestinal transplantation. Newer immunosuppressive drugs have reduced the impact of rejection after transplantation and brightened the outlook for patient who experience this problem. Rejections however can still occur despite adequate medications. Determining rejection can be difficult and relies on experience, clinical exams, and an endoscopy with a biopsy. Treatment generally is successful using higher dose of immunosuppressive drugs such as Tacrolimus, steroids, or OKT3. Unsuccessful treatment or complications of treatment requires removal of the transplanted intestine. This need for this procedure is infrequent but when it occurs, generally requires 1 to 2 operations and is associated with infections, mechanical ventilator support, and ICU management. After the intestine is removed patients generally recover but death from infection can occur. Also, patients are left with intestinal failure and require TPN again. In this condition, patients will many time require retransplantation of the same or

different type. To be eligible for retransplantation, patients need to recover from their first transplant and undergo re-evaluation for another transplant. Candidacy will be assessed as before with recommendations made to the patient and family.

5. **Kidney** failure or insufficiency can occur and is frequently associated with infectious problems. Kidney problems can be associated with drug therapies such as antibiotics and immunosuppression.

Your chances of having one or more of these complications cannot be predicted. Every effort will be made to identify the problem and take corrective action or treatment in a timely manner. If you have any questions regarding your risks related to this procedure, please contact one of your transplant team members.

LIFE AFTER INTESTINAL TRANSPLANTATION

After discharge from the hospital, patients should expect close follow-up during the early post-transplant period. Typically, patients require blood laboratory analysis 1 to 2 times per week and clinic checks once a week. Once the patient is more stable the frequency of these checks is diminished. At one year after transplant, patients are typically seen in clinic once per month and have blood laboratory analysis once to twice per month. Once patients are stable and further out from their transplant, they are seen approximately 4 times per year. Re-hospitalizations can occur and should be expected. Patients are required to take their medications until instructed to stop them by a transplant physician. The drugs that are taken to prevent rejection must be taken for the remainder of a patient's life. Life-long medical care by a transplant team experienced in intestinal transplantation is required. At UCLA, we are committed to our transplant patients and plan on caring for them indefinitely. Patients initially stay in the Los Angeles area until they are stable to return to their homes. Patients will also follow-up with their primary and referring doctors who work with the UCLA transplant team to assist in patient care needs.