SARS Laboratory Diagnosis

WHO SARS Team

17 June 2003 = day x+93
Today

- Contribution of laboratory diagnosis to SARS control
- Current stage of development of laboratory tests
- Obstacles and challenges
- Gaps and need
SARS → use of laboratory tests

- Patient treatment/management
- Understanding of the natural history of the disease
SARS Diagnosis

- SARS suspect
- SARS probable

Pneumonia cases

Contacts

admission
SARS laboratory diagnosis

- **Indicators of infection**
  - Presence/excretion of virus
  - Measurable immune response

- **Challenges to laboratory diagnosis**
  - Antibody development late
  - Relatively low virus excretion at beginning
  - Seroconversion and virus/RNA excretion without any/typical symptoms
  - Long excretion of RNA in stool

**Graph:**
- Detectable immun-response
- Respiratory
- Stool
- %
- 0 2 3-5 6-8 9-11 12-14 15-17 18-20 21-23 day
SARS laboratory tests 1

- Immune response: ELISA/Westernblot
  - CDC Atlanta, CDC Beijing; HKU, Hong Kong SAR; ...
  - Detection of IgM/IgG against various virus components
  - Ag: whole virus; recombinant (various virus proteins)
    - ELISA: large scale screening
    - WB: confirmatory test; no large scale testing

→ Antibody detection reliably only late in disease

→ No standardization yet; one ring-trial so far
SARS laboratory tests 2

- Immune response 2: Immune-fluorescence assay
  - Reliable, robust test; cumbersome for large scale screening
  - Detection of IgM/IgG
  - Ag: whole virus fixed in cells on glass slide
    - Antibody detection only late in disease (>day 10)
    - No standardization yet
SARS laboratory tests 3

- Presence/excretion of virus
  - Virus isolation in tissue culture/animal models
    - Sophisticated lab; low sensitivity
  - Antigen detection by serological methods
    - currently not feasible
    - monoclonal antibodies?
  - Detection of genetic material (NAAT)
SARS Nucleic Acid Amplification Techniques

- **PCR**
  - Reiterative process for amplification of viral genetic material;
    - Target: multiple regions of viral genome
  - High specificity and relatively high sensitivity
  - Various techniques (nested; real-time…)

- **Conditions**
  - Experienced laboratory staff and/or sophisticated equipment
  - High laboratory quality assurance standards

- **No standardization yet; one ring trial so far**
Summary: positive laboratory results

- Important adjunct to clinical diagnosis
  - Virus isolation and seroconversion: definitive answer
  - NAAT very useful: require additional verification and quality assurance
  - However:
    - Seroconversion and consistent virus/RNA excretion only late in disease
    - Epidemiological significance unclear of RNA excretion in milder/asymptomatic cases and after disease resolution
Summary: negative laboratory results

- No additional significance for case management and initiation for disease control measures
  - Virus/RNA excretion low during initial phase
  - Ab reaction detectable only during late phase
  - NAAT: sensitivity too low for exclusion of disease
SARS - Do we need diagnostic tests?

- Yes: particularly at the tail end of the outbreak.
  - Quick tests
    - SARS
    - Other respiratory diseases (Influenza)
SARS laboratory diagnosis: priorities

- Requires concerted efforts of various partners for common public health goal
  - Incentives for long-term investments necessary
  - Public health
    - Establish pedigreed panel of specimens for test validation
    - Standardizing reagents (reference virus and serum) for test performance assessment
    - Genetic diversity databank
    - Repository of reagents and isolates
If you think research is expensive - try disease. Mary Lasher 1901-1994
Provision of standardizing reagents through WHO

61 countries; 11 June 2003