**Neisseria meningitidis** Group A Bactericidal Activity Assays using Pooled Human Complement

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**Background**

*Neisseria meningitidis* is an obligate human pathogen with the following characteristics:
- **Obligate human pathogen**
  - No reservoir outside of the human host.
  - Aerobic, non-spore-forming Gram-negative
  - Well adapted to inhabit human mucous membranes

**Immune responses to Neisseria meningitidis**: Polysaccharide encapsulated organism

**Research Outline**

**Properties**
- Immune correlates of protection are a likely mechanism for licensure of future meningococcal vaccines
- Anti-capsular antibodies – ELISA
- Complement mediated bacterial killing – SBA
- IgM, IgG, anti-class 4 antibodies

**Methods**
- Clinical isolates of *Neisseria meningitidis* from the Meningitis Vaccine Project (MVP) of Phase I studies conducted in Indian adults were used to compare complement pools.
- Various criteria were developed for pooling complement.
- 3 independent complement pools were created:
  - Predominantly intrinsic killing
  - Predominantly rSBA criteria
  - Multifactorial: intrinsic and rSBA criteria combined

**Results – Screening Sera**

- **Group A Intrinsic Bactericidal Assay**
  - **Immune correlates of protection are a likely mechanism for licensure of future meningococcal vaccines**
  - **Anti-capsular antibodies** – ELISA
  - **Complement mediated bacterial killing** – SBA
  - **IgM, IgG, anti-class 4 antibodies**

**Results – Pooled Complement Lots**

- **Human Complement Pools Tested with Adult Post Immunization Sera**
  - **Group A Intrinsic Bactericidal Assay**
  - **Immune correlates of protection are a likely mechanism for licensure of future meningococcal vaccines**
  - **Anti-capsular antibodies** – ELISA
  - **Complement mediated bacterial killing** – SBA
  - **IgM, IgG, anti-class 4 antibodies**

**Results - hSBA Titers Pre- and Post Immunization With Polysaccharide or Conjugate Vaccines**

**Summary**

- Suitable donors were identified among normal healthy U.S. adults
- Screening to exclude sera with intrinsic killing and or **SBA titers > 1:8** was sufficient to identify acceptable sera
- Pooling 6 to 9 sera resulted in independent complement pools that gave reproducible hSBA titers for a range of sera
- Differences between the immune response to conjugate vaccine vs. polysaccharide vaccine were detected by hSBA, even in an adult population

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