

IMMUNIZATIONS IN THE IMMUNOCOMPROMISED HOST

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I have no actual or potential conflict of interest in relation to this program

Outline of Presentation

Challenges

- Introduction
 - High-dose corticosteroid scenario
 - Live-attenuated vaccines in selected groups
 - Inactivated/non-live vaccines in selected groups
 - Passive immunizing agents
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Objectives

- To highlight the challenges in adequately immunizing the immunocompromised host.
 - To discuss the roles and safety of specific vaccines.
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Vaccines in Immunocompromised Hosts: Challenges

- Compliance
- Safety concerns
- Effectiveness

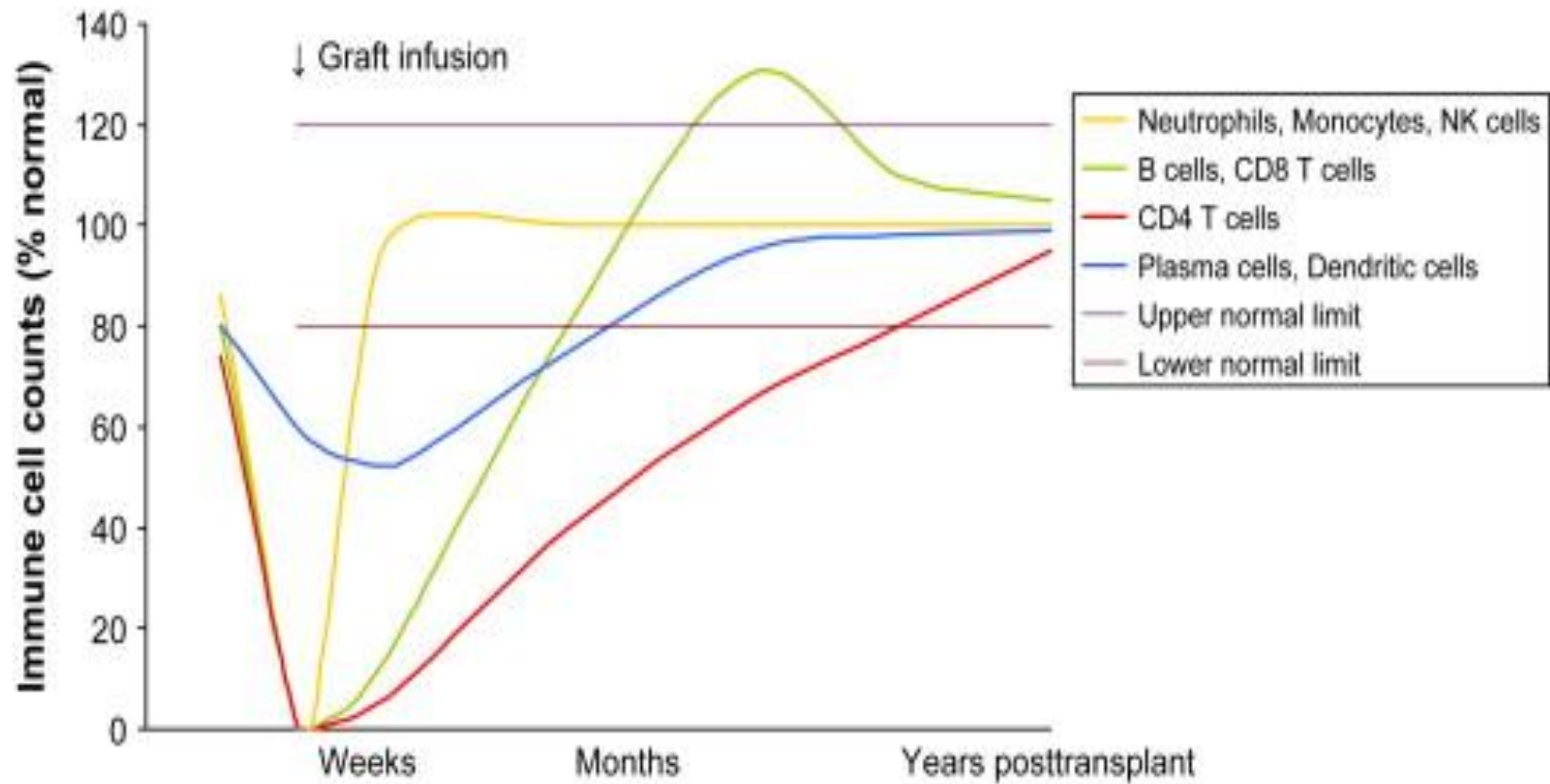
Fluctuating immune status

Increasing use of potent immunosuppressants

Heterogeneous patient groups with variable immune deficits

The Problem of Heterogeneity: HSCT Scenario

- Degree of functional immune deficit
 - Recipient age
 - Underlying disease
 - Previous treatment
 - Conditioning regimen
 - Source of stem cells
 - Degree of HLA mismatch
 - GVHD
 - Concomitant infections
 - Pre-existing immunity
-



Tomblyn et al. Biol Blood Marrow Transplant 2009;15:1143-1238

Current Acute Lymphoblastic Leukemia (ALL) Protocols Induce Loss of Humoral Immunity to Viral Vaccination Antigens

Study of children with ALL; N = 43

- Continuous first remission for a median of 5 years (range 2-12)
- Before ALL diagnosis, children were immunized against MMR
- # vaccines doses received = 1-2 depending on age.
- MMR serology performed after revaccination while in remission.

Nilsson A, et al <http://pediatrics.org/cgi/content/full/109/6/e91>

Immune Status in Patients with ALL after Chemotherapy

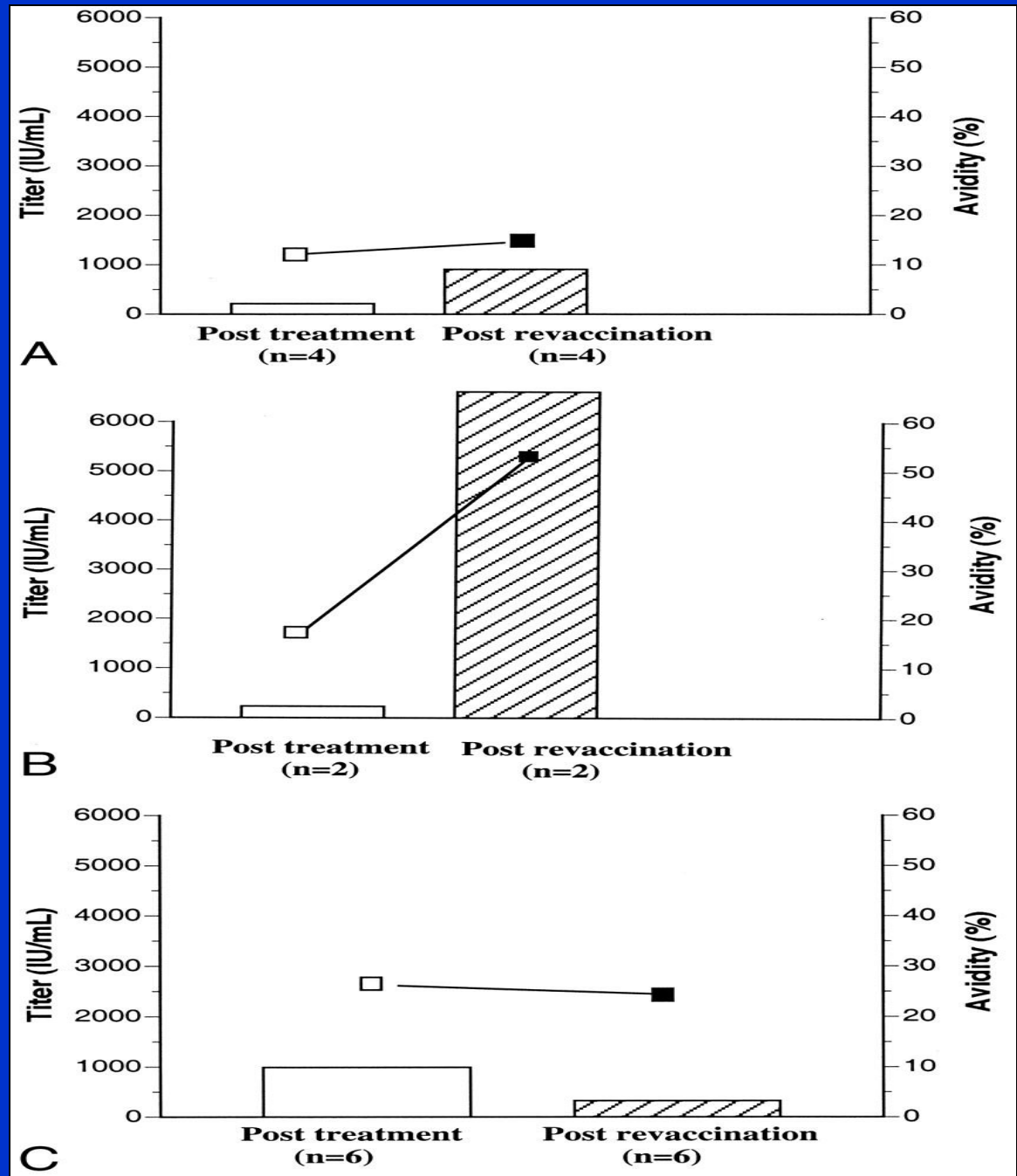
Patients' Status	Measles	Rubella
Immune	26/43 (60%)	31/43 (72%)
Non-immune	17/43 (40%)	12/43 (28%)

Nilsson A, et al <http://pediatrics.org/cgi/content/full/109/6/e91>

Primary immune response

Secondary immune response

Non responder



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**Live Attenuated
Vaccines**



Patient receiving high-dose
corticosteroids;

Is it safe to administer the varicella
or MMR vaccines?

Live Vaccines and High-dose Steroid Therapy

Definition of high-dose steroids

≥ 2 mg per kg/day of prednisone or
equivalent to a total of ≥ 20 mg/day for those
weighing more than 10 kg.

Live Vaccines: Intervals Post Steroid Therapy

<u>Dose of Steroids</u>	<u>Duration of Delay</u>
High-dose steroids for ≥ 2 weeks	1 month
High-dose steroids for < 2 weeks	2 weeks

Live Vaccines: Intervals Post Steroid Therapy

<u>Dose of Steroids</u>	<u>Duration of Delay</u>
Topical (skin or resp. tract)	No delay
Local injection	No delay
Physiologic	No delay
Low or moderate systemic	No delay

12 year old cancer patient; what are the recommendations for use of the varicella or MMR vaccines?

Live Vaccines: Intervals Post-Immunoablative Therapy

Sources	Duration of Delay
AAP Redbook	At least 3 months No firm recommendations
UK Survey	6-12 months
Australia	12 months
NACI 2003	≥ 12 months

References: Redbook 2009; Aust Fam Physician 2003;32.
Med and Pediatr Oncology;2003;40.

Live Vaccines in Selected Patient Populations

Varicella Vaccine

Still controversial in leukemics. May be considered if;

- Patient is in remission for 1 year
 - Lymphocyte counts $> 0.7 \times 10^9/L$
 - Platelets $> 100 \times 10^9/L$
 - Vaccinated as part of a research protocol, with close monitoring.
-

12 year old HSCT or solid organ
transplant patient; what are the
recommendations
for use of the varicella or MMR vaccines?

Live Vaccines in Selected Patient Populations

Patient Group	Varicella Vaccine Use	MMR Vaccine Use
SOT Recipients	No	No
HSCT Recipients	No	Yes*
HIV	Yes if CD4 \geq 15%	Yes Unless severely compromised

*At 24 months assuming immune recovery and no GVHD.

**Sustainability of humoral responses to varicella
vaccine in pediatric transplant
recipients following a pre-transplantation immunization strategy**

*Barton M, Wasfy S, Melbourne T, Hébert D, Moore D, Robinson J,
Marchese RD, Allen UD.*

Pediatr Transplant. 2008 Dec 15. [Epub ahead of print]

Can siblings of a cancer patient
receive the varicella vaccine?



Low but definite risk of transmitting vaccine virus.

Disease in such cases tends to be mild and does not outweigh the more significant risk of the immunocompromised child acquiring natural varicella infection.

If siblings of a cancer patient receive the measles vaccine, is there any risk of transmission of measles to the immunocompromised child?



Measles vaccine will not result in transmission of measles of vaccine virus.

Important to vaccinate siblings against measles. This will reduce the risk that the immunocompromised patient will become exposed to measles in the home.

Can mumps vaccine virus
be transmitted?



Vaccinated persons do not transmit
mumps vaccine virus.

Can the rubella vaccine virus
be transmitted?



Vaccinees intermittently shed small amounts of virus from the pharynx 7-28 days after vaccination. However, no evidence of transmission of the vaccine virus has been documented (2009 Redbook).

**Inactivated / Non-live
Vaccines**



Non-live Vaccines: Interval Post-Immunoablative Therapy

- Give when total lymphocyte count exceeds $0.5 \times 10^9/L$
 - Can be done during maintenance chemotherapy.
 - Boosters required at > 3 months after the end of chemotherapy.
-

Post-Transplant Vaccination if Not Vaccinated Pre-Transplantation

DTaP	0, 2, 4 months starting 1 year post-Tx Booster at 18 mths & 4-5 years post-Tx
IPV	0, 2, 4 months starting 1 year post-Tx Booster at 18 mths & 4-5 years post-Tx
HIB	Doses vary with age of initiation

Post-Transplant Vaccination if Not Vaccinated Pre-Transplantation

Hepatitis B	Full series at 12 mths post Tx
Hepatitis A	Consider in high-risk at 12 mths
Influenza	Start at 6-12 mths post Tx

Post-Transplant Vaccination if NOT Vaccinated Pre-Transplantation

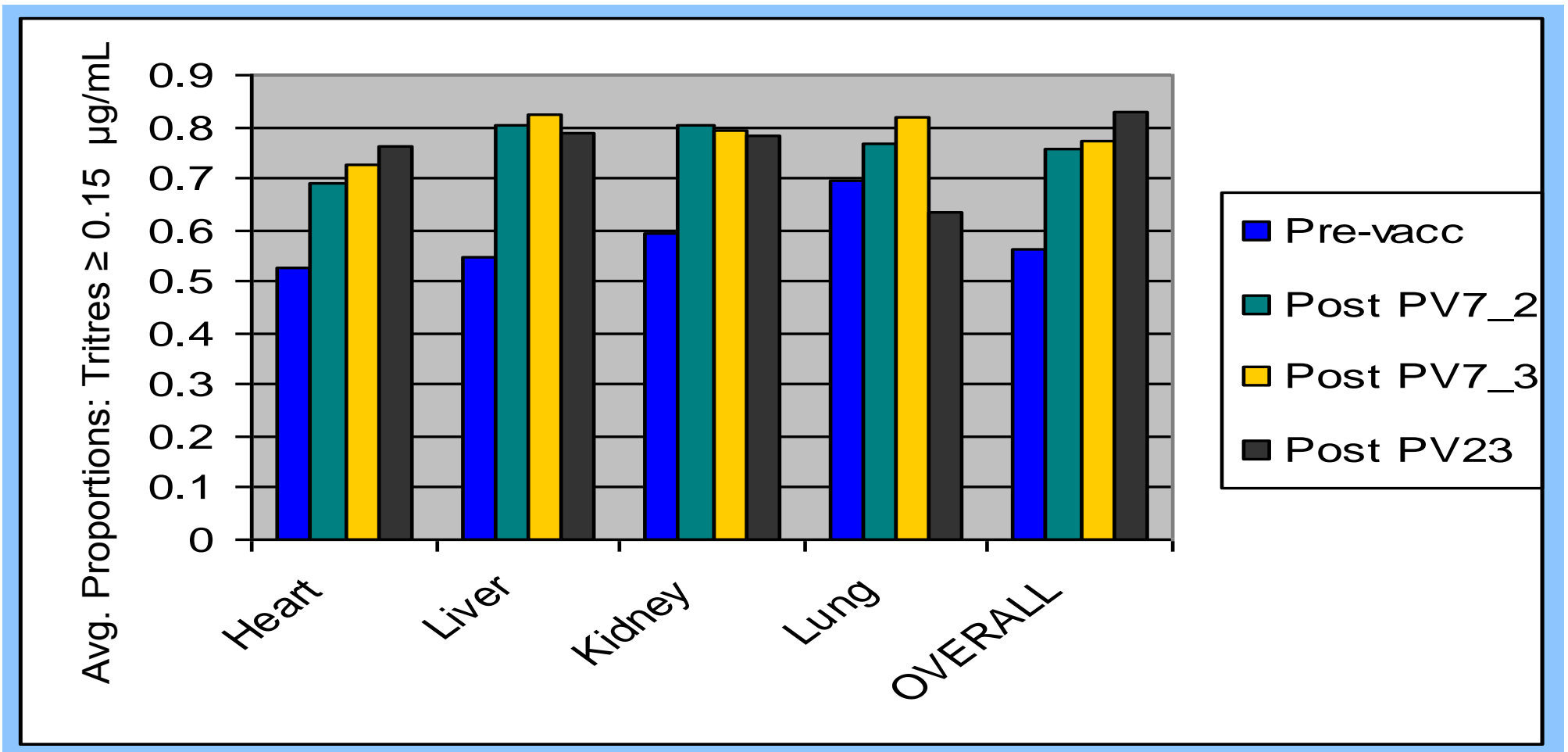
Pneumococcal	7-valent vaccine plus 23-valent booster Start at 6-12 months post-Tx
Meningococcal	1 dose if polysaccharide; 12 mths post-Tx # doses of conjugate varies with age.
Rabies	Pre and post exposure prophylaxis
Travel	Pre-travel ID consult recommended

**Seven-valent pneumococcal conjugate vaccine in pediatric
solid organ transplant recipients:
a prospective study of safety and immunogenicity.**

*Barton M, Wasfy S, Dipchand AI, Hébert D, Ng V, Solomon M,
Fecteau A, Stephen D, Allen U.*

Pediatr Infect Dis J. 2009 Aug;28(8):688-92.

Proportions of Transplant Recipients with Titres $\geq 0.15 \mu\text{g/mL}$ after Vaccination with PV7 + PV23



Proportions of Transplant Recipients with Titres $\geq 0.15 \mu\text{g/mL}$ after Vaccination with PV7 + PV23

- Cardiac & lung recipients demonstrated additional benefit from a third dose of PCV7.
- Cardiac recipients showed most benefit from boosting with PV23, with significant increases in GMC's ($P < \text{or} = 0.008$).

Barton et al. *Pediatr Infect Dis J.* 2009 Aug;28:688-92

Post-Transplant Vaccination if Vaccinated Pre-Transplantation

DTaP	Booster at 12 mths & 4-5 years post-Tx
IPV	Booster at 12 mths & 4-5 years post-Tx
HIB	Booster at 12 mths post-Tx
Influenza	Start at 6-12 mths post Tx

Post-Transplant Vaccination if Vaccinated Pre-Transplantation

Hepatitis B	Check serology post Tx
Hepatitis A	Consider in high-risk at 12 mths
Influenza	Start at 6-12 mths post Tx

Post-Transplant Vaccination if Vaccinated Pre-Transplantation

Pneumococcal	PV23: Booster 12 mths & 4-5 yrs post-Tx Conjugate: Booster 12 mths followed by PV23
Meningococcal	Booster at 12 mths post-Tx
Rabies	Pre and post exposure prophylaxis
Travel	Pre-travel ID consult recommended

Immunization of HSCT Recipients

Vaccine	Time after HSCT		
	12 months	14 months	24 Months
DTaP*	+	+	+
IPV	+	+	+
HIB	+	+	+
Pneumococcal	+ #		+
Meningococcal	+ ?		+ ?
Flu	≥ 6 months post-transplant		
HBV	+	+	+
HAV	Selective use		

*Td if ≥ 7 years;

if polysaccharide vaccine

Thank You

