Coronavirus Overview as it Relates to Vaccine Development
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Course Number PB-VI01P: Development of a Vaccine During a Pandemic
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Outline

- Coronavirus Virology & Biology
- Transmission
- Pathophysiology
- Clinical features
- Diagnostics
- Immunology
Coronavirus Virology

• >30 known animal CoVs in four genera – A, β, Δ, Γ
• Virus spillover occurs with bats and rodents likely sources of human CoVs
• Seven CoVs known infect humans
  ▪ HCoV-229E, and HCoV-NL63 (alphaCoVs)
  ▪ HCoV-OC43, and HCoV-HKU1 (betaCoVs)
  ▪ SARS-CoV, SARS-CoV-2, and MERS-CoV (betaCoVs)
Coronavirus Virology

• Positive-stranded RNA viruses – prone to mutation

• Genetic drift occurs with SARS-CoV-2 S, N and M proteins potentially complicating vaccine development
Endemic Coronavirus Biology

- Worldwide distribution
- Major cause of common cold-like illness in all ages
- Infection marked seasonal and cyclical patterns
- ~50% of endemic CoV infections are asymptomatic
- Endemic CoVs have a high rate of reinfection; in volunteers it can occur within a year of prior infection
Endemic Coronavirus Biology

• One study, 81.5% of newly infected individuals had pre-existing virus specific neutralizing antibody

• Uncertain whether pre-existing neutralizing antibody modifies the severity of subsequent re-infections

• Endemic CoV infections involve mainly the surface of the respiratory tract, it is possible that secretory IgA antibody plays a more direct role in protection, as is the case with swine CoV infections
SARS-CoV-2 Transmission

• Primarily human to human
• Respiratory –droplets/contact - portal of entry: eyes/nose
  • Medical students touch their eyes, nose and or mouth an average of 10 times an hour
• Oral-fecal?
• No recognized mother to fetus transmission

Kwok YLA, et.al., Face touching_ A frequent habit that has implications, Am J Infect Control 43_112-4, 2015
COVID-19 Transmission Dynamics

• Research suggests that seasonality is likely to play only a minor role in the epidemiology of COVID-19

• Public health interventions strongly associated with reduced epidemic growth:
  ▪ restrictions of mass gatherings
  ▪ school closures
  ▪ measures of social distancing

COVID-19 Pathophysiology(?)

• Virus binds to ACE2 receptors on oral, nasal and ocular mucosal epithelial cells initiating infection
• Infection extends to lungs leading to pneumonia
• Viremia may develop in some patients with dissemination and injury of visceral organs, i.e., heart, renal, gastrointestinal tract (with fecal shedding)
• In some, infection triggers immune dysregulation and immunopathological (autoimmune) responses

COVID-19 Clinical Features Important in Vaccine Development?

• Hypoxia
• Pneumonia
• Organ failure (heart, kidney, multi-organ)
• Hepatitis
• Shock
• Stroke
• Venous thromboembolism
• Pediatric Multi-System Inflammatory Syndrome
SARS-CoV-2 Diagnostics

• Acute infection
  ▪ Virus culture
  ▪ Viral nucleic acid (RNA) detection
  ▪ Antigen detection

• Serologic assays
  ▪ ELISA
  ▪ Lateral-flow
  ▪ Virus neutralization
  ▪ Pseudovirus neutralization
SARS-CoV-2 Immunology

• Antibody seroconversion— IgM appears day 8-12 and is gone by week 13. IgG appears around day 14
  ▪ Serum contains neutralizing antibody; convalescent plasma appears to have some therapeutic benefit

• Both CD4+ and CD8+ T cells are detected about 7 days after onset of symptoms
  ▪ SARS-CoV-1 mouse studies showed that induction or passive transfer of virus-specific CD4+ and CD8+ T cells increased survival. Other studies found that some vaccines could induce detrimental T cell responses

SARS-CoV-2 Unknowns

• What proportion of the population need to become infected and/or immunized to afford to community immunity (herd immunity)?

• Will COVID-19 infection protect against SARS-CoV-2 reinfection?

