

# Donor Selection

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- Donor selection topics
  - Extended criteria donors
  - PHS increased social risk
  - Hep B core Ab+ donors
  - Hep C Ab+ donors
  - Hepatic steatosis
  - Domino liver transplantation
  - Split liver transplantation
  - Auxiliary transplantation
  - Donation after cardiac death
  - Living donor selection

- Extended criteria donor (ECD) livers
  - Sometimes referred to as “marginal” grafts
  - Conceptually, ECD livers are at increased risk of early failure (PNF, DGF) or predisposes to inferior outcomes
  - No precise definition

- Generally accepted ECD variables
  - Advanced donor age (>70)
  - Prolonged WIT (>12 hours)
  - Prolonged CIT (>40 min)
  - Graft steatosis ( $\geq 30\%$ )
  - DCD grafts
  - “Orphaned” grafts

### ○ ECD outcomes

- At high volume centers, patient and graft survival is similar to recipients of SCD livers
- Experience and appropriate recipient selection are key to achieving good outcomes

### ○ PHS increased social risk (PHS IR)

- In 2013, PHS published criteria defining deceased donors at increased risk for HIV, HBV, and HCV transmission to potential organ transplant recipients
- Donors with a history of specific social behaviors are deemed PHS IR
- These were integrated into OPTN policy; use of livers from these donors requires the patient's informed consent

People who have had sex with a person known or suspected to have HIV, HBV, or HCV infections in the preceding 12 months
Men who have had sex with men (MSM) in the preceding 12 months
Women who have had sex with a man with a history of MSM behavior in the preceding 12 months
People who have had sex in exchange for money or drugs in the preceding 12 months
People who have had sex with a person who had sex in exchange for money or drugs in the preceding 12 months
People who have had sex with a person that has injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the preceding 12 months
A child who is ≤18 months of age and born to a mother known to be infected with, or at increased risk for HIV, HBV, or HCV infections
A child who has been breastfed within the preceding 12 months and the mother is known to be infected with, or at increased risk for HIV infection <i>(Recommendation 4 in the PHS Guideline further recommends that the birth mother, if available, should be interviewed about behaviors that may have placed her at risk for HIV, HBV, or HCV infection)</i>
People who have injected drugs by intravenous, intramuscular, or subcutaneous route for nonmedical reasons in the preceding 12 months
People who have been in lockup, jail, prison, or a juvenile correctional facility for more than 72 hours in the preceding 12 months
People who have been newly diagnosed with or have been treated for syphilis, gonorrhea, Chlamydia, or genital ulcers in the preceding 12 months
Donors who meet the following criterion should be identified as being at increased risk for recent HCV infection only:
People who have been on hemodialysis in the preceding 12 months

Seem, Debbie L, Ingi Lee, Craig A Umscheid, and Matthew J Kuehnert. PHS Guideline for Reducing Human Immunodeficiency Virus, Hepatitis B Virus and Hepatitis C Virus Transmission through Organ Transplantation. *Public Health Reports* 128, Jul-Aug 2013: 247-344

## ○ PHS IR livers

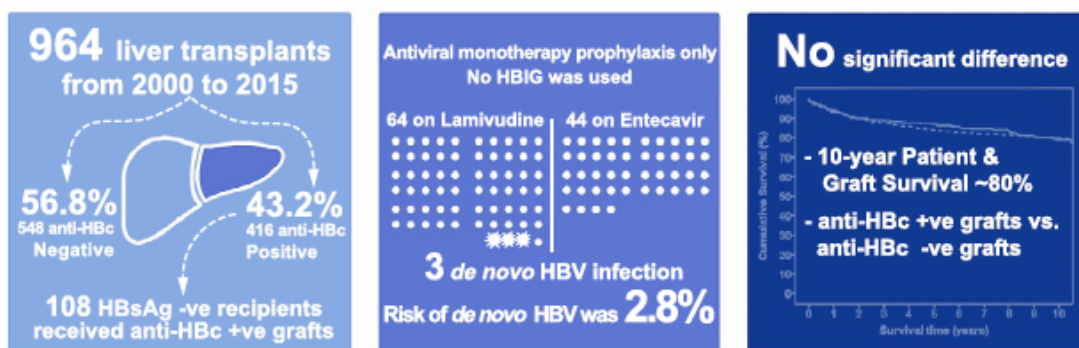
- Utilization is associated w decreased waitlist mortality and improved survival
- In general, these livers are physiologically equal or better than non-IR liver grafts
- Transplant centers need protocols for monitoring/suveillance for disease transmission post transplant

## ○ Hep B core Ab + donors

- Anti-HBc+, HBsAg-
- Relatively common (5-10% of deceased donors)
- May harbor occult infection; HBV DNA in serum or liver
- Most centers use these grafts selectively for HBV naïve recipients
- No consensus re post transplant prophylaxis regimen, trend towards less HBIG and entecavir > lamivudine

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### Liver Transplantation Using Hepatitis B core Positive Grafts with Antiviral Monotherapy Prophylaxis A Single Centre, Retrospective Study of Adult Liver Transplant



Wong TC, Fung JY, Cui TY, et al. Liver transplantation using hepatitis B core positive grafts with antiviral monotherapy prophylaxis. *J Hepatol.* 2019;70(6):1114-1122. doi:10.1016/j.jhep.2019.03.003

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## ○ Hepatitis C antibody + donors

- Utilization of HCV+ livers is increasing
  - Opioid crisis – more HCV+ donors w/o established liver disease
  - DAA therapy – high efficacy post LT
- 2 types
  - Viremic – HCV RNA positive by nucleic acid testing (NAT+)
  - Nonviremic – HCV RNA negative by nucleic acid testing (NAT-)

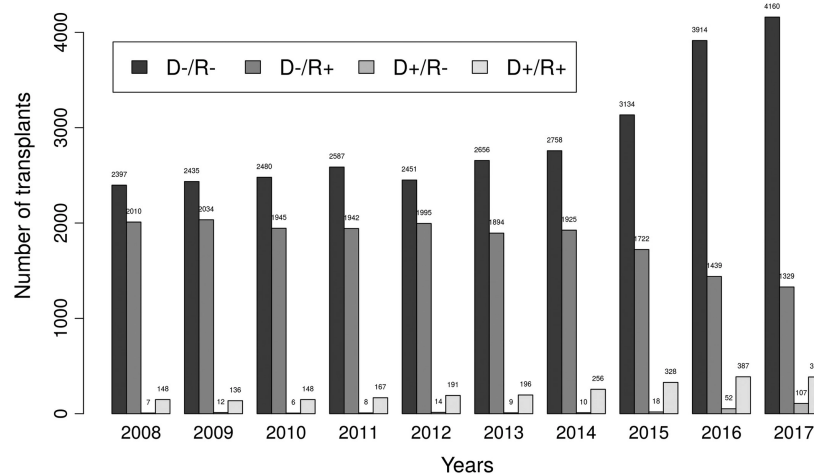


TABLE 1. Advantages and Disadvantages of Utilizing HCV-Positive Donors for HCV-Negative Recipients

Advantage	Disadvantage
<ul style="list-style-type: none"> <li>- Increase pool of currently available donors</li> <li>- Decrease wait-time mortality for very sick recipients (FHF, high MELD &gt;30)</li> <li>- Potentially younger donors without other comorbidities</li> <li>- DAA regimens have a very high rate of cure</li> <li>- Similar longterm graft and patient outcome than HCV-negative donors</li> </ul>	<ul style="list-style-type: none"> <li>- 100% risk of transmission of HCV for recipients</li> <li>- High cost of DAA</li> <li>- Limited access to DAA regimens</li> <li>- Requirement for preapproval by drug companies or insurance companies*</li> <li>- Possible interaction between DAA regimens and immunosuppression</li> <li>- Ethical/society barrier</li> </ul> <p>*only for countries where insurance companies cover the costs</p>

Selzner N, Berenguer M. Should organs from hepatitis C-positive donors be used in hepatitis C-negative recipients for liver transplantation? [published correction appears in Liver Transpl. 2018 Aug;24(8):1152]. *Liver Transpl.* 2018;24(6):831-840. doi:10.1002/lt.25072

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## ○ HCV+ donor livers

- HCV transmission
  - Ab+/NAT- → 15%-20%
  - Ab+/NAT+ → 100%
- Grafts w/o significant inflammation/fibrosis are considered
- Genotype of NAT+ donors is unknown at time of procurement

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### ○ Transplant center protocol

- Use selectively for appropriate candidates
- Informed consent
- Post LT serologic monitoring
- Timely access to and initiation of DAA's is critical

### ○ Hepatic steatosis

- Hepatocytes contain triglyceride vacuoles
- Macrovesicular – large vacuoles w peripheral displacement of the nucleus
- Considered ECD grafts – associated with poor outcomes
- Macro >> microsteatosis

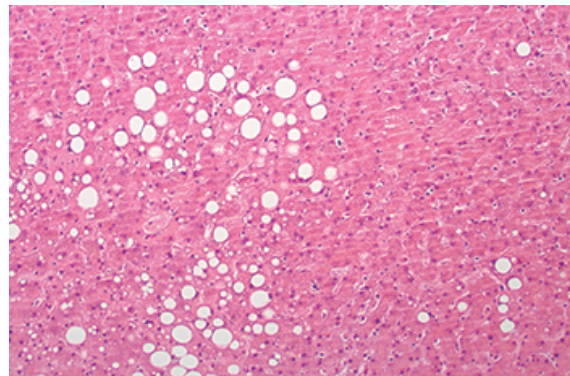


## ○ Assessment of the steatotic graft

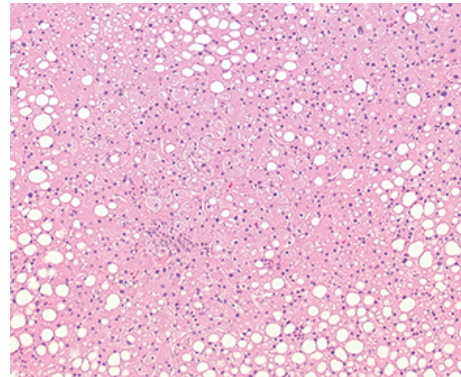
- Preprocurement imaging may be helpful (if available)
  - US - ↑ in liver echogenicity (brightness) relative to kidney
  - CT w/o contrast – absolute liver attenuation <40 HU (or 10+ < spleen)
- Liver biopsy - semiquantitative
  - Mild – 5%-33%
  - Moderate – >33%-66%
  - Severe – >66%

## ○ Mild 5%-33%

- Suitable for LT



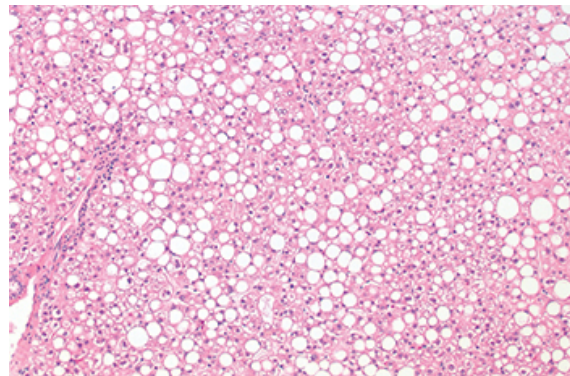
- Moderate >33%-66%
  - Use selectively
    - ↓ MELD
    - Short CIT



Yerian L. Liver donor organ evaluation. CAP Today [Internet]. 2015 Feb [cited 2020 Jun 7]. Available from: <https://www.captodayonline.com/liver-donor-organ-evaluation/>

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- Severe >66%
  - Use is relatively contraindicated



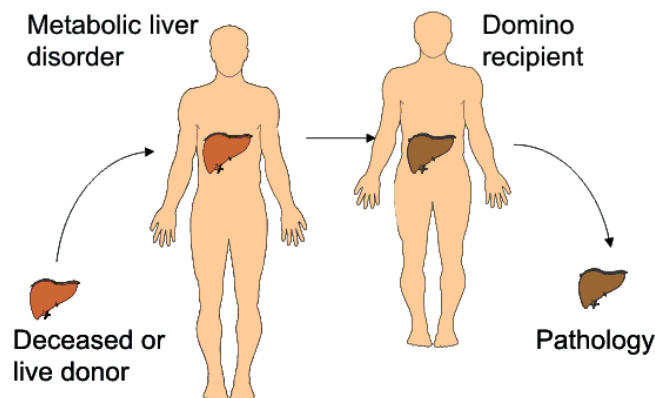
Yerian L. Liver donor organ evaluation. CAP Today [Internet]. 2015 Feb [cited 2020 Jun 7]. Available from: <https://www.captodayonline.com/liver-donor-organ-evaluation/>

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## ○ Domino liver transplant

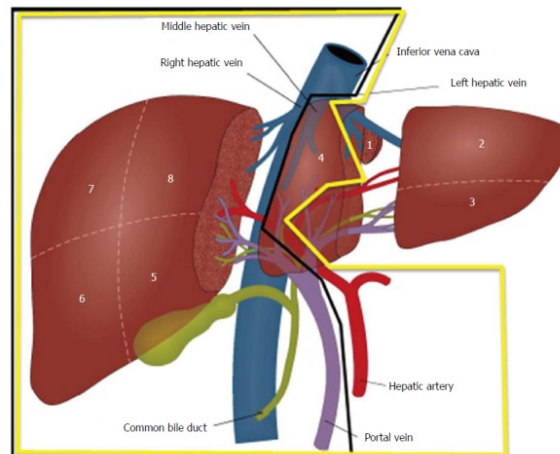
- Involves utilizing the native liver from a recipient for another patient
- The domino donor liver is usually anatomically and functionally normal except for a single metabolic defect
- The domino liver recipient is typically older and is unlikely to encounter symptoms related the defect during their lifetime
- Classic example, familial amyloidotic polyneuropathy

## Domino liver transplantation – the Concept

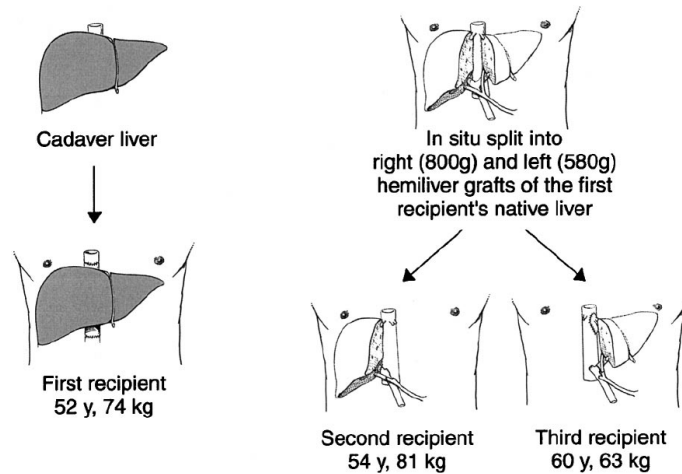


## ○ Split LT

- 1988, pioneered Pichlmayr and Bismuth
- Applies knowledge of liver segmental anatomy to divide a single graft for 2 recipients
- Technically and logistically demanding
- Classic split – LLS (seg 2,3) for a child or small adult; eRL (seg 1,4-8) for an adult



Hackl C, Schmidt KM, Süsal C, Döhler B, Zidek M, Schlitt HJ. Split liver transplantation: Current developments. *World J Gastroenterol.* 2018;24(47):5312-5321. doi:10.3748/wjg.v24.i47.5312



Azoulay D, Castaing D, Adam R, Mimoz O, Bismuth H. Transplantation of three adult patients with one cadaveric graft: wait or innovate. *Liver Transpl.* 2000;6(2):239-240. doi:10.1002/lt.500060208

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## ○ Auxiliary LT

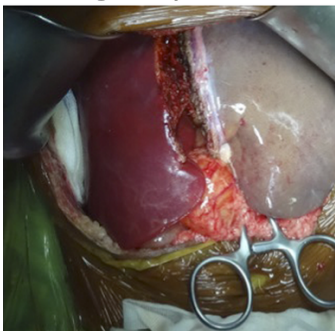
- Definition – providing additional or supplementary support
- APOLT – auxiliary partial orthotopic liver transplant

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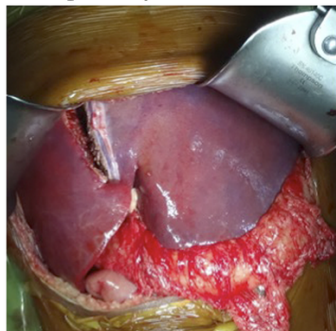
## ○ APOLT

- LT where a portion of the native liver is left in place after partial hepatectomy to create space implantation of a segmental liver graft
- Indications –
  - FHF
  - MLD (non-cirrhotic)
- When used for FHF, the goal is withdrawal of immunosuppression after native liver regeneration

Prior to graft reperfusion



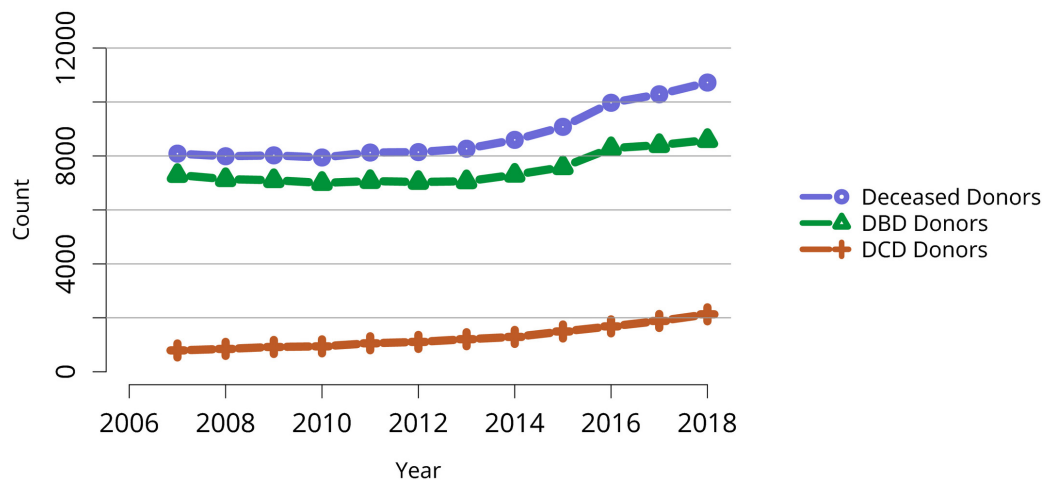
Post graft reperfusion

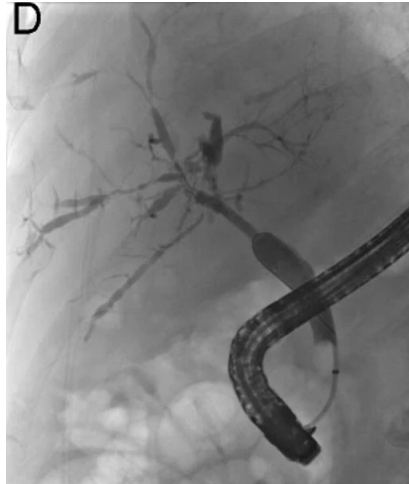


- Left sided APOLT for MLD. Graft implantation in progress. The child underwent native extended left hepatectomy to provide sufficient space for an adult LLS graft donated by her mother.

## ○ Donation after cardiac death

- Organ procurement after circulatory death criteria
- ECDs –
  - Use selectively (donor age and BMI)
  - Minimize CIT
  - Select “appropriate” recipient
- Warm ischemia + agonal time < 30 min
- ↑ risk for PNF, DGF, and ischemic cholangiopathy



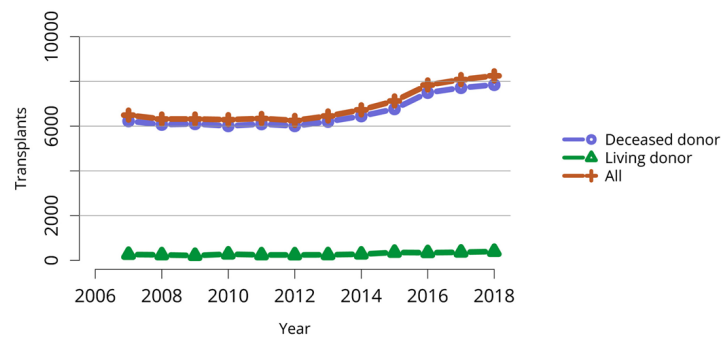


Kohli, D.R., Pannala, R., Crowell, M.D. *et al.* Interobserver Agreement for Classifying Post-liver Transplant Biliary Strictures in Donation After Circulatory Death Donors. *Dig Dis Sci* (2020). <https://doi.org/10.1007/s10620-020-06169-7>

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## ○ Living donor selection

- Donor safety is paramount
- Morbidity 15-25%
- Mortality 0.5%



American Journal of Transplantation 2020, Volume: 20, Issue: s1, Pages: 193-299

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### ○ Living donor selection

- Adult, age 18-60, ABO compatible
- Mentally and physically healthy, no comorbidities
- BMI <30, minimal hepatic steatosis (<10%)
- Vascular and biliary anatomy favorable
- Graft size –
  - Big enough for recipient (GRWR 0.80 or >)
  - Not too big for the donor (RLV  $\geq$ 30%)