Early Investigations of MERS-CoV

Lab – Epi Integration

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World Health Organization

The Big Questions – MERS-CoV

- **How transmissible?**
  - **Secondary attack rate – in households, HCF, work place.**
  - **Ro**
  - **Roll of risk factors and settings – e.g. chronic illness and institutions**
- **Source of the virus**
  - **Animal reservoir**
  - **Time of emergence**
- **Clinical spectrum of severity**
  - **Proportion of severe/mild cases**
  - **Types of complications – e.g. renal failure**
- **Exposures that result in human infection**

Types of Protocols Needed

- Generic interview form with open ended questions
- Case control study of exposures
  - Determine exposures that result in transmission from non-human sources
  - Comparison of index/sporadic cases to random, matched controls
  - Could use serology to determine controls but not critical for a novel, rare infection.
- Health Care Facilities
  - Evidence of human-to-human transmission
  - Types of exposures that result in infection (e.g. medical procedures)
  - Case control study of exposed and unexposed HCW
  - Infections or seropositives in cohort of all exposed

Types of Protocols Needed

- **Contact study**
  - **Rates of human-to-human transmission (difficult)**
  - **Spectrum of disease, rates of mild disease (if prospective w/ acute and convalescent sera)**
  - **Rates of sero(+) in different exposure-type cohorts of case exposure environment(s): e.g. farm, home, workplace, bridge club – not really about contact w/ case**
- **Serial cross-sectional surveys of risk groups**
  - **Population studies can look at rates of infection**
  - **Prospective cohort study to determine exposures that result in infection**
- **Animal surveys: source of virus**

Laboratory Issues

- **PCR was quickly available and labs offered support**
  - **Initial global discussions led to identification of appropriate targets for screening and confirmation**
  - **Local capacity varied – lab support helped**
  - **Unclear initially which specimens most appropriate: upper vs. lower**
- **Early recommendations included:**
  - **Retrospective testing of stored specimens from SARI surveillance**
  - **Testing of all unexplained pneumonia in affected countries**
  - **Inclusion of testing in SARI surveillance algorithms.**
- **Cost and human resources were limiting factors**

Laboratory Issues

- **Serological assays being developed by multiple institutions on a variety of formats, using different protein substrates**
  - **ELISA, IFA, LIPS, protein arrays, neutralization**
  - **Spike protein, nuclear protein**
- **Challenges to development include limited number viruses and positive sera**
  - **Difficult to know sensitivity**
  - **Not possible to know the comparability without standards**
  - **Antibody kinetics unknown – though Jordanian cases had (+) 1 year later**
- **Epi implications:**
  - **Very useful tor comparing relative positivity of groups of people**
  - **Need to include controls in sero-epi studies – background rates of positivity related to cross reactivity or previous infection unknown.**
  - **Not yet possible to use for diagnostic purposes – positives are classified as "probable"**

Lessons Learned

- **Serological assays can take a long time to perfect**
  - **Actually, they are never perfect but imperfect assays are useful, especially in comparing groups.**
  - **Serological data, like epi data, are "messy" but can provide critical understanding about risk groups, infection rates, and spectrum of disease**
  - **International collaboration critical to development.**
- **Much misunderstanding among epi about what test means in an individual**
  - **Cross-reactivity not widely appreciated or understood**
  - **No single test is going to be definitive**

Thank you for your kind attention