Immunisation and transplantation

Peter McIntyre

National Centre for Immunisation Research and Surveillance, CHW and University of Sydney

Structure of Talk

- **Current immunisation schedule**
  - Children, Adolescent and Adult
- **Transplant scenarios**
  - Solid Organ vs BMT
  - Children vs Adults
  - Disease risks
- **Immunisation Recommendations**
  - Handbook 2008
  - Literature updates
- **Case studies**
- **Are we walking the walk ?**

NIP schedule to 4 years of age

Age	Vaccines administered					
Birth	Hepatitis B					
2/12	DTPa	Hib	HepB	IPV	7vPCV	Rota
4/12	DTPa	Hib	HepB	IPV	7vPCV	Rota
6/12	DTPa	Hib	HepB	IPV	7vPCV	annual influenza (6+ months onwards med at risk only)
12/12	MMR	Hib	Mening C			
18/12	VZV					
3.5 yrs	DTPa	IPV	MMR			

NIP schedule for adolescents and adults

Age	Vaccines administered				
12-15 years	Hepatitis B	VZV (negative history)	HPV	dTpa	23vPPV (Indigenous only)
ATSI ≥50 years	23vPPV	Annual influenza			
All ≥ 65 years	23vPPV	Annual influenza			

Haemopoetic Stem Cell Transplants (HSCT)

- Antibody titres to VPDs decline progressively post transplant, autologous < allogeneic
- Functional impairment varies but little data to support different approach for autologous vs allogeneic
- Disease risk highest for encapsulated bacteria (Hib, pneumococcus) and for measles, varicella, influenza. Also high long-term risks with HPV……..
- Routine re-immunisation needed but…….
- Evidence of risk-benefit for vaccines favourable but mainly indirect

Development of Immunity post HSCT

- Time post transplant crucial
- B lymphocytes
  - Zero first 1-3 months
  - Normal numbers by 3-12 months, but maturation of responses delayed – longer in adults
- T lymphocytes
  - Naïve T cells that can respond to new antigens do not appear until 6-12 months, earlier in children
  - T cell responses to pathogens or vaccines encountered pre-transplant earlier (adults)
- Useful responses can still occur with GVHD, so increasing evidence not to postpone esp in children

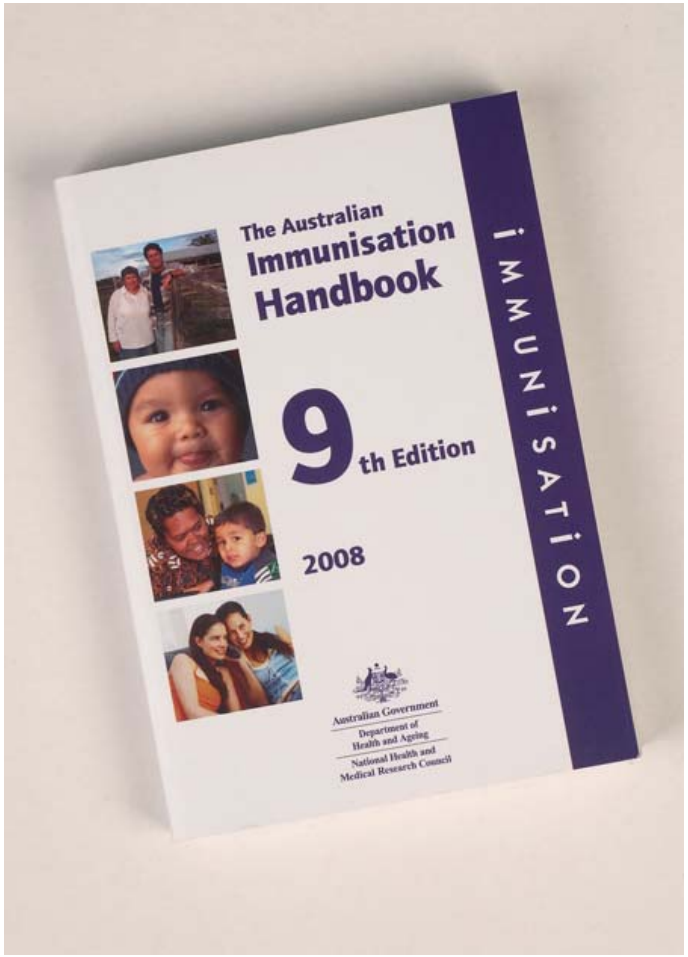
Solid Organ Transplants – kidney/liver

- Compared to HSCT, immunosuppression often long term
- Focus should thus be on ***pre***-transplantation vaccination
  - Define susceptibility by serology
- A problem in children – often young and urgent t'plant
  - Can accelerate schedules to complete primary series
- Live viral vaccines at least one month pre-transplant
- Adverse events (except for live vaccines)
  - rare and comparable to immunocompetent individuals
  - no evidence that immunisation triggers allograft rejection, but good evidence for infection…….

For all transplant recipients…….

- Immunise/serologically evaluate all household and health care worker contacts
  - Influenza
  - MMR
  - Varicella
  - Pertussis

Australian Immunisation Handbook – 2008



Recommended vaccination for solid organ transplant (SOT) recipients - children

Inactivated Vaccine	Pre	Post	Comments
Hib vaccine	Yes	Yes	If possible complete vaccination at least 6 weeks before transplantation.
Hepatitis A vaccine	Yes	Yes	Recommended for all seronegative SOT recipients.
Hepatitis B vaccine	Yes	Yes	Recommended for all seronegative SOT recipients.
Influenza vaccine	Annual vaccination starting before transplantation for people ≥6 months of age.		
7vPCV	Yes, if <10 yrs	Yes, if <10 yrs	The primary schedule should be completed before transplantation.
23vPPV	Yes	Yes	
Inactivated poliovirus vaccine (IPV)	Yes	Yes	The primary schedule should be completed before transplantation.
HPV	Yes	Yes	In girls aged 12-17 years only
Diphtheria-tetanus- pertussis vaccine	Yes	Yes	The primary schedule should be completed before transplantation DTPa for children <8 years of age; dTpa for people ≥8 years of age).
Meningococcal C conjugate vaccine (MenCCV)	Yes,	Yes	If ≥1 year of age
Meningococcal polysaccharide vaccine (4vMenPV)	Yes	Yes	If >2 years of age, give 4vMenPV at an interval of at least 2 weeks after MenCCV.
Live Vaccines	**Pre**	**Post**	
MMR vaccine	Yes	Contraindicated	
Varicella vaccine	Yes	Contraindicated	

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

9th Edition *The Australian Immunisation Handbook* 2008

Recommended vaccinations for solid organ transplant (SOT) recipients – adults

Inactivated Vaccine	Pre	Post	Comment
Hepatitis A vaccine	Yes, if seronegative	Yes, if seronegative	Recommended for all seronegative SOT recipients.
Hepatitis B vaccine	Yes, check serology	Yes, check serology	Recommended for all seronegative SOT recipients.
Influenza vaccine	Annual vaccination starting before transplantation for people ≥6 months of age.		
23vPPV	Yes	Yes	
Inactivated poliovirus vaccine (IPV)	Yes	Yes,	The primary schedule should be completed before transplantation. If no booster in past 10 years
Diphtheria-tetanus-pertussis vaccine dTpa	Yes	Yes	The primary schedule should be completed before transplantation.
Meningococcal C conjugate vaccine (MenCCV)	Yes	Yes	
4vMenPV or 4vMenCV	Yes	Yes	Give 4vMenPV at an interval of at least 2 weeks after MenCCV.
Live Vaccine	**Pre**	**Post**	**Comment**
MMR vaccine	Yes, unless 2 documented doses	Contraindicated	The primary schedule should be completed before transplantation provided the recipient is no longer on immunosuppressive therapy.
Varicella vaccine	Yes	Contraindicated	Vaccination should be completed before transplantation provided the recipient is no longer on immunosuppressive therapy.

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

9th Edition *The Australian Immunisation Handbook* 2008

Post-transplantation vaccination schedules for HSCT

Inactivated Vaccines	Months after HSCT			Comments
	12	14	24	
Diphtheria-tetanus-pertussis (DTPa for children <8 years of age; dTpa for people ≥8 years of age)	Yes	Yes	Yes	For recipients ≥8 years of age, give first dose as dTpa followed by 2 doses dT. If dT unavailable, dTpa may be used for all 3 doses.
Hib	Yes	Yes	Yes	
Hepatitis A	Not routinely recommended			
Hepatitis B	Yes	Yes	Yes	High dose (H-B-VAX II dialysis formulation) vaccine is recommended.
Influenza	Annual vaccination for life, starting 6 months post HSCT, for people ≥6 months of age.			
MenCCV	Yes, ≥1 year of age			People ≥1 year of age should receive 1 dose of MenCCV.
4vMenPV	Yes, ≥2 years of age			People ≥1 year of age should receive 1 dose of MenCCV followed by a dose of 4vMenPV when ≥2 years of age or, if already aged >2 years, give after an interval of at least 2 weeks following the MenCCV.
7vPCV	Although there are limited data on the effectiveness of 7vPCV in HSCT recipients, vaccination is recommended for children ≤9 years of age starting 6 months post HSCT			
23vPPV	Yes			Adjunctive antibiotic prophylaxis is recommended for patients with chronic GVHD.
IPV	Yes	Yes	Yes	
Live Vaccines	**Months after HSCT**			**Comments**
	12	14	24	
Varicella vaccine	No	No	Yes	Vaccination of seronegative HSCT recipients at 24 months post HSCT is recommended, provided that immunosuppressive therapy has been discontinued, there is no chronic GVHD, and cell-mediated immunity has been reconstituted.
MMR	No	No	Yes	Vaccination of measles or rubella seronegative HSCT recipients at 24 months post HSCT is recommended, provided that immunosuppressive therapy has been discontinued, there is no chronic GVHD, and cell-mediated immunity has been reconstituted.

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

9th Edition *The Australian Immunisation Handbook* 2008

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

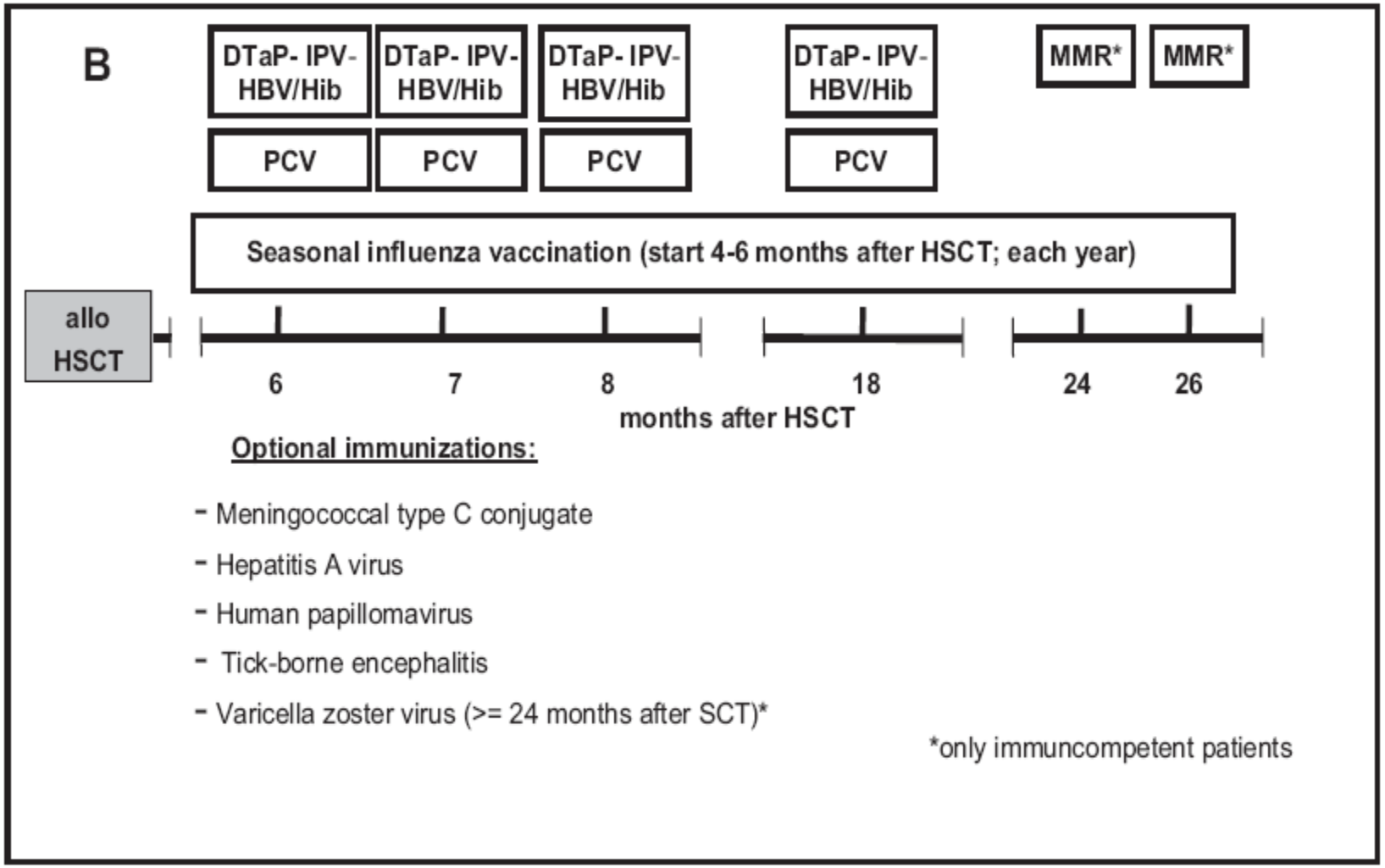
Some more recent evidence……..

Vaccination in chronic GVHD - Report from an International Consensus Conference

- Universally recommend 6 months as the time to start vaccination – change from previous
- Vaccination can proceed despite GVHD given high risk of vaccine-preventable infections and response in children
- In adults, postpone until immunosuppression is reduced to a double combination or prednisone < 0.5 mg/kg

Vaccine 2011;29:2825–2833

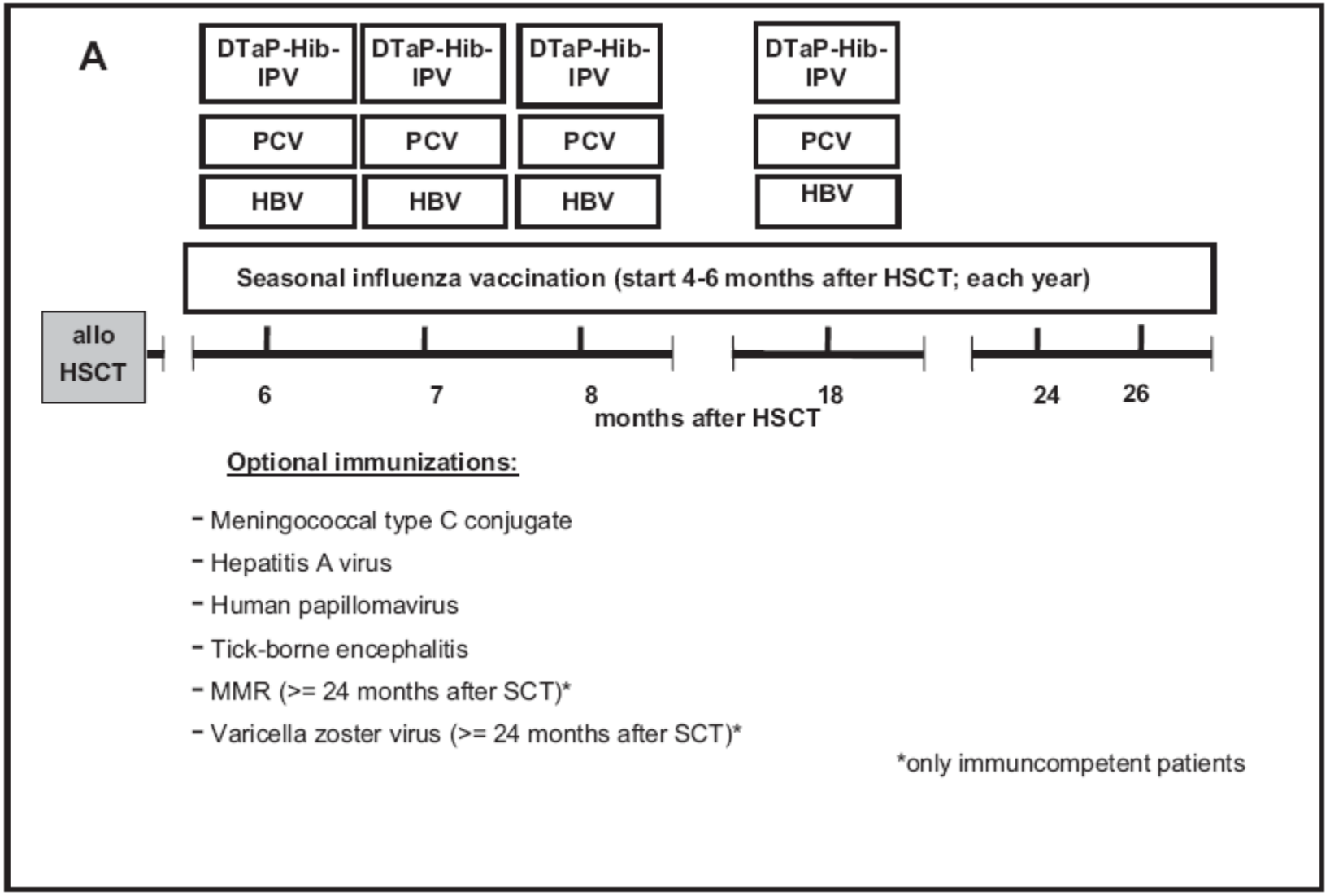
Recommended vaccines for children aged <18 years



Vaccine 2011;29:2825–2833

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

Recommended vaccines for Adults aged ≥18 years



Optional immunizations:

- Meningococcal type C conjugate
- Hepatitis A virus
- Human papillomavirus
- Tick-borne encephalitis
- MMR (>= 24 months after SCT)*
- Varicella zoster virus (>= 24 months after SCT)*

*only immuncompetent patients

NATIONAL CENTRE FOR IMMUNISATION RESEARCH & SURVEILLANCE

Vaccine 2011;29:2825–2833

Table 3
Recommendations for vaccinations after allogeneic HSCT for adults.

	Type of vaccine	Start of vaccination (months after HSCT)	Number of doses	Strength of recommendation
Bacteria				
H. influenzae type b	Conjugated	6 (boost: 18)	3+1	BII
B. pertussis	Acellular	6 (boost: 18)	3+1	BIII
S. pneumoniae	Conjugated	6 (boost: 18)	3+1	BI
N. meningitidis type c	Conjugated	6-12	3	CIII
Diphtheria/tetanus	Toxoid	6 (boost: 18)	3+1	BII
Viruses				
Hepatitis A	Inactivated	6–12	3 (+1 boost)[a]	CIII
Hepatitis B	Inactivated	6 (boost: 18)	3+1 boost	BII
Influenza	Inactivated	(4–) 6	1	AII
Measles–mumps–rubella	Live	>24	1–2	CII/III (for immunocompetent pts) EIII (<24 months post-HSCT, active cGVHD or on immunosuppression)
Poliomyelitis	Inactivated	6 (boost: 18)	3+1 boost	BII
Human Papillomavirus	Inactivated	6–12	3	CIII
Tick-borne-encephalitis	Inactivated	6–12	3	CIII

[a] If a vaccine combining immunization against Hepatitis A and B is used.

Vaccine 2011;29:2825–2833

Table 4
Recommendations for vaccinations after allogeneic HSCT for children and adolescent (<18 years).

	Type of vaccine	Start of vaccination (months after HSCT)	Number of doses	Strength of recommendation
Bacteria				
H. influenzae type b	Conjugated	6 (boost: 18)	3 + 1	BII
B. pertussis	Acellular	6 (boost: 18)	3 + 1	BII
S. pneumoniae	Conjugated	6 (boost: 18)	3 + 1	AII
N. meningitidis type c	Conjugated	6–12	3	CIII
Diphtheria/tetanus	Toxoid	6 (boost: 18)	3 + 1	BII
Viruses				
Hepatitis A	Inactivated	6–12	2	CIII
Hepatitis B	Inactivated	6 (boost: 18)	3 + 1	BII
Influenza	Inactivated	(4–) 6	1–2 (~age)	AII Every year
Measles–mumps–rubella	Live Attenuated	≥24	2	BII (for immunocompetent pts) EIII (<24 months post-HSCT, active cGVHD or on immunosuppression)
Poliomyelitis	Inactivated	6 (boost: 18)	3 + 1	BII
Varicella-Zoster-virus	Live Attenuated	≥24	2	CIII(for immunocompetent pts) EIII (<24 months post-HSCT, active cGVHD or on immunosuppression)
Human Papillomavirus	Inactivated	6–12	3	CIII
Tick-borne-encephalitis	Inactivated	6–12	3	CIII

Vaccine 2011;29:2825–2833

Specific vaccines - HSCT

- Inactivated
  - Diphtheria, Tetanus, Pertussis – use DTPa not dTpa
  - Conjugate pneumococcal (immunise donor if related)
  - In outbreak, influenza vaccine if >4 months post Tx
  - HBcAb and HBsAg need lamivudine +/- Ig + high dose Hep B vaccine
- Live attenuated
  - Measles – all children and seronegative adults (more likely if immunised than previously infected)
  - Varicella and Zoster vaccines – more limited data
  - Contraindications more liberal in children

Specific vaccines - SOT

- Inactivated
  - Hepatitis A and B need emphasis pre-immunisation
- Live attenuated
  - Serologically test all for measles and varicella irrespective of vaccination history pre–transplant
  - Specific recommendation for Zoster vaccine for those “anticipating immunosuppression” ……..

Some case scenarios

Case scenario 1 – VZV post renal transplant

- 41 year old male
- Living-related renal transplant
  - Ongoing immunosuppressives
- 4 years post transplant
  - 6 day h/o non-resolving ear pain
  - odynophagia and dysgeusia
- Day 12 dizzy with unstable gait
  - left facial paralysis horizontal diplopia
- Vesicles erupted on left pinna and beard area
- VZV antigen positive

R.A. Mortada et al. *Transplant Infectious Disease* 2009;11:72-74

- Ramsay Hunt syndrome
- Acyclovir, myringectomy
- Unusual presentation
  - delay in onset of vesicles

- ? Zostavax in this population

R.A. Mortada et al. *Transplant Infectious Disease* 2009;11:72-74

Case scenario 2 - Measles and Liver transplant

- 31 year old liver transplant 13 years previously
  - Tacrolimus therapy ongoing
- Teacher in 2008 - measles outbreaks in Germany
- April 7 saw GP with stiff neck 3 days + low grade fever
  - erythematous and maculopapular rash
    - started on forehead proceeded to the trunk
    - lasted 7 days

- 23 days later elevation of LFT (30th April)
- Abdominal ultrasound - enlargement of liver
- Liver transplant rejection diagnosed on biopsy

T.Sternfield et al. *International Journal of Infectious Diseases* 2010;14:528-530

- Vaccinated as a child
- Serology never been checked even before transplant
- Serology 9th April (4 days post rash)
  - IgM 0.520 mIU/L and IgG 22.9 mIU/l

- Messages:
  - Consider post exposure prophylaxis or re-immunisation
  - Ensure serology checked pre and post transplant

T.Sternfield et al. *International Journal of Infectious Diseases* 2010;14:528-530

Case scenario 3

- 12 month old child
- Liver failure post biliary atresia, on transplant list
- MMR and varicella vaccine given
- Suitable donor liver becomes available 3 days later……

T.Sternfield et al. *International Journal of Infectious Diseases* 2010;14:528-530

Compliance with revaccination guidelines - Australia

- Survey in 2008 (Torda and Alexander. *Int Journ Med* 2009; 39:216-221)
  - Survey of Australian BMT physicians and recipients
  - Lack of consensus re benefit among physicians (N=20)
  - Patients often not aware and/or not reminded
  - ? Hospital or GP

Summary

- Handbook a very useful resource
- Some important updated recommendations
- Well understood and implemented vaccination policies are important for disease prevention in this vulnerable population
- This includes household and health care worker contacts……

Acknowledgements

- Dr Jane Jelfs – font of Handbook wisdom and literature searcher extraordinare
- Dr Nicky Gilroy – a rarity – adult physician interested in immunisation and lead author for this section of Handbook
- Ms Lyn Benfield – NCIRS