Ethical Considerations in Rabies mAb Development

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Rabies Prevention/Treatment

- Mass dog vaccination
- Mass human vaccination
- Post exposure prophylaxis (PEP)
- Public education
- Provider education
- Bite treatment centers

Challenges

• Human Rabies immune globulin (RIG)
  – Product
    • “Inconsistency between batches,
    • Potential contamination with blood borne diseases, and
    • ...severe allergic reactions (with equine RIG)
  – Expense
  – Supply in low resource settings where incidence highest and rising

Goal

- “Safer, efficacious, and potentially more economical alternative biologic.”
  - Rabies monoclonal antibody (RmAb) cocktail

Considerations

• Beneficence/Study Design
  – conducting PEP trials of RmAb as an alternative to available RIG

• Respect/Vulnerable Populations
  – conducting PEP trials in children

• Justice/Exploitation
  – conducting PEP trials in rural/developing areas
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Study Design

• What is the standard of care?
  – Prompt wound care followed by:
    • 1 dose RIG into and around wound as well as intramuscularly
    • 4 doses of vaccine

Source: MMWR 2010
Study Design

• Randomized controlled trial
  – Placebo trial
    • Wound cleaning and vaccine v. wound cleaning, mAb and vaccine
  – Superiority trial
    • Wound cleaning, vaccine w/mAb ≥ wound cleaning, vaccine w/RIG (standard)
  – Equivalency trial
    • Wound cleaning, vaccine w/mAb = wound cleaning, vaccine w/RIG (standard)

Source: MMWR 2010
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Vulnerable Population

- Rabies disproportionately effects children in countries where it is endemic
- 40% of those bitten by rabid dogs are children under 15

Source: WHO 2013; WHO 2017
Vulnerable Population

• Research with children allowed when
  – No more than minimal risk, or
  – More than minimal risk with potential for direct benefit, or
  – No more than minimal risk with potential for benefit to children with disease/condition

*otherwise not approval, referred to expert panel

Source: WHO 2013
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Exploitation

• Exploitation
  – A exploits B when A receives an unfair level of benefits and/or B receives unfair burden of risks as a result of interacting with A

• Non-exploitation
  – Only those likely to benefit from results ought to be exposed to risk and burden of research enrollment

Exploitation

• What increases likelihood of exploitation?
  – Less experience with scientific research
  – Less local infrastructure for health care and treatment
  – Less ability to give voluntary informed consent, due to social, gender, class inequities
  – Less experience or capacity with scientific and/or ethical review
  – Less infrastructure to conduct own research

Source: UNAIDS(2007)
Exploitation

• How do we minimize risk of exploitation?
  – Where is the study being conducted?
  – In what types of capacity building ought investigators invest?
  – Who will have access to the intervention if research is a success?
    • Who is responsible for assuring access?
Exploitation

• Why is research proposed in the low resource setting?
  – Greater prevalence
  – Question/intervention more relevant there
  – Convenience/familiarity: preexisting relationship
  – Cost/expediency: relevant but not decisive

Source: Kass (2013)
Rabies Prevention/Treatment

- Mass dog vaccination
- Mass human vaccination
- Post exposure prophylaxis
- Public education campaign
- Provider education
- Bite treatment centers