CORRELATES OF IMMUNITY: SUMMARY OF 12/10/2007 SESSION

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SEASONAL INFLUENZA

- **CHACTERISTICS OF IMMUNITY**
  - **Homotypic immunity is powerful and long-lived**
  - **Heterotypic immunity varies with the extent of antigenic variation**
  - **Both are highly correlated with serum anti-HA antibodies to the infecting virus**
  - **For optimal/maximal immunity, the mediator must be present at the time of exposure; activation from ‘memory’ can ameliorate but not prevent infection**

CORRELATES/SURROGATES

There is considerable redundancy in immune protective modalities; all are desirable.

- **Anti-HA is the most powerful mediator of immunity to infection; anti-HA can reduce severity of infection. Both serum and secretion antibody are necessary/desirable.**
- **Anti-NA can reduce the severity of infection and prevent infection, if in secretions.**
- **Anti-M2 can reduce the severity of infection in mice; titers in humans are low, and proof of the value of anti-M2 in man is lacking.**
- **CTLs (cytokines) can reduce the severity of infection, and data are emerging for effectiveness in seasonal influenza.**

COCHRANE COLLABORATION

- **Vaccine Efficacy Assessed**
  - **Identified all field trials possible (N=338)**
  - **Only 4 were RCTs with very low bias**
  - **Examples were homotypic and heterotypic protection: very high efficacy with homotypic challenge (up to 93%); good protection vs. heterotypic challenge (~53%)**
  - **Strong plea for high quality RCTs**

T CELLS (1)

- **Dissection of the components of recognition and understanding of the responses to influenza antigens are expanding rapidly**
- **Role in mouse model is clear; potential significance in humans is clear**
- **Immunodominance and a tiny fraction of T cell epitopes inducing responses characterizes virus encounter**

T CELLS (2)

- **Major determinants of responses include binding affinity, T cell repertoire, processing, ? others**
- **Internal proteins can immunize and protect**
- **Unknowns: Features/requirements for optimal benefit have not been demonstrated conclusively; e.g., precursor cell frequency**

STUDIES OF HUMAN CELLS AFTER VACCINATION

- **Live vs. TIV in infants, children, adults**
- **T cell responses-FACS analysis for surrogates; B cell responses (ASCs)**
- **Differences by age and vaccine were noted**
- **CD8 increases in children after live, not adults**
- **ASCs up at day 9, down by day 28**
- **CD4 level best predictor for Ab response**
- **Some expected and some curious findings**