Newborn Screening for SCID: clinical impact

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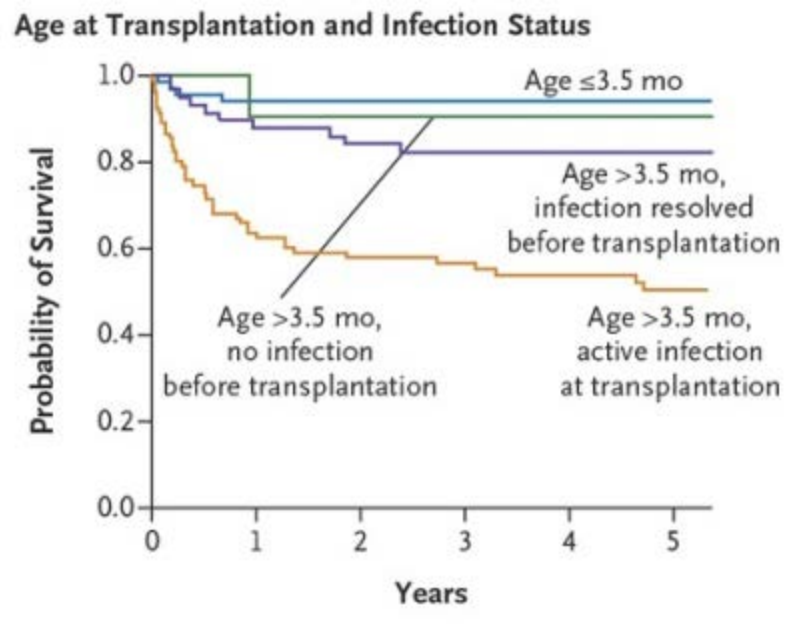
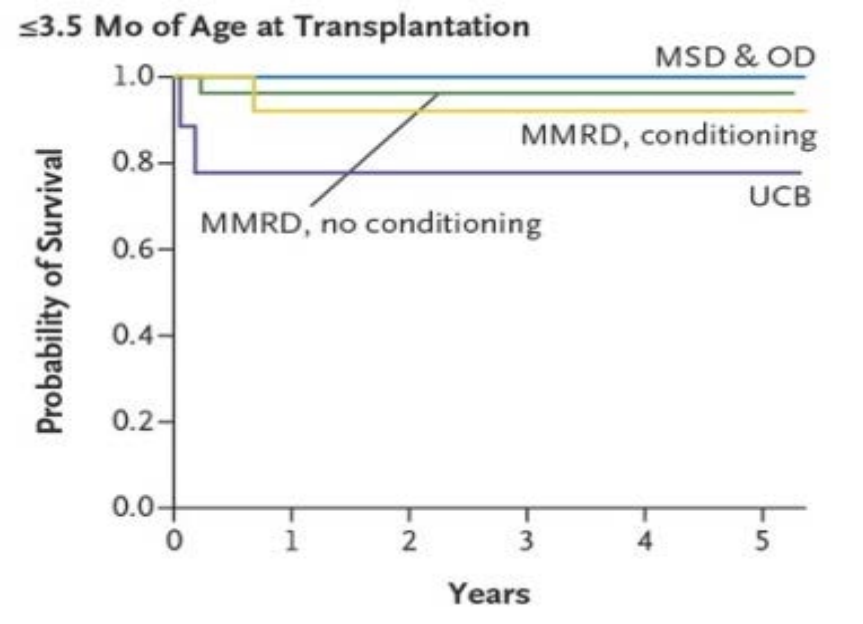
Early Diagnosis = Better outcomes

- Key publication by Pai, et al. using data from the Primary Immune deficiency treatment consortium showed a marked improvement in survival for transplants done at <3.5 months of age.





Diagnosis + treatment ≤ 3.5 mos = 94% survival at 5 years

Pai SY NEJM 2014

What we learned: first 11 states screening

- Data from 11 programs (10 states + Navajo nation) screened over 3 million infants:
  - Identified 52 cases of SCID – population incidence of 1:58,000
  - Survival was 45/52 infants overall and in 45/49 who received a hematopoietic cell transplant (92%)
  - Non-SCID T-cell lymphopenia occurred in 1:14,000 infants
  - Causes of non-SCID TCL: DGS/22q11 DS (n=78), trisomy 21 (n=21), Ataxia-telangiectasia (n=4), Trisomy 18 (n=4), CHARGE (n=3), Jacobsen (n=2), assorted others single cases
- Paper was critical in identifying the population birth prevalence of SCID, which was nearly double the previous estimates of 1:100,000

Kwan A et al. JAMA 2014

More States data

- Wisconsin data 2008-2011: 5 cases (207,696 births) or ~ 1:41,000 births
  - In addition 4 patients with 22q11 DS, 5 with Idiopathic TCL, 10 with other syndromes
  - 4/5 SCID patients had been transplanted at the time of publication. 1 was on PEG-ADA replacement, all were alive
- New York data 2010-2012: 9 cases (485,912 births) or ~ 1:54,000
  - In addition 19 cases with idiopathic TCL, 28 with other syndromes
  - 8/9 with HCT, one on PEG-ADA, all were alive
- California data 2010-2016: 26 cases from CA and 6 from other states
  - 94% were alive
  - Transplant outcomes: all with T cell reconstitution, 50% with B cell reconstitution
  - Types of SCID: IL2RG (7),ADA (6), DCLERC1 (5), Il7R (4), RAG1 (4), RAG2 (4), JAK3 (1), RMRP (1)
  - Non SCID TCL – mostly DiGeorge syndrome, also Ataxia-telangiectasia, CHARGE
  - 1 patient died prior to transplant

Verbsky J Jo Clin Immun 2012, Vogel B Jo Clin Imm 2014, Dorsey M JACI 2017

Georgia experience

- Screening started June 2016
- 3 cases of SCID identified for 129,700 births or ~ 1:43, 200 births
- 1 IL7RA, 1 PNP, 1 unknown
- 3/3 have been transplanted. All are alive
- 1 Idiopathic TCL, 2 CHARGE syndrome, 3 22q11 DS, 1 absent thymus, several other genetic/syndromic defects

Impact of SCID NBS

- Early *presymptomatic* identification is happening in 46/50 states with most infants being seen by a specialist within weeks of identification through NBS
- Several recent papers highlighted the cost savings for early identification and intervention for infants with SCID

Outcome	Screening	No Screening
Total cost screening + diagnosis	$741,376	N/A
Treatment costs for surviving infants	$197,258	$457,401
Treatment costs for infants dying PT transplant	$27,234	$83,996
Treatment cost reduction w/ screening	$316,905	N/A
Net direct cost w/ screening	$424,470	N/A
Cost per life-yr-saved	$35,311	
Benefit-cost ratio	2.7-5.3*	

** Ratio varies depending on the healthcare costs from Ding J Peds 2016*

Conclusions

- As implied in the Kwan paper, SCID is more common that previously appreciated
- As expected, outcomes for infants with SCID identified at birth are better with less infectious complications and hospitalizations prior to transplant and to-date better outcomes post-transplant
- Another impact has been the focus on gathering data on the outcome of treatments for SCID with an emphasis on improving treatment outcomes through multicenter prospective trials
- BUT – barriers remain
  - Access to specialists and treatment for infants in underserved areas (developing referral networks)
  - Cost issues for diagnostic testing and treatment at institutions specializing in primary immune deficiencies
  - Creation of central repositories for data on NBS for SCID – epidemiology, pre transplant treatment and transplant outcomes, and long-term outcomes
    - Efforts by the Association of Public Health Laboratories, New Born Screening and Translational Research Network and Next Steps have been important

Thank you

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