Diagnosis of Severe Acute Respiratory Syndrome (SARS)

- Clinical characteristics of illness
- Epidemiologic link to SARS, i.e. ,travel or contact
- Laboratory evidence of SARS-CoV infection
  - Type of specimen
  - Timing of specimen collection
  - Laboratory assay to detect infection

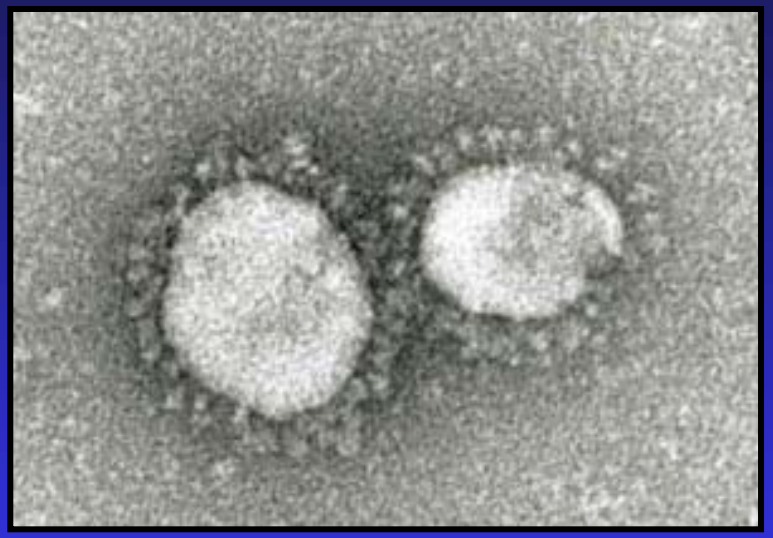
Association Between SARS-CoV and SARS Disease

- **Infection in SARS patients – virus and serology**
  - CDC
  - Germany, Canada, Hong Kong, Taiwan, Singapore, France, China, Thailand, etc.
- **Neg-serology in non-SARS patients** (~1000 sera at CDC, 280 HK)
- **Virus in lung tissue/BAL specimen**
- **Identical sequences different outbreaks (c/w point source)**
  - US; Hong Kong, Thailand, Singapore, Taiwan, Vietnam, Canada, Germany
- **Pulmonary pathology in monkey model**
- **Questions – histopathology and rate of positivity**

CDC

SARS Etiologic Agent

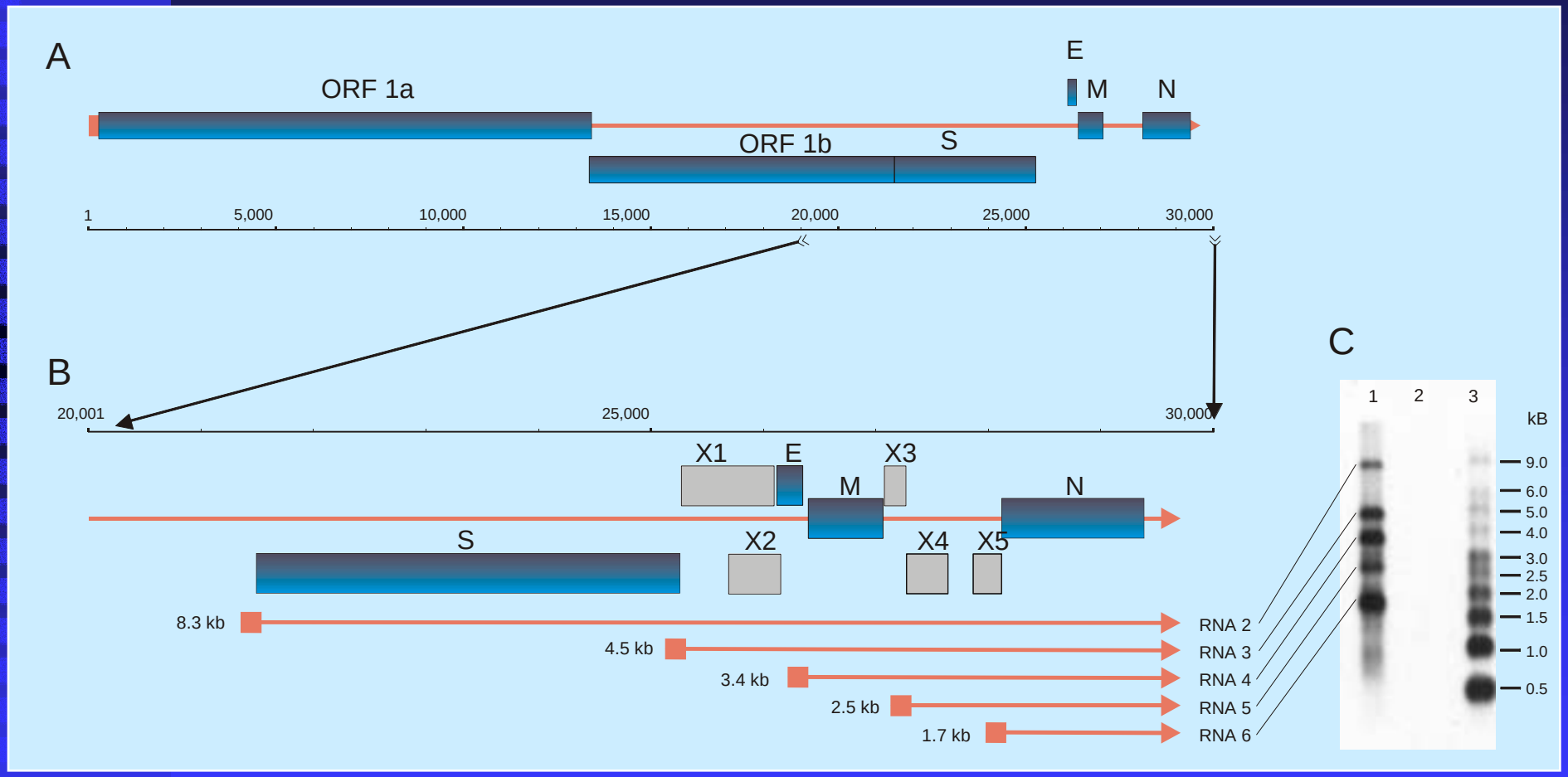
- Order: Nidovirales
  - Family: Coronaviridae
    - ♦ *Torovirus*
    - ♦ *Coronavirus*
      - Grp I
      - Grp II
      - Grp III



Coronaviruses, Hosts and Diseases

Antigenic Group	Virus	Host	Respiratory	Enteric	Other
I	HCoV-229E	human	X		
	TGEV	pig		X	
	PRCoV	pig	X		
	FIPV	cat	X	X	X
	FECoV	cat		X	
	CCoV	dog		X	
II	HCoV-OC43	human	X	??	
	MHV	mouse	X	X	X
	RCoV	rat	X		X
	HEV	pig	X		X
	BCoV	cattle	X	X	
III	IBV	chicken	X		X
	TCoV	turkey		X	

SARS-CoV Genome Organization and mRNA Synthesis



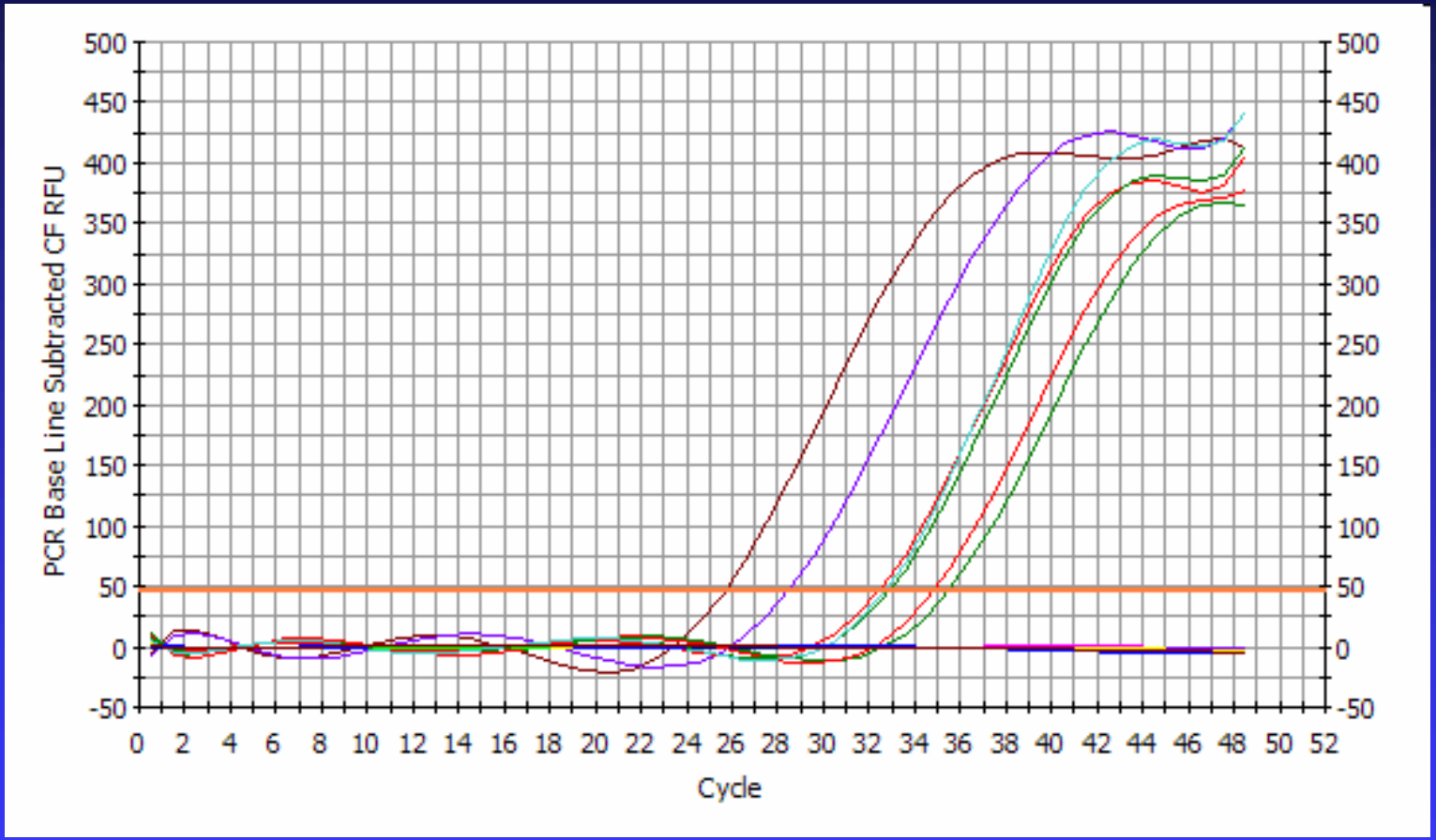
Laboratory Diagnosis of SARS Infection

- Type and timing of specimen collection (we need to know more)
- Type of assays
  - Sensitivity
  - Specificity
  - Interpretation of results

Laboratory Assays for SARS

- Detection of virus
  - EM in clinical specimens (CoV-like particles)
  - Isolation of virus
  - Detection of viral antigens (IHC for tissue, ?sensitivity of IFA or ELISA for respiratory specimens)
  - Detection of viral RNA (PCR)
    - Respiratory secretions
    - Stool specimens
    - Urine specimens
    - Tissue – lung and kidney
- Detection of SARS-specific antibody
  - IFA
  - ELISA
  - Neutralization

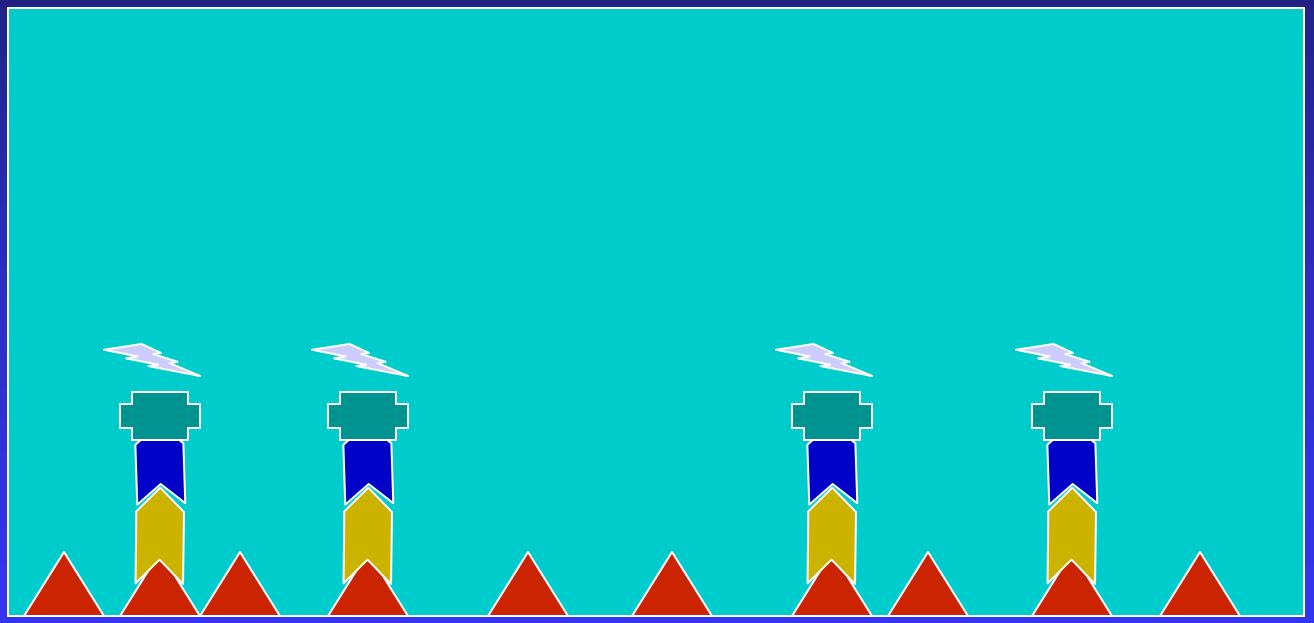
Real-Time RT-PCR (TaqMan)



Characteristics of SARS-CoV PCR

- Limited experience/data
- Specimens
  - Upper respiratory maybe ~50% positivity in acute-phase specimens
  - Stool possibly higher sensitivity later in illness, e.g., 10-14 days
  - Sputum/BAL probably higher rate of positivity
  - Other specimens, urine, blood, tissues, ?
- Interpretation of Results
  - Negative -- does not rule out SARS-CoV infection
  - Positive – possibility of false positive (test error/contamination)

SARS CoV Antibody Assays



Characteristics of SARS-CoV Antibody Assays

- Limited data
- Very low or absent antibody in controls and persons without acute SARS
  - Acute sera may be positive as early as 6 days after onset of sera
  - Convalescent sera should be positive by 21 days after onset
- Interpretation of results
  - Single positive sera indicative of acute infection
  - Later diagnostic rise in antibody between acute- and convalescent-phase sera or IgM antibodies may be need to diagnose acute infection
  - Convalescent-phase serum specimen collected >21 days after onset of illness is required to confirm lack of antibody response to infection
  - False positive/false negative results

Other Tests for SARS Infection

- Limited data
- Tissue culture isolation
- Electron microscopy for CoV-like particles
- Immunohistologic or in situ studies of tissue specimens
- IFA or ELISA assays SARS-CoV antigens in respiratory or other specimens (? Likely to be sufficiently sensitive)

Conclusions

- SARS is a clinical and epidemiologic diagnosis
- Laboratory testing can diagnose SARS-CoV infection during the acute illness
- Laboratory testing can not rule out infection until the convalescent phase of illness
- Dual infections, e.g., SARS-CoV and human metapneumovirus, can occur in patients with SARS