Live varicella vaccine in solid organ transplant recipients
Dawn of a new era?

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Disclosures

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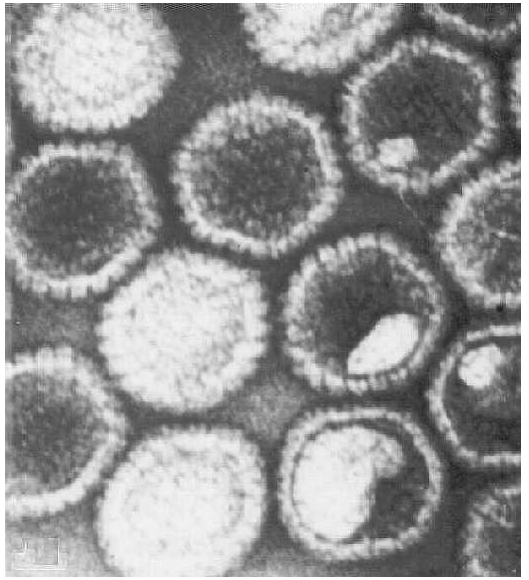
- Not received any personal payments

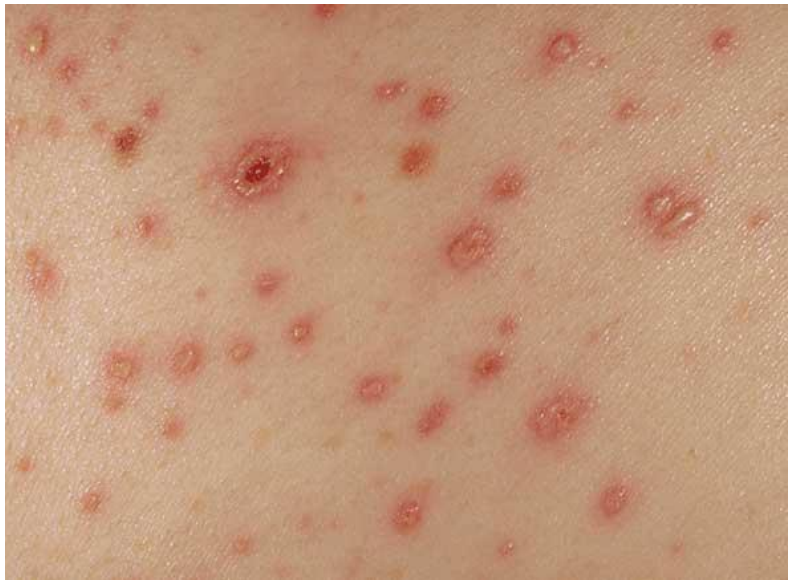
Transmission

- ~90% risk of infection if non-immune and exposed
- Incubation period 10-21 days (usually 14-15 days)
- Immunocompromised: Contagious for several wks



The disease

- Fever
- Very itchy rash
- General symptoms
  - Headache, malaise, reduced feeding



- Complications
  - Bacterial infection
  - Spread to organs – brain, lungs
  - Death is rare (2-4 per 100,000 cases) – higher in immunocompromised

What can we do to prevent this?

- 6yr old boy, never had chickenpox or vaccine
- 3yr old sister recently Δd chickenpox

- What are the chances of him getting it? >90%
- He has previously had a liver transplant – what should we do?

Varicella Zoster Immunoglobulin (VarIg)

- From pooled plasma of blood donors
- High anti-varicella antibodies (prevent infection)
- Donors screened for HIV, Hepatitis B & C, etc. as normal
- 1 intramuscular injection
  - 50% effective in preventing chicken pox
- Very limited supply

Case

- 6yr old boy, never had chickenpox or vaccine
- 3yr old sister recently Δd chickenpox

- What are the chances of him getting it? >90%
- He has previously had a liver transplant – what should we do? VarIg

- He develops a vesicular rash 14 days after his sister
- Now what can we do?

Treatment

- Usually only symptomatic Rx
  - Acetominophen
  - Topical or systemic treatment for itching
  - Keep well hydrated
- Intravenous acyclovir (anti-viral) for immunocompromised children
- Antibiotics for bacterial infection if needed

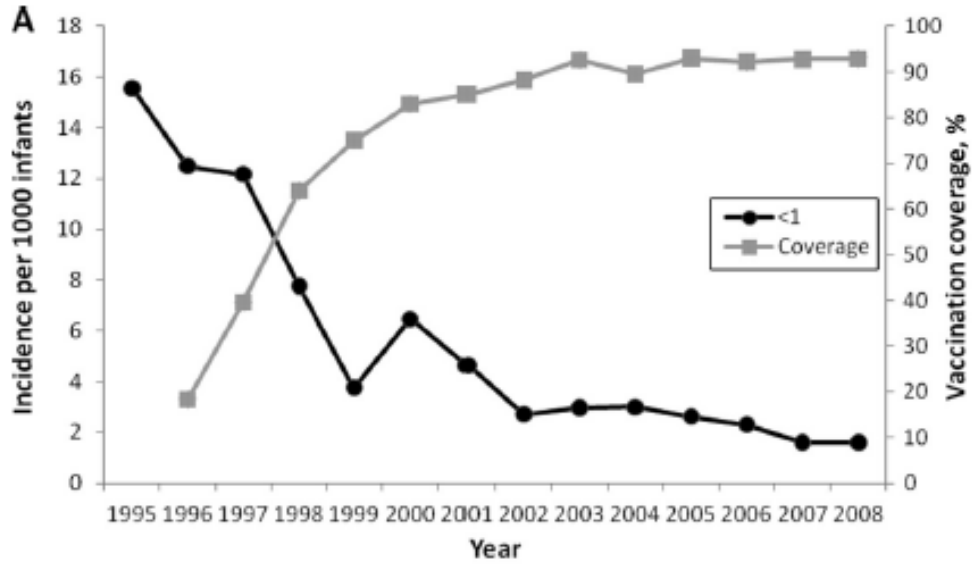
Prevention -- Varicella Vaccine

- Live, attenuated vaccine = weakened form of the virus
  - Developed in Japan
- Single vaccine or combined with MMR
- Side effects
  - Vaccine-induced rash
  - Febrile seizures with MMRV

The vaccine has been highly effective

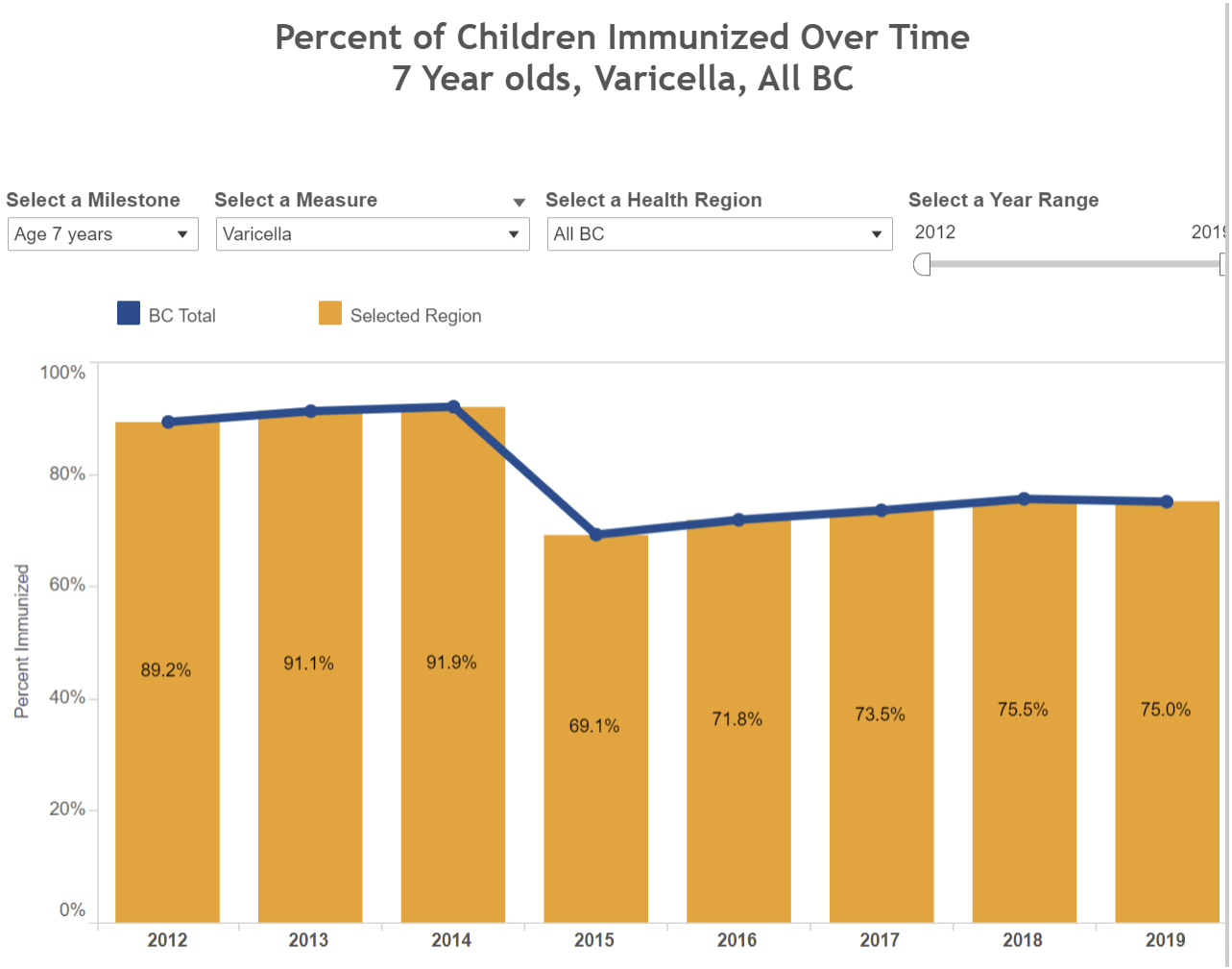
- Clinical trials
  - 98% effective for prevention of all varicella

- In the real world
  - 70-90% for prevention of all varicella
  - 97% against moderate/severe disease
  - 100% against severe disease



We cannot rely on the 'herd'

- http://www.bccdc.ca/health-professionals/data-reports/childhood-immunization-coverage-dashboard



Need 85-90% coverage to protect everyone

Varicella Vaccine in immunocompromised children

- Has been contra-indicated (of course it has!!)

- Were part of original childhood studies
- Protective antibody response in 89-100%
- Reduced occurrence of natural varicella
  - Only 8-16% after exposure (normally 90%)
- Vaccine rash in 6-47%
  - ↑risk with ↑immunosuppression
  - 40-50% in acute leukemia

What do we now know?

- Safety
  - Breakthrough rash in 3/97 HIV+ patients (well-controlled HIV)
  - Breakthrough rash in 3/25 rheumatology patients receiving treatment
  - No serious adverse events

  - Well tolerated in children with 22q11- with mild/moderate immunosuppression
  - Acute leukemia: 36% rash →10% transmission to siblings
    - Reports of fatalities during maintenance chemo

What do we now know?

- Effectiveness
  - HIV+: 82% effectiveness (*vs.* >95% in healthy)
  - 191 children in remission from leukemia
    - Vaccinated: 18% developed disease after exposure
    - Pre-vaccine: 90%
  - 2/25 children with rheumatologic conditions developed varicella after 1 dose within 32 months follow up

The new reality for SOT patients

ORIGINAL ARTICLE

WILEY

Live vaccines after pediatric solid organ transplant: Proceedings of a consensus meeting, 2018

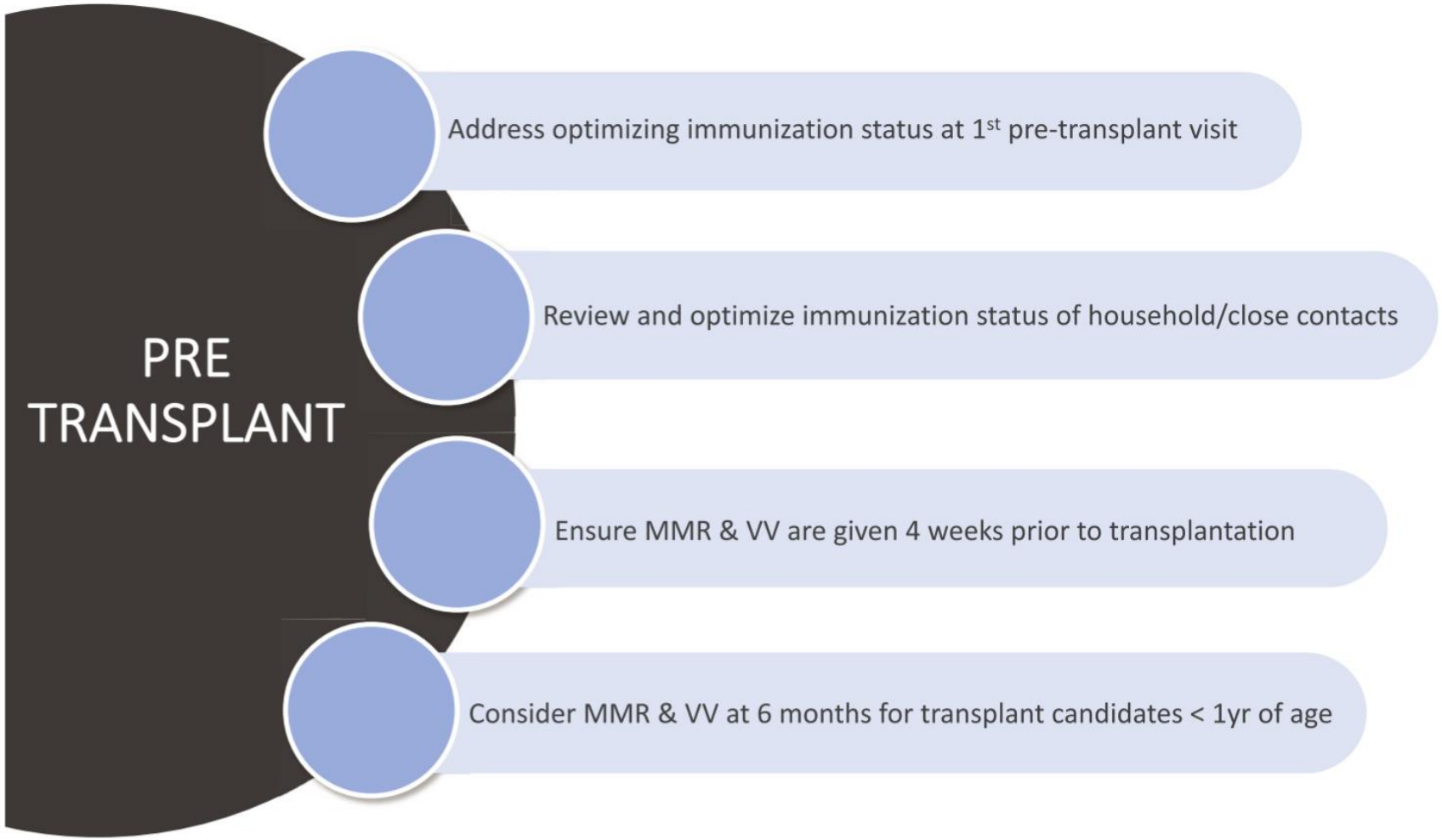
Sneha Suresh[1] | Julia Upton[2] | Michael Green[3] | Anne Pham-Huy[4] | Klara M. Posfay-Barbe[5] | Marian G. Michaels[3] | Karina A. Top[6] | Yaron Avitzur[7] | Catherine Burton[8] | Pearlie P. Chong[9] | Lara Danziger-Isakov[10] | Anne I. Dipchand[11] | Diane Hébert[12] | Deepali Kumar[13] | Shaun K. Morris[14] | Nadya Nalli[15] | Vicky Lee Ng[7] | Sarah Kogan Nicholas[16] | Joan L. Robinson[17] | Melinda Solomon[18] | Bruce Tapiero[19] | Anita Verma[20] | Jolan E. Walter[21,22] | Upton D. Allen[23]

Varicella vaccine post organ transplant in children

- Kidney
- Liver
- Small bowel

- Rash in 0-25%
- Effective immune response in 50-100%
  - Over 60% in most studies

Before transplant



BCCH guideline

- Eligible for live varicella vaccine
  - Age 1–19 years
  - Clinically well
  - At least 1 year post-transplant
  - On maintenance immunosuppression
  - Stable graft function for at least 6 months
  - No antibodies against varicella
  - Normal immune function tests

BC Children's Hospital Research Institute

Optimizing Varicella Immunization in Children and Youth with Solid Organ Transplants to Prevent Disease and Improve Long-Term Health

Study Initiation Meeting 07 Jan 2020

Karina Top, MD, MS

Canadian Center for Vaccinology

Objectives

- Among health care providers, identify barriers and facilitators to implementing a clinical guideline for administering live varicella vaccination in pediatric SOT recipients;
- Among parents/caregivers of children with SOT, evaluate acceptability and uptake of LAVV, and impact of possible and confirmed VZV exposures on participation in daily activities and parent/child stress;
- Among SOT recipients, vaccinated with LAVV, estimate seroconversion after LAVV (VZV IgG $\geq$150 mIU/ml);
- Among SOT recipients, estimate the frequency of adverse events following LAVV that interfere with daily activities or require medical attention.

Resources

- BCCH Family Immunization Clinic
  - http://www.bcchildrens.ca/our-services/clinics/family-immunization
- BCCDC
  - http://www.bccdc.ca/health-professionals/clinical-resources/communicable-disease-control-manual/immunization
- ImmunizeBC
  - https://immunizebc.ca/
- CanImmunize App
  - https://www.canimmunize.ca/en/home

Thank you

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