Unintended consequences: pertussis re-emergence

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Vaccines are essential to controlling pertussis

Figure courtesy of CDC, USA.
Pertussis is re-emergent, despite continued high vaccine coverage.
Pertussis is re-emergent across the globe, but with distinct patterns

Associated with early waning of aP induced immunity
Associated with adaptation of BP to aP induced immunity

Bento & Preston, unpub.
WCV v ACV

• Th1/Th17 v Th2/Th17
• aP induced immunity wanes earlier than that from WCV
• aP induced immunity protects from disease, but less well against colonization

• Does use of aP increase/alter the pool of susceptible hosts?
• Does use of aP increase circulation of \textit{B. pertussis}?
**B. pertussis** adaptation

- Certain key SNPs associated with selective sweeps but, mutation rate of *B. pertussis* is low
- Horizontal gene transfer is undetectable
- *B. pertussis* genome is plastic

Bart et al. 2014. mBio. DOI: [10.1128/mBio.01074-14](https://doi.org/10.1128/mBio.01074-14)

Pertactin Deficiency

Generally, around 10 years after switch to aP but also observed in some wP countries (e.g. Argentina)

Prn-deficiency

- Prn+ strains are fitter in naïve hosts
- Prn-ve strains are fitter in aP-vaccinated hosts
- Children vaccinated with aP have greater risk of infection by Prn- than Prn+ strain
- No obvious difference in disease presentation due to Prn+ v Prn- strains
So, modified new/vaccines?

More antigens?
- OMVs
- AC - CyaB

Adjuvants?
- Th2 → Th1

BPZE1
- Live, attenuated BP
- ILIAD Biotech
- Regulatory hurdles
Key decision: what do we need from pertussis vaccines?

- Protect young babies from disease?
- Lifelong protection from disease?
- Prevention of colonisation (and transmission)?
- What is possible?
Observations

• Changes in host alter selection pressures on the pathogen
• Adaptation will be selected
• Adaptation may be subtle, and may take a long time to manifest
• Before implementing an intervention, can the consequences be anticipated?
  • Modeling
  • Models require data...
The host...human interactions are changing rapidly

Climate change

Changing population epidemiology

Evolving interaction networks

Incidence of pertussis in 2021 was very low
Continued (increased) surveillance is essential
  • Pathogen, not disease, focused
  • Global
  • Genomics + metadata
  • Phenotypes (requires isolates and relevant assays)

Big data offers insight into both host and pathogen

New models to incorporate all available data
  • Backed up by the ability to test model outcomes

Lab studies remain essential
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