Transplant Handbook

TABLE OF CONTENTS

(click on bookmarks to the left to navigate to a page)

TABLE OF CONTENTS (continued)
(click on bookmarks to the left to navigate to a page)

Introduction

No doubt, the transplant rotation is challenging. But it is also potentially one of the best.

Challenge

- This is a busy service. IU has one of the largest transplant programs in the world.
- Patients are sick. They all have organ failure and associated disease. They are all immusuppressed. This means weird drugs and weird infections.
- Operations are complex and therefore leads to difficult complications.

Opportunity

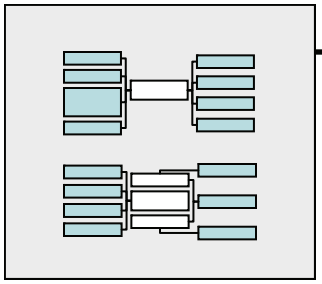
There is unique exposure to unique surgical issues:

- **Open vascular techniques and complex operations.** Gi sugery and vascular anastomoses over and over.
- **Unbelievable anatomy:** Check out a multiorgan procurement.
- **Surgical care of organ failure:** end-stage renal disease, cirrhosis, and/or diabetes mellitus
- **Surgical care of immunosuppression.**

Stretch

The transplant rotation will stretch the resident's comfort-zone, but under extremely controlled and supportive circumstances:

- Transplant drugs are complicated, but we have transplant pharmacists you can always turn to.
- The fellows are a constant buffer between you and the attending. You can always run things by them
- The liver service has very experienced nurse practitioners. They have been around a long time and usually know exactly what is expected. They are a great resource.
- On what other service do attending write all the progress notes?



Transplant Service Organization

IU Transplant is one of the busiest transplant services in the country, with the highest volume in pancreas and intestinal transplants. This is a well oiled machine, with our own floor, ICU and OR team. We also have a number of fellows and nurse practitioners.

Rounds

In general, the entire team (attending, pharmacist, nurse practictioner, fellow, residents, med student) gather and go over patients in detail, concentrating especially on meds, labs, tests, Xrays, and then setting out the plan for the day.

We usually go over:

- allograft function
- immunosuppression (drug levels)
- ID issues (cultures, antibiotics, lines)
- Fluid and electrolytes
- Medical issues like blood pressure control, vent
- GI issues. Diet, nutrition. Prerounds should include finding out about the bowel status (flatus, BM).
- Studies done (XR, scope, biopsies)

We prefer to round where there are multiple computers; rounds are more efficient if the resident has Cerner open to answer questions (what's the FK level) and gets XR studies up while the notes are written. Generally, all XRs are reviewed, not just the report.

Documentation

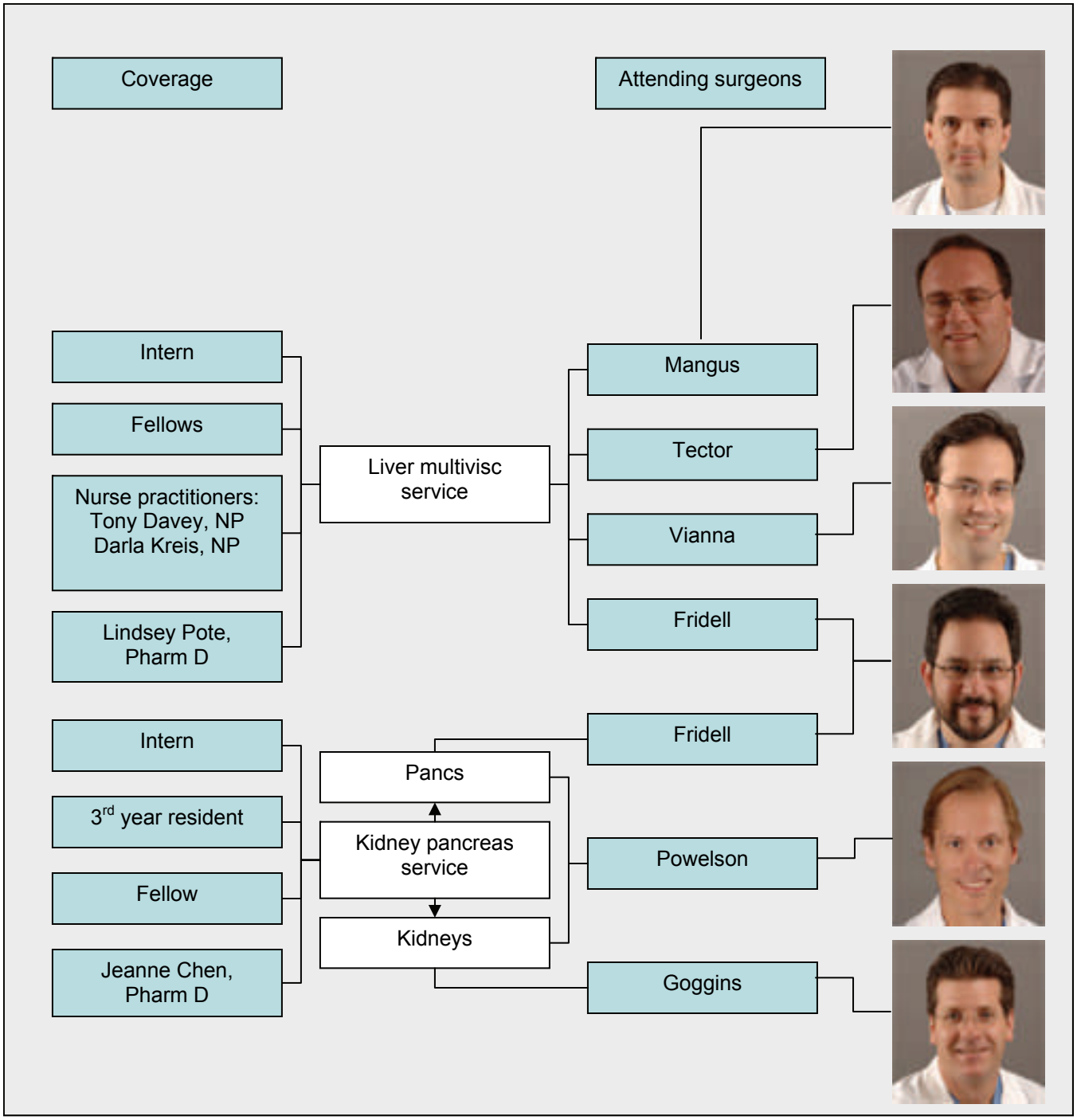
***Progress notes*:** Attendings write them.

***History and physicals*:** Residents, fellows if no resident

Discharge summaries: Must be completed on discharge day. Please note that delinquent discharge summaries lead to attending OR privilege suspension.

IU Transplant national rank by volume

- Pancreas program (kidney/pancreas and pancreas alone) : ……..….# 1
- Intestine program : ……..….# 1
- Abdominal program (pancreas, intestine, liver and kidney) : ……..….# 3
- Liver program:……. ……...# 7
- Kidney program : ……...#12



Approach to the transplant patient

For more detailed information, go to:

www.asts.org/FellowshipTraining/ResidentEducation/Resident1.aspx

Excellent educational series are available (log in under "INIM" as center).

In most surgical patients, the goal is to harness the body's natural healing power, intervening at critical points, but mostly stepping aside and letting nature do its thing. In transplant surgery, that approach would surely fail, since the natural response is to reject the organ. So things are much more complicated with transplant patients.

Nevertheless, there are three general areas to consider when caring for these patients.

Allograft Status

No matter what's going on, this is key —even if the problem at hand does not appear to be related to the allograft.

I have had many calls from residents about, say, pneumonia on a kidney transplant patient. But when I ask about the creatinine, the resident will say "let me check". That should never happen. No matter what the issue, always know the allograft status.

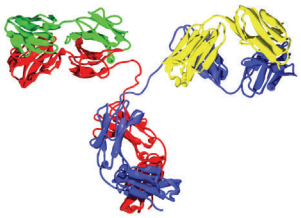
Associated Disease

Know the common associations:
Kidney patients often have heart disease and hypertension. Diabetics (panc patients) have GI issues (gastroparesis, neuropathic bowel)

If patients have a problem, go with common things. They'll be commonly present.

Immunosuppression

Each medication has predictable side-effects, so knowing the patient's immunosuppression is key. Also, immunosuppressed patients are susceptible to different infections at different time periods. Knowing that can point to a diagnosis. (more on immunosuppression and infections later).



Transplant immunology

For more detailed information, go to:

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Overview

Following is a brief, very basic introduction to immunology as it applies to transplantation. In many ways, it's an oversimplification, because immunology is very complicated. But it'll give you a general way of thinking about it and clinical issues that derive from it.

Immunology and Transplant Immunology:

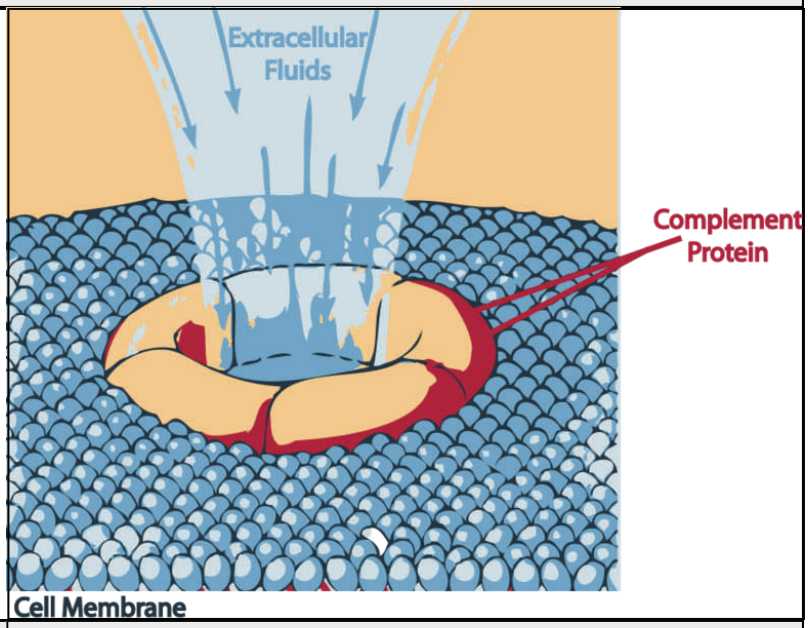
We are under attack by bacteria, viruses, fungi, parasites and cancers. The immune system provides us with protection from these invaders. Basically, they're all considered non-self and whatever is non-self, the immune system tries to get rid of.

In transplantation, we're transplanting non-self organs. Not surprisingly, the immune system attacks —rejects—these organs. Nevertheless, the immune system does not have a specific module for rejection. Rejection is a coincidental by-product of the normal functioning of the immune system. In addition, the violence of the rejection reaction, in comparison to a reaction to an infection, begs for an explanation. The answer to that conumdrum —basically how the MHC/HLA system works —should be clear after you read this.

Approach:

Transplant immunology is the normal immune reactions as applied to a transplanted organ. So we will look at the major actors of the immune system, from the most primitive (complement) to the most recently evolved (T cells) and outline how this works.

Complement



The complement system is the grenade of the immune system. If you set it off, it'll blast away whatever it touches. But it's pretty indiscriminate.

Complement is a system of small proteins found in the blood. When stimulated, it results in a biochemical cascade with positive feedback that creates a cell-killing membrane attack complex.

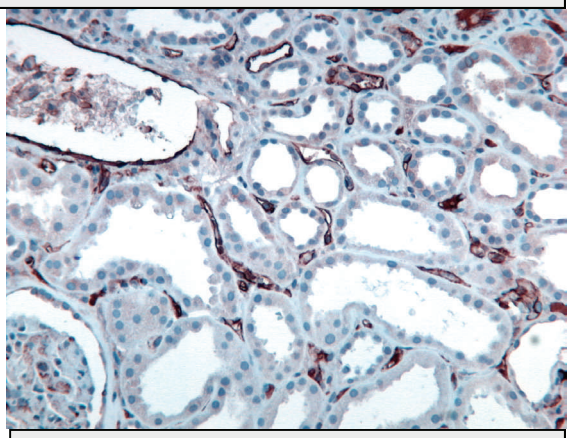
Complement is a primitive part of the immune system that is not adaptable (like humoral or cell-mediated immunity).

Complement in transplantation

Complement doesn't come up much clinically in classical transplantation. However, it's one of the major barriers to **xenotransplantation:** xenoorgans can activate complement, leading to immediate rejection.

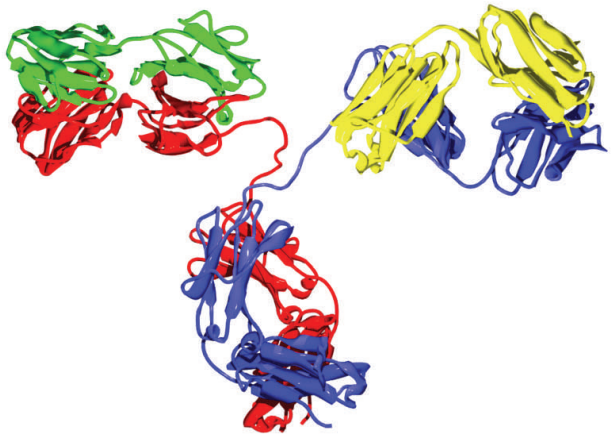
Complement is largely synthesized by the liver. Dr Tector has shown that the acutely failing liver tends to be unable to make complement. Therefore, he believes that xenotransplantation could be easier in fulminant hepatic failure.

Stay tuned….



C4d staining. Complement is activated by antibodies. So when humoral rejection occurs (antibodies attacking allograft), the reaction is detected by staining the C4d complement protein that provides indirect —but very specific— evidence for antibody attack. The above picture shows a kidney graft undergoing humoral rejection. C4d , a complement protein is stained. C4d is present because it is attached to antibodies.

Antibodies in transplantation



Antibodies are produced by B-cells, are in lymph nodes and can also circulate freely. They have specific binding sites. There's a huge variety, around 10^8 .

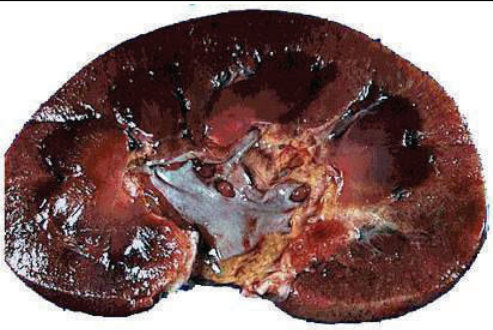
Immunosuppressants don't work on antibodies

Most of the medications we give in transplantation affect cellular metabolism and enzymes. Since antibodies are not cells, immunosuppressive medications are not very effective.

Cross match

The easiest approach to this problem is to simply avoid doing transplants in patients who have preformed antibodies against the planned allograft. This is the purpose of the crossmatch. Positive crossmatch means antibodies are present.

Antibody-mediated rejection types



Hyperacute rejection (above)

If the patient has pre-existing antibodies in circulation reperfusion of the organ is immediately followed by a very dramatic reaction; the kidney turns black, thromboses and immediately necroses.

Humoral rejection

Similar to hyperacute rejection, in that antibodies are deposited in kidney (see section on complement for picture). However, the reaction is less violent and can be reversed.

Chronic rejection

Despite immunosuppression, antibodies against a transplanted allograft are induced and cause a low grade chronic injury to the allograft. Over time, this results in gradual failure. (Chronic rejection is not well understood and likely has other mechanisms besides antibody-mediated injury).

Desensitization

For years, *positive cross-match* meant *no transplant*. There are now ways of reducing the antibody count enough to allow transplantation. The caveat is that this has to be a scheduled transplant (ie living donor) because the transplant is the culmination of the antibody reduction. If antibodies are reduced with plasmapheresis and no transplant occurs, a rebound almost always takes place and the patient is worse off.

Steps in desensitization
(also treatment of humoral rejection):

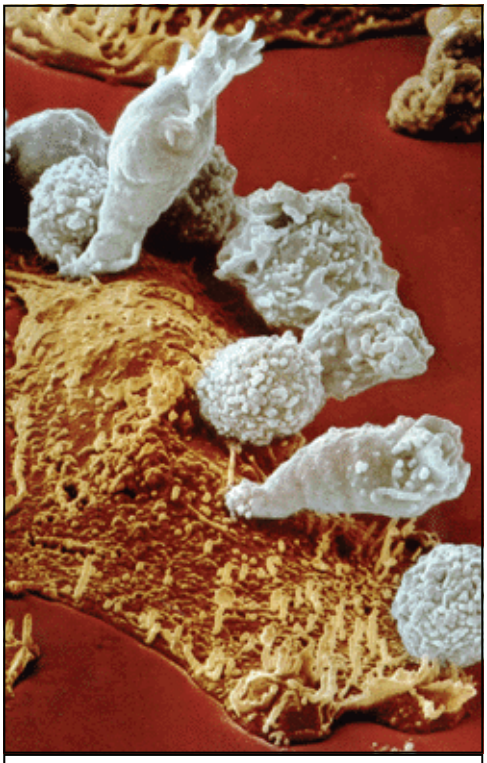
- Plasmapheresis: reduces antibody titers by mostly by dilution. This is performed serially for around 5 seesions, until a low titer is achieved.
- IVIg. Probably works with a combination of dilution and by binding lymphocytes
- Rituxan. Monoclonal antibody targeting B-cells, the producers of antibodies.
- Rarely splenectomy

Panel Reactive Antibody (PRA)

Blood test performed on patients waiting for kidneys. Measures anti-human antibodies in the blood. The PRA score is given as a percentage and can be from 0% to 99%. The PRA represents the percentage of the U.S. population that the anti-human antibody reacts with.

Someone is "highly sensitized" if they have high PRA (>20%). The higher the PRA, the longer the wait on the list.

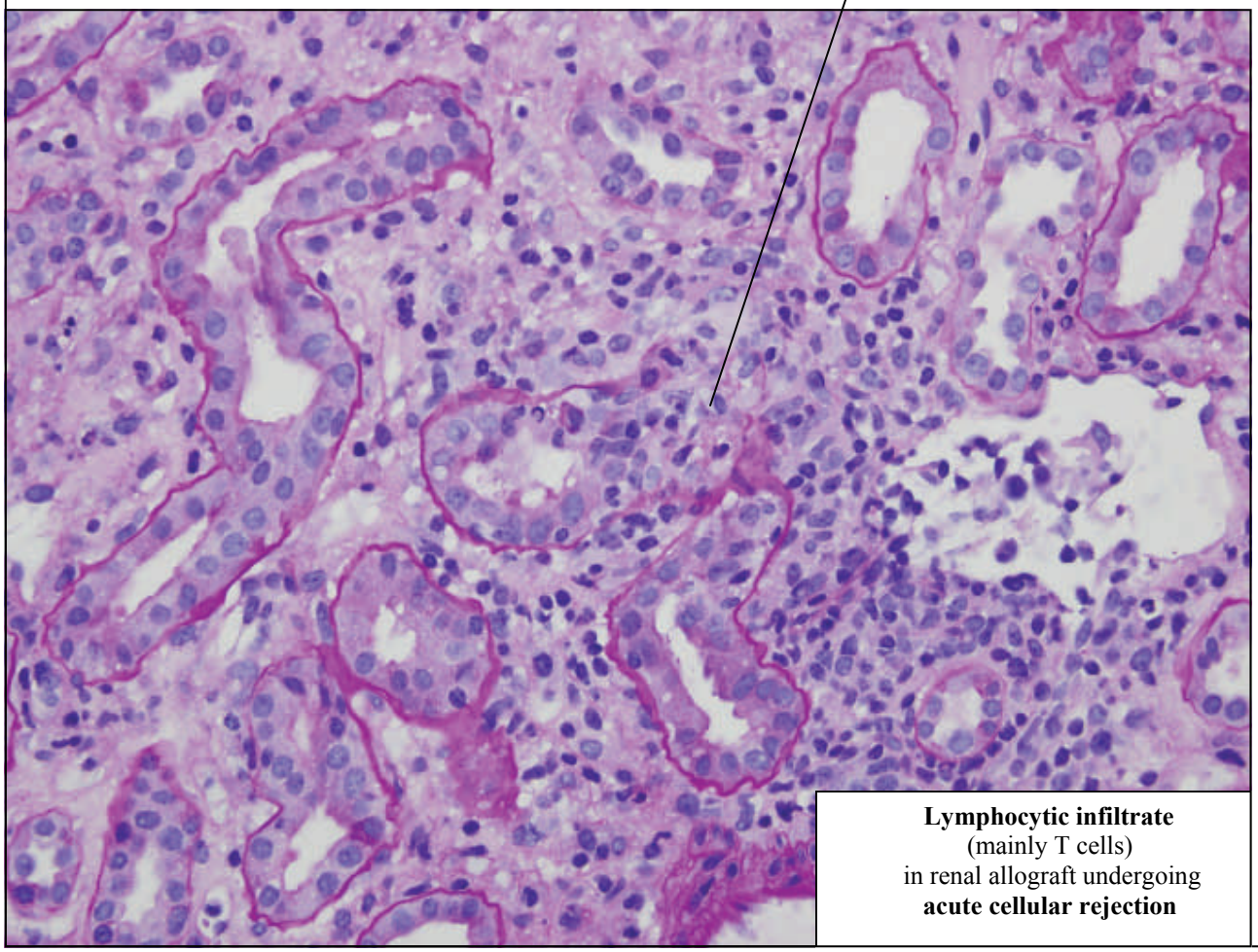
T cells in transplantation



T cells attacking a cell

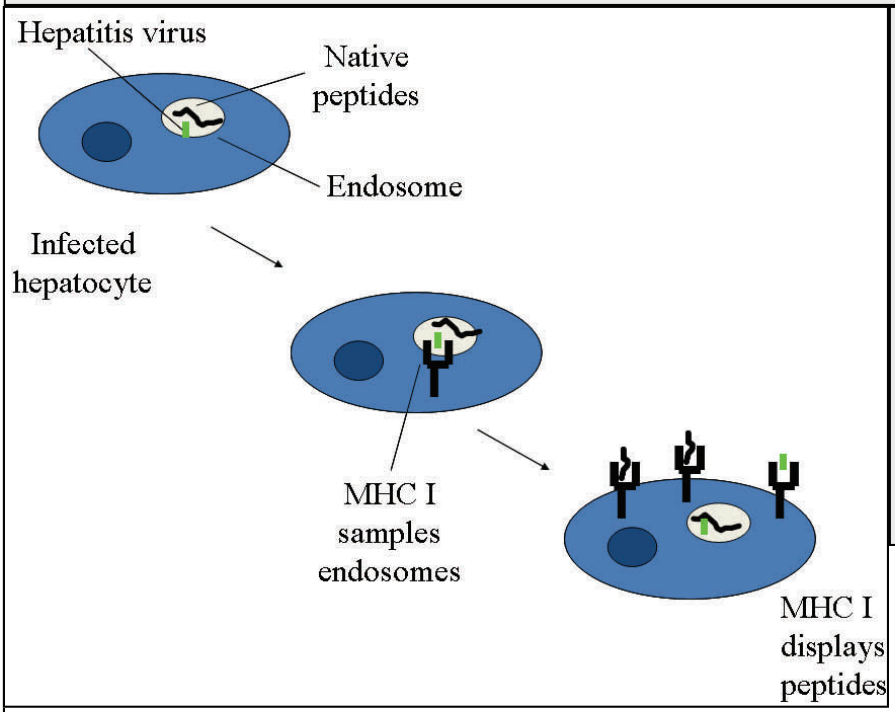
T cells are the **central actors in acute cellular rejection** which is mainly an consequence of cellular immunity (as opposed to humoral immunity which is the province of antibodies).

Tubulitis
(lymphocytes within boundary of tubular basement membrane). Tubule is losing basement membrane integrity due to inflammation



Lymphocytic infiltrate
(mainly T cells)
in renal allograft undergoing
acute cellular rejection

T cells and MHC

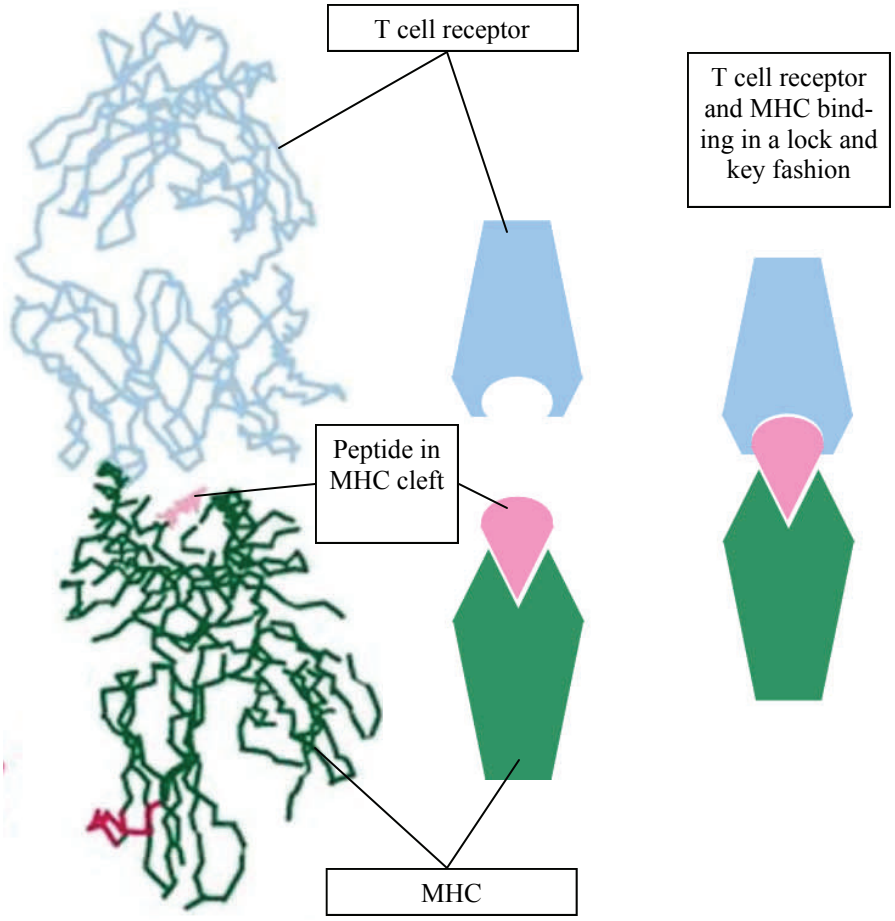


Endosomes inside a cell (in this case a liver cell) break down proteins and deliver the resultant peptide to the MHC molecule.

The MHC displays the peptide on the cell surface.

The MHC peptide combination, if not infectious, is ignored. If infectious, it is a target for the T cell receptor.

Non immune cells have MHC I which bind CD8 T cells; immune cells have MHC II, which bind CD4 cells.



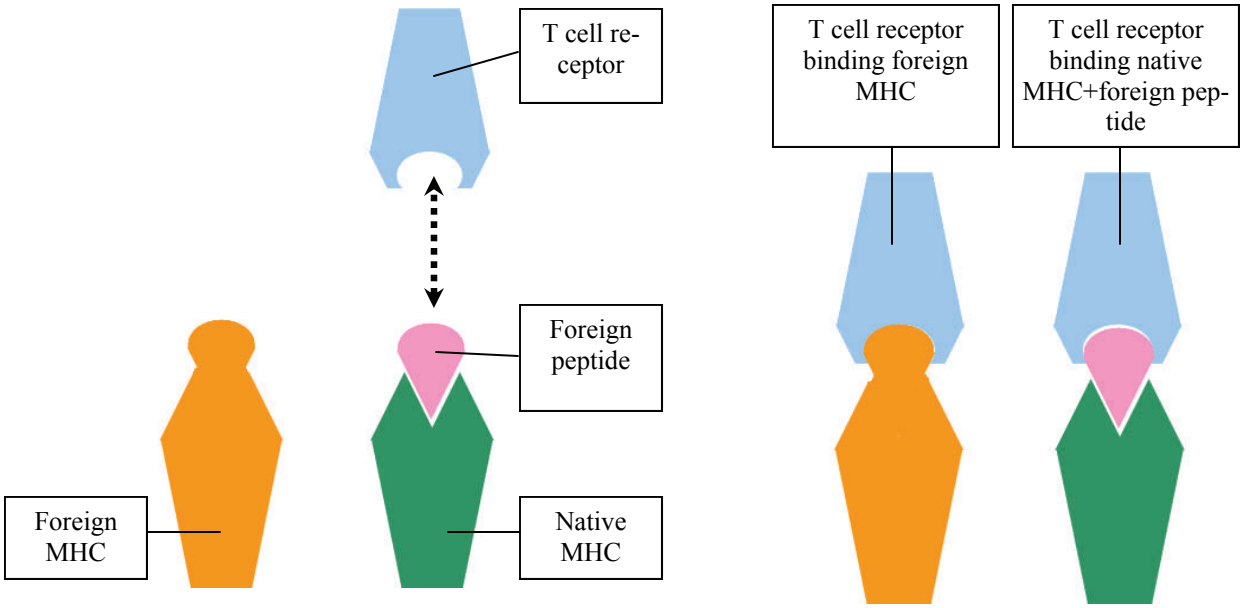
MHC
Major Histocompatibility Complex

The binding of the T cell receptor to the MHC + peptide is highly specific, like a lock and key.

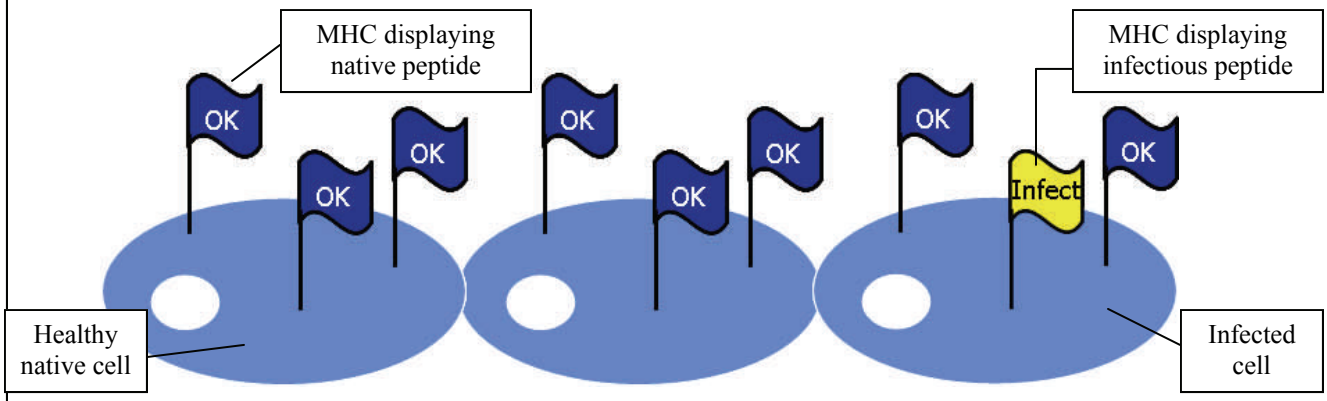
In the case of humans, MHC is called HLA

HLA= Human Leukocyte Antigen

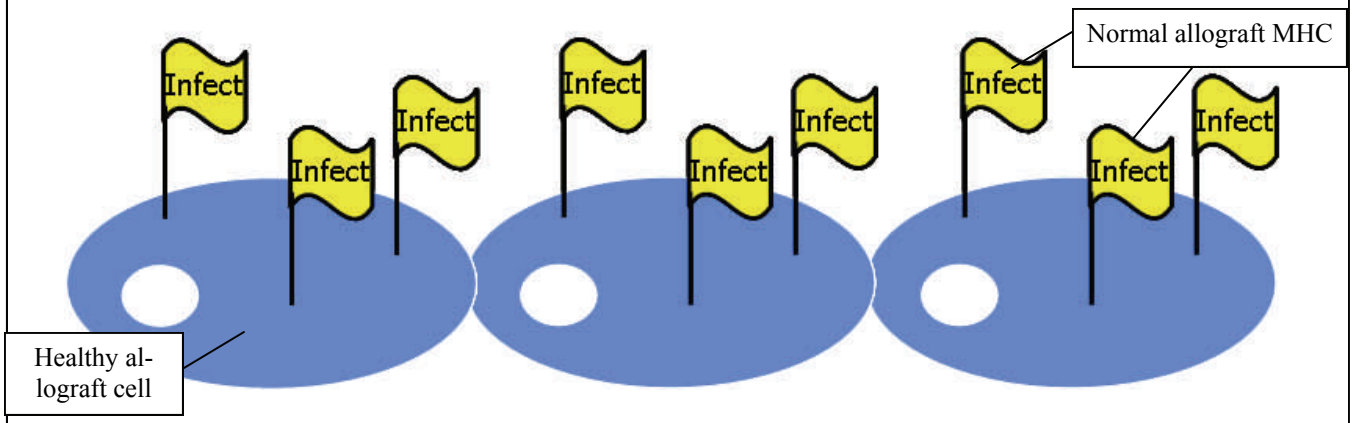
Why are allografts so immunogenic?



Native MHC + foreign protein is the normal incompatibility target for the T cell receptor. However, foreign MHC can be equally incompatible and therefore be a target for the T cell receptor. MHC is highly polymorphic. The degree of incompatibility of the MHC molecule can be assessed by HLA typing (HLA = MHC for humans).



The MHC molecule is like a flag that displays to outside the cell the health of inside the cell. In this case, one native cell is infected, so it displays a non-native infectious peptide and becomes a target of the T cell receptor.



In the case of an allograft, every single MHC looks like an infection to the T cell. This is far more immunogenic than an infection of a native organ, which explains the magnitude of the acute cellular rejection response.

Transplant immunosuppression

For more detailed information, go to:

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Overview

Since cellular immunity (T cells) is responsible for acute cellular rejection, transplant immunosuppression is largely focused on modulating the the T cell response.

There are three stages of immunosuppression in transplantation:

1. induction:

This refers to a brief and intense course of early immunosuppression given primarily to deplete T cells. The idea is that the T cells clones activated by the transplant are eliminated, leading to the possibility of a long lasting effect, even after inducution is complete.

Induction agents tend to be T cell depleting, and include thymoglobulin and campath (alentuzumab). They are designed for a brief, single course.

2. maintenance:

Induction agents have long-standing effects but they don't induce tolerance, so maintenance immunosuppression is required. These are agents like prograf, cellcept and rapamune which affect cellular metabolism and as a result impair cellular immunity.

3. Treatment of rejection

If rejection occurs, then the immune system has to be tamped down (steroid pulses) and T cells beaten back (thymoglobulin)

Infections

In the early years, transplant patients died of numerous infections, because immunosuppression was global. With more focused immunosuppression that targets T cells, infections controlled by T cells (mainly viruses like EBV and CMV) are the main threat.

Immunosuppressive agents

These are described in the order that they are used clinically at IU.

Thymoglobulin:

T cell depletion=> used for induction and acute cellular rejection treatment

Anti-T cell rabbit derived antibodies. It is used for induction or rejection treatment because it depletes T cells. It stops working after prolongued administration.

Thymoreaction like sepsis syndrome

Initial administration causes lysing of t cells and release of cytokines. Not surprisingly then, this can cause a syndrome similar to sepsis (sepsis syndrome is largely cytokine mediated): fever, hypotension, ARDS. The pulmonary complication is more likely is the patient is fluid overloaded. To prevent this, the initial thymoglobulin administration is one with high dose steroids, Tylenol and Benadryl.

Fever also often occurs around the last dose or two of thymo. This is not usually associated with a full blown reaction and is therefore likely a different mechanism.

Thymo can be very caustic is it extravasate. It is therefore given, if possible, through a central line. The fever that occurs after 5 days of thymo can also be due to a line infection.

Simulec (basiliximab):

Binds T Cell receptor for IL2

Interleukin 2 plays a central role in T cell activation, so activated T cells have an IL2 receptor (CD25, the T cell activation antigen, or TAC). Anti Tac monoclonal antibodies like simulec are therefore excellent induction agents because it specifically impairs the T cells that are activated by the allograft.

Corticosteroids: too many side-effects to be used routinely

Solumedrol and prednisone:
(solumedrol is IV, prednisone is PO)

While steroids used to be the mainstay of immunosuppression, they have widespread undesirable effects beyond the immune system (diabetes, osteoporosis, weight gain, cataracts). Even in the immune system, they are very broad in their effect; as a result, they tend to be associated with all kinds of infections (fungi, bacteria, viruses; steroids are associated with hepatitis virus reactivation for are avoided as much as possible in liver transplantation).

As a result, modern immunosuppression avoids steroid use in favor of agents directed more specifically at the part of the immune system (t cells) responsible for rejection.

Nevertheless, steroids are still used for specipic purposes:

Thymoglobulin administration;
Thymoglobulin can be associated with a violent reaction due to activation of the immune system. Solumedrol is used as an anti-inflammatory prevent that reaction.

Steroid taper: the classic transplant is performed with high dose steroids in part for thymo, in part to knock out the immune system. On the kidney service, this is done as a 5-day wean with prednisone. On the pancreas service, we dropped the wean in favor of two solumedrol doses upfront.

Acute rejection treatment:
Acute rejection can be treated with three solumedrol pulses (500mg IV QDx3), sometimes followed by a prednisone taper.

Maintenance immunosuppression:
Sometimes, when other agents are associated with bad side effects, prednisone is used for maintenance. This is rare nowadays.

Maintenance immunosuppression is like cancer chemotherapy: several agents are used for an additive effect on the immune system. But each can be used in combination at a lower level than as a single agent; a lower dose has fewer side effects.

The three maintenance agents (prograf, cellcept and rapamune):

Prograf, rapamune and cellcept are the principal maintenance agents. Prograf is the main one:if at all, possible, this one is used. Most kidneys are also on cellcept. Kidney pancreas patients are on rapamune instead of cellcept because cellcept causes a lot of GI toxicity, which is common problem with diabetes.

If neither cellcept or rapa is tolerated, some patients go on imuran, an older antimetabolite.

Prograf (Tacrolimus, FK 506), cyclosporin:

These drugs are known as calcineurin inhibitors. They bind to the immunophilin FKBP1A, followed by the binding of the complex to calcineurin. Calcineurin is involved involved in cellular replication (in helping the transition from G_0 to G_1 part of the cell cycle). Both are used for maintenance immunosuppression (usually prograf).

Kidney transplant patient on prograf comes in with higher creatinine. What do you do?

This is the classic conundrum of kidney transplantation. If there's rejection, you should raise Prograf levels, if prograf toxicity, you should decrease levels.

Frequently, a biopsy is required to settle the issue.

In practice, the patients undergoes hydration and the prograf level is checked. If level normal and creat still up, then biopsy.

Prograf is considered the more potent drug, so is mainly used. Side effects for both drugs include renal failure, hyperkalemia, hypertention, which obviously complicates the management of kidney transplant patients.

Prograf tends to cause more neurologic issues like seizures and tremors, than cyclosopin. Cyclosporin can cause gingival hyperplasia. Prograf causes hair loss, cyclosporin causes excess hair.

Both drugs require monitoring of daily levels. Various drugs increase levels (like fluconazole ketokonazole, and erythromycin); other drugs decrease levels (dilantin).

Some clinical states can change levels. Postop ileus can be associated by increased levels. Diarrhea and vomiting can lead to decrease levels.

Rapamycin (rapamune, sirolimus):

It binds to FKBP1A like tacrolimus, however the complex does not inhibit calcineurin but another protein, mTOR, preventing transition from G1 to S phase of the cell cycle. Therefore, sirolimus acts synergistically with tacrolimus. Sirolimus prevents B cell differentiation into plasma cells, reducing production of IgM, IgG, and IgA antibodies.

Rapamune, an antiproliferative agent.

Good: for cardiac stents, to prevent cancers.
Bad for wound healing, may cause hernias.

Rapamune is in large part an antiproliferative agent. It is used for example cardiac stents to prevent intimal hyperplasia. It can also slow some cancers: if a transplant patient has a lot of skin cancerr s a switch to rapamume can help clear them. In the case of wound healing, however, this effect is detrimental. For that reason, sirolimus may in fact be associated with incisional hernia. Therefore, is a transplant patient undergoes a hernia repair, if possible, rapamune is discontinued and replaced by something else (usually cellcept).

Rapamune can sometimes potentiate the nephrotoxic effect of calcineurin inhibitors, so this can become an indication for changing it.

Finally rapamune is known to cause hyperlipidemia.

Cellcept (mycophenolate mofetyl):

Cellcept: lots of GI side-effects

Mycophenolic acid acts as a non-competitive, selective, and reversible inhibitor of Inosine-5′-monophosphate dehydrogenase (IMPDH), which is a key enzyme in the de novo guanosine nucleotide synthesis. In contrast to other human cell types, lymphocytes B and T are very dependent on this process so this is a good agent for maintenance immunosuppression.

Cellcept is used for kidney transplant patients in combination with prograf. As mentioned for kidney pancreas patients, rapamune is used instead of cellcept. However, pancreas alone

patients tend to have more rejection. So they get a triple drug regimen: prograf, rapamune and half dose cellcept.

All bone marrow cells, not just lymphocytes, are affected by cellcept. So anemia and leucopenia are predictable side-effects and sometimes require aranesp or neupogen administration to boost marrow production.

Cellcept is the new and improved imuran

Imuran is much more likely than cellcept to cause anemia and leucopenia.

Cellcept is known to cause GI issues (nausea, vomiting, diarrhea, constipation).

Imuran, azathioprine

interferes with the synthesis of purines (adenine and guanine), which is required for DNA synthesis. Fast-growing cells, including T-cells and B-cells, are particularly affected by the inhibition of purine synthesis.

Cellcept is a new and improved imuran. Because cellcept affects a denovo pathway, it is more specific to activated T and B cells. Imuran is not used much anymore.

Rituxan (rituximab)

Rituxan uses:

- Desensitization
- Humoral rejection
- PTLD (B cell lymphoma)

Anti CD20 monoclonal antibody. CD 20 is mostly found on the surface of B cell, so this a good agent for B –cell mediated phenomena. It's therefore used for desensitization and in the treatment of humoral rejection. There is some evidence that chronic rejection is antibody mediated.

Finally most post transplant lymphoproliferative disease (PTLD) is CD20 positive (ie B cell proliferation). Riuxan is therefore used for that as well.

Liver Multivisceral Rotation

Members:

- One intern
- Fellows (currently three)
- Two nurse practitioners:
    1. Tony Davey, NP
    2. Darla Kreis, NP
- Lindsey Pote, Pharm D.

Rounds:

Once a day with entire team and whichever attending is covering.

PM rounds: team usually meets with fellow in PM to go over day's events and results

Intern Duties:

- Write orders, TPN
- Implement orders (contact consults, arrange for studies)
- Look up results and report to team
- Go over all consults and report to team
- bedside procedures (wound care, lines etc…) under fellow supervision
- History and physicals
- Discharge summaries. These must be dictated on day of discharge.

Division of Labor:

Depending on the number of nurse practitioners and fellows, the ICU, floor and Riley are divided up. This varies.

OR Coverage:

The transplant operations are generally covered by the fellows. However, the intern will typically cover fascial closures, which is a good opportunity to learn how to close an abdominal wound.

Resources for Intern

- Tony Davey has been around for years. He knows exactly what the attendings want. He's a good resource to run things by.
- Darla Kreis is in a similar role, though more recent addition.
- Lindsey Pote, Pharm D. Almost all med orders should be run by her.

Progress Notes

Written by the attending (How sweet is that?). Residents do history and physicals, however.

Discharge Summaries

All discharge summaries must be dictated on the day of discharge. (if dictation are delinquent, the attending get privileges yanked, so this becomes very bad for resident).

Who dictates: Whoever operates on the patient dictates the D/C summary: the fellow will do most transplants, the third year resident other cases, and the intern will dictate nonoperative admissions.

Pointers for fast dictation:

- These do not have to be done in exhaustive detail. A quick list of the procedures and major events of the hospitalization is all that's needed.
- Look at the most recent progress note. Some of them have a running list of events during the hospitalization. This simplifies dictation.

Liver
Intestine
Multivisceral
Protocols

Liver alone (no kidney)

No immunosuppression x48hrs

Rationale
The liver is relatively resistant to rejection. Delaying immunosuppression allows for anti-donor clonal expansion. Starting immunosuppression at 48 hrs can then theoretically wipe out these clones.

Preop

No immunosuppression

Antibiotic prophylaxis
Unasyn 3 g IVon call to OR
If PCN allergy = anaphylaxis:
Ciprofloxacin 400 mg IV
Vancomycin 1000 mg IV
Fluconazole 200 mg IV on call to OR

First 48 hours Postop:
(48 hrs from time of graft reperfusion)

No immunosuppression

Antibiotic prophylaxis
Unasyn 3 g IVPB q 6 hrs x 48 hrs
if PCN allergy:
Ciprofloxacin 400 mg IV q 12 h
Vancomycin 1000 mg IV q 12 h
Fluconazole 200 mg IVPB qd x 48 hrs

GI
Pepcid 20 mg IV q 12 hrs
When taking po:
Zantac 150 mg po q hs \

Or

Nexium 40 mg IV q 24 hrs
When taking po:
Nexium 40 mg po once daily

Solumedrol and thymo premedication

Solumedrol is a steroid immunosuppressant, of course, and therefore plays a role in preventing rejection. In addition, as an anti-inflammatory agent, it prevents or blunts the thymo reaction. Tylenol and benadryl are also given as anti-inflammatory agents against the thymo reaction

Thymoglobulin

Made from antibodies against rabbit thymus. Therefore an anti-T lymphocyte agent. Since T lymphocytes are the principal actors in rejection, thymo is a potent immunosuppressive agent.

Thymo reaction

By lysing T-cells, thymo causes the release of cytokines, which can precipitate a violent reaction. The syndrome resembles sepsis, with which it shares a similar mechanism: fever, hypotension (from vasodilatation) and pulmonary edema (from leaky capillaries, like ARDS). Thymo pulmonary edema is more likely in the fluid overloaded state

Prograf

Anti-T cell agent used for maintenance immumnosuppression (T cells are the principal actors in rejection). Prograf is the mainstay of long-term immunosuppression.

Rituxan

Anti-B cell agent. Used to prevents anti-donor antibody formation and thus reduce chronic rejection. Also used in B-cell lymphoma treat-

Starting 48 hrs postop:
(48 hrs from time of graft reperfusion)

POD 2

30 minutes prior to thymo:

- **Solumedrol** 500 mg IV (30 min prior to Thymo)
- Tylenol 650 mg
- Benadryl 25 mg

Thymoglobulin

- 150 mg IV over 6-8 hours
- If pt < 60 kg, give 2 mg/kg (rounded to nearest 25 mg)

Start Prograf

- Start at 2 mg po BID
- Order Prograf levels q AM
- Target trough = 6-8 ng/mL by POD 7.

POD3

Rituxan 150 mg/m^2 on POD 3

- Initial infusion rate at 50 mg/hr. If no hypotension or other infusion-related reactions, may increase by 50 mg/hr Q 30 min to max rate of 400 mg/hr.
- Monitor temp Q hr during infusion.
- Monitor BP, RR, HR:
  q 15 min x 60 min, q 30 min

POD4

30 minutes prior to thymo:
- **Solumedrol** 250 mg IV
- Tylenol 650 mg
- Benadryl 25 mg

Thymoglobulin (same as initial dose)

POD 6

30 minutes prior to thymo:
- **Solumedrol** 125 mg IV
- Tylenol 650 mg
- Benadryl 25 mg

Thymoglobulin (same as initial dose)

When tolerating PO:
- ASA chewable 81 mg po daily
- **Septra** SS 1 tablet po daily
- **Valcyte** 900 mg po daily
  adjust for renal function
  (CrCl < 60 or age >65 yrs)
- Colace 100 mg po BID
- MVI po daily

Septra (bactrim)

Prevents PCP

Valcyte (valgancyclovir)

Antiviral agent.
T-cells, being the principal agents of rejection, are the main target for immunosuppression. However, T cell mediated immunity is the main protection against viruses of the herpes family (CMV, EBV, VZV, HSV). Since T-cell mediated immunity is impaired by transplant immunosuppression, antivirals are added at the time of maximal immunosuppression (first months and during rejection treatment) to prevent activation or reactivation of these viruses.

Liver and kidney

Preop

No immunosuppression

Antibiotic prophylaxis
Unasyn 3 g IVon call to OR
If PCN allergy = anaphylaxis:
Ciprofloxacin 400 mg IV
Vancomycin 1000 mg IV
Fluconazole 200 mg IV on call to OR

Postop:

Antibiotic prophylaxis
Unasyn 3 g IVPB q 6 hrs x 48 hrs
if PCN allergy:
Ciprofloxacin 400 mg IV q 12 h
Vancomycin 1000 mg IV q 12 h
Fluconazole 200 mg IVPB qd x 48 hrs

GI
Pepcid 20 mg IV q 12 hrs
When taking po:
Zantac 150 mg po q hs \

Or

Nexium 40 mg IV q 24 hrs
When taking po:
Nexium 40 mg po once daily

Solumedrol and thymo premedication

Solumedrol is a steroid immunosuppressant, of course., and therefore plays a role in preventing rejection. In addition, as an anti-inflammatory agent, it prevents or blunts the thymo reaction. Tylenol and benadryl are also given as anti-inflammatory agents against the thymo reaction

Thymo reaction

By lysing T-cells, thymo causes the release of cytokines, which can precipitate a violent reaction. The syndrome resembles sepsis, with which it shares a similar mechanism: fever, hypotension (from vasodilatation) and pulmonary edema (from leaky capillaries, like ARDS). Thymo pulmonary edema is more likely in the fluid overloaded state

Thymoglobulin

Made from antibodies against rabbit thymus. Therefore an anti-T lymphocyte agent. Since T lymphocytes are the principal actors in rejection, thymo is a potent immunosuppressive agent.

Prograf

Interferes with T cell function, used for maintenance immumnosuppression (T cells are the principal actors in rejection). Prograf is the mainstay of long-term immunosuppression.

Cellcept

Inhibits with activated lymphocyte proliferation. Used for long-term immunosuppression.

POD 1

30 minutes prior to thymo:

- **Solumedrol** 500 mg IV (30 min prior to Thymo)
- Tylenol 650 mg
- Benadryl 25 mg

Thymoglobulin

- 150 mg IV over 6-8 hours
- If pt < 60 kg, give 2 mg/kg (rounded to nearest 25 mg)

Start Prograf

- Start at 2 mg po BID
- Order Prograf levels q AM
- Target trough = 6-8 ng/mL by POD 7.

Start Cellcept

- 1000 mg po BID
- 500mg PO BID if recipient HCV+

Rituxan

Anti-B cell agent. Used to prevents anti-donor antibody formation and thus reduce chronic rejection. Also used in B-cell lymphoma treat-

POD2

Rituxan 150 mg/m^2 on POD 3
- Initial infusion rate at 50 mg/hr. If no hypotension or other infusion-related reactions, may increase by 50 mg/hr Q 30 min to max rate of 400 mg/hr.
- Monitor temp Q hr during infusion.
- Monitor BP, RR, HR:
  q 15 min x 60 min, q 30 min

POD3

30 minutes prior to thymo:
- **Solumedrol** 250 mg IV
- Tylenol 650 mg
- Benadryl 25 mg

Thymoglobulin (same as initial dose)

POD 5

30 minutes prior to thymo:
- **Solumedrol** 125 mg IV
- Tylenol 650 mg
- Benadryl 25 mg

Thymoglobulin (same as initial dose)

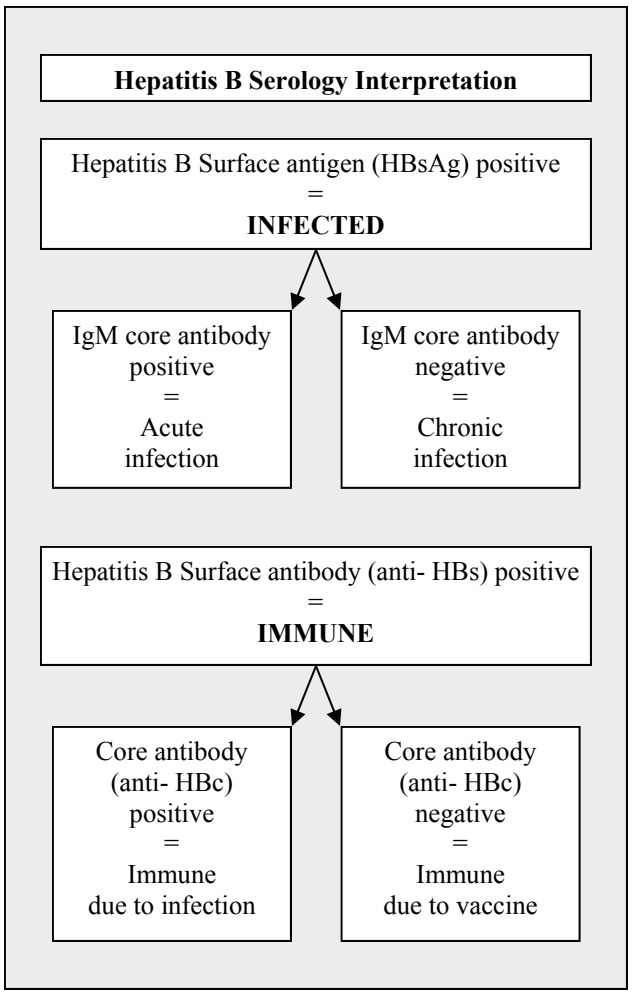
Septra (bactrim)

Prevent PCP

When tolerating PO:
- ASA chewable 81 mg po daily
- **Septra** SS 1 tablet po daily
- **Valcyte** 900 mg po daily
  adjust for renal function
  (CrCl < 60 or age >65 yrs)
- Colace 100 mg po BID
- MVI po daily

Valcyte (valgancyclovir)

Antiviral agent.
T-cells, being the principal agents of rejection, are the main target for immunosuppression. However, T cell mediated immunity is the main protection against viruses of the herpes family (CMV, EBV, VZV, HSV). Since T-cell mediated immunity is impaired by transplant immunosuppression, antivirals are added at the time of maximal immunosuppression (first months and during rejection treatment) to prevent activation or reactivation of these viruses.



Hepatitis protocols

Hepatitis B
HBIG
(to be given within 72 hours post-txp)

Lamivudine 100mg PO once daily for life
HBIG 9,360 IU IV once daily x 7 days
Followed by HBIG 1560 IU IM once a month x 6 months

HBV core positive liver recipients

Lamivudine 100mg PO once daily for life

Intestine multivisceral protocol

Preop:

Isolated bowel recipients only
IV Ig 10% :
1 g/kg (round to nearest 5 g increment)

Highly sensitized patients only:
(Combined Class I and 2 PRA ≥ 100)
IV Ig 10%
2g/kg (round to nearest 5 g increment)

For all patients

Thymoglobulin 150 mg IV to OR (2 mg/kg round to 25 mg increment if wt < 60 kg)

Solumedrol 500 mg IV to OR

Antibiotic prophylaxis
Zosyn 3.375 g IVPB on call to OR
If PCN allergy = anaphylaxis:
Meropenem 500 mg IVPB
Vancomycin 1000 mg IVPB

Fluconazole 200 mg IV on call to OR

Solumedrol and thymo premedication

Solumedrol is a steroid immunosuppressant, of course, and therefore plays a role in preventing rejection. In addition, as an anti-inflammatory agent, it prevents or blunts the thymo reaction. Tylenol and benadryl are also given as anti-inflammatory agents against the thymo reaction

Thymoglobulin

Made from antibodies against rabbit thymus. Therefore an anti-T lymphocyte agent. Since T lymphocytes are the principal actors in rejection, thymo is a potent immunosuppressive agent.

Thymo reaction

By lysing T-cells, thymo causes the release of cytokines, which can precipitate a violent reaction. The syndrome resembles sepsis, with which it shares a similar mechanism: fever, hypotension (from vasodilatation) and pulmonary edema (from leaky capillaries, like ARDS). Thymo pulmonary edema is more likely in the fluid overloaded state

Prograf

Anti-T cell agent used for maintenance immumnosuppression (T cells are the principal actors in rejection). Prograf is the mainstay of long-term immunosuppression.

Rituxan

Anti-B cell agent. Used to prevents anti-donor antibody formation and thus reduce chronic rejection. Also used in B-cell lymphoma treat-

Postop:

Immunosuppression Protocol

Thymoglobulin
150 mg IV to OR (2 mg/kg round to 25 mg increment if wt < 60 kg), same as preop dose.

30 min prior to infusion:
premedicate with daily steroid dose, Tylenol 650 mg, and Benadryl 50 mg

Steroids:

POD 1:	Solumedrol	250 mg IV x 1 dose
POD 2:	Solumedrol	250 mg IV x 1 dose
POD 3:	Solumedrol	250 mg IV x 1 dose
POD 4:	Solumedrol	120 mg IV x 1 dose
POD 5:	Solumedrol	80 mg IV x 1 dose
POD 6:	Solumedrol	60 mg IV x 1 dose
POD 7:	Solumedrol	40 mg IV x 1 dose
POD 8:	Solumedrol	20 mg IV x 1 dose
POD 9:	Solumedrol	10 mg IV x 1 dose
POD 10:	Prednisone	10 mg PO Daily

Rituximab 150 mg/m^2 IV on POD 1
Initial infusion rate at 50 mg/hr. If no hypotension or other infusion-related reactions, may increase by 50 mg/hr Q 30 min to max rate of 400 mg/hr.

During infusion, monitor:
- temp Q hr .
- BP, RR, HR q 15 min x 60 min, q 30 min with each rate escalation , then q 60 min once max rate reached.

Prograf: Route/Dose will be determined by attending/fellow in OR.
J tube on day one (start with 2 mg BID)
Target level = 15-20 ng/mL.
All multivisceral trps should receive J tube administration of Prograf
Isolated bowel trps should receive J tube administration of Prograf until NG tube pulled, then
can switch to G tube or oral administration

Zenapax: 1 mg/kg (rounded to 25 mg increment) POD 21 and q month x 6-12 months
Given to all Isolated Bowel/Modified MVT
Multiviscerals: Zenapax only given if highly sensitized or increased creatinine

Additional IVIG on POD 18: **For "highly sensitized" pts only** (Combined Class I and 2 PRA ≥ 100!!!)
2 gm/kg (max 140 gm)

Antibiotic prophylaxis

Zosyn 3.375 g IV q 6 hrs x 10 days
if PCN allergy:
Meropenem 500mg IV q 12 h x 10 days
Vancomycin 1000 mg IV q 12 h x 10 days
Fluconazole 200 mg IVPB qd
At POD 7,
change fluconazole to 100 mg po/g tube QD

GI
Nexium 40 mg IV Q24H

*

Postop:

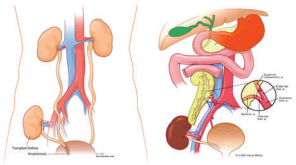
3. Based on donor and recipient CMV status –

- Ganciclovir 5 mg/kg IV Q 12 hrs (for D+/R-, D+/R+, and D-/R+)
- Ganciclovir 2.5 mg/kg IV Q12 hrs (for D-/R-)
- Cytogam 150 mg/kg/dose (round to 2.5 g increment) with 72 hours of OR,

Additional “Condiments” when tolerating PO

Septra ss tab or 10 ml suspension po/gtube QD
Valcyte 900 mg po/gtube QD – adjust dose for renal function
ASA chewable 81 mg po/gtube QD
MVI 1 tab po QD

*****Note: J tube to be used for feedings and Prograf administration only. All other meds must be administered either orally or through the gastric tube.**



Kidney Pancreas Rotation

Members

- One intern
- One third year resident
- One fellow
- Jeanne Chen, Pharm D

Rounds

Kidneys: Dr Goggins mostly rounding once a day —Dr Powelson covers when Dr Goggins is out of town and on half the weekends.

Pancs: Either Dr Fridell or Powelson round once a day. On most weekdays, the panc service meets at 3:30PM in Dr Powelson's office to go over the day.

Intern and Resident Duties

- Write orders, TPN
- Implement orders (contact consults, arrange for studies)
- Look up results and report to team
- Go over all consults and report to team
- bedside procedures (wound care, lines etc…) under resident or fellow supervision
- History and physicals
- Discharge summaries. These must be dictated on day of discharge.

OR Coverage

- Fellow has first dibs on OR coverage of transplant operations and laparoscopic living donation.
- Third year resident has first dibs on hernias, access surgery, and any transplant operation not covered by fellow.
- Intern is encouraged to come to the OR to close wounds, especially on Dr Powelson's cases. There are plenty of wounds to do subcuticular closures on, but you have to make yourself easily available.

Resources

- Jeanne Chen, Pharm D, has been around for years and knows exactly what the attendings want on almost any transplant issue. Good person to run things by.

Progress Notes

Written by the attending (How sweet is that?). Residents do history and physicals, however.

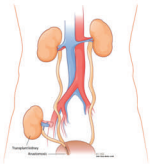
Discharge summaries

All discharge summaries must be dictated on the day of discharge. (if dictation are delinquent, the attending get privileges yanked, so this becomes very bad for resident).

Who dictates: Whoever operates on the patient dictates the D/C summary: the fellow will do most transplants, the third year resident other cases, and the intern will dictate nonoperative admissions.

Pointers for fast dictation:

- These do not have to be done in exhaustive detail. A quick list of the procedures and major events of the hospitalization is all that's needed.
- On the panc patients, the progress notes usually have a summary of the hospital course as it develops, Use that .



Kidney Transplantation

Why kidney transplantation?

A patient with kidney failure has two options:

- Dialysis
- Transplantation.

Both of these fall under the heading of *renal replacement therapies*.

Kidney Function

Despite their small size (about 10x5cm, and 150gm), the kidneys receive about 20% of the cardiac output. Their most obvious function is filtering the blood, but they have numerous other regulatory functions including:

- Blood pressure control
- Fluid and electrolytes
- Acid-base balance
- Calcium metabolism (also phosphorus and vitamin D)
- Red cell production (epogen).

Dialysis

Dialysis is life-saving if you have no kidney function. It works pretty well at filtering, though misses some molecules that the kidney would remove. However, even with careful medical management of blood pressure, calcium, epo etc… dialysis cannot fine tune as well as the kidney. In addition, dialysis requires access (line, fistula, graft, PD catheter) all of which come with complications.

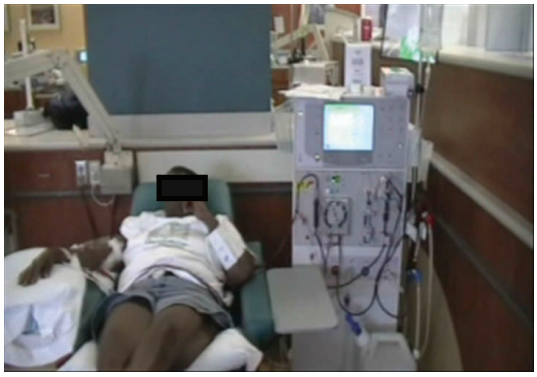
Transplantation

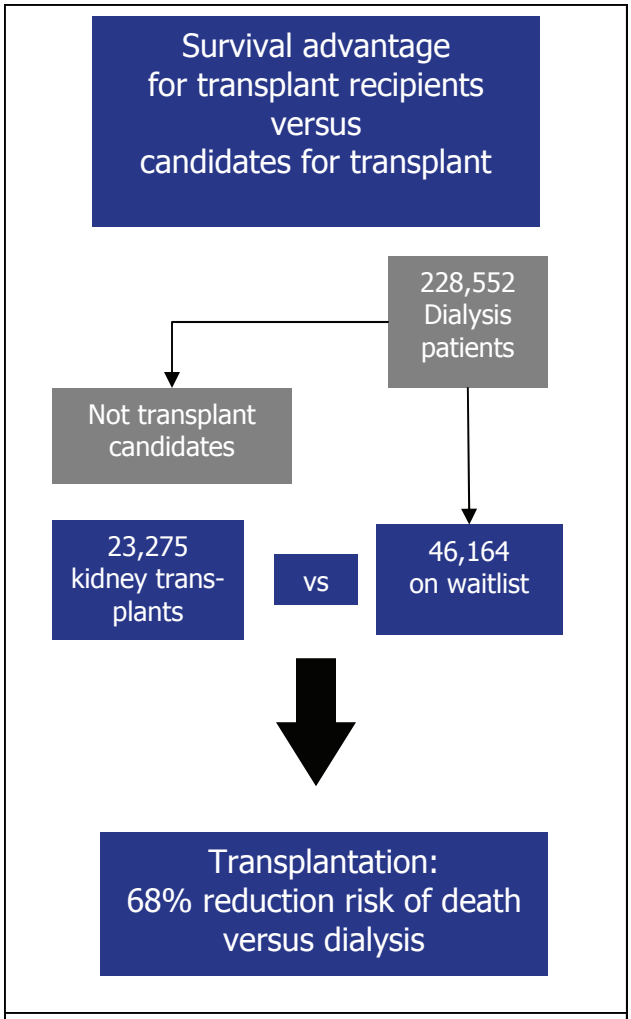
Transplantation results in normal kidney function. The price of admission is a large operation and immunosuppression.

Transplantation versus dialysis

Since transplantation requires a large operation up front, and since heart disease is common in renal failure patients, transplant patients require careful preoperative screening. Assuming a patient passes that screening, transplantation is better than dialysis on three counts:

- **Quality of life**. That transplantation leads to better quality of life has been shown in numerous parameters, but most transplant patients report a marked increase in energy.





The problem with comparing survival in dialysis patients versus transplant patients is that to be approved for transplantation, you need to be healthier than most dialysis patients; so better survival is expected in that healthier subgroup.

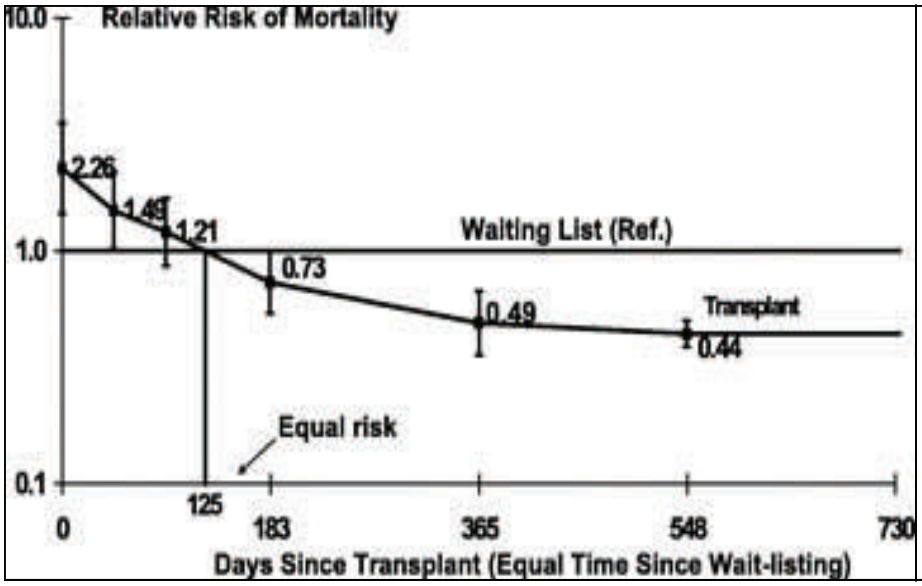
This study gets around that issue by taking the subgroup of dialysis patients on the waitlist: healthy enough to be transplanted but still on dialysis. A fair comparison group for transplantation, which leads to better survival than dialysis.

Kidney transplantation: Better survival than dialysis

Because dialysis tends to make you feel tired each dialysis day. Transplant patient will say a veil has been lifted.

- **Survival**. Transplantation leads to a survival benefit in all age groups, even the elderly, compared to dialysis
- **Quality of life**. Dialysis does not clear all the toxins cleared by a biologic kidney. These slowly accumulate and choke up the body, leading to complications like neuropathy. Dialysis is also very intermittent, leading to swings of energy level. Many dialysis patients feel tired for hours after dialysis. Not surprisingly, quality of life is better with a transplant.
- **Cost.** Transplantation is cheaper for Medicare than dialysis. Sure, the first year after transplantation is more expensive than dialysis, because of the operation. However, after that, and overall, transplantation is much cheaper.

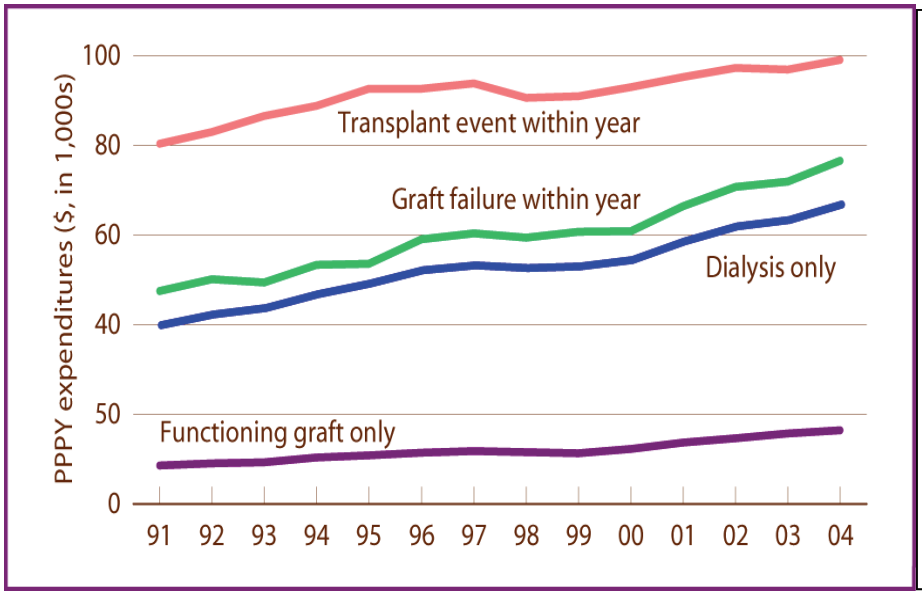
Transplantation: better for >70 year old



Mortality RR (95% CI) for 2078 first deceased donor kidney transplant recipients versus 5667 wait-listed dialysis patients older than 70 years of age.

Renal transplantation in elderly patients older than 70 years of age: results from the Scientific Registry of Transplant Recipients.Rao PS; Merion RM; Ashby VB; Port FK; Wolfe RA; Kayler LK. Transplantation. 83 (8):1069-74, 2007 Apr 27.

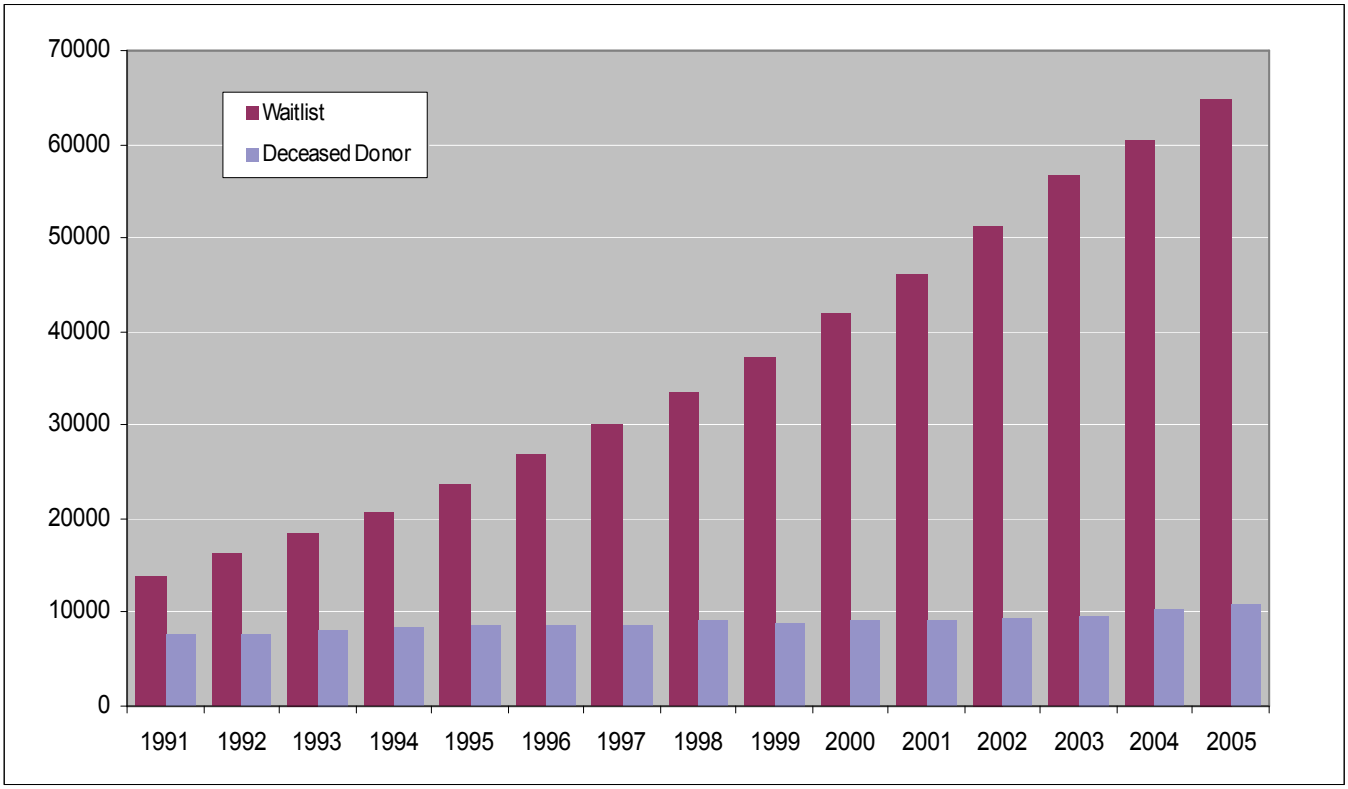
Transplantation: cheaper than dialysis



As long as the transplant lasts more than one year (which most do), it is a much cheaper treatment than dialysis.

USRD data.

Transplantation: victim of its success



Because transplantation is better than dialysis in all age groups, and because of an explosion in the incidence of renal failure in the US, more and more people are being listed for transplantation. Although the number of deceased donors is also increasing, it's not keeping up. As a result, candidates for transplantation are waiting longer and longer.

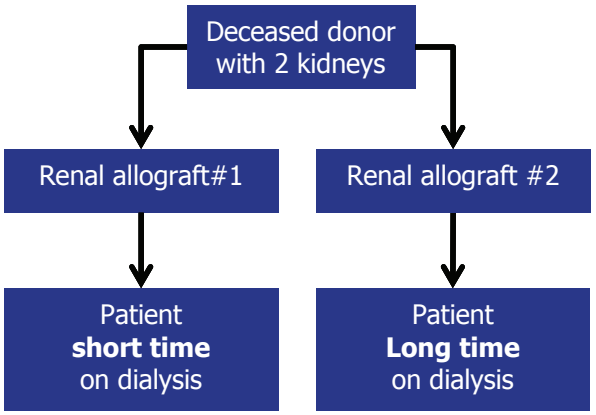
Who gets listed?

- Creatinine clearance < 20
- Free of cancer or infections (some exceptions like hepatitis C)
- Safe for surgery (generally means no cardiac disease)
- Psychosocial evaluation predicts compliance.

Kidney waitlist rules

- Separate listing by blood group
- Time waiting most important factor
- Geography important (local donors for local patients, generally)
- 0-HLA mismatch trumps time and geography (0-mismatch kidneys will be offered nationally before locally).
- Special lists: ECD (older kidneys, hep C) can shorten waiting time (fewer patient but

Shorter time on dialysis is better



2405 paired Kidney transplants

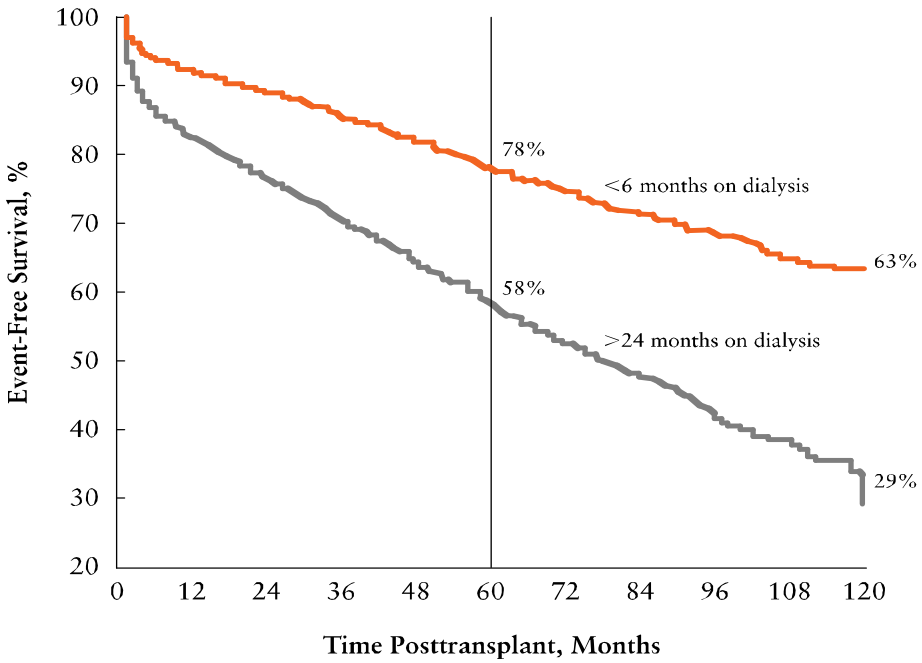
This is a clever study on the long-term effects of dialysis.

Since each cadaveric donors can donate two kidneys, the authors found kidney pairs from the same donor where one recipient happened to have been on dialysis a short time, and the other recipient a long time. Since the quality of the kidney is clearly the same, and the populations were otherwise similar, the difference in survival is attributed to dialysis. It appears that longer dialysis results in problems that are irreversible, even by a transplant.

This is a strong argument in favor of living donation, since the waitlist for a cadaveric kidney is longer than 24 months.

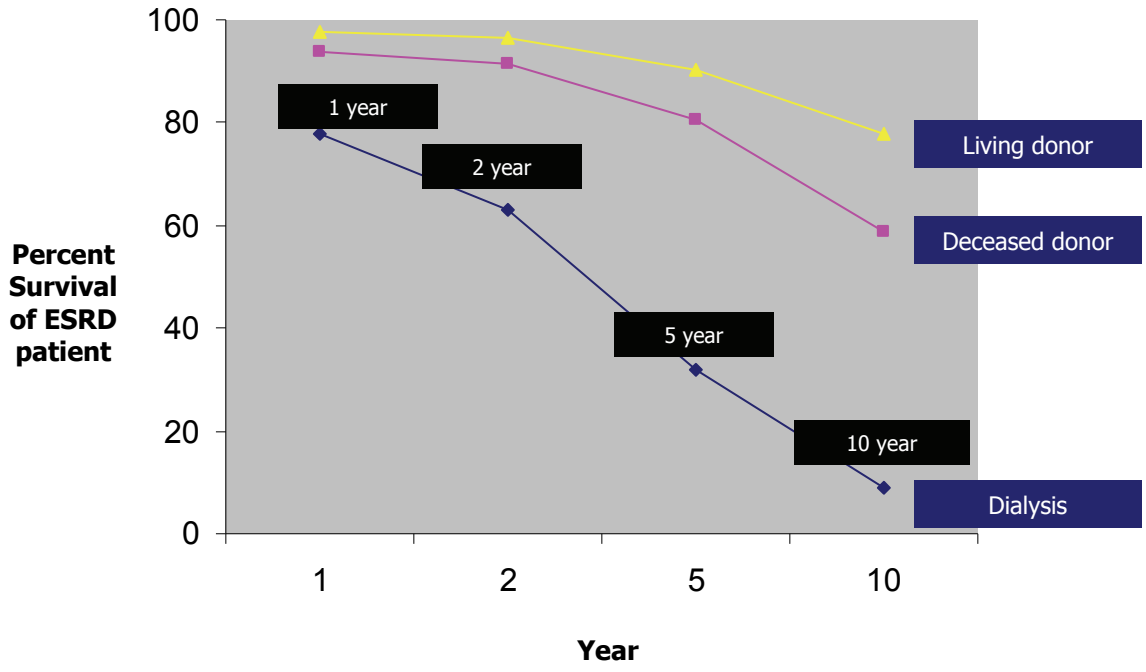
Meier-Kriesche HU, et al. Transplantation. 2002;74:1377-1381.

Difference in survival after transplantation?

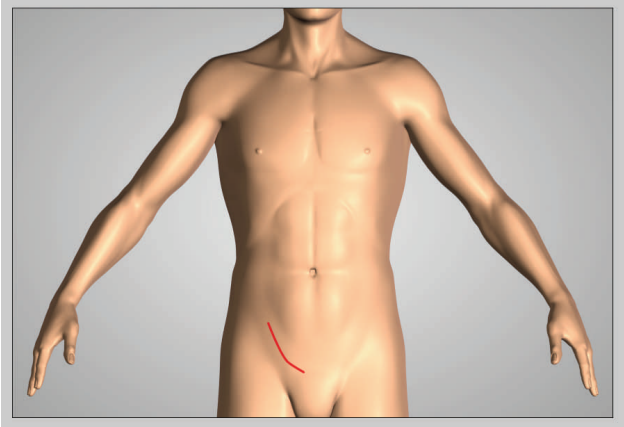


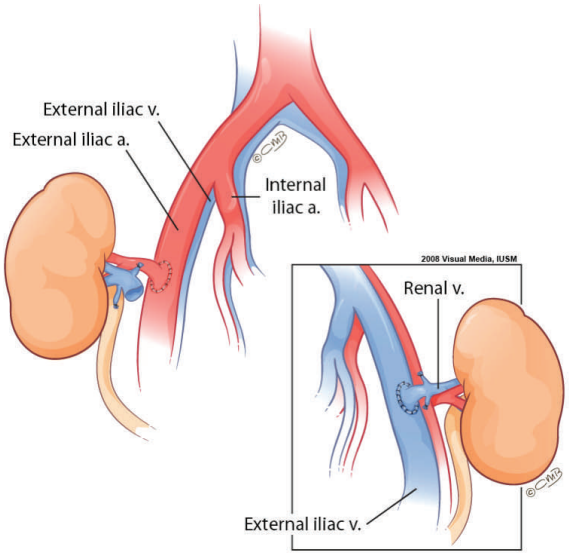
More dialysis => worse survival after transplant

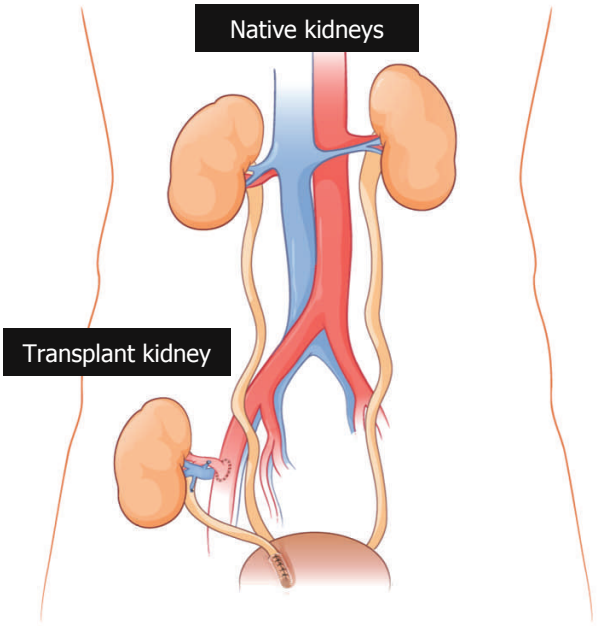
Living donation transplantation is the best treatment for renal failure

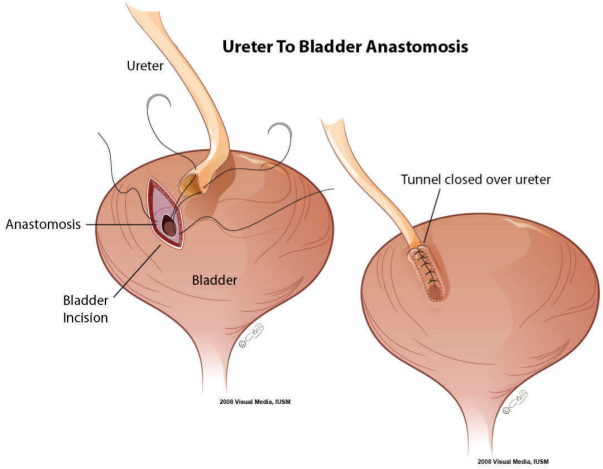


USRDS end-stage renal failure data







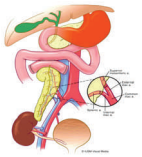


Kidney transplant operation

Top and bottom right: *the incision is in the right or left lower quadrant. This provides easy access to inflow and outflow vessels and to the bladder. Generally, the best lie will be left donor kidney to right and vice versa; this matches the renal vein and artery to the iliac vessels best, but this is not an absolute rule. The native kidneys are generally left in place. Exception: in the case of polycystic kidney disease, the transplant incisions made a little higher and longer, can be used to remove one native kidney at the time of transplantation*

Top left: *the renal vein is generally anastomosed first, then the artery. This part of the surgery is the warm ischemia time (the kidney is off ice, which allows cold ischemia time), so generally needs to be done swiftly.*

Bottom left: *the ureter is anastomosed directly to the bladder. A stent is usually inserted.*



Pancreas Transplantation

Why pancreas transplantation?

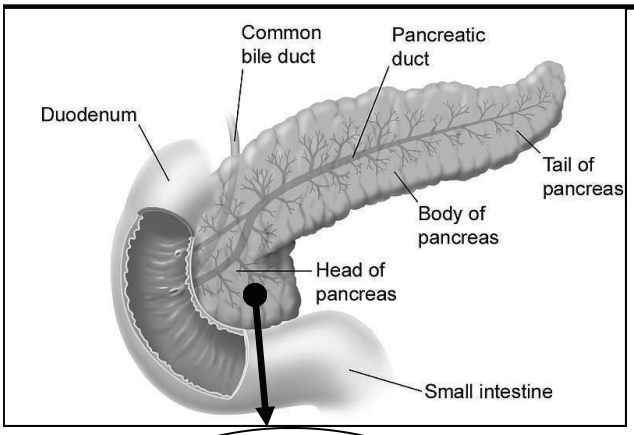
The pancreas is transplanted as treatment for diabetes. The purpose is to establish an insulin-independent and normoglycemic state; and to prevent and possibly improve, secondary complications of diabetes.

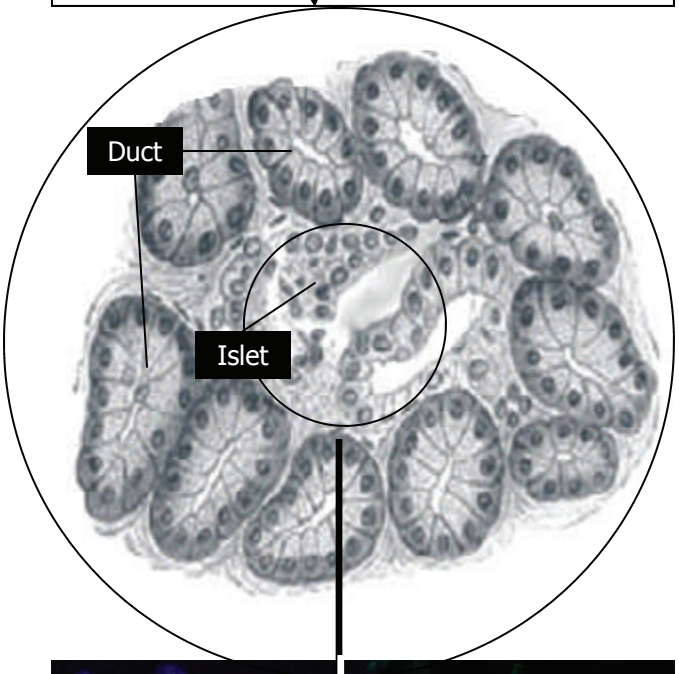
There are two general categories of pancreas transplant patients:

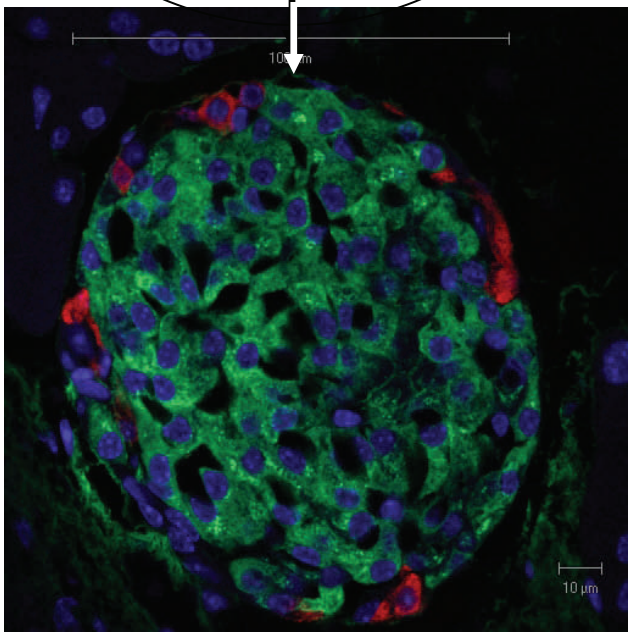
- **Pancreas alone**. These are diabetics which such bad sugar control that pretty much only a pancreas will help. Because the diabetes has become life-threatening, the risk of the operation + immunosuppression is justified.
- **Pancreas with kidney transplant.** These are diabetics with renal failure. Since they need immunosuppression for the kidney transplant anyway, adding a pancreas has an easier risk benefit profile than in the case of a pancreas alone. This can be one of the following:
    - a simultaneous kidney and pancreas transplant.
    - A kidney first (for example from a living donor) and then a pancreas. The rationale is that the waiting time for a pancreas alone is much shorter than for a kidney pancreas.

The **keys to pancreas transplantation** are understanding the following areas:

- The mixed functions of the pancreas, both endocrine (what we want, the insulin) and exocrine (means we need to make a bowel anastomosis) .
- The vascular anatomy that is shared with the liver. This is the key to the backbench reconstruction of the pancreas.
- The complications of diabetes, primarily bowel, which are the most common reason for readmission post-transplant.







Short primer on diabetes

The pancreas has both exocrine function —the secretion into the duodenum of digestive enzymes— and endocrine function —the secretions into the blood stream of regulatory hormones, including insulin.

Simplifying things a little, *type 1 diabetes* means no secretion of insulin. *Type 2 diabetes* means peripheral resistance to insulin. In practice though, the two are not quite so distinct, with type 2 sometimes ending up with no insulin production as well. Generally speaking, however, when talking about pancreas transplant we are dealing with type 1 diabetics.

Diabetes is associated with numerous complications, including *blindness*, *renal failure*, *peripheral vascular disease* and *neuropathy*. The neuropathy affects:

- peripheral nerves (pain and numbness)
- the brain (inability to sense hypoglycemia, or hypoglycemia unawareness, which is life-threatening and the main indication for pancreas transplant alone.
- the GI plexus of nerves, resulting in gastroparesis and poor bowel motility. This is one of the main reason for readmission post pancreas transplant.

Top left: *The pancreas secretes digestive enzymes into the duodenum*

Middle left: *a microscopic view of the pancreas reveals ductal tissue (for exocrine function of digestive enzymes) surrounding an islet (literally, a small island) of langherhans .*

Bottom left: *an islet has different hormone producing cells. In green, the beta-cells (65-80%), that produce insulin. In red, the alpha-cells (15-20%), that produce glucagon. Nuclei are blue.*

Not stained, but also present in the islets: delta-cell (3-10%) that produce somatostatin; PP cells that produce pancreatic polypeptide (3-5%); and epsilon cells that produce ghrelin (<1%).

Anatomic challenges of the pancreas allograft

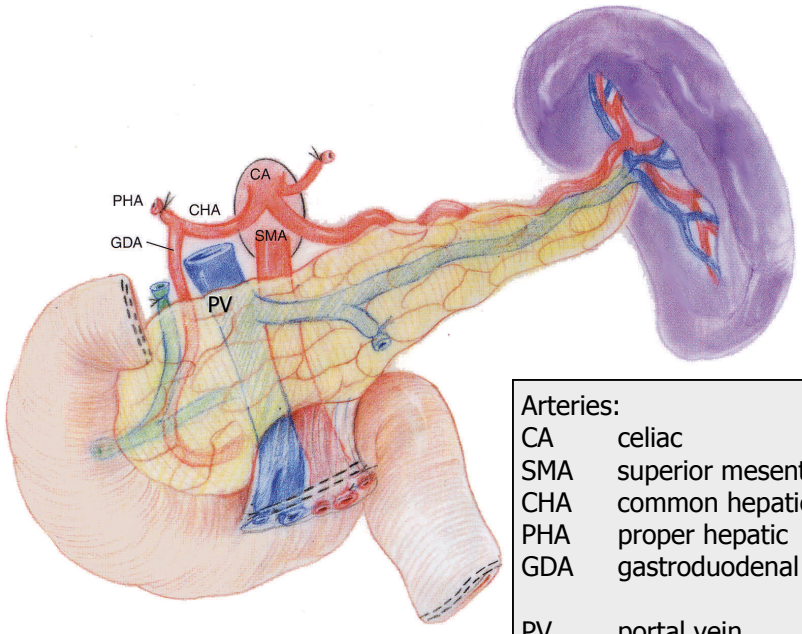
- *What to do with exocrine secretions?*
- *How to reconstruct the arterial blood supply, from superior mesenteric artery and celiac artery into one vessel, while preserving the blood supply of the liver allograft?*
- *How to use the portal vein as venous drainage of the allograft?*

Pancreas transplant anatomy

Exocrine function
The point of pancreas transplantation is to transplant the islet cells. However, until islet cell transplantation alone is clinically feasible, the whole organ pancreas has to be transplanted to allow islet cell function.

The pancreas secrete exocrine enzymes from the pancreatic duct into the duodenum. To take care of this, the pancreas allograft comes with its own donor duodenum segment, which is then anastomosed for drainage into either a segment of recipient small bowel (most common nowadays) or bladder (old style, not common now).

Vascular anatomy
The following page shows how the arterial and venous anatomy of the pancreas allograft.



Arteries:

CA	celiac
SMA	superior mesenteric
CHA	common hepatic
PHA	proper hepatic
GDA	gastroduodenal
PV	portal vein

Portal vein (PV)

The pancreas sits astride over the portal vein, which provides venous drainage of the pancreas and inflow into the liver. This arrangement allows an intimate connection between the glucose regulating hormones secreted by the pancreas and the carbohydrate and fat storage function of the liver.

Arterial blood supply

The pancreas is supplied by

- ***celiac axis (CA):*** *gastroduodenal artery GDA to head of pancreas,, and splenic artery (SA) to tail.*
- ***Superior mesenteric artery (SMA),*** *which supplies the head of the pancreas (pancreatico-duodenal artery, which connects to GDA).*

Celiac + hepatic arteries

To liver allograft

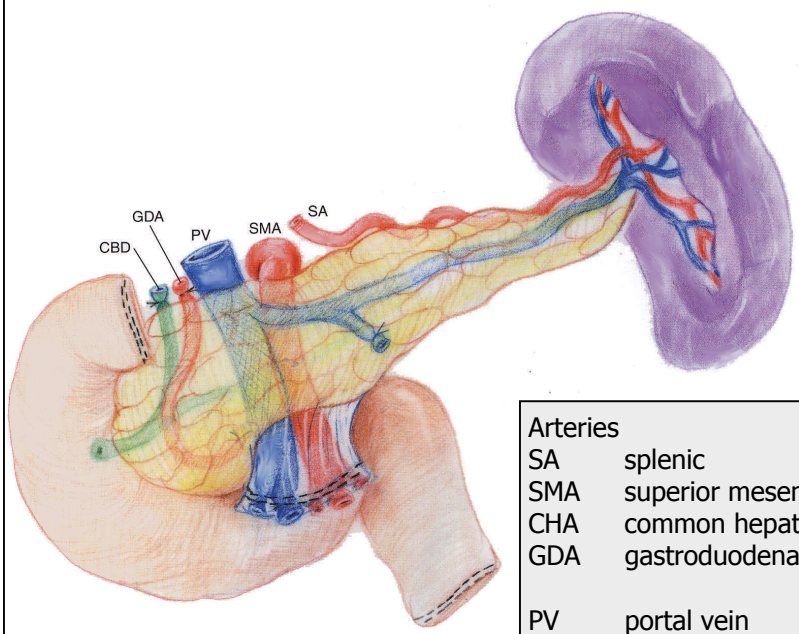
Superior mesenteric + splenic arteries

To pancreas allograft

Almost as a rule, deceased donors that are good enough to be a pancreas donor are good liver donors as well. The problem is that the liver and pancreas share blood supply. To separate them:

The celiac axis, except for the splenic artery, goes with the liver

The superior mesenteric artery and splenic artery go with the pancreas.



Arteries

SA	splenic
SMA	superior mesenteric
CHA	common hepatic
GDA	gastroduodenal
PV	portal vein
CBD	common bile duct

Despite missing the celiac artery, as long as the pancreas keeps the splenic artery and the SMA, the pancreas is entirely supplied:

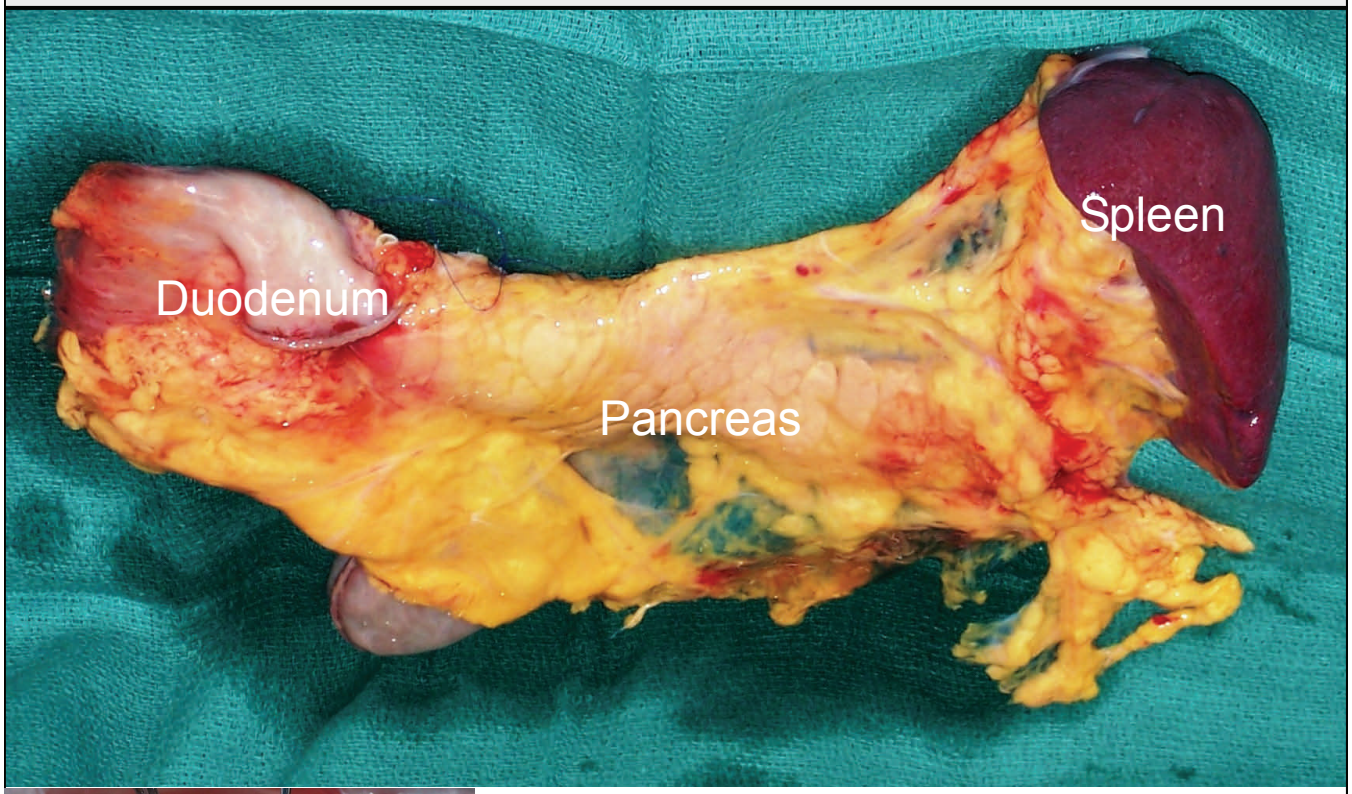
- *the splenic artery supplies the tail.*
- *the pancreatico-duodenal supplies the head so the GDA is not needed.*

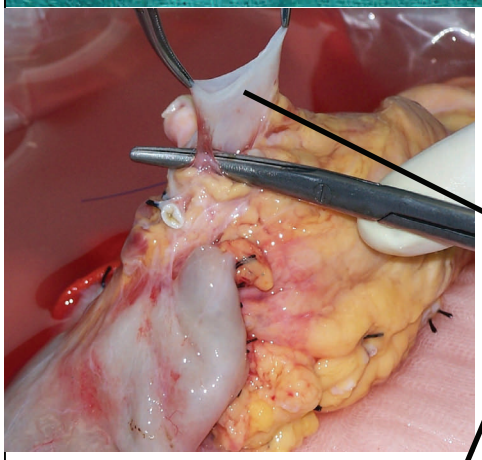
How to join these two arteries into one is the main purpose of the bench work (next page)

Note that the pancreas allograft is really pancreas + duodenum. The duodenum cannot be removed, because it is intimitally associated with the pancreatic head (this is the rationale for the Whipple).

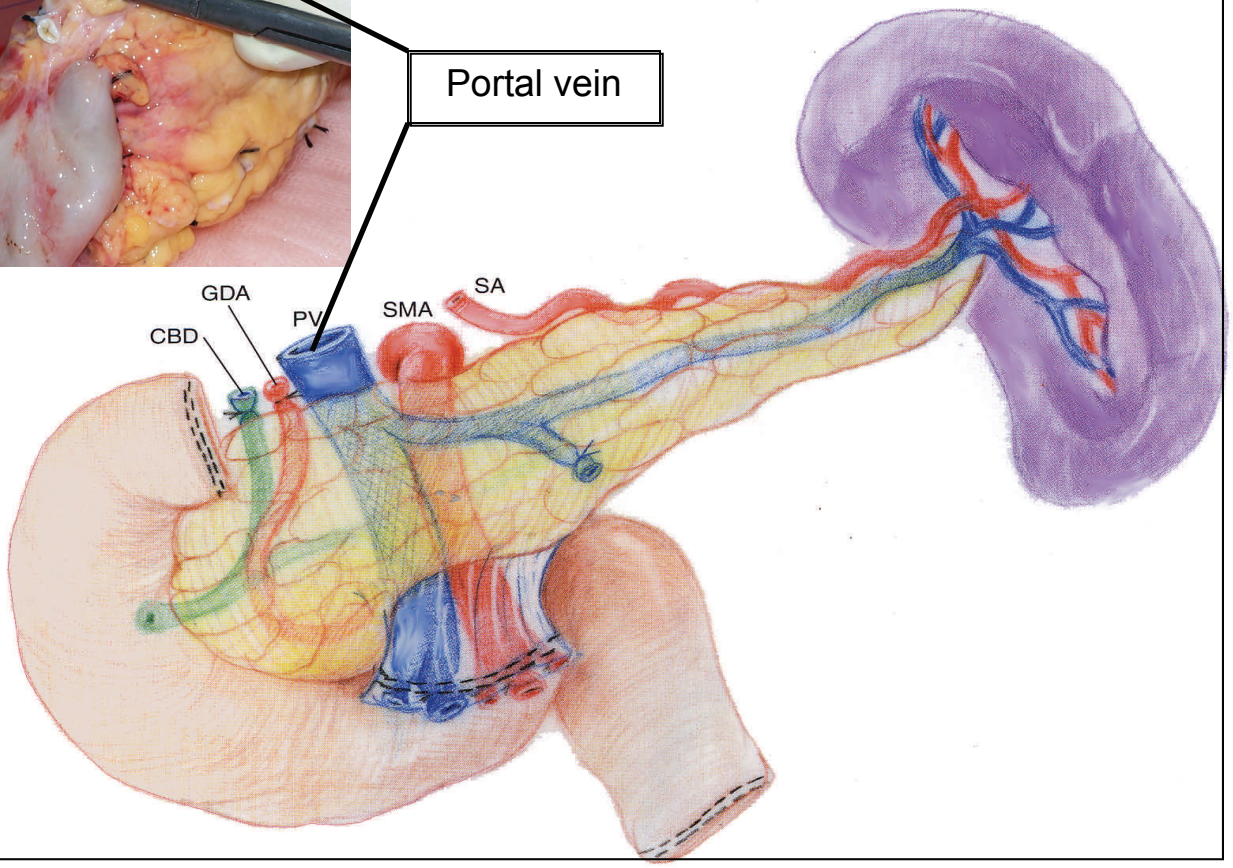
On the other hand, these pictures show the spleen. This is not left in place in the allograft. However, it is harvested with the allograft because it is a convenient handle. The less you mess with the pancreas, the better...

Pancreas allograft backbench preparation

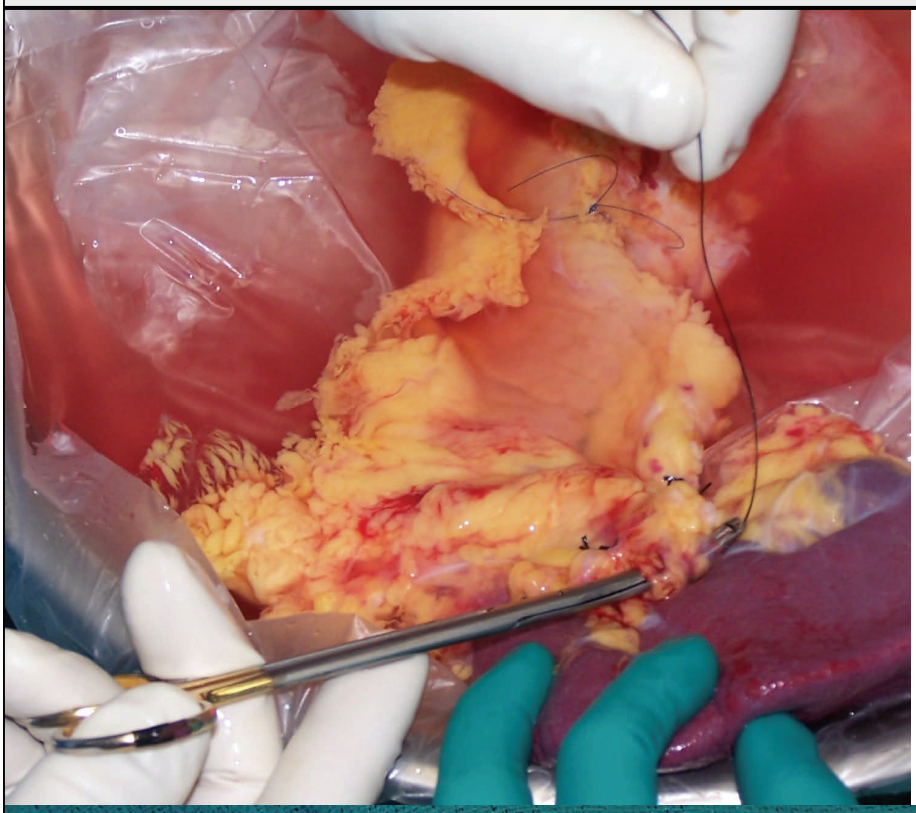


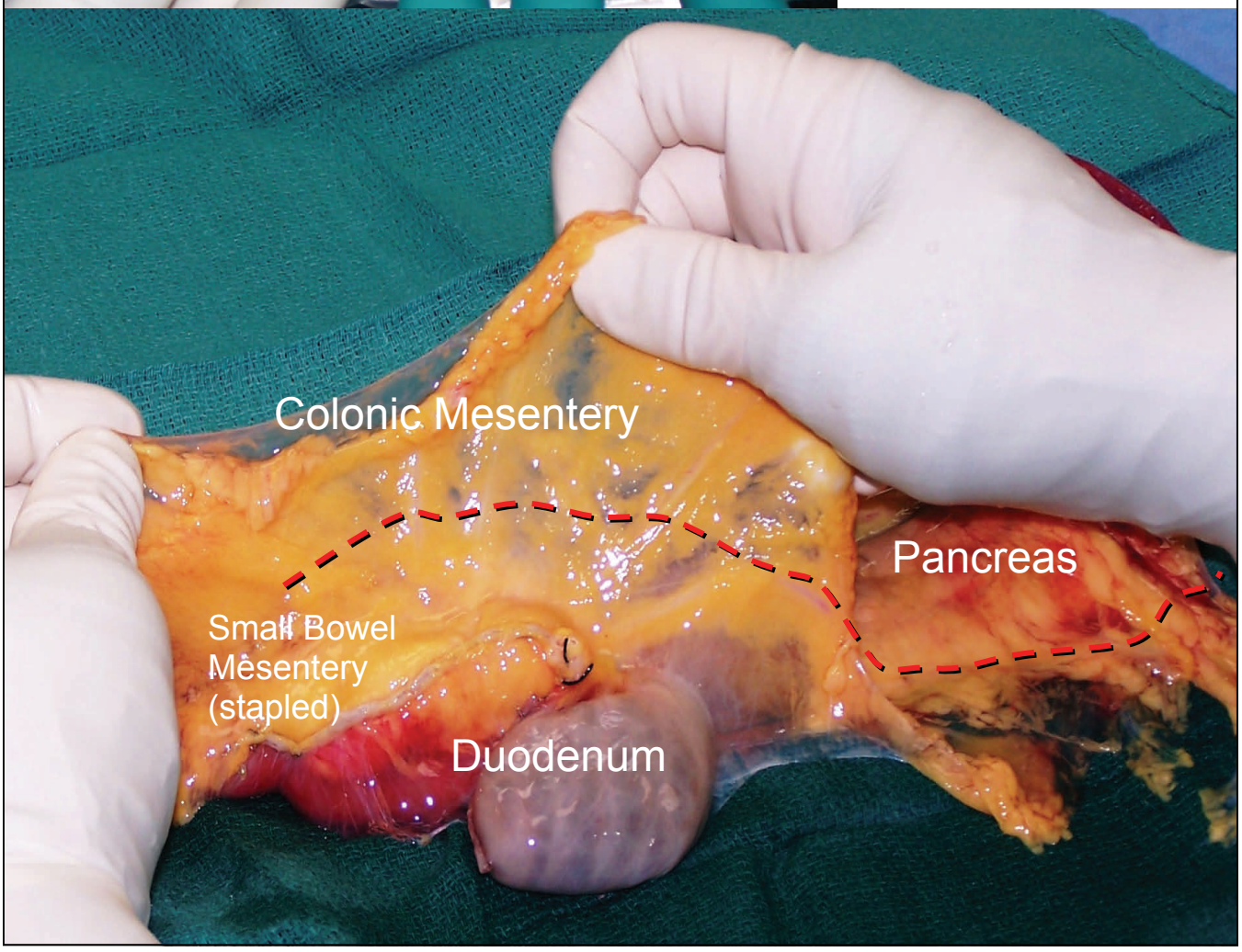


Portal vein

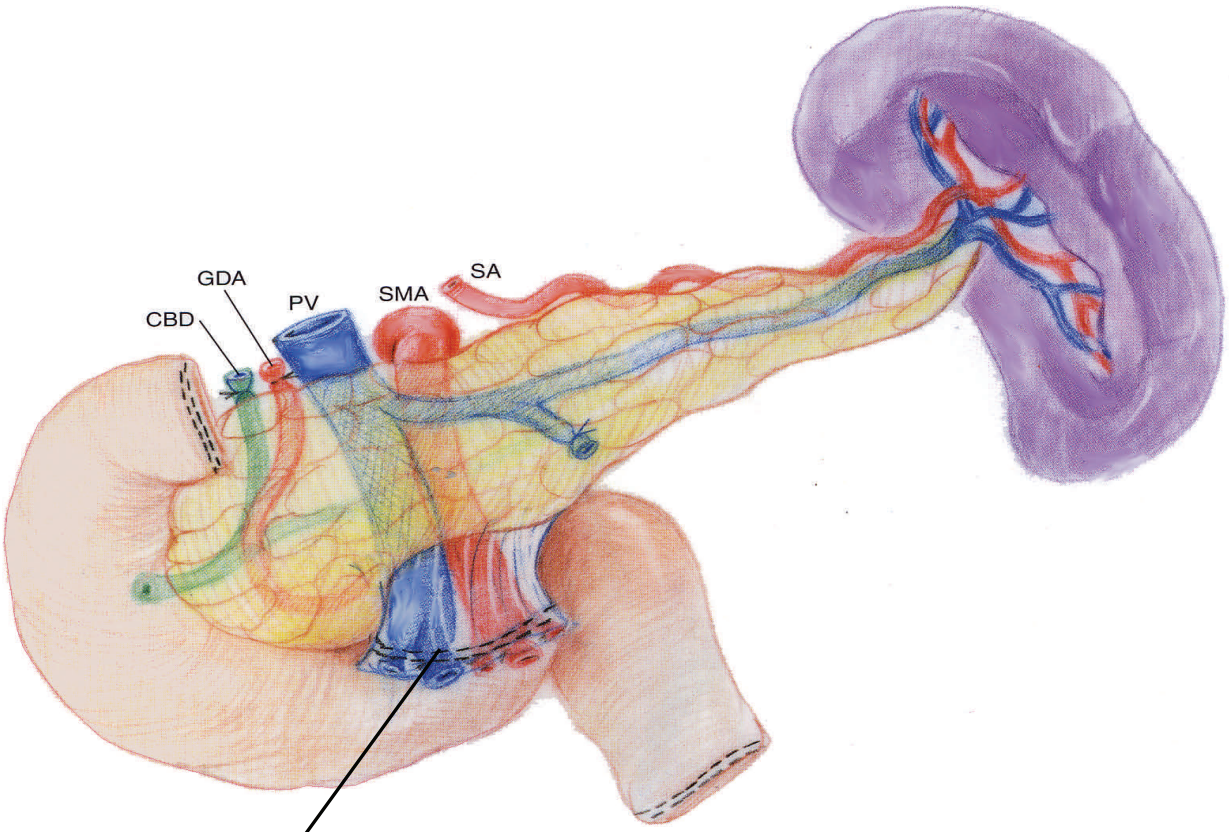


Pancreas allograft backbench preparation



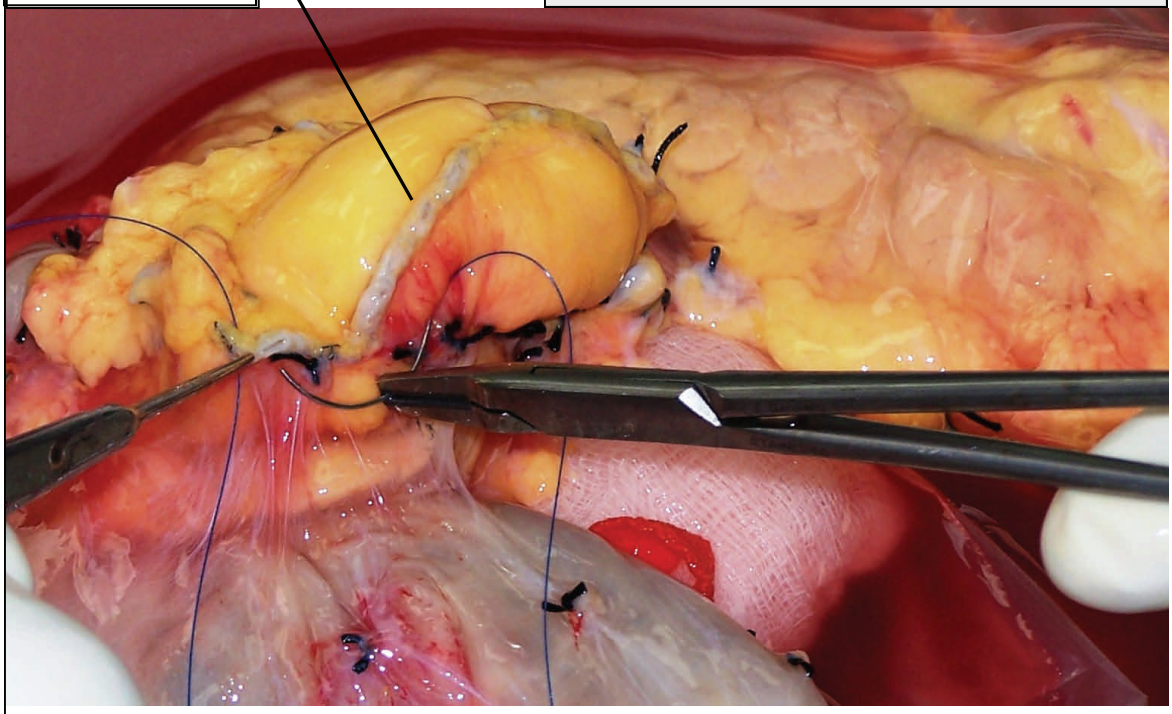


Pancreas allograft backbench preparation

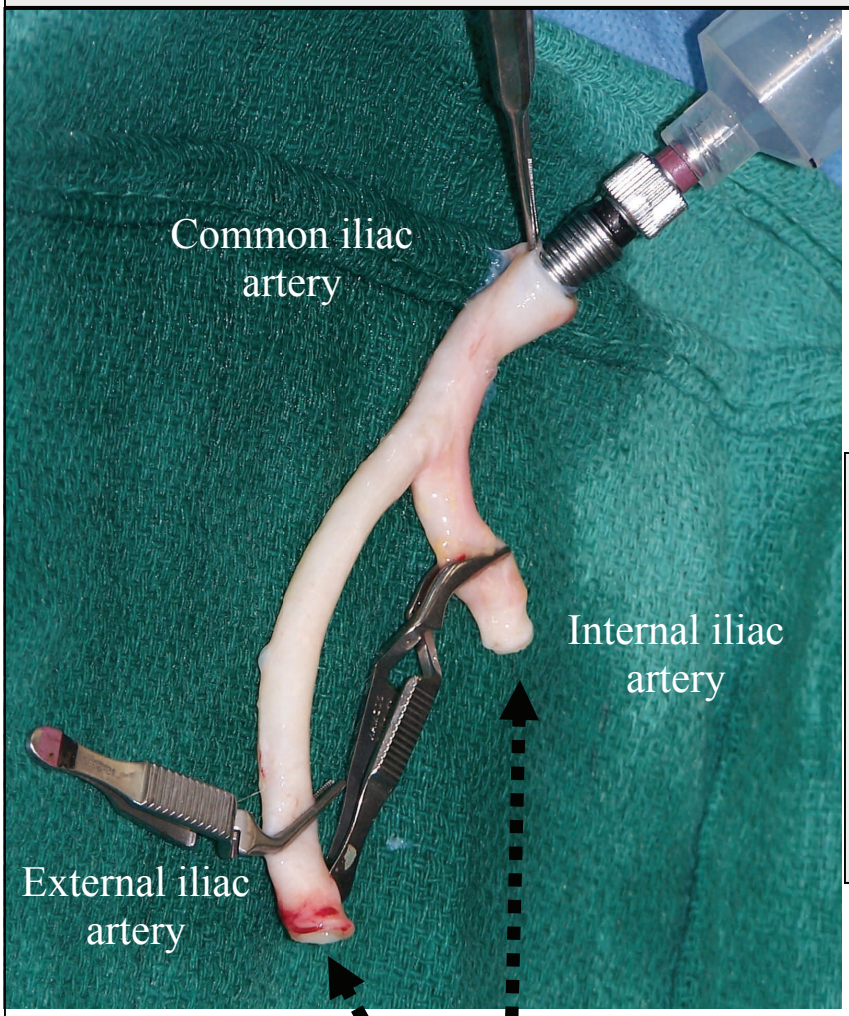


Small Bowel Mesentery (stapled)

The small bowel mesentery, which contains major vessels, is oversewn to prevent bleeding.

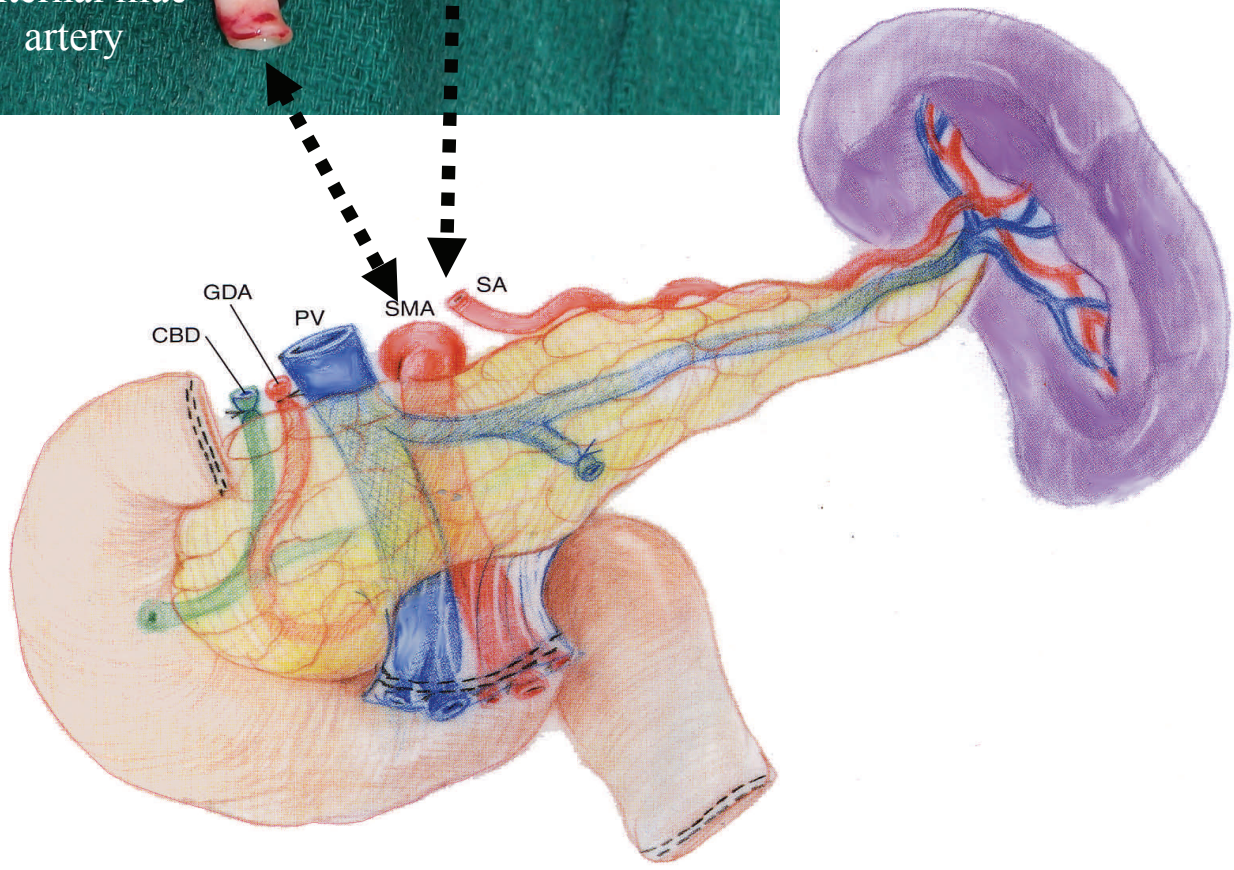


Pancreas allograft backbench preparation

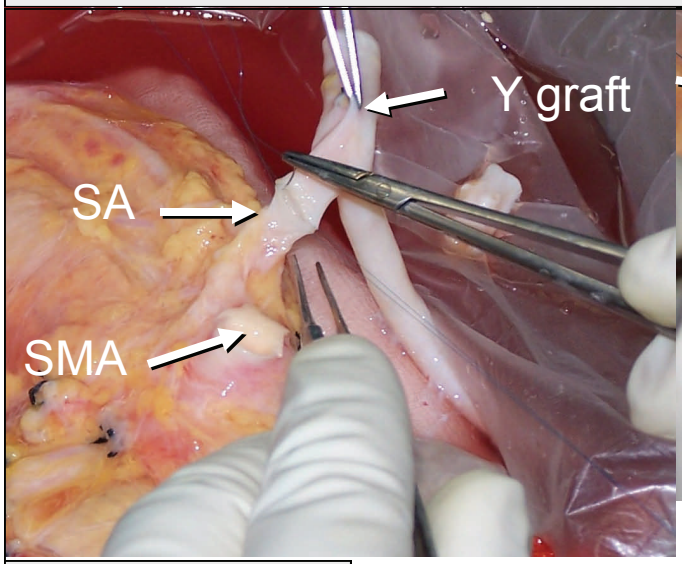


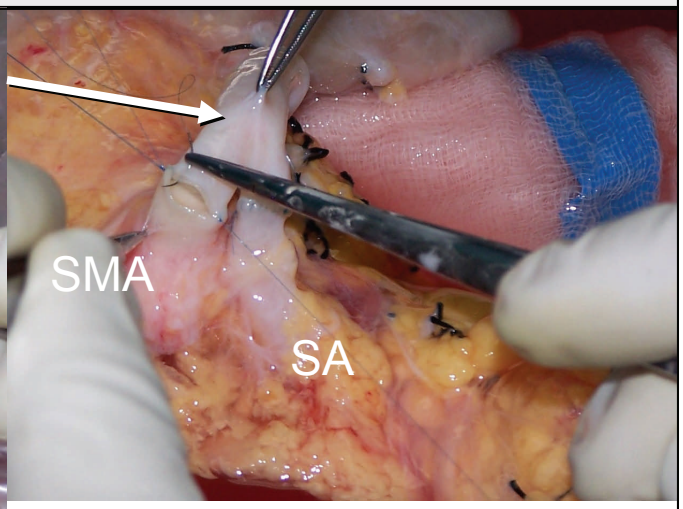
After the liver allograft blood supply is removed, ***the pancreas allograft is left with two separate arteries:*** *the splenic and superior mesenteric. It would be nearly impossible to sew these in separately into the recipient.*

The solution is to use a Y-graft of donor iliac arteries*. The internal iliac is sewn to the splenic, the external to the SMA, and voila. There is now a single artery (the common iliac) to sew into the recipient.*



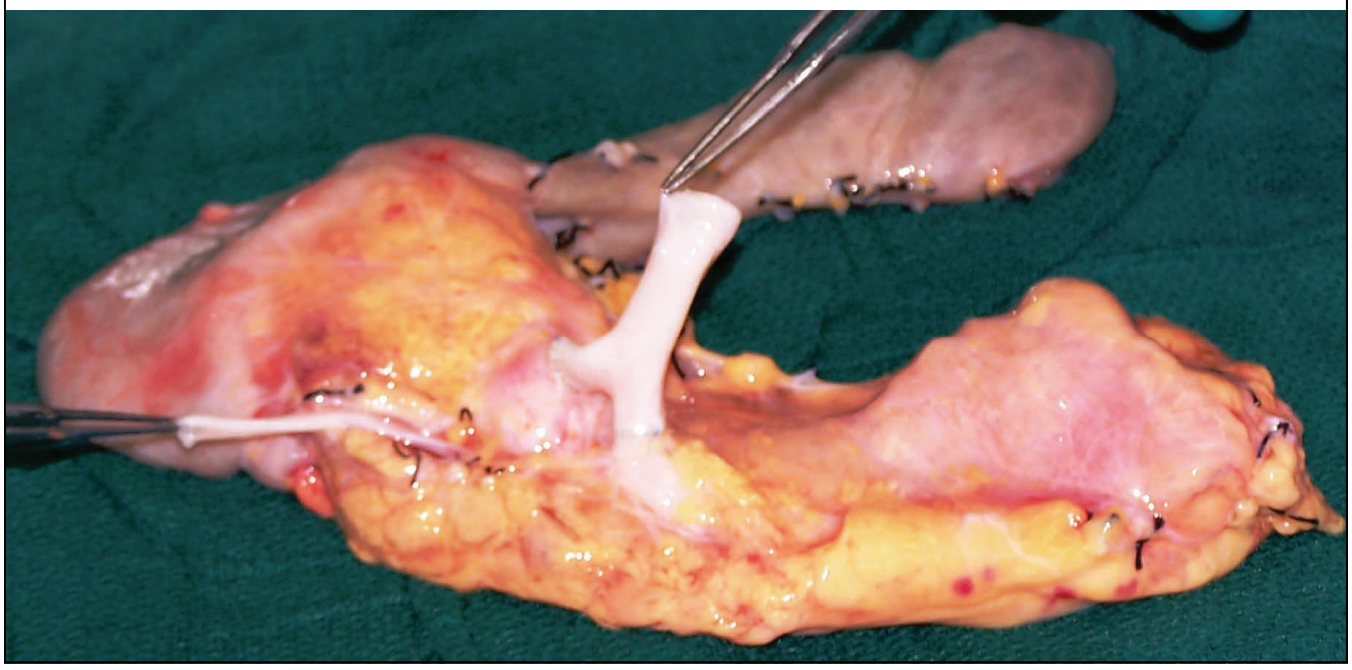
Pancreas allograft backbench preparation





SA= splenic artery
SMA= superior mesenteric artery
Y graft is donor iliac arteries (common, external, internal)

Using Y-graft of donor iliac arteries, the internal iliac is sewn to the splenic, the external to the SMA. There is now a single artery (the common iliac) to sew into the recipient.



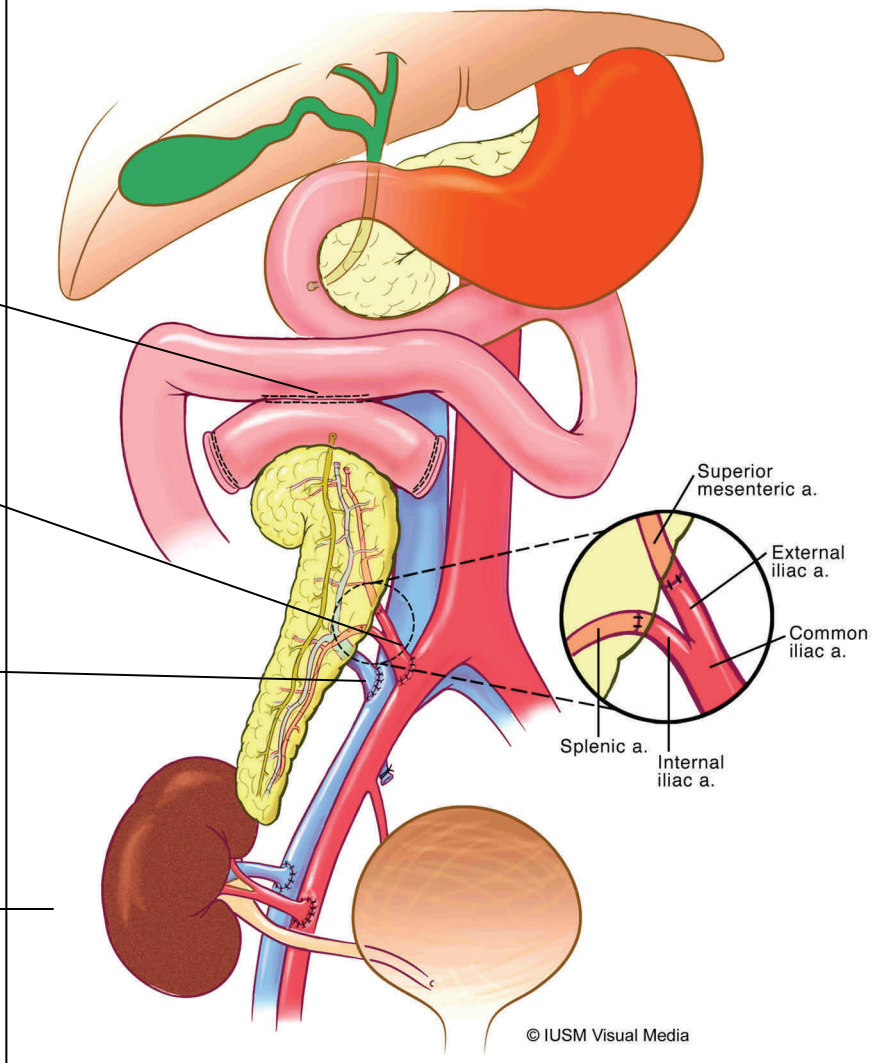
Pancreas Transplant operation

Donor duodenum to recipient jejunum anastomosis

Y-graft arterial inflow to iliac artery

Donor portal vein (venous outflow of pancreas) to vena cava or iliac vein

Kidney transplant (not for pancreas alone operation)



Step 1: dissection
Midline incision, right colon reflection, dissection of vena cava, common iliac artery. For kidney pancreas transplants, external iliac artery and vein also dissected.

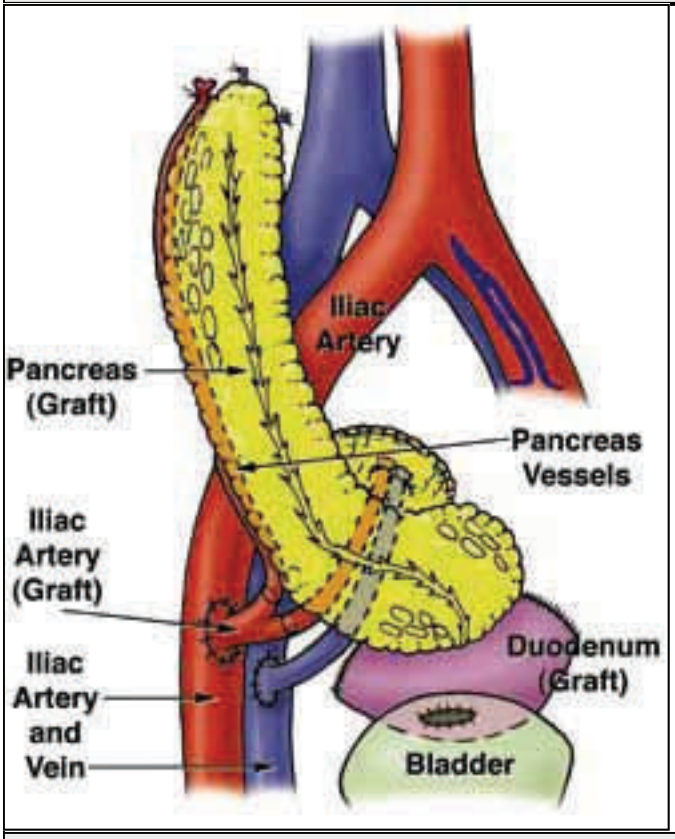
Step 2: vascular anastomoses.
The portal to cava anastomosis is done first, from the right side of the OR table. The artery (donor iliac used for Y-graft, to recipient iliac) is then done.

Step 3: reperfusion.
The vascular anastomoses are released and hemostasis is obtained (after perfusion, bleeder are in evidence).

Step 4: enteric anastomosis.
The donor duodenum is anastomosed to the recipient jejunum using an EEA stapler. All suture lines are then oversewn.

Step 5 (in KP recipients): kidney transplant.
This is done after the pancreas because it's distal. Therefore the pancreas arterial blood supply is not clamped. We do it on the right side to save the left side in case a future kidney is needed. Other programs do it on the left.
The transplant is done like a standard kidney transplant except the kidney is intraperitoneal, not retroperitoneal, and the exposure is more difficult because excessive retraction on the pancreas has to be avoided.

Pancreas Transplant with bladder drainage



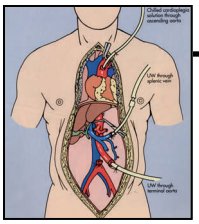
Pancreas transplant with bladder drainage

In the early era of pancreas transplantation, most transplants were drained of exocrine secretions into the bladder. The rationale was that a leak to the bladder was easier to deal with than a bowel leak (this was in the era of high steroid use, so leaks were more likely and more lethal); also the amylase and lipase could be measured in urine, allowing monitoring of the gland function for rejection (although in practice, this was not very easy to do, since there were wide variations in amylase output and it was diluted by urine).

The downside was that the pancreatic secretions were often very harsh on the bladder mucosa, resulting in hematuria. Also, patients developed metabolic acidosis requiring bicarbonate supplementation to compensate for pancreatic secretion.

Conversion of bladder drainage to enteric drainage

Bladder drainage operation is not done much anymore. However, it is encountered on our service when patients who underwent a bladder drainage in the past have complications that require conversion to enteric drainage. The operation consists of closing the bladder orifice and doing a donor duodenum to recipient jejunum anastomosis. The end result is similar to a standard pancreas transplant, except that the gland is oriented in the opposite direction



Deceased Organ Donation

When a patient is brain dead, all organs are being perfused. So brain death makes possible multi-organ donation. Brain death is associated with some unstability (for example the loss of the pituitary can result in liters of diuresis, it's usually possible to support the cadaver for 24-48 hours, allowing time to place multiple organs and coordinate multiple teams procuring different organs. (see

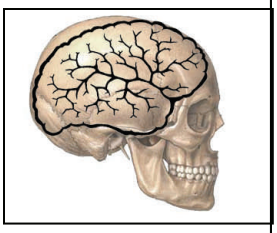
There are two types of deceased donors:

- **Brain dead, with continued perfusion**. In this case, the brain is dead (see next page as an explanation of how this is possible). Relatively leisurely organ allocation is possible. There are several subtypes:
    - Standard donation
    - Expanded criteria donor (ECD)

  These are kidney donors who are predicted to have a slightly worse renal allograft outcome; for example a 65 year old who died of a stroke. However, for many patients, this kidney would still be better than dialysis. This program is sometimes referred to as "old kidneys for old patients" although that's not exactly the case.
    - Two for one. Two slightly compromised kidneys are given to one patient. In total, the patient receives adequate nephron mass.

- **Donors after cardiac death (DCD)** These donors typically have irreversible massive-brain injury and poor outlook but are not dead. A decision for terminal wean has been made. At that point, families are offered the chance to donate organs once the patient is dead. The patient is brought to the OR for a terminal wean, where the patient is taken off the ventilator. If the patient expires within 30-60 minutes, then donation proceeds. A kidney first (for example from a living donor) and then a pancreas. The rationale is that the waiting time for a pancreas alone is much shorter than for a kidney pancreas.

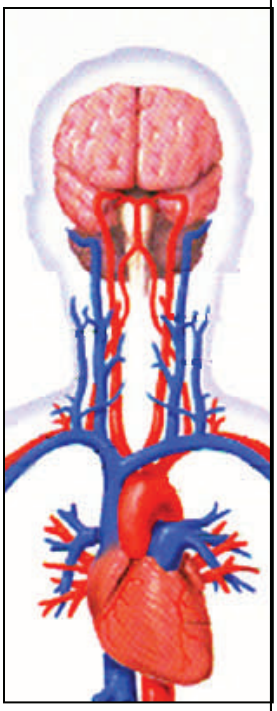
Brain death



Brain swelling → Intracranial pressure

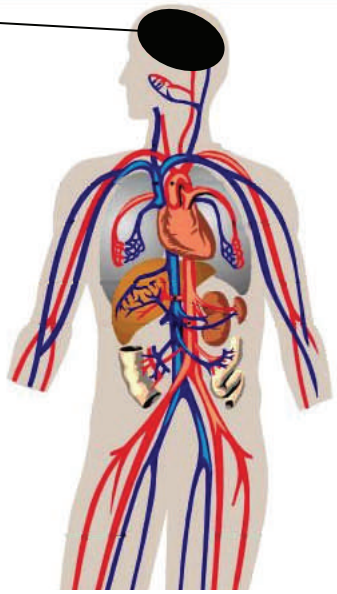
Trauma → Brain swelling

Intracranial pressure → Decrease Perfusion pressure → Increase Pump pressure



Brain death allows continued perfusion of:

- Lungs
- Heart
- Liver
- Pancreas
- Kidneys
- Intestine



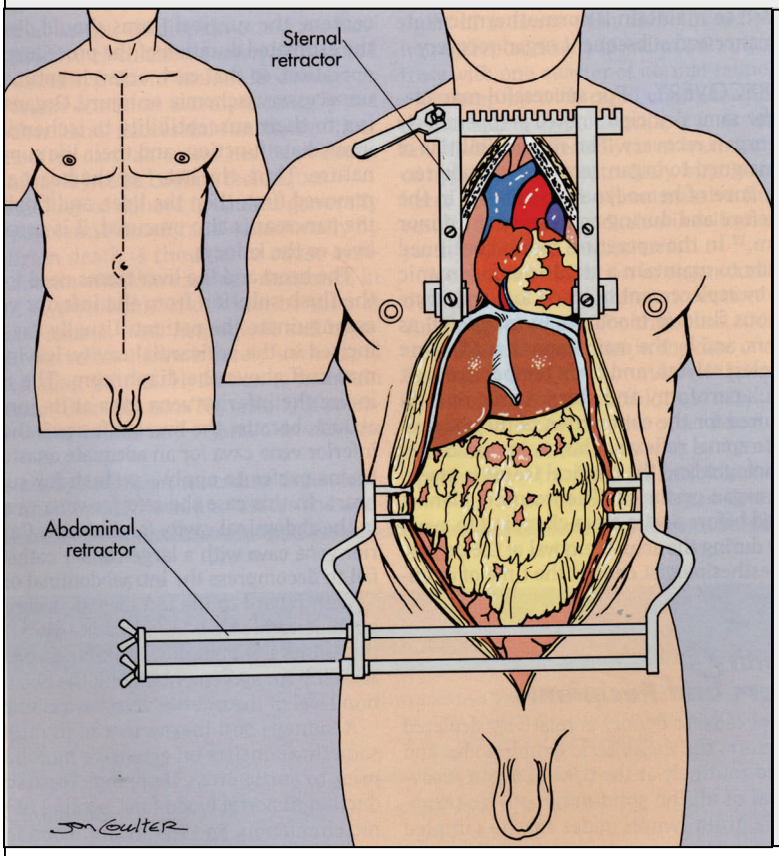
How is brain death even possible?

Brain death means the brain is gone: liquified, without any recognizable structure or perfusion. This is distinctly different from other organs dying. For example a dying kidney goes into ATN but continues to be perfused and is recognizable as a kidney.

Brain death occurs because the brain is encased in a hard unyielding shell, the skull. Normally, the pump pressure of the heart ensures brain perfusion. However, if brain swelling occurs, the intracranial pressure (ICP) opposes the perfusion pressure. If the ICP increases enough, perfusion to the brain stops and brain death ensues. This is why brain death can occur, and yet other organs continue to be perfused.

Brain death is an unstable state, however, because the brain's neurohumoral regulation is not present. Thus brain dead donors tend to have diabetes insipidus with hourly urine outputs of one liter, because of the absence of Anti-diuretic hormone (ADH) from the pituitary.

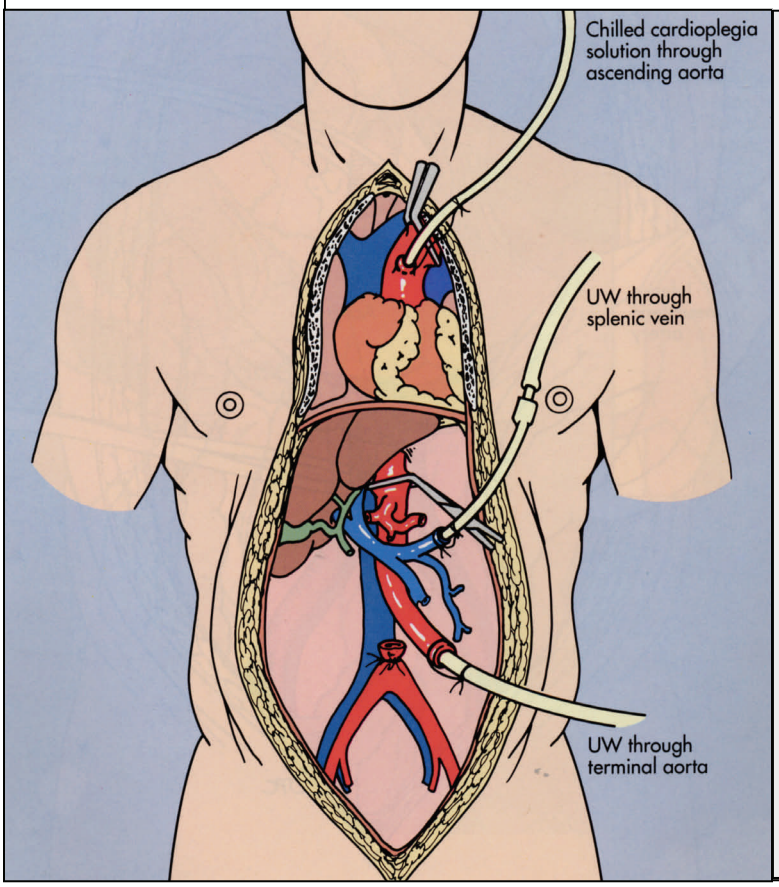
Multiorgan donor operation



START

The operation is done through a long midline incision. Several teams are typically present: heart, lung, abdomen.

This is an incredible anatomy lesson. Residents are encouraged to go on at least one donor.



END

The operation needs to accomplish the following:

The vasculature of each donor organ is defined, so that organs can be separated.

Flushing cannulae are inserted in the chest and abdomen to flush blood out of these organs, cool the organs and infuse them with preservation solution. A clamp on the proximal abdominal aorta separates the chest and abdominal flushes.