Plenary Session 2: Landscape

Mucosal Vaccine Delivery

Next-Generation Vaccine Delivery Technology Meeting

Geneva, Switzerland

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"Most pathogens access the body through the mucosal membranes. Therefore, effective vaccines that protect at these sites are much needed".

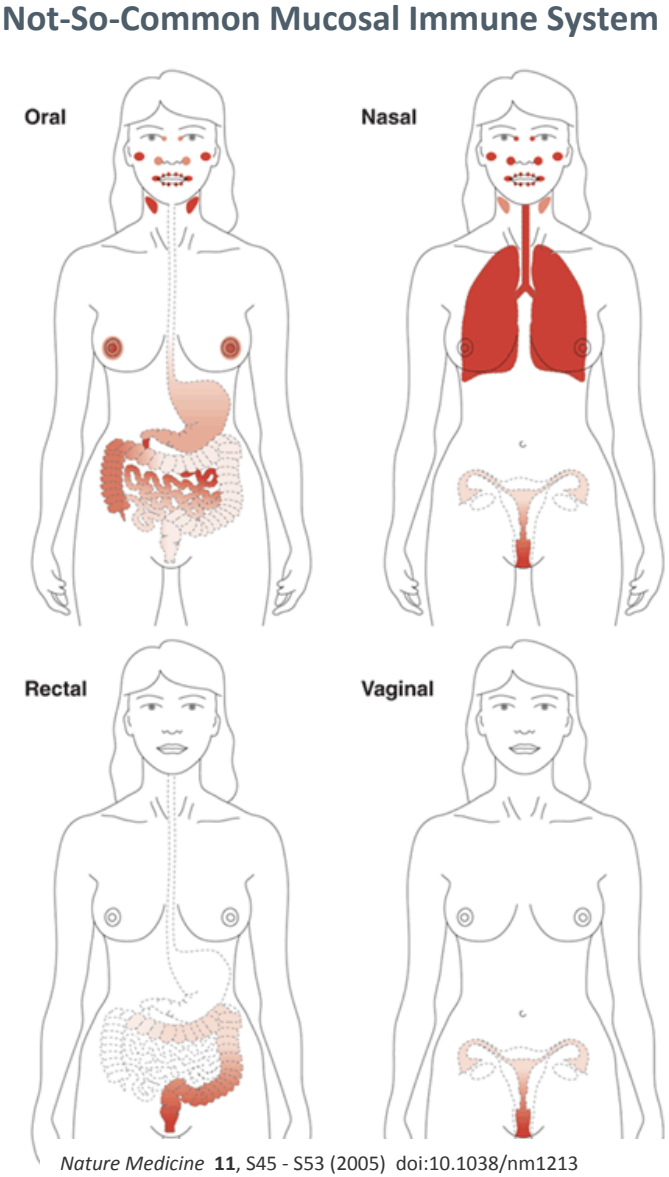
www.nature.com/reviews/immunol

doi:10.1038/nri3251

Mucosal Delivery: Oral, rectal, nasal, vaginal, sublingual

Live *versus* subunit:

- **Live organisms**: mucosal portal of ***infection***
  - **Success**: polio, rota [oral]
    LAIV, (measles) [airways]
  - **Moderate**: Salmonella, cholera, (shigella [oral]
    - Multivalent live disappointing
  - ***Attenuation<>immunity***
    - viruses more established?
- **Subunit / killed**: route of ***immunisation***
  - Non-immunogenic or weak
    - Multiple doses, short lived
      (oral cholera, ETEC)
  - Adjuvants: toxicity / ineffective (Ivag)

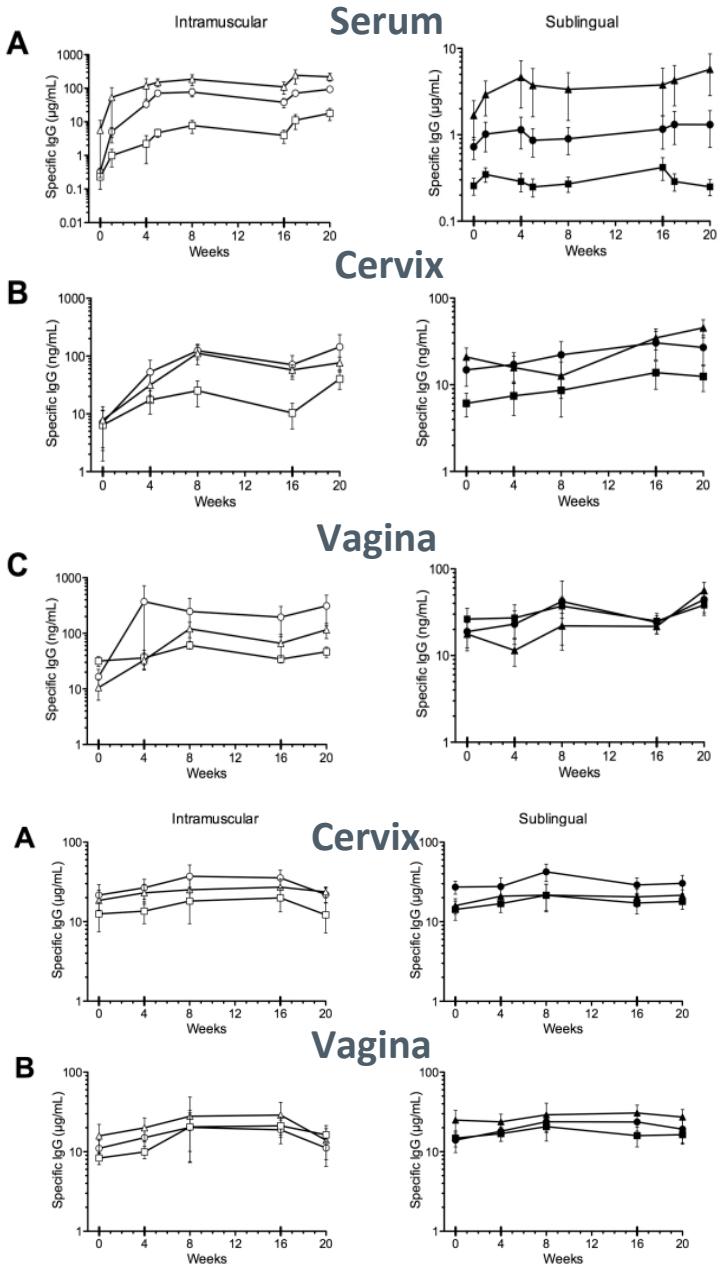


Nature Medicine **11**, S45 - S53 (2005) doi:10.1038/nm1213
Jan Holmgren & Cecil Czerkinsky

Mucosal IgA: Necessary and effective? (in humans)

Overview:

- Dogma that mucosal delivery will induce protective SIgA whereas IM will not:
  - Alum adjuvanted Gardasil high protection against cervical basal cell (openly exposed) HPV infection
    - IgG can protect mucosal surfaces – no IgA
  - eIPV can prevent mucosal polio transmission via IgG
  - IM Shigella/Salmonella **conjugates**
  - Confusing story over HIV STEP trial correlation with serum IgA, impact of gut adeno CMI?
- Series of failed Phase 1 trials of mucosal prime- parenteral boost



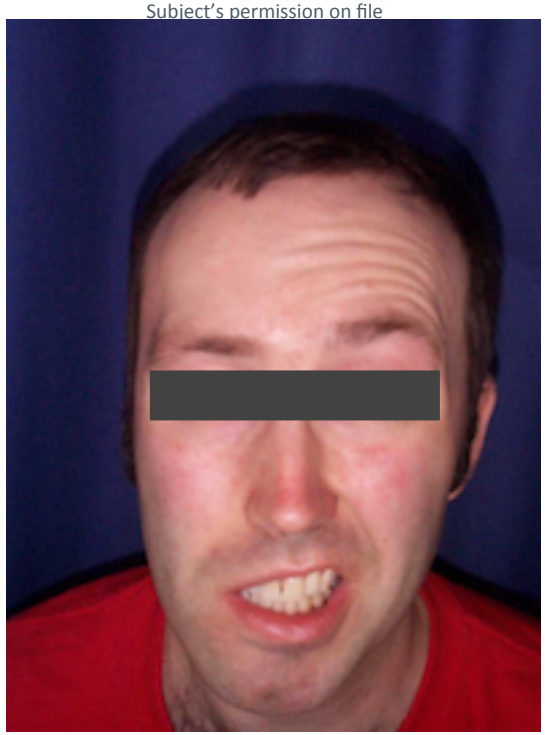
Correlates: Models don't predict mucosal responses

Description:

- Small animals do not always predict
  - Rabbit noses / vaginas respond to anything. Anatomy different
  - Primates (human & non-human) needed ?? Especially reactogenicity?
- Industrialized country citizens do not predict globally

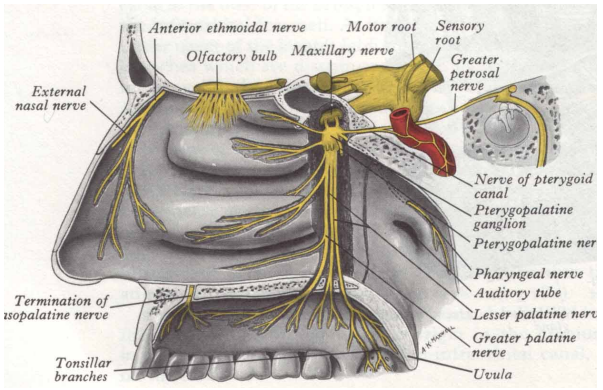
Bell's Palsy after nasal LT-toxoid delivery

Subject's permission on file



Status:

- Correlates of protection / reactogenicity may differ when localised mucosal immunity / reactions in place
  - LAIV – serum HAI???
  - How to measure and model ??



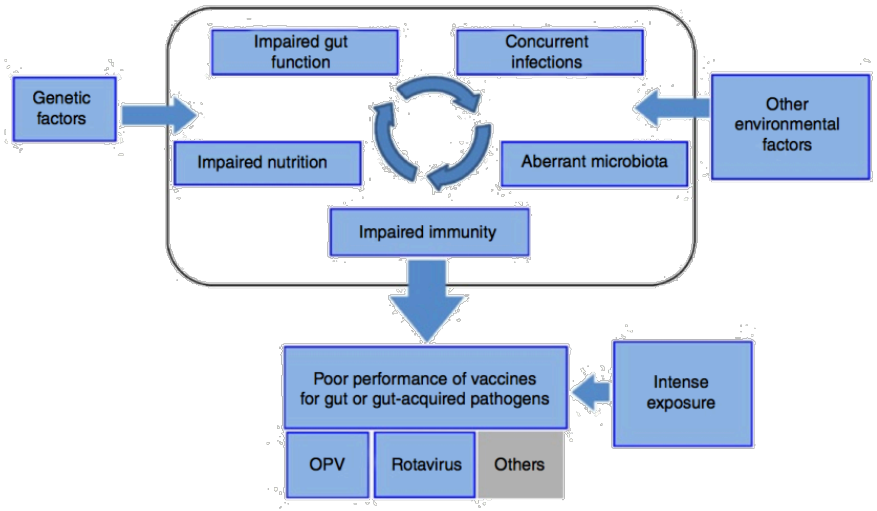
Mucosal vaccines: Benefits and Challenges

Benefits:

- Needle-free : ~~HIV/HBV/HCV~~
- *Maybe SIgA induced?????*

Challenges:

- **Tropical Barriers**
- Weak, short lived responses
  - failure to mucosal prime
- Mucosal adjuvants / toxicicity / attenuation / high antigen doses
- Clean Water Supply
- Delivery devices / buffers / 2-stage immunisations / days–> EPI



Mucosal vaccines: Opportunities + Way Forward

Global Public Health Challenge:

- Most infections via mucosal surface
  - HIV / TB / STDs / pneumonia / gastroenteritis / meningitis

Technology Availability:

- Live viral vaccines – available and potentially adaptable to mucosal delivery
- Cheap, reliable devices to convert existing syringe/needle combination for mucosal delivery, integrate into EPI
- Better understanding of mucosal immunity – antigens – mIgG – adjuvants – duration – magnitude – targeting
- Multivalent parenteral subunit vaccines, adjuvanted, conjugates? GMMAs? – safe injection devices?
- **Expectations management for what mucosal delivery offers**