Cadaveric Organ Procurement
Historical Origins

- 1933 - First cadaveric donor surgery performed – Dr. Yuily Voronov
  - Kidney procured from a cadaver, implanted into thigh 6 hours later. Recipient died two days later from rejection/sepsis.
- First donor surgeries all done after cardiac death:
  - 1950 – Kidney transplant by Dr. Richard Lawler at Little Company of Mary Hospital, Illinois
  - 1962 – Liver transplanted by Dr. Thomas Starzl at the University of Colorado
  - 1962 – Lung transplanted by Dr. James Hardy at the University of Mississippi
- For all these cases, donors were transferred to the OR, and mechanical ventilation was stopped. Organ retrieval could start only when the donor’s heart stopped beating.

- 1963 - First brain-dead donor surgery done by Dr. Guy Alexandre at the Catholic University of Louvain in Belgium.
  - Graft worked immediately after transplant, and creatinine normalized.
  - Patient died of sepsis on POD #87.

Dr. Alexandre and colleagues established a set of criteria to constitute brain death

Disclosure

I have no relevant financial relationships with any companies related to the content of this course.
Establishment of Formal Brain Death Criteria
Harvard Criteria for Brain Death

- 1968 – In part as a result of the demands created by the growth of transplantation, an "Ad Hoc Committee of the Harvard Medical School" established criteria for diagnosis of brain death.

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Irreversible cerebral damage</th>
<th>Irreversible coma of recent onset</th>
<th>Irreversible cessation of circulatory and respiratory functions</th>
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<tbody>
<tr>
<td>Criteria</td>
<td>Papilledema and dilated and misdirected pupils</td>
<td>No reaction to plantar or corneal stimulation</td>
<td>No reaction to tracheal suctioning</td>
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<td></td>
<td>No spontaneous eye opening or upward gaze</td>
<td>No response to verbal commands</td>
<td>No response to tracheal suctioning</td>
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<td>No urine or stool production</td>
<td>No response to verbal commands</td>
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Re-emergence of Donation after Cardiac Death
Current Practice Patterns in the US

- 1990s – increasing demand for organs, with growing waitlist time and pre-transplant mortality. Some centers began re-examining donation after cardiac death in selected patients.
- Pittsburgh group pioneered the rapid DCD procurement protocol
- 2000 – IOM study released on Non-Heart Beating Organ Transplantation
- "All organ procurement organizations (OPOs) should explore the option of nonheartbeating organ transplantation, in cooperation with local hospitals, health care professionals and communities."

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UDDA: Codifying the Diagnosis of Brain Death
Uniform Determination of Death Act

- 1981 – President’s Commission for the Study of Ethical Problems in Medicine and Behavioral Research enacted the Uniform Determination of Death Act (UDDA).
- The act states that, "An individual who has sustained either (1) irreversible cessation of circulatory and respiratory functions or (2) irreversible cessation of all functions of the entire brain, including the brain stem, is dead."
- Rapidly led to the expansion of donation after brain death in the US and abroad, which became the predominant form of cadaveric donation.

Growth of DCD Procurement Surgery in the United States

- Growth of DCD procurement surgery in the United States has shown steady increase over the years.
Organ Procurement Surgery: DBD

WARM dissection

- Two components: WARM (pre-crossclamp) and COLD (organ cut-out)
- The ABC’s: ABO confirmation, Brain death documentation, Consent for donation
- Discussion with other procurement teams: timing considerations, anticipated cross-clamp delays
- Positioning, instrumentation, lines
- Time out/prepared statement/moment of silence
- Incision: from sternal notch to pubis. Cruciate incision possible if additional exposure needed


Organ Procurement Surgery: DBD

WARM dissection

- Evaluation of the organs, assessment for evidence of malignancy, infection
- Liver: assess for fat content, masses, liver edges (blunting). Take down falciform ligament, left triangular ligament, and gastrohepatic ligament. Assess here for a replaced left hepatic artery. If found, mark and preserve.
- Palpation in foramen of Winslow for replaced right hepatic artery pulse.


Organ Procurement Surgery: DBD

WARM dissection

- Extended kocherization/Cattell-Braasch
- Purpose is to expose the retroperitoneum for cannulation of vessels.


Organ Procurement Surgery: DBD

WARM dissection

- Retroperitoneal structures are visualized, including IVC, left renal vein, and right kidney.
- Inferior vena cava and inferior mesenteric vein are anastomosed with ties for later cannulation.

Organ Procurement Surgery: DBD

WARM dissection

- Goal of cannulation is to flush both arterial and portal circulation after cross-clamp.
- However cannulas are not actually inserted until immediately prior to cross-clamp when patient is systemically heparinized.

Organ Procurement Surgery: DBD

WARM dissection

- Once vasculature is encircled, gallbladder incised and flushed.
- Goal is to flush bile out of CBD, to reduce risk of ischemic cholangiopathy.

Organ Procurement Surgery: DBD

WARM dissection

- Supraceliac aorta is identified and mobilized.
- Cross-clamping is essential for good organ perfusion to prevent unintended losses of flush into non-procured tissues.
- Ready for heparinization and cross-clamp once certain criteria met:
  - Organs inspected and acceptable
  - Malignancy/infection ruled out
  - Retroperitoneum exposed and vessels for cannulation encircled
  - Gallbladder flushed
  - Supraceliac aorta dissected free for cross-clamp.
Organ Procurement Surgery: DBD

**WARM** dissection
- IV Heparin administered, commonly ~300U/kg
- Distal aorta below cannula ligated
- Cannulas flushed and inserted. Cannulas secured in place.
- Shown here are two illustrations of cannulas in position and the vasculature they perfuse.


Aseni et al., *Multiorgan Procurement for Transplantation*, 2016 Springer

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Organ Procurement Surgery: DBD

**WARM** dissection into **COLD**
- Once coordinated with all teams, multiple things happen quickly:
  - Supraceliac aorta is crossclamped.
  - Flush is started.
  - Venous outflow is vented into chest (IVC/RA incision) or abdomen (infrarenal IVC).
- Cold flush is immediately packed throughout the chest and abdomen.
- Perfusate solution commonly University of Wisconsin; goal to stabilize cold organs, reduce osmotic stress.


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Organ Procurement Surgery: DBD

**COLD** dissection
- Thoracic organs removed.
- Intestines removed, small bowel mesentery clamped and SB cut out to prevent loss of flush into bowel.
- Once flush run in, remainder of GI tract is excised and removed from abdomen.
- Organs then carefully cut out individually or en bloc, depending on circumstances.


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Organ Procurement Surgery: DBD

**COLD** dissection
- Liver and pancreas are split in situ, or taken en bloc and separated on the back table.
- Aberrant liver arterial anatomy can preclude pancreas procurement – replaced right hepatic arteries create challenges for division of resources between organs. Liver takes precedence.

The kidneys are removed last, and are removed en bloc, leaving as much length and tissue on the ureters as possible.

The kidneys are then split from each other on the back table.

Once removed, all organs placed in cold slush, flushed, separated, and examined on the backtable, and packaged.

Although organs are FLUSHED immediately after crossclamp, they are not truly COLD until they are removed from the body.

EXTRACTION TIMES have become a relevant predictor of graft function.

Extraction times impact graft function:

- 576 kidney recoveries from 2006-2008
- 5 year follow up
- Tracked extraction time (crossclamp->organs out) and correlated with primary nonfunction (PNF; loss w/in 90d), delayed graft function (DGF; HD w/in 7d), and overall allograft survival.

Extraction times >60 mins correlate with decreased graft survival. If >120 mins, associated with 20% PNF.
Extraction times impact graft function

The Impact of Deceased Donor Liver Extraction Time on Early Allograft Function in Adult Liver Transplant Recipients

- Extraction times from 2012-2016
- DCD, re-transplant recipients, and split liver grafts were excluded
- Correlated extraction time with Model of Early Allograft Function (MEAF) score: peak ALT, INR, bilirubin levels in first 3d.
- Validated predictor of patient and graft survival.

Organ Procurement Surgery: DCD

- Highly protocolized, to ensure no conflict of interest, and that the donation and procurement process in no way interferes with or impacts the care of the patient from whom support is being withdrawn.
- Pre-withdrawal anticoagulation, vasoactive medications, and intravascular cannulation are areas of debate.
- Withdrawal, patient care, and declaration of death happen entirely independent of the transplant team.
- After circulatory death is confirmed, team enters room and rapidly performs laparotomy, secures iliac arterial access for perfusate flush. “Super rapid technique.”
- Goal: incision to flush in <2 mins.
- Unlike DBD surgery, there is no extended warm dissection (barring ECMO as done by U. Mich).
Organ Procurement Surgery: DCD

- Times matter in DCD:
  - (A) Time from withdrawal of vent support to hypoperfusion of organs (blunt or MAP<50)
  - (B) Time from hypoperfusion until declaration of death
  - (C) Waiting period for confirmation of death
  - (D) Time from declaration of death to move and prep patient, make incision, dissect, cannulate, and begin flush.

- A-D constitute the total warm ischemic time. B-D constitute the “true” warm ischemic time.

DCD vs DBD: increased risk of graft failure

- DCD livers have an increased risk of graft failure, with an odds ratio of 1.85.
  - Along with graft failure, increased rates of EAD (as defined by INR >1.6 or bilirubin >10 at POD#7, or peak AST/ALT >2000) among DCD recipients.
  - However graft failure risk after receipt of DCD donor liver is not simply perioperative risk from acute early dysfunction, but continues to be increased for first 12-24 months.

DCD donation also associated with biliary complications

- UPenn group was first to describe increased risk of biliary complications in DCD recipients. Single-center retrospective series, 15 DCD vs 221 DBD, 1996-2001.
  - Overall rate of biliary complications was 33% in DCD cohort, vs. 9.5% in DBD cohort.
  - Majority of these were intrahepatic, ischemic-type strictures.

Predictors of graft failure in DCD livers

- Michigan/Mayo groups analyzed SRTR database data 2001-2009 for all liver-only DCD recipients (N=1557), completed graft failure with donor, recipient, and transplant characteristics.
Predictors of graft failure in DCD livers

Conclusions
- Organ donation only possible thanks to the incredible generosity of donors and families in a time of great hardship
- Donor procurement surgery is a technically complex operation that happens in an unfamiliar OR, often late at night, and requires coordination, communication, and professionalism between multiple teams.
- Re-emergence of DCD donation as the demand for organs continues to rise
- Increased risks with DCD donation, specifically for graft failure, EAD, and biliary complications.
- Risks can be mitigated by careful donor selection (age, weight) and technical aspects (minimizing cold and warm ischemia).
- For both DCD and DBD, the data clearly demonstrate: TIME MATTERS