# Transplantation for TTR Amyloidosis 2011

# Steve Zeldenrust, MD, PhD Mayo Clinic



Scottsdale, Arizona

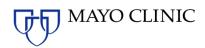


Rochester, Minnesota



Jacksonville, Florida





#### Rationale

- Why liver transplant?
  - Removing source only known cure
  - Majority of circulating TTR made in liver
  - Not for asymptomatic gene carriers
- What about transplanting other organs?



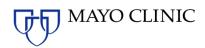
# **Liver Transplant**

- First liver transplant performed in Sweden 1990
- The FAP World Transplant Registry:
  - Updated 12/31/09
  - 1782 OLT performed worldwide
  - 120 transplants/year
  - Portugal, France and Sweden account for over two-thirds



#### **Outcomes**

- Low mortality rate (3%)
- Predictors of outcome:
  - mBMI
  - Disease duration (?)
  - Mutation (V30M vs non-V30M)
  - Autonomic neuropathy



#### **V30M Outcomes**

- Neuropathy stable or improved in up to 40%
- Nutrition improves in up to 80%
- Cardiac progresses in ~50%
- Kidney involvement unaffected
- Eye deposits progress



#### Non-V30M Outcomes

- Small numbers make prediction difficult (n=108)
- Neuropathy autonomic most likely to improve, sensory variable
- Gl improves in most
- Eye and brain can worsen due to local production of variant TTR



# Non-V30M Outcomes

- Cardiac progresses in many
- Evidence that pace of deposition can increase after transplant
- Cardiac deposits develop in those with no heart involvement at dx.
- New deposits contain normal TTR made by transplanted liver



# **Heart Transplant in ATTR**

- FAPWTR:
  - Liver + heart 19
  - Liver + previous heart 8
  - Liver + sequential heart 1
  - Liver + heart + kidney 1



# **Heart Transplant in ATTR**

- Outcomes similar to other indications for heart transplant
- Some centers advocating combined heart/liver transplant in non-V30M
- Controversy over timing (combined vs. sequential)



# **Kidney Transplant in ATTR**

- Kidney involvement in most at diagnosis
- Only symptomatic in ~10%
- FAPWTR: Liver + kidney 39
- Survival worse than liver alone, but related to low mBMI



## What Does It All Mean?

- Known:
  - Survival improved with liver transplant in V30M
  - Most effective if early
  - Major benefit is nutrition
  - Combined liver + heart and liver + kidney feasible



## What Does It All Mean?

- Unknown:
  - When is it futile?
  - Which mutations benefit?
  - If heart involved need combined heart + liver?
  - Is amyloid halted, slowed, reversed or accelerated?



# **Implications**

- ATTR clear indication for liver transplant
- Early and accurate diagnosis critical
- Possibility of domino shortens wait time
- Need for multiple organs lengthens wait time



#### **Future Directions**

- Better follow-up needed to answer important questions (disease progression, etc.)
- Impact of new treatments (alternative to transplant vs. adjunct to transplant)