Viruses in May

RCAP- Katoomba

Nigel Crawford

Rotavirus and other ……. vaccinations, outcomes and experiences in high-risk groups

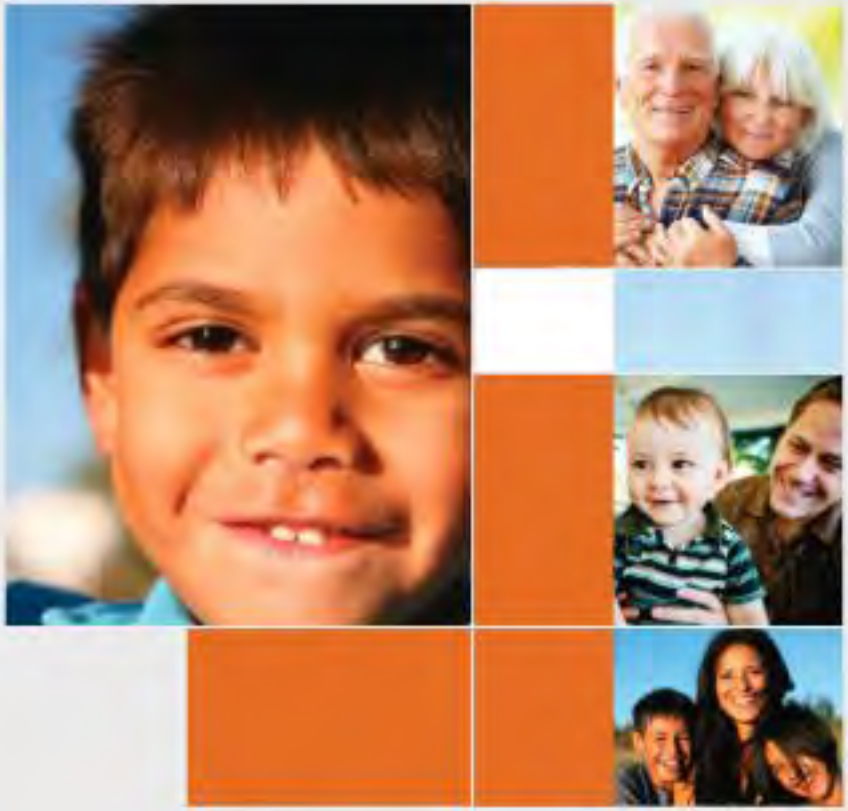
Presentation outline

1. Special risk
   - Definitions
   - Immune suppression
2. Vaccines:
   - Rotavirus
   - HPV
   - Herpes Zoster

- Case studies
- Adverse events following immunisation (AEFI)

The Australian Immunisation Handbook

10th Edition 2013



IMMUNISATION

The Australian Immunisation Handbook 10th Edition

Page last updated: 06 March 2017

THE AUSTRALIAN IMMUNISATION HANDBOOK 10TH EDITION

Part 3 Vaccination for Special Risk Groups

Page last updated: 06 March 2017

Special risk categories

Those who have:

- special immunisation requirements
  - (e.g. children/ adolescents with a chronic medical condition)

and/or

- a suboptimal response to immunisation
  - (e.g. due to impaired immunity)

↑Risk: Underlying Conditions or their Therapy

Chronic medical condition

- E.g. CF

Healthy physiological status

- pregnancy

Anatomical breach of defences

- E.g. CSF leak

Immune deficiency

- Developmental eg preterm
- Primary
- Secondary

↑Risk: Epidemiological Exposure

Day care

- Rotavirus, influenza

Increased medical attendances

- Influenza

Health care workers

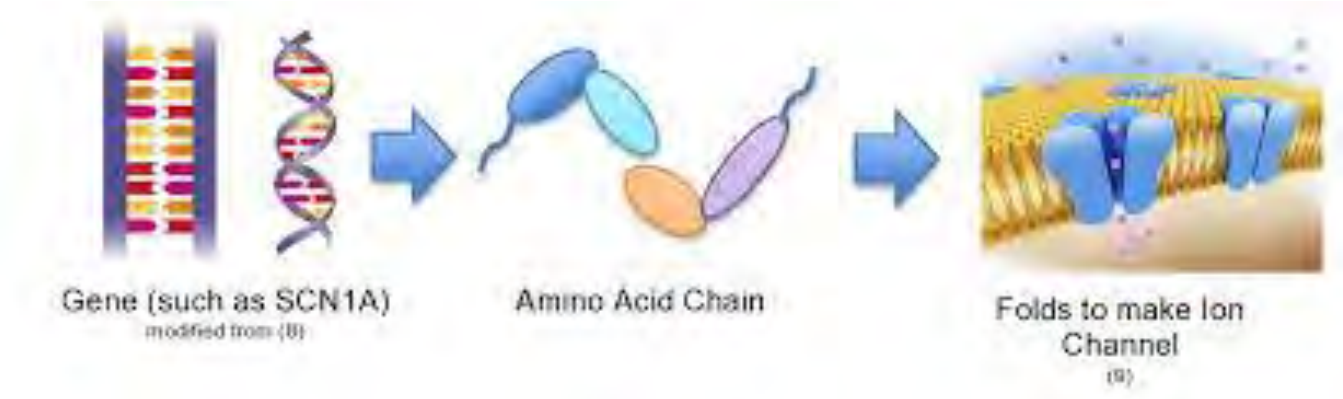
- Influenza, Pertussis, Measles, TB

Microbiology lab

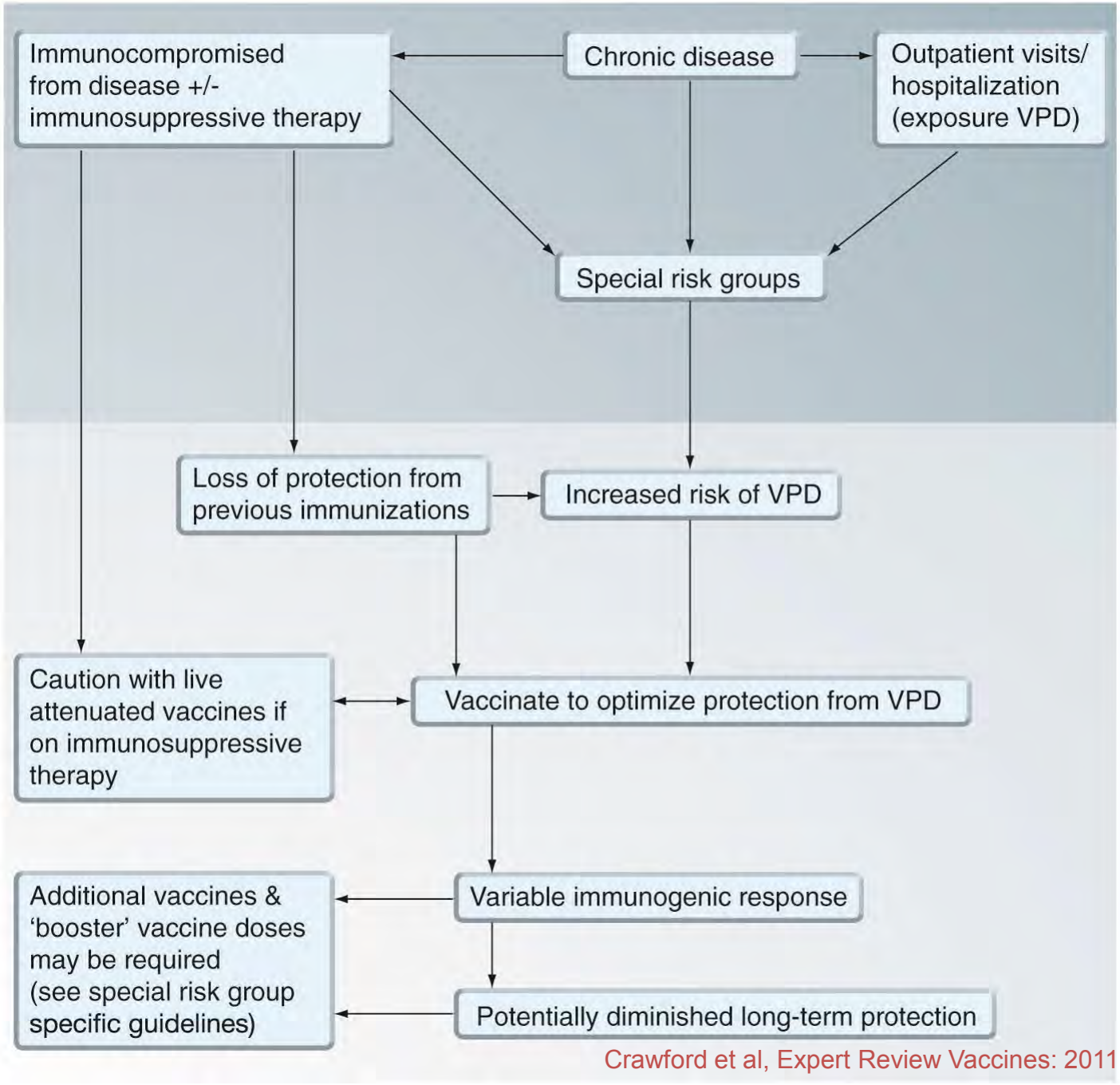
- meningococcus

↑Risk of Adverse Event Following Immunisation (AEFI)

- Immune suppressed
- ? genetic predisposition
  - Dravet's (severe myoclonic epilepsy)

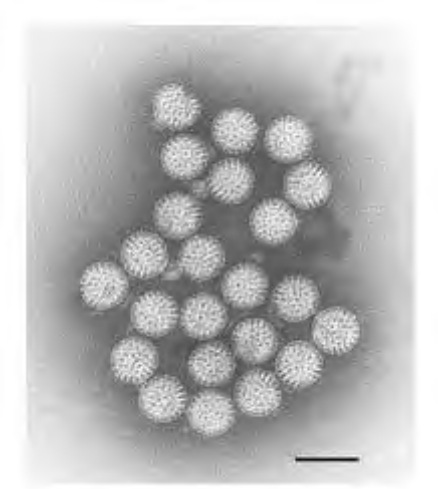


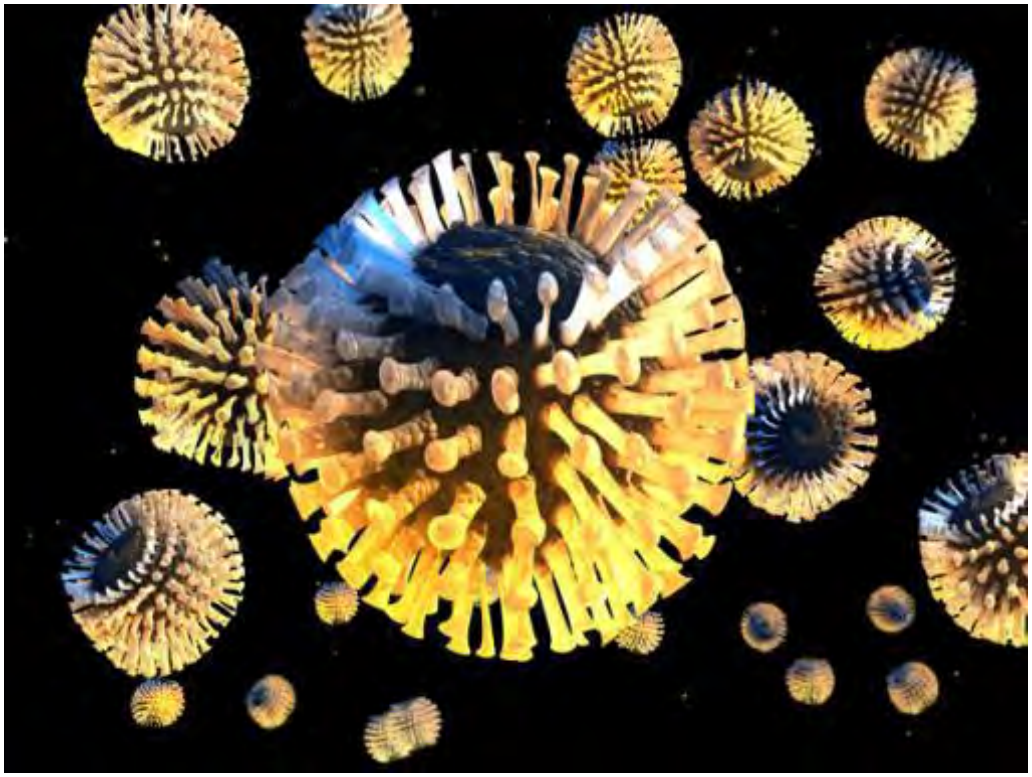
https://www.ncbi.nlm.nih.gov/pubmed/20447868



Crawford et al, Expert Review Vaccines: 2011, 10(2):175-86

Rotavirus vaccine

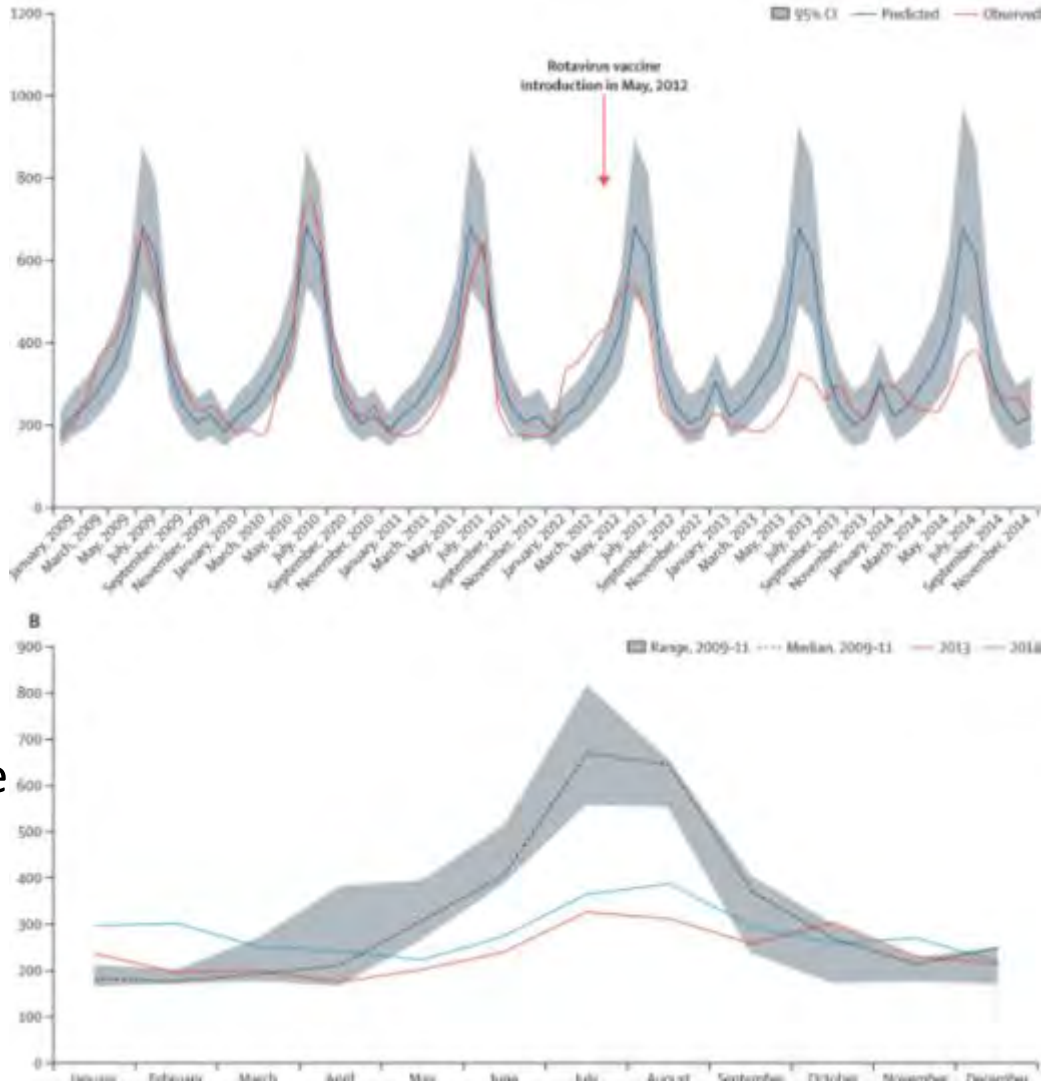




Rotavirus vaccines

Vaccines

- Introduced NIP 2007-
- Two products used in Australia
- RotaTeq
  - pentavalent bovine-human reassortant vaccine
- Rotarix
  - a human monovalent vaccine



http://thelancet.com/journals/langlo/article/PIIS2214-109X(15)00270-3/fulltext

	Rotarix	RotaTeq
Origin	Human monovalent strain P[8]G1	Human–bovine pentavalent strains P[8]G1–G4
Presentation	Lyophilised, reconstituted	Liquid
Administration	Oral, by applicator	Oral, squeeze tube
Storage	2–8°C	2–8°C
Number of doses	2	3
Timing of administration	1st dose at 6–13 weeks of age, 2nd dose ≥4-week interval at 14–24 weeks	1st dose at 6–12 weeks of age, 2nd and 3rd doses with 4–10-week intervals completed by 32 weeks
Phase III trials: safety	11 countries in Latin America, Finland, Singapore, Taiwan, Hong Kong (n=63 225)	USA, Mexico, Costa Rica, Guatemala, Jamaica, Puerto Rica, Belgium, Finland, Germany, Italy, Taiwan (n=70 301)
Intussusception	1·89 in vaccine group vs 2·21 in placebo group, both per 10 000, within 30 days of either dose	1·73 in vaccine group vs 1·44 in placebo group, both per 10 000, within 42 days of any dose
Decrease in rotavirus gastroenteritis (95% CI)*		
Any disease	ND	74% (67–79)
Severe†	85% (72–92)	95% (91–97)
Hospital admission	85% (70–94)	96% (90–98)
Severe disease†		
G1	92% (74–98)	95% (92–97)
G2	41% (−79 to 82)‡	88% (<0–99)
G3	87% (63–97)§	93% (49–99)
G4		89% (52–98)
G9		100% (67–100)
Decrease in all-cause gastroenteritis hospital admission (95% CI)	42% (29–53)	59% (52–65)
Virus shedding after first dose	50–80%	9%

Diarrhoea following vaccine

Case 1

- 4/12 old- 3-days following 2nd dose
- Severe vomiting, pale, floppy, unresponsive
  - ? HHE
  - Hypotonic Hyporesponsive Episode (HHE)
  - ?? intussusception
- More history- 1st Bottle cows milk 2-hours prior

Case 2

- 6-week old
- 1-day following vacciantion
- V+D
- 2-day admission for NGT re-hydration…..

Diarrhoea following vaccine

Case 1

- Severe cows milk allergy
- FPIES

Case 2

- Adenovirus

Case 3

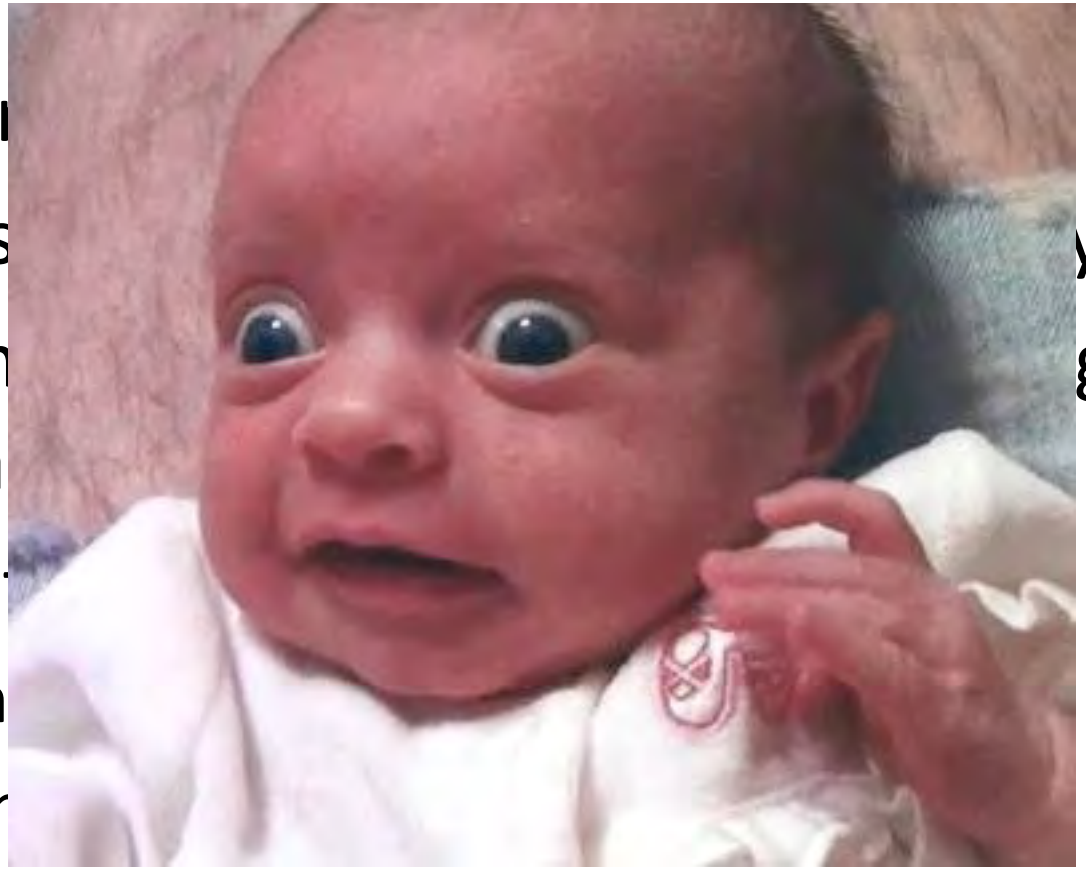
- Mother with Crohn's disease, treated with Adalimumab [Humira] – TNF blocker-
  - $T_{1/2}$- 10-20 days, 50-110 days (3-months)
- Ceased before 3rd trimester
  - 26 –weeks gestation.
- Subsequently developed maternal HTN (HELP syndrome), emergency LUSC @ 33-weeks.

Case 3

- Advised to not administer live vaccines to infant, but not documented anywhere….
- At 6-weeks received routine vaccines (including Rotateq).
- Developed diarrhoea 2-days later requiring hospitalisation, lasted 10-days.

- Stools – positive on PCR- awaiting typing

bDMARDS, Pregnancy and Infant Risks



- "Bewar
- Increas y
- predon gylated Fab fra
- Active
  - Main
  - Ofter
  - Measured in baby up to 7 months of age

Slide courtesy of Jim Buttery

Journal of Crohn's and Colitis (2010) 4, 603–605

ELSEVIER

available at www.sciencedirect.com

ScienceDirect

SHORT REPORT

Case Report: Fatal case of disseminated BCG infection in an infant born to a mother taking infliximab for Crohn's Disease

Kuldeep Cheent [a], Jonathan Nolan [a], Sohail Shariq [a], Liina Kiho [b], Arabinda Pal [a], Jayantha Arnold [a,*]

Severe combined immune deficiency [SCID]

ARTICLE IN PRESS

Letter to the Editor

Rotavirus vaccine induced diarrhea in a child with severe combined immune deficiency

posttransplant and last detected at 13.5 months of age, thus excreted for at least 7.5 months.

doi:10.1016/j.jaci.2009.07.005

SCID

Case

- Chronic diarrhoea
- 1st noted following @ 6-weeks, then 4 and 6 months
- Not hospitalised
- Investigated for nil weight gain @ 9-months

Enteric virus lab (RCH/MCRI)

- Carl Kirkwood/ Julie Bines
- Ruth Bishop
  - RV3 vaccine

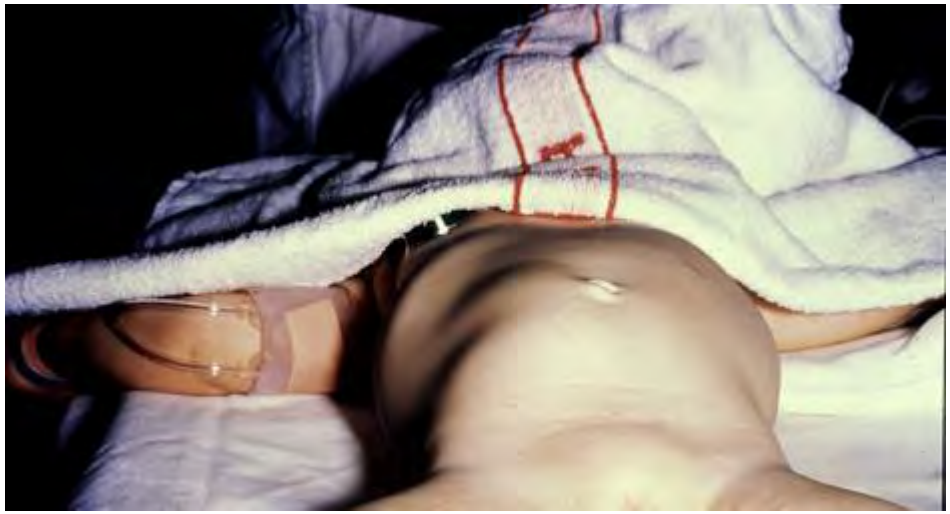
- VP6 RT-PCR amplicons sequenced and compared with the known sequence of the RotaTeq vaccine and wild-type strains

SCID

- Studies of RotaTeq have shown that viral shedding occurred
  - In 9% of after dose
  - 1 % after dose 2, and 0.3% after dose 3
- usually ~days 1 to 15 after the dose

- This case stopped excretion following HSCT…

Intususception

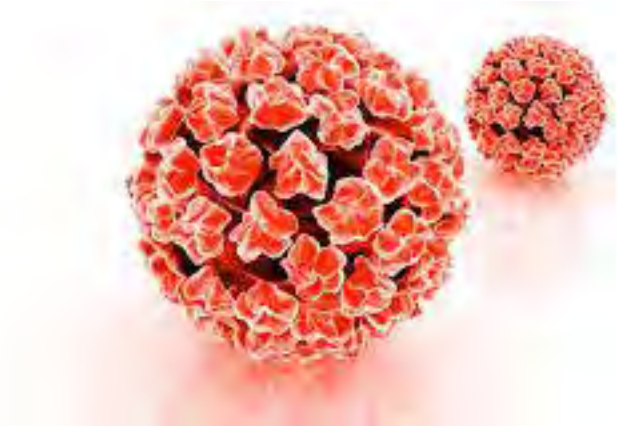


Clin Infect Dis. 2013 Nov;57(10):1427-34. doi: 10.1093/cid/cit520. Epub 2013 Aug 26.

Intussusception risk and disease prevention associated with rotavirus vaccines in Australia's National Immunization Program.

Carlin JB[1], Macartney KK, Lee KJ, Quinn HE, Buttery J, Lopert R, Bines J, McIntyre PB.

HPV vaccine in special risk

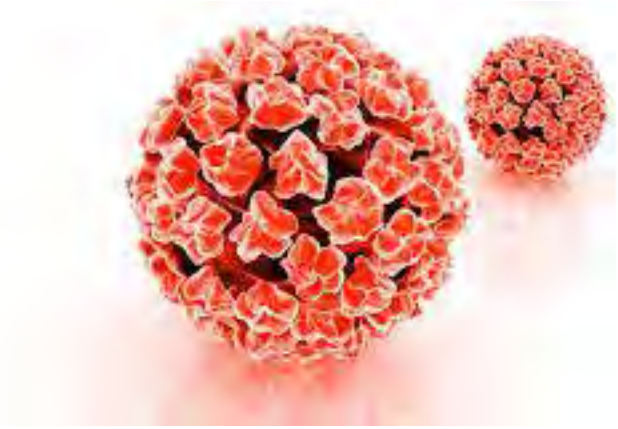


Current program

- 4vHPV [6,11,16,18]
- Year 7 (12-13 years)
  - Females 2007
  - Males 2013

- **Future**
  - 2-dose schedule
  - 9vHPV vaccine

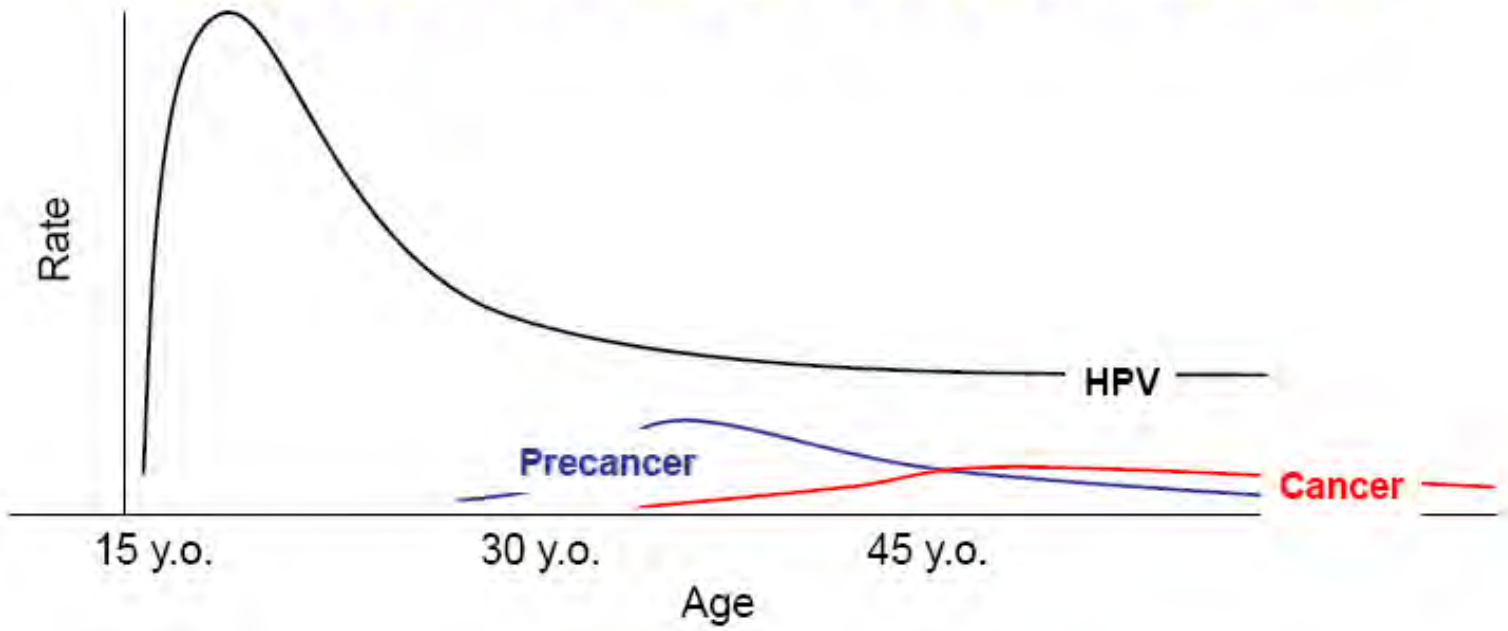
HPV vaccine in special risk



Risk

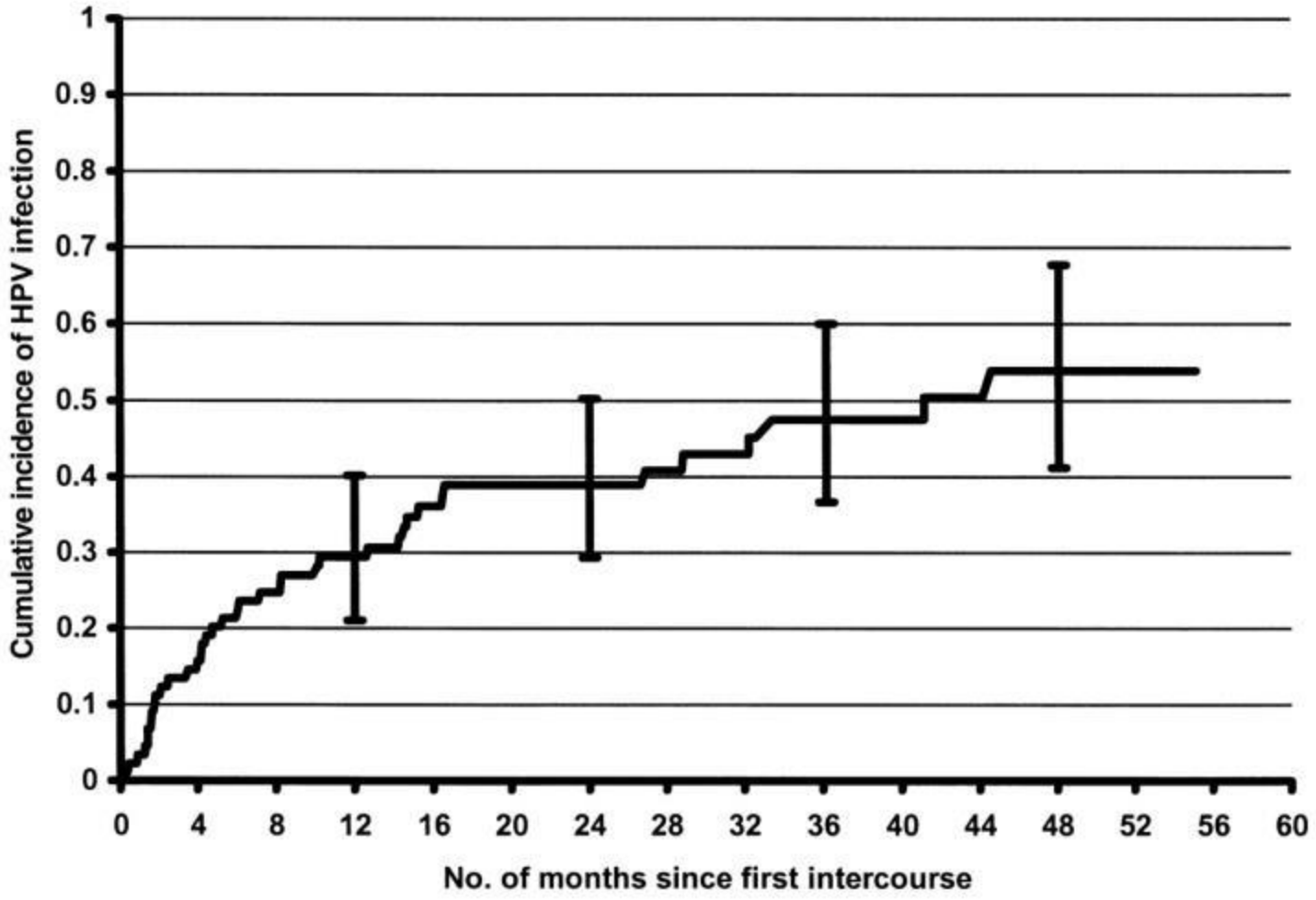
- Exposure
- Disease
  - IBD
  - Paediatric Rheumatology
  - Childhood Cancer

Time Line of Cervical HPV Infections And Progession to Cervical Cancer



Adapted from Schiffman & Castle NEJM 2005; 352:2101-05

FIGURE 2. Cumulative incidence of human papillomavirus (HPV) infection from time of first sexual intercourse (n = 94) among women in Washington State, 1990–2000.



Winer R L et al. Am. J. Epidemiol. 2003;157:218-226

American Journal of
EPIDEMIOLOGY

Level of Immune suppression

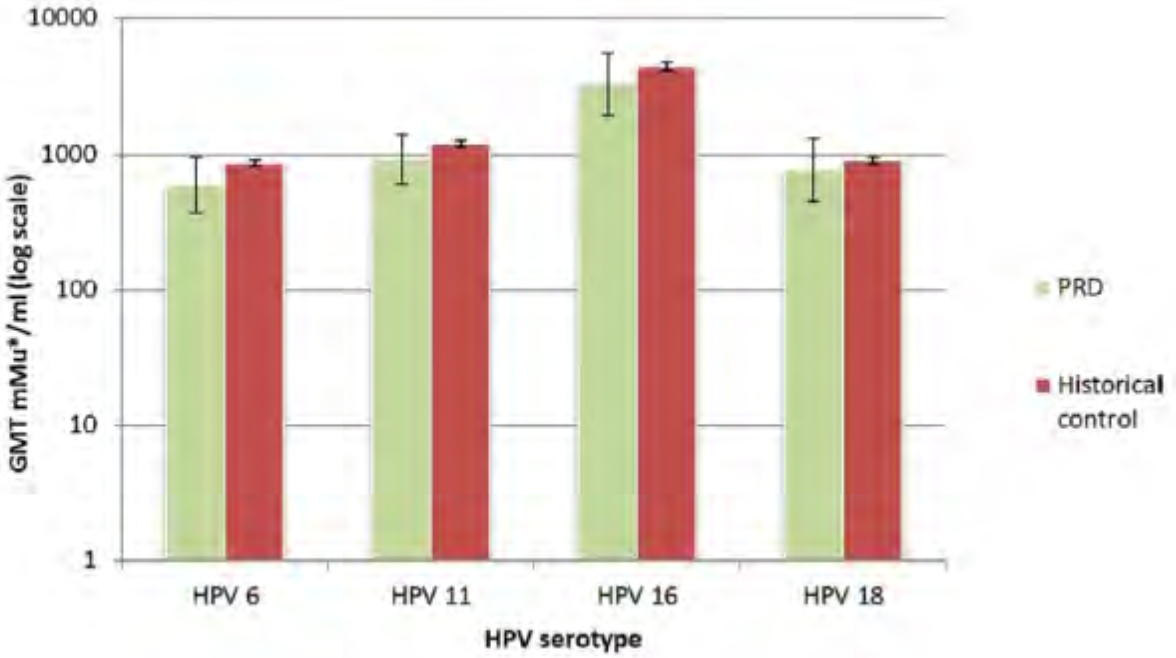
- Level 0
  - no therapy or NSAIDs only
- level 1
  - single DMARDs or low-dose corticosteroids
- level 2
  - high dose corticosteroids (>2.0 mg kg per day or 20mg)
  - biological agents or combination of DMARD and corticosteroid or combination of DMARDs

Table 3 Diagnoses and degree of immunosuppression of 38 girls with paediatric rheumatic diseases in whom serostatus after HPV vaccination was assessed (RCH, Melbourne)

Diagnosis	No.	Immunosuppression level[a] (no.)		
		0	1	2
Juvenile idiopathic arthritis (JIA)	28	3	10	15
Systemic lupus erythematosus	6	0	5	1
Juvenile dermatomyositis	2	0	0	2
Scleroderma	1	0	1	0
Sjogren's disease	1	0	1	0
TOTAL	38	3	17	18

[a] Level 0, no therapy or NSAIDs only; level 1, single DMARDs or low-dose corticosteroids; level 2, high dose corticosteroids (>2.0 mg kg^{-1} day^{-1}) or biological agents or combination of DMARD and corticosteroid or combination of DMARDs

Fig. 1 Post-immunisation antibody titres to HPV vaccine serotypes of 38 girls with paediatric rheumatic disease (PRD) compared with historical healthy controls. *GMT mMU*, geometric mean titre milli Merck units



Curr Rheumatol Rep (2014) 16:432

Alert

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A- A+ Share

Zostavax vaccine

Safety advisory – not to be used in patients with compromised immune function

7 March 2017

The TGA has received a report of a death occurring in a person with pre-existing compromised immune function after receiving Zostavax – a live, attenuated varicella-zoster virus vaccine that is used to prevent shingles and prevention/treatment of nerve pain associated with the virus.

Man dies following GP's Zostavax error

8 March, 2017 6 comments

An elderly man with compromised immune function has died after being given the shingles vaccine Zostavax in error. Health authorities are urging vigilance about contraindications for...

“Shingles” HZV vaccine

- Zostavax national campaign commenced November 2016 (70-79 year olds)
- Single dose
- Live-attenuated
- Oka/Merck strain of VZV
- Each 0.65-mL dose contains a minimum of 19,400 PFU (plaque-forming units)
  - ~ 14-fold – varicella vaccine [infants schedule]

Immune suppression

- Complexity increasing in adults
- May appear well….
- “Stacking” of special risk factors
- New medications- targets
  - ? Dose
  - ? Duration

Mechanism of action	Examples*	Safe dose**	Comments
Anti-TNF	Etanercept Infliximab Adalimumab	NONE	Vaccinate 1 month before treatment initiation **OR** 12 months after treatment cessation
IL-1 inhibition	Anakinra	NONE	
Costimulation blockade	Abatacept	NONE	
B-cell depletion/inhibition	Rituximab	NONE	
Immunomodulators (antimetabolites)	Azathioprine 6-Mercaptopurine Methotrexate	≤3.0 mg/kg/day ≤1.5 mg/kg/day ≤0.4 mg/kg/week	If on higher dose, vaccinate 1 month before treatment initiation **OR** 3 months after treatment cessation
Corticosteroids	Prednisone	<20 mg/day for <14 days	
T-cell activation/inhibition	Tacrolimus Cyclosporine	NONE	Vaccinate 1 month before treatment initiation **OR** 3 months after treatment cessation
Others	Cyclophosphamide Mycophenolate Sulfasalazine	NONE	

http://www.ncirs.edu.au/assets/provider_resources/fact-sheets/zoster-vaccine-FAQ.pdf

Summary

- Special risk groups
  - Risk of exposure (infection)
  - Modified vaccine response
  - Adverse events following immunisation

- Role immune suppression
- Thresholds / recommendations
  - Live-attenuated *versus* inactivated vaccines

Acknowledgements

- Collaborators at Melbourne Children's campus

- Jim Buttery