Vaccines and Therapeutics: Key Issues

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Potential Role of Vaccines in Pregnancy

■ **Pregnant women as a target**: Prevention of microcephaly is a primary goal, but several expressed concern about use of vaccines in pregnancy:
  - Need for demonstrated safety in non-pregnant adults before testing in pregnant women
  - Potential need for sterilizing immunity
  - Rapidity of immune response
  - Limits approaches – e.g., live-attenuated

■ Several invoked **rubella** approach (target broad population in order to protect)
Preclinical development issues

- **Strain selection** – data showing excellent cross-reactivity

- **Immune correlates** – have one for JE and recently for dengue (both neutralizing Ab titers)

- **Harmonized assays** – e.g., reporter virus particles for neutralization

- **Animal models** – good model for viremia curves in NHPs; gap for pathogenesis
Clinical development issues

- **Potential trial pathways**: traditional vs. Phase 2b vs. human challenge/Phase 2

- Key questions about **efficacy endpoints**, particularly given current diagnostics

- Need to locate trials well for high incidence

- Potential role of **human challenge**
  - Could provide immune correlate (at least immune profile)
  - Could offer demonstration of sterilizing immunity
  - Efficacy in small N
  - Questions about GBS, sexual transmission and prevention of pregnancy
Other questions and critical gaps

- Potential role of prior flavivirus exposure
- Pathogenesis and risk of Guillain-Barré syndrome
- Critical gaps for vaccine developers:
  - Viral samples from endemic settings
  - Sera from endemic settings, particularly to define likely neutralizing Ab target
  - Standardized assays
  - Well characterized animal models
  - More information on viral structure and contact points for neutralizing antibodies
Use of drugs in pregnancy

- Outlined specific considerations for drugs in pregnancy
  - Impact of pregnancy physiology
  - Specific preclinical information needed (special tox, placental transfer)
  - Ethical considerations

- Potential use cases – chemoprophylaxis vs. treatment after infection

- Approved drugs vs. novel drugs (including monoclonals)
Other issues/critical gaps

- Kinetics of viral infection and disease; implications for therapeutic window
- Replication sites in humans
- Potential use of monoclonals – early stage but could be long-lasting; concerns about cost and placental transfer
- Animal models – including microcephaly, accurate placental transfer