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 for 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