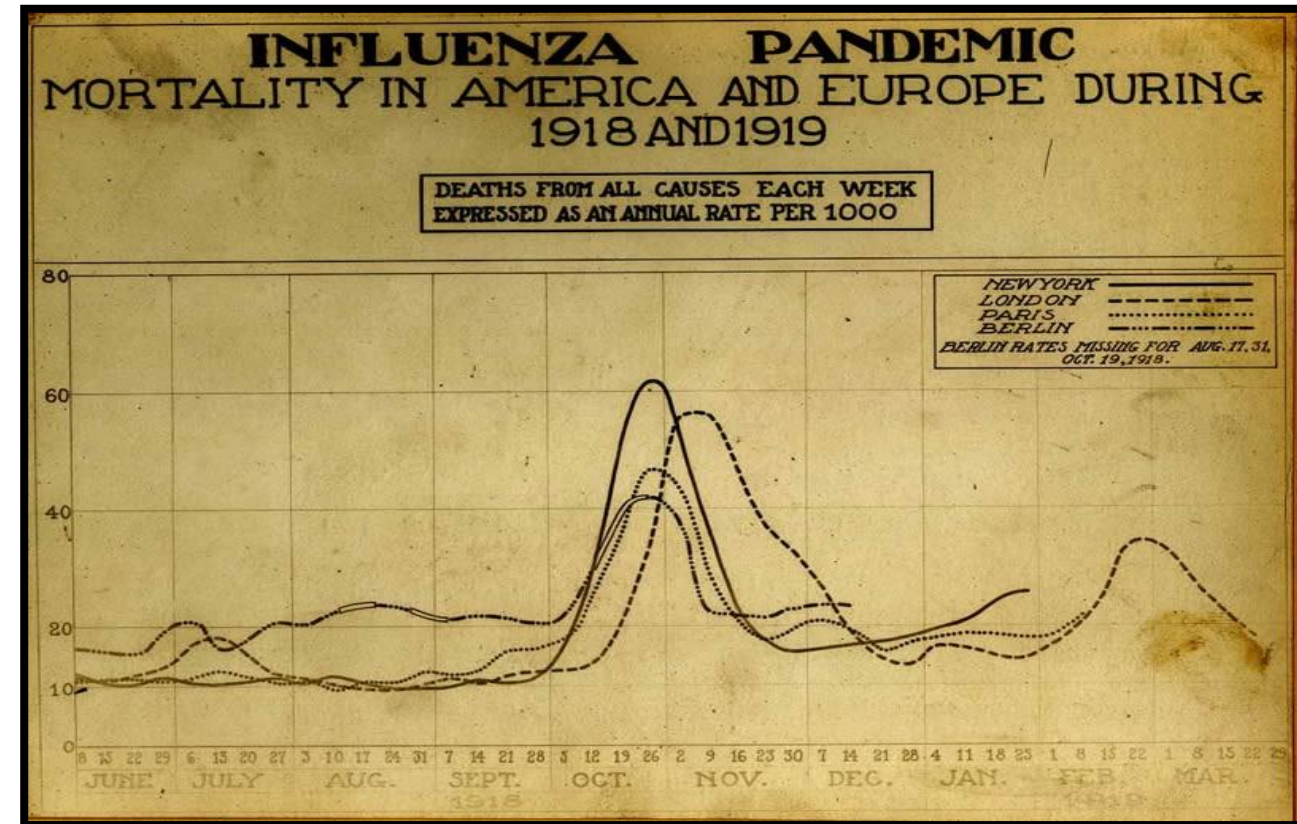


Understanding the Scale of the 1918 Pandemic and the Role of Bacterial Coinfections on Mortality

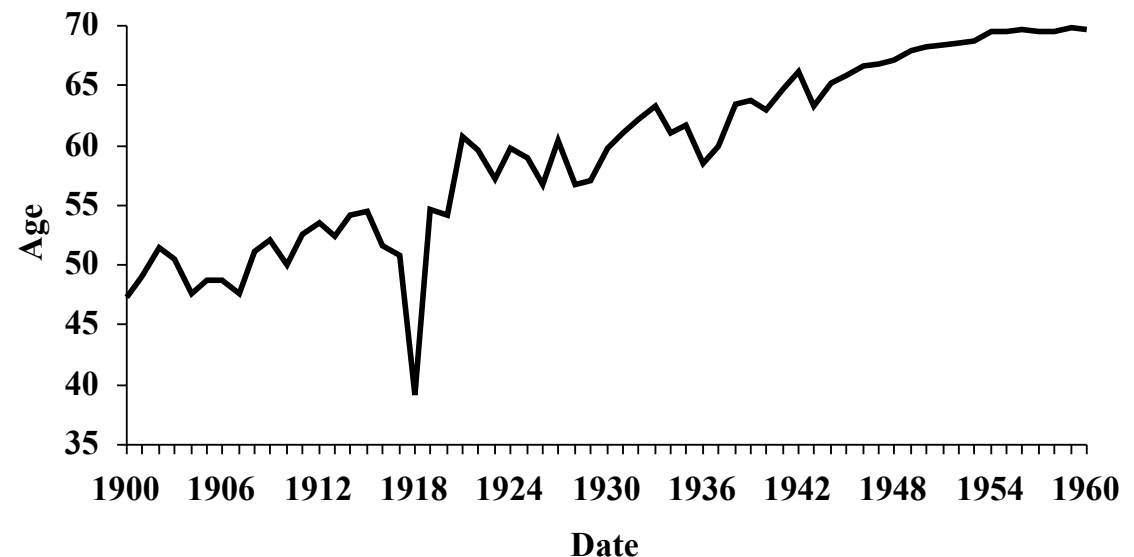
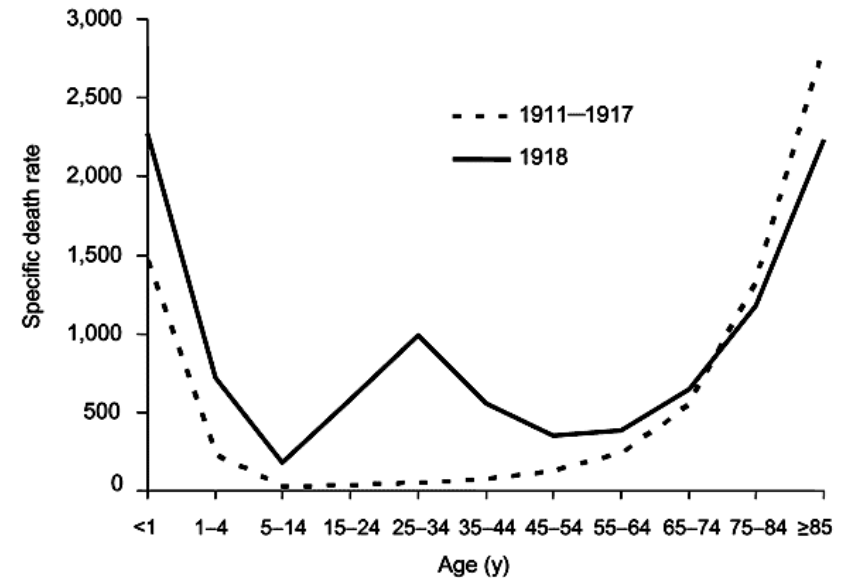


Jeffery K. Taubenberger, M.D., Ph.D.
NIAID, NIH
March 2, 2022

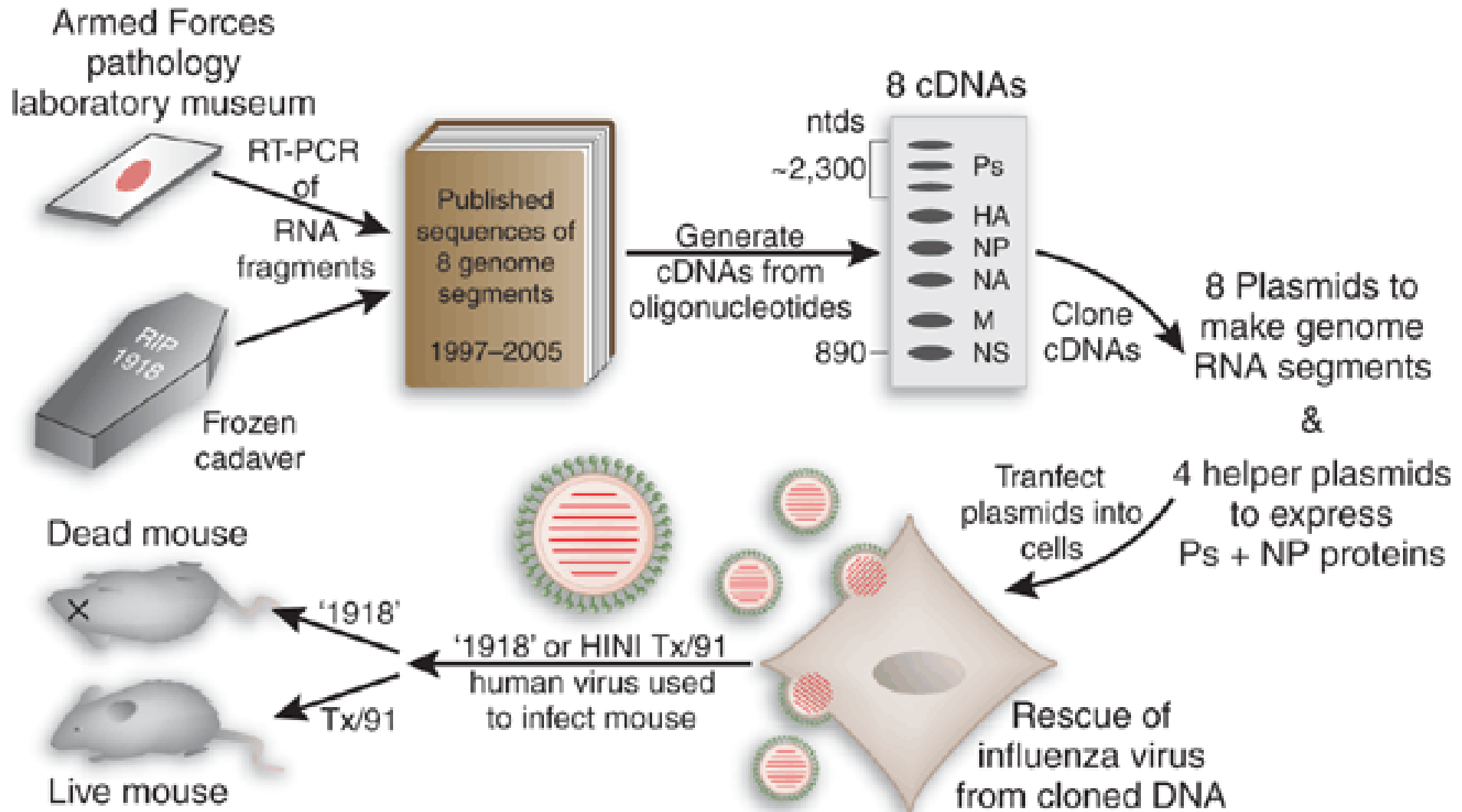


1918 'Spanish' Influenza Mortality

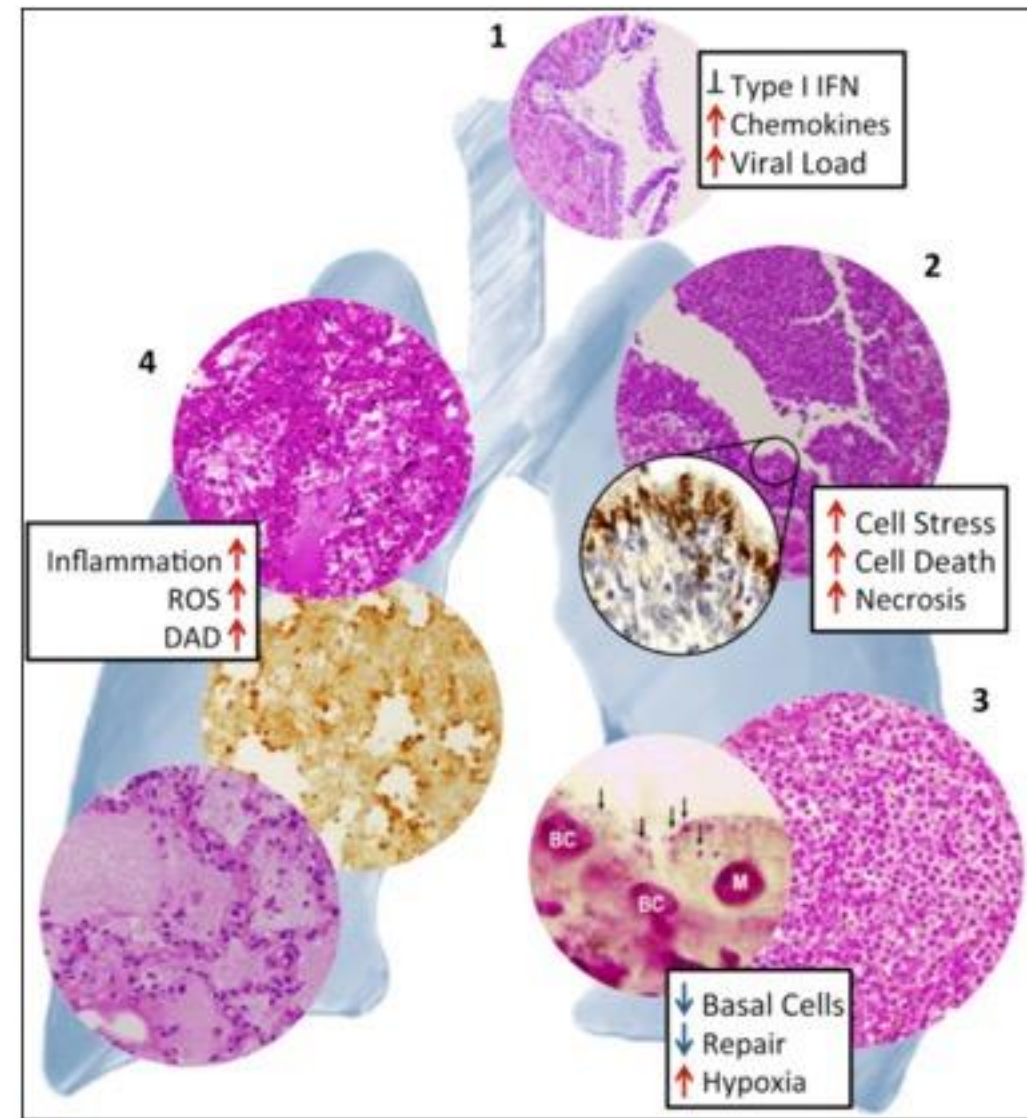
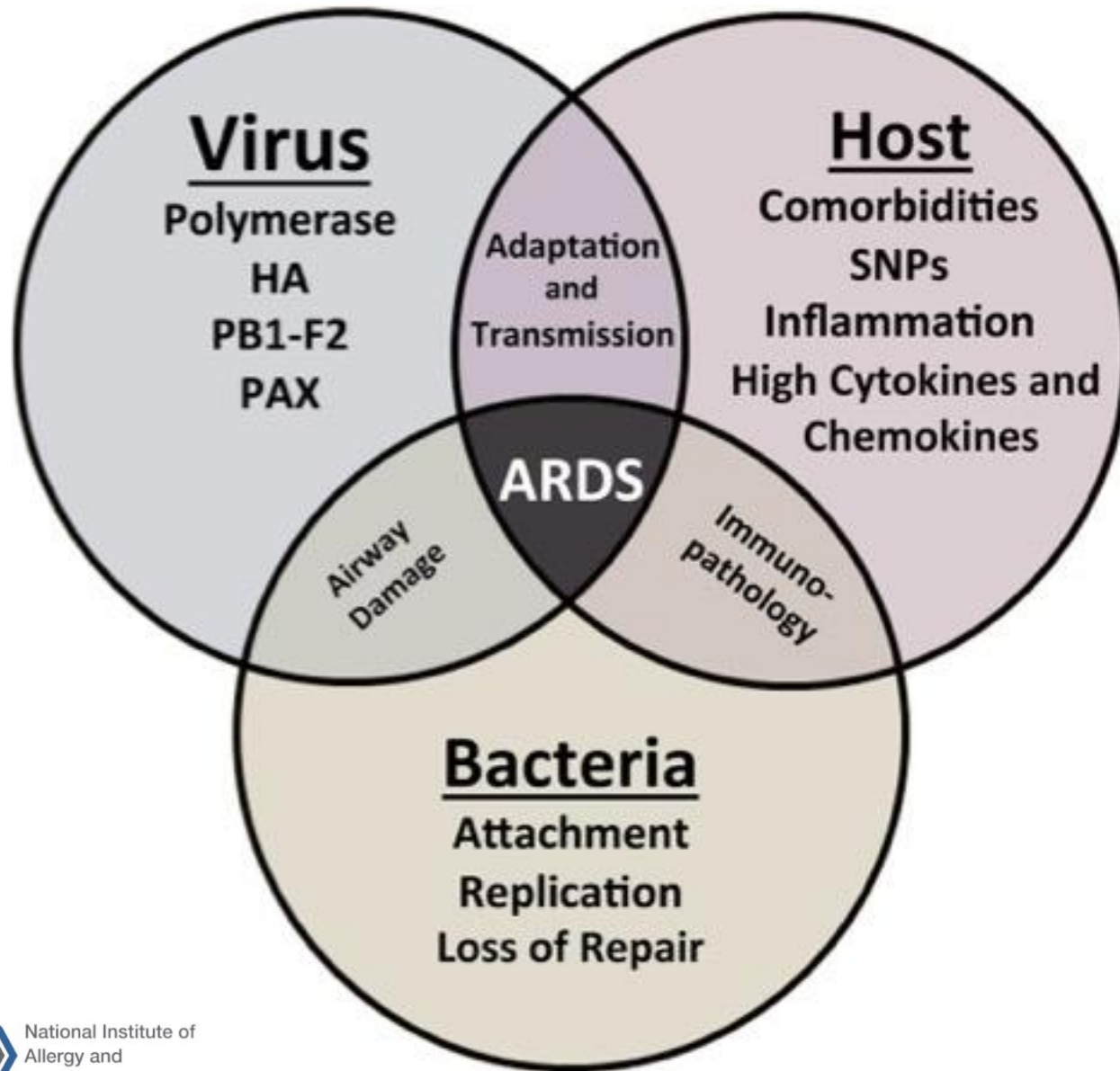
- Total global deaths in the 9 months of the pandemic in 1918-1919 estimated to be 50-100 million (1918 world population ~1.8b)
- U.S. Deaths = 675,000 (U.S. pop. ~100m)
- Flu deaths in Philadelphia in October 1918 = 10,959. Total flu deaths = 15,785
- U.S. Military deaths to flu = 43,000 (out of ~100,000 U.S. Troop casualties in WWI)



'Resurrecting' the 1918 Influenza Virus



Factors in Influenza Pathogenesis



Predominant Role of Bacterial Pneumonia as a Cause of Death in Pandemic Influenza: Implications for Pandemic Influenza Preparedness

David M. Morens, Jeffery K. Taubenberger, and Anthony S. Fauci

National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland

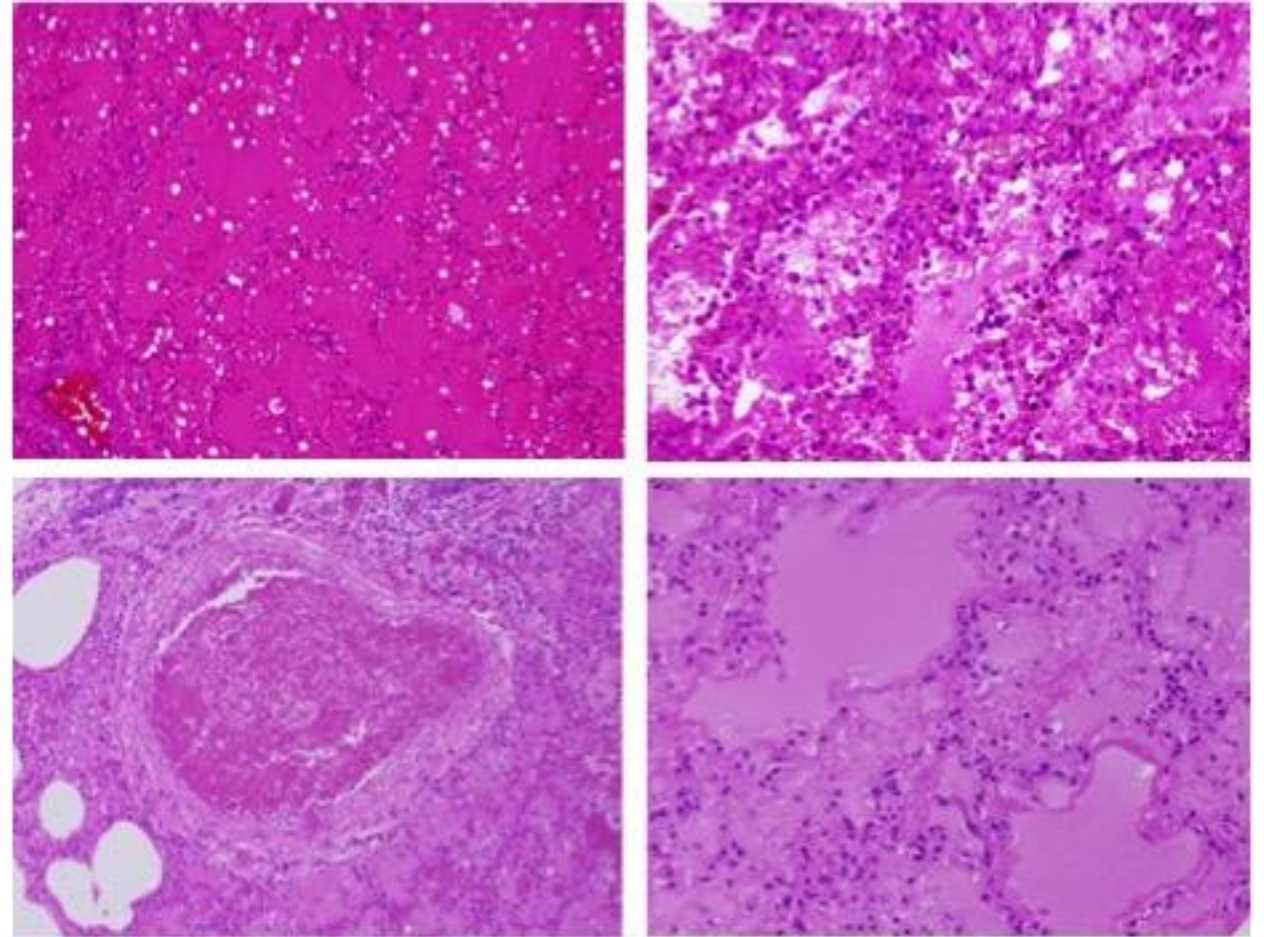
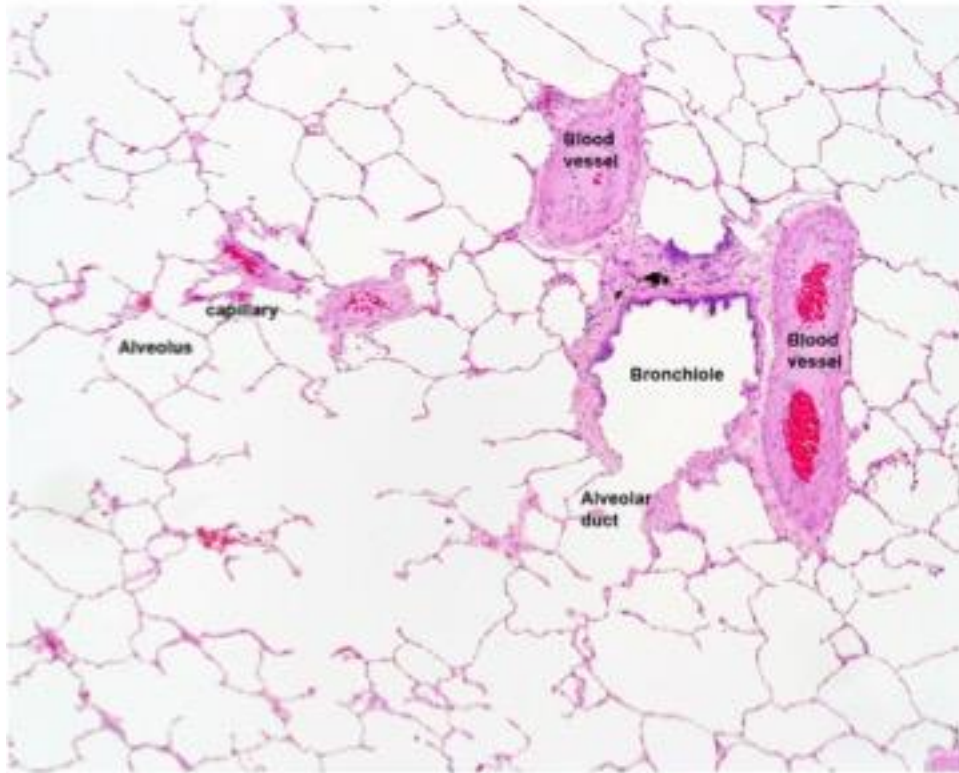
- The importance of secondary bacterial pneumonias in severe and fatal influenza infections were widely recognized by clinicians, pathologists, and microbiologists during the 1918 pandemic, but somehow this critical fact seemed to have been forgotten in modern times
- Review of >8000 published autopsy studies in 1918-19 showed bacterial pneumonia in >94% of cases

“If grippe condemns, the secondary infections execute” [1, p. 448].

—Louis Cruveilhier, 1919

1918 Lung Pathology

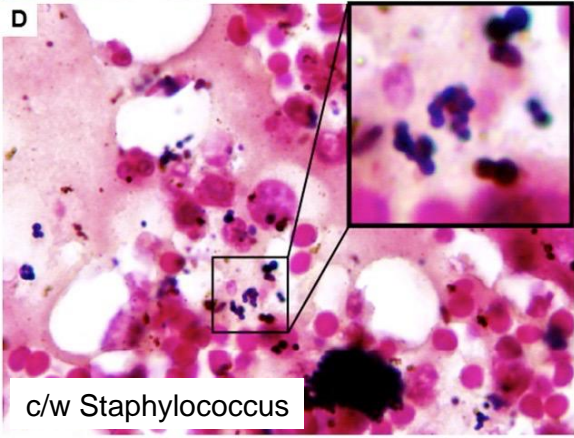
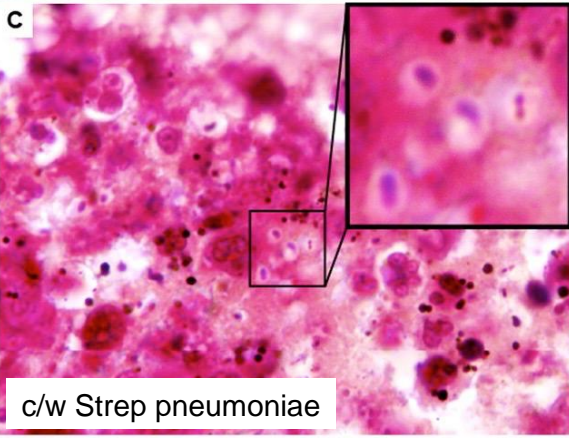
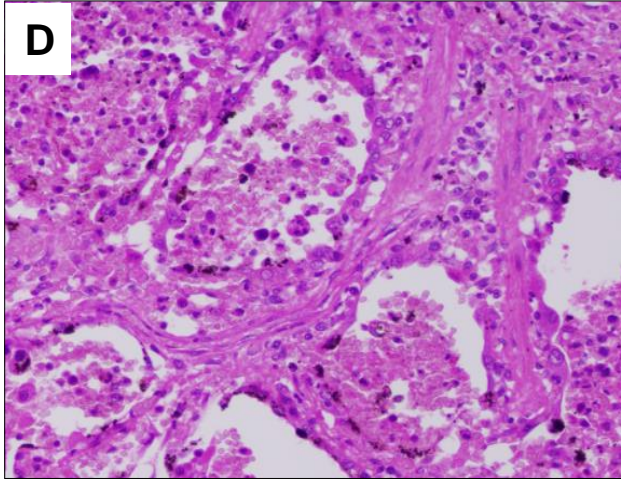
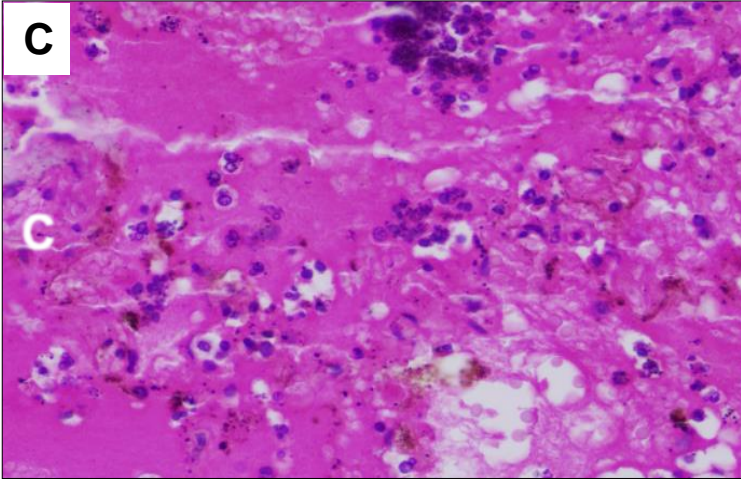
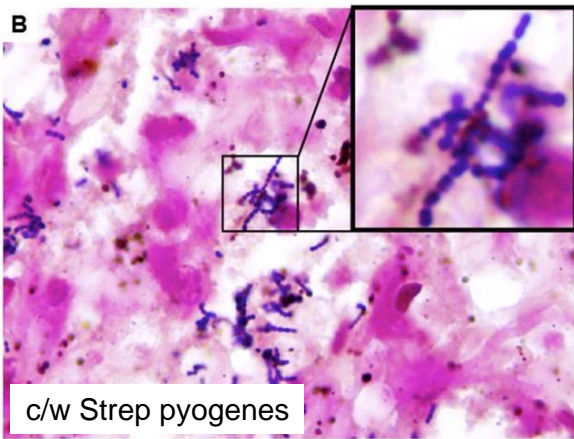
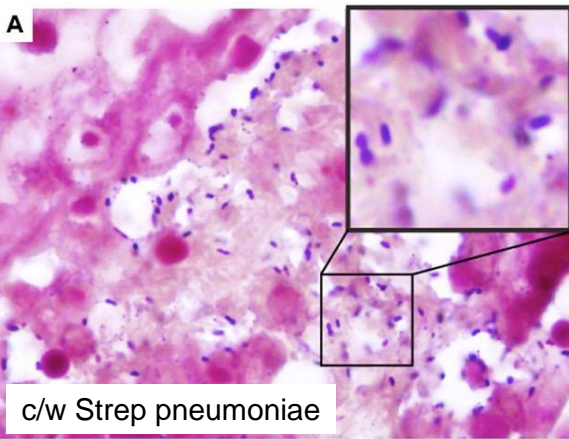
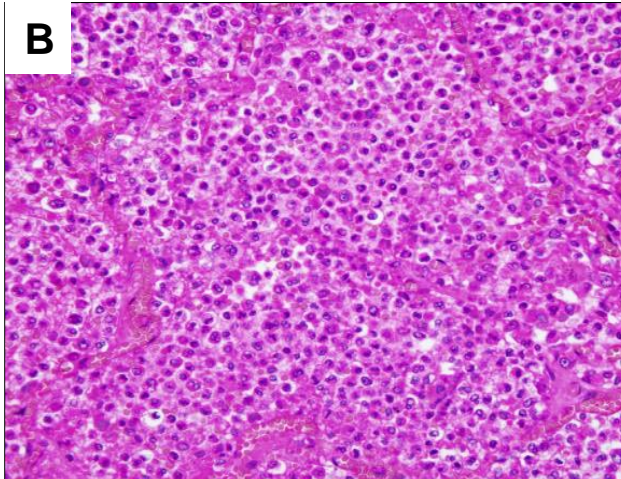
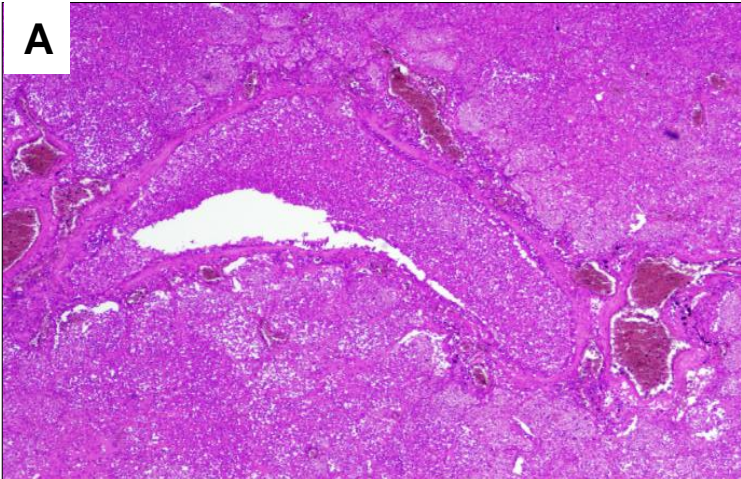
Primary Viral Pneumonia: DAD with edema, alveolitis, thrombi



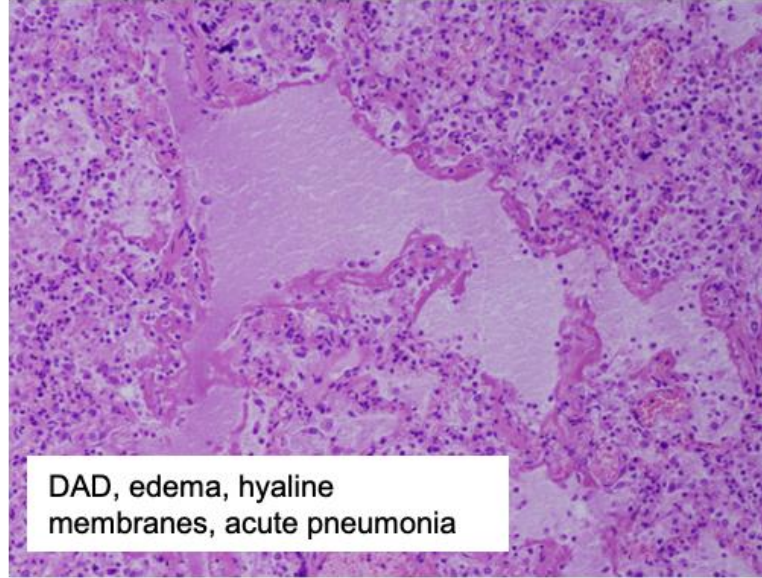
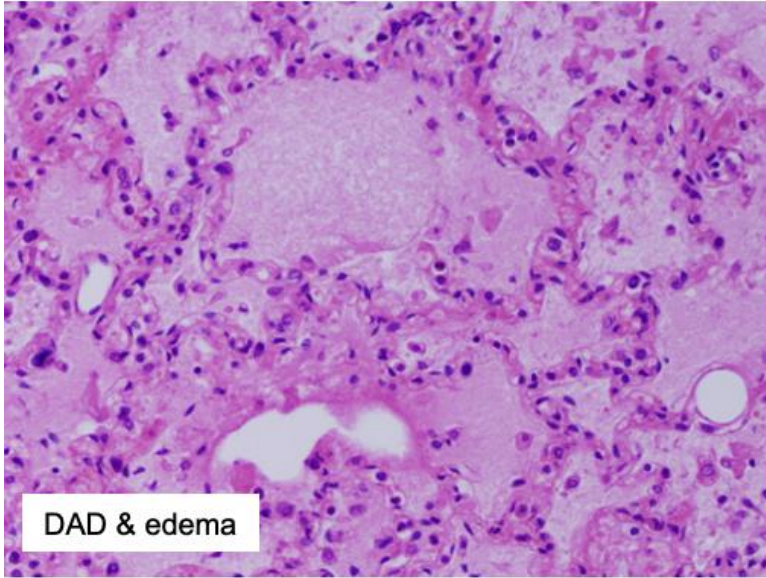
Taubenberger & Morens 2008 *Ann Rev Path* 3:499
Morens, Taubenberger & Fauci 2008 *JID* 198:962
Kuiken & Taubenberger 2008 *Vaccine* 26(S4):D59

1918 Lung Pathology

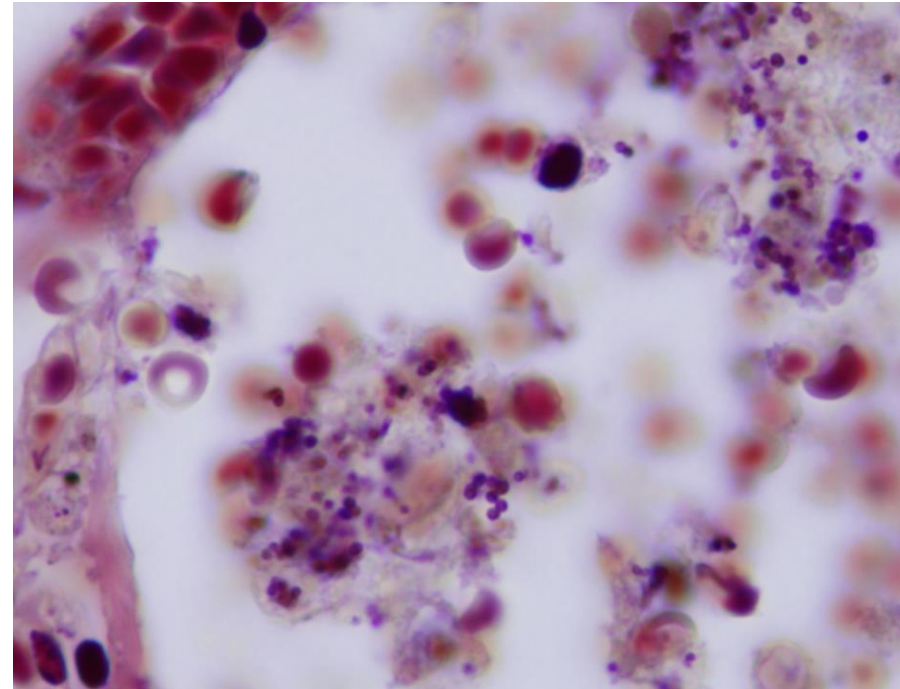
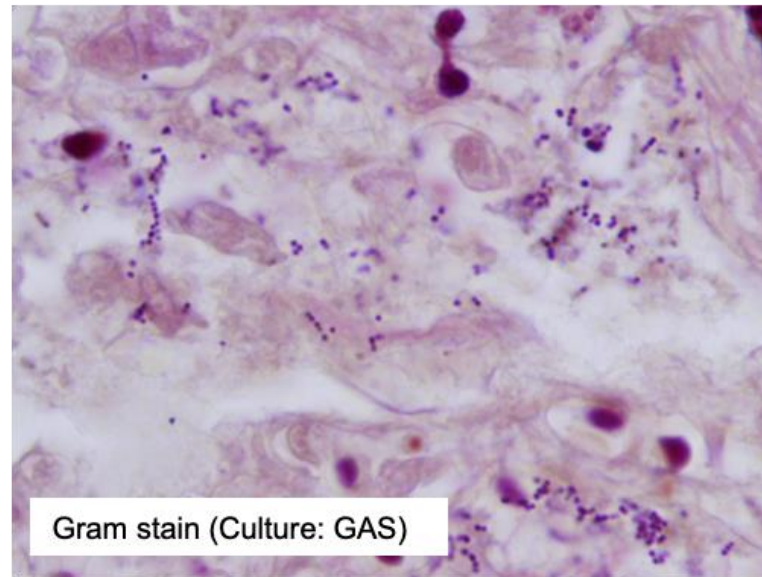
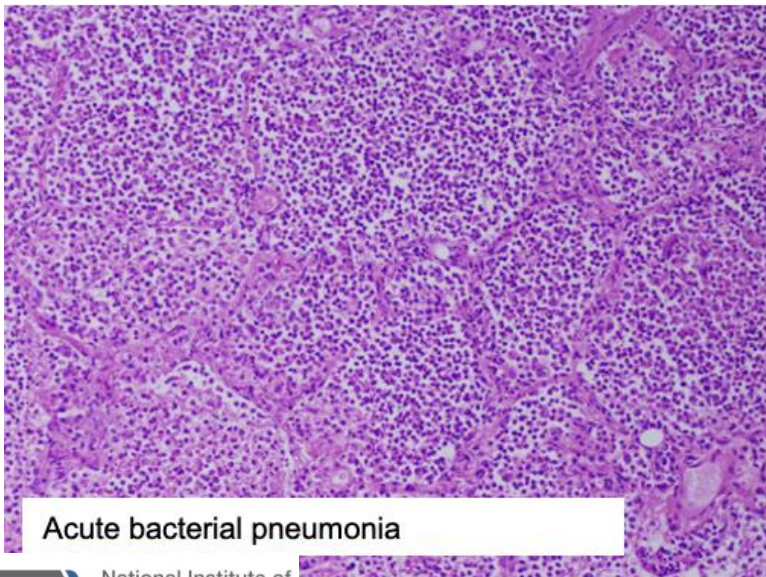
Secondary Bacterial Pneumonia and Repair



2009 Autopsy Pathology

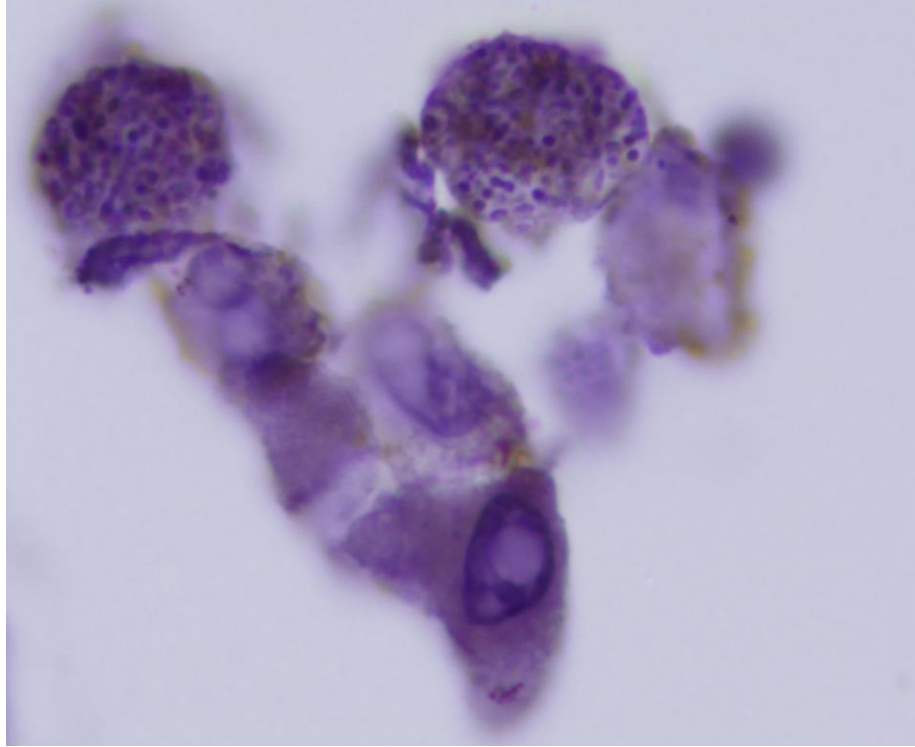


Bacterial pneumonia common (55%), mainly *Strep pneumoniae*, Group A Strep, Staph (including MRSA), most community acquired

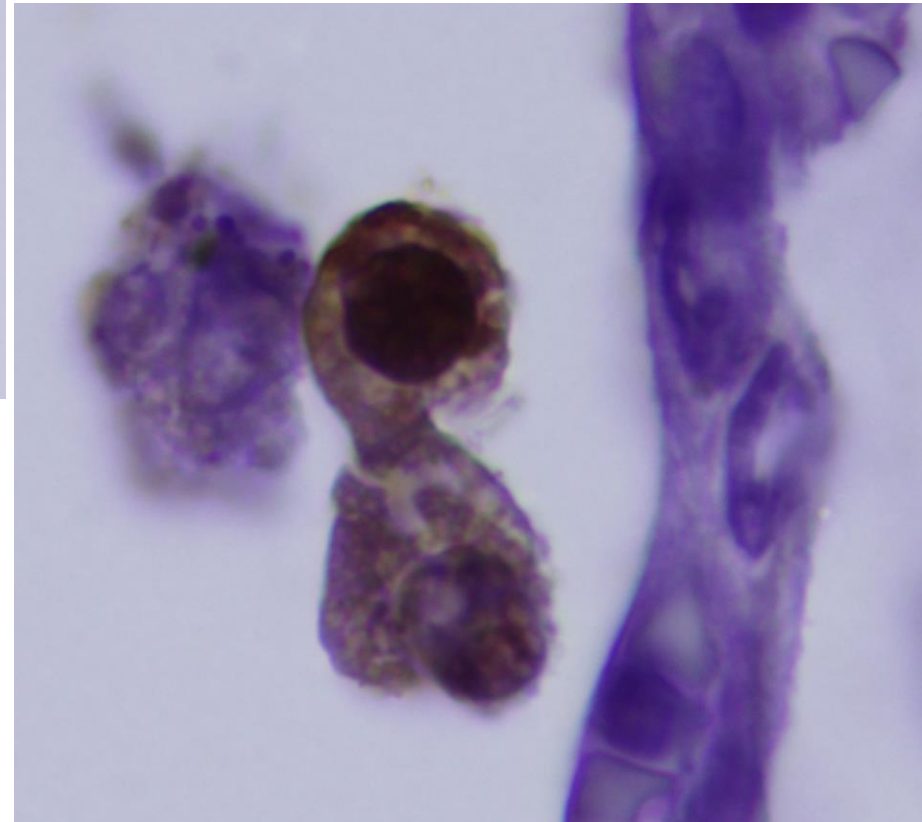


Necrotizing acute pneumonia with MRSA

2009 Autopsy Pathology

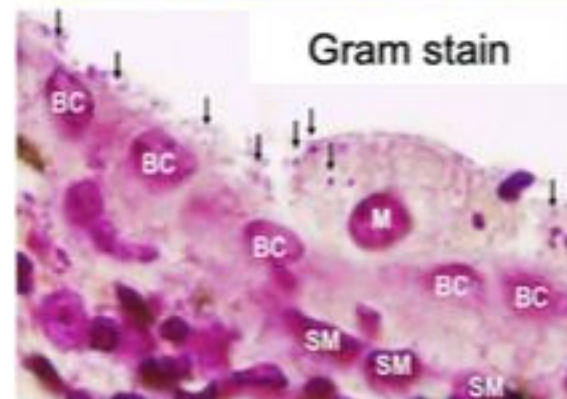
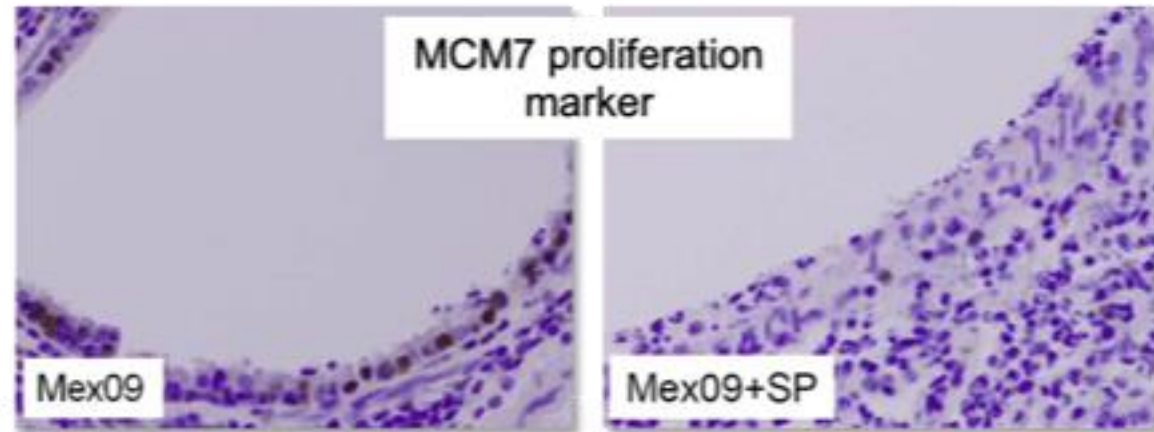
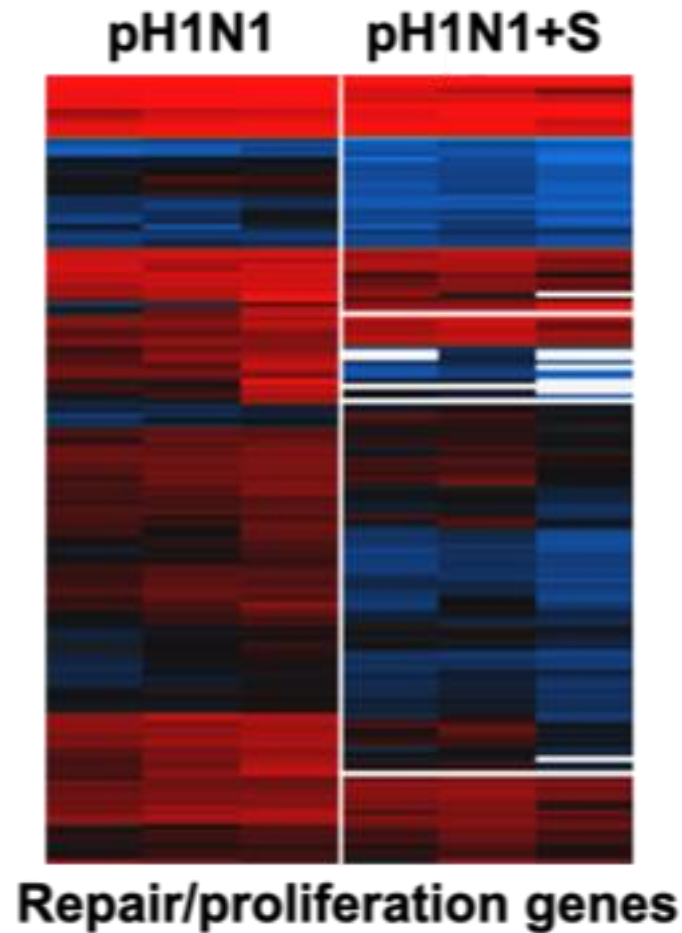


Alveolar macrophages
with Strep pneumo and
influenza antigen



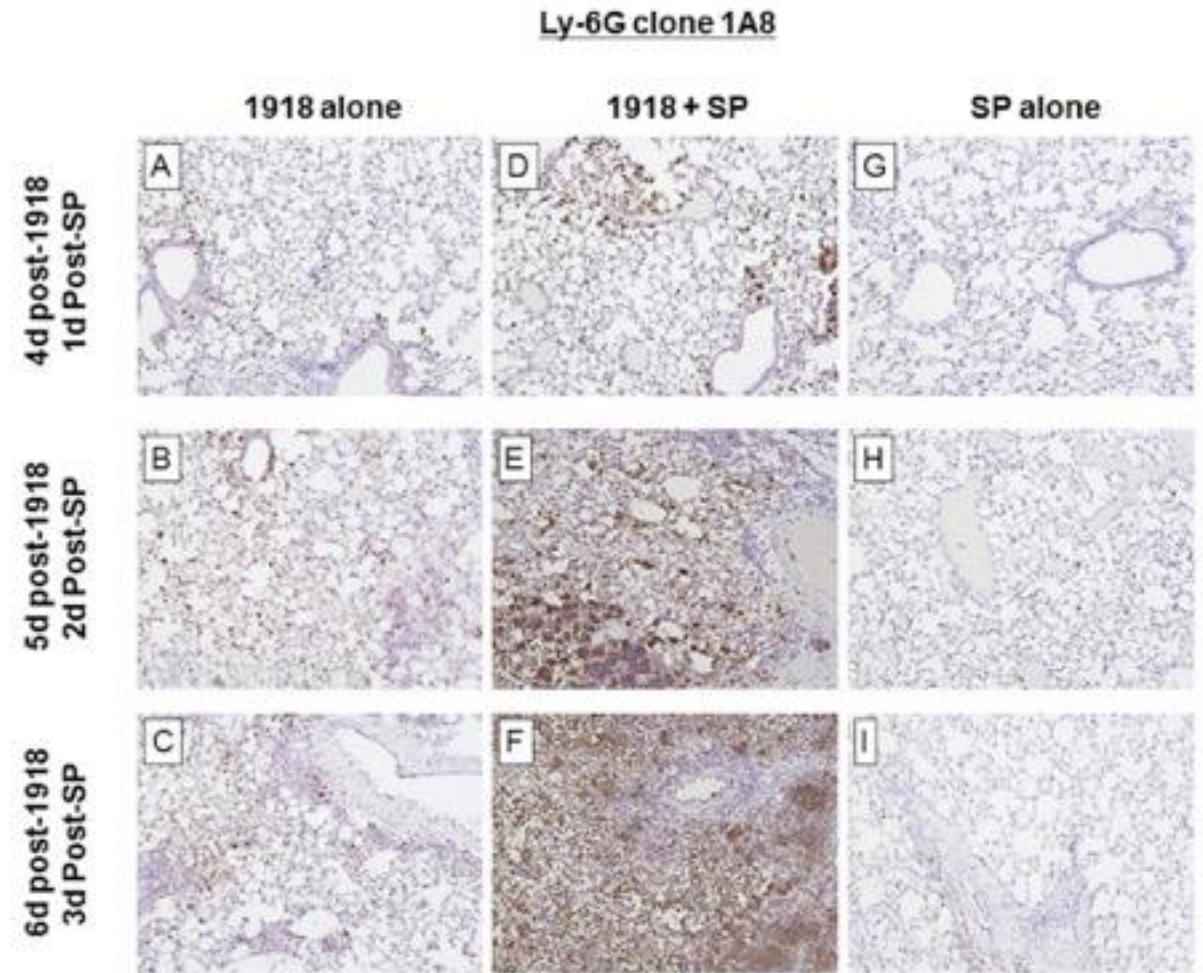
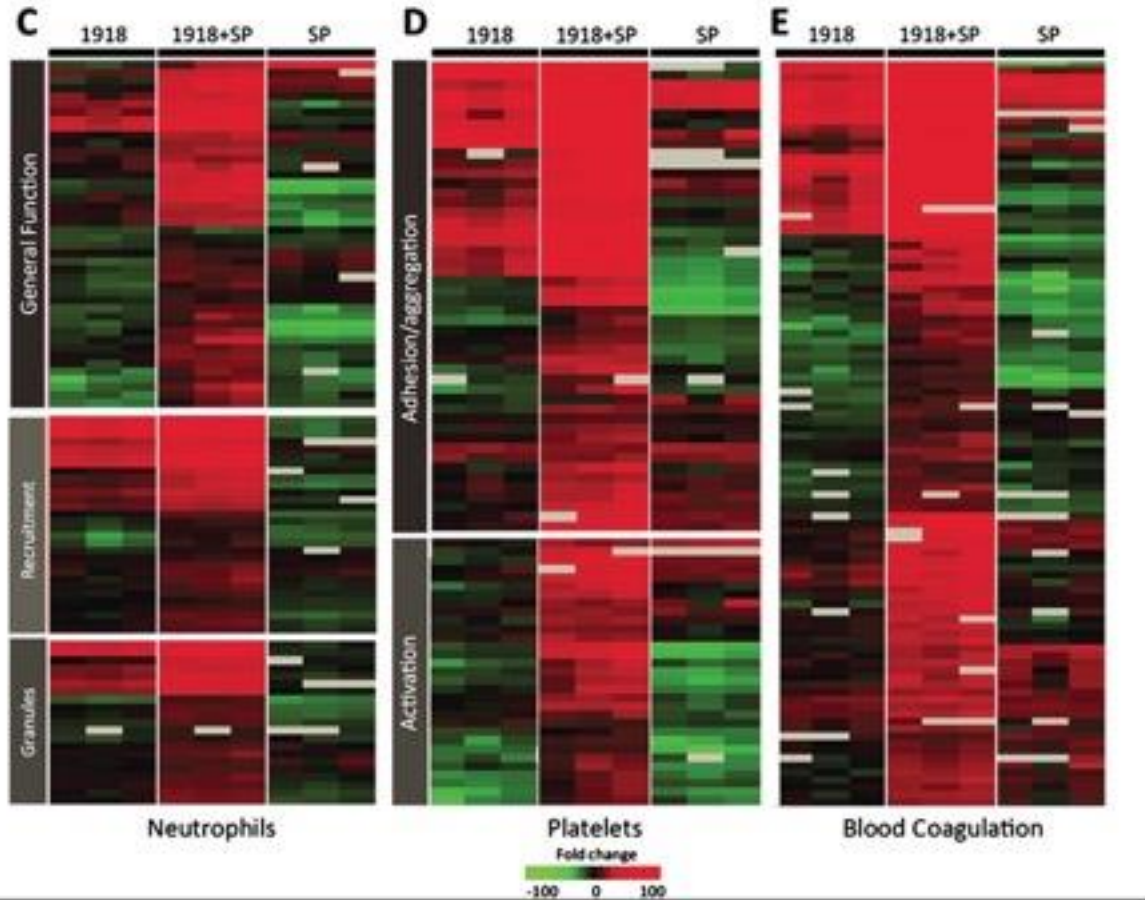
Viral & Bacterial Copathogenesis

pH1N1+SP infection associated with loss of basal cells and absence of re-proliferation and repair of airway epithelial cells

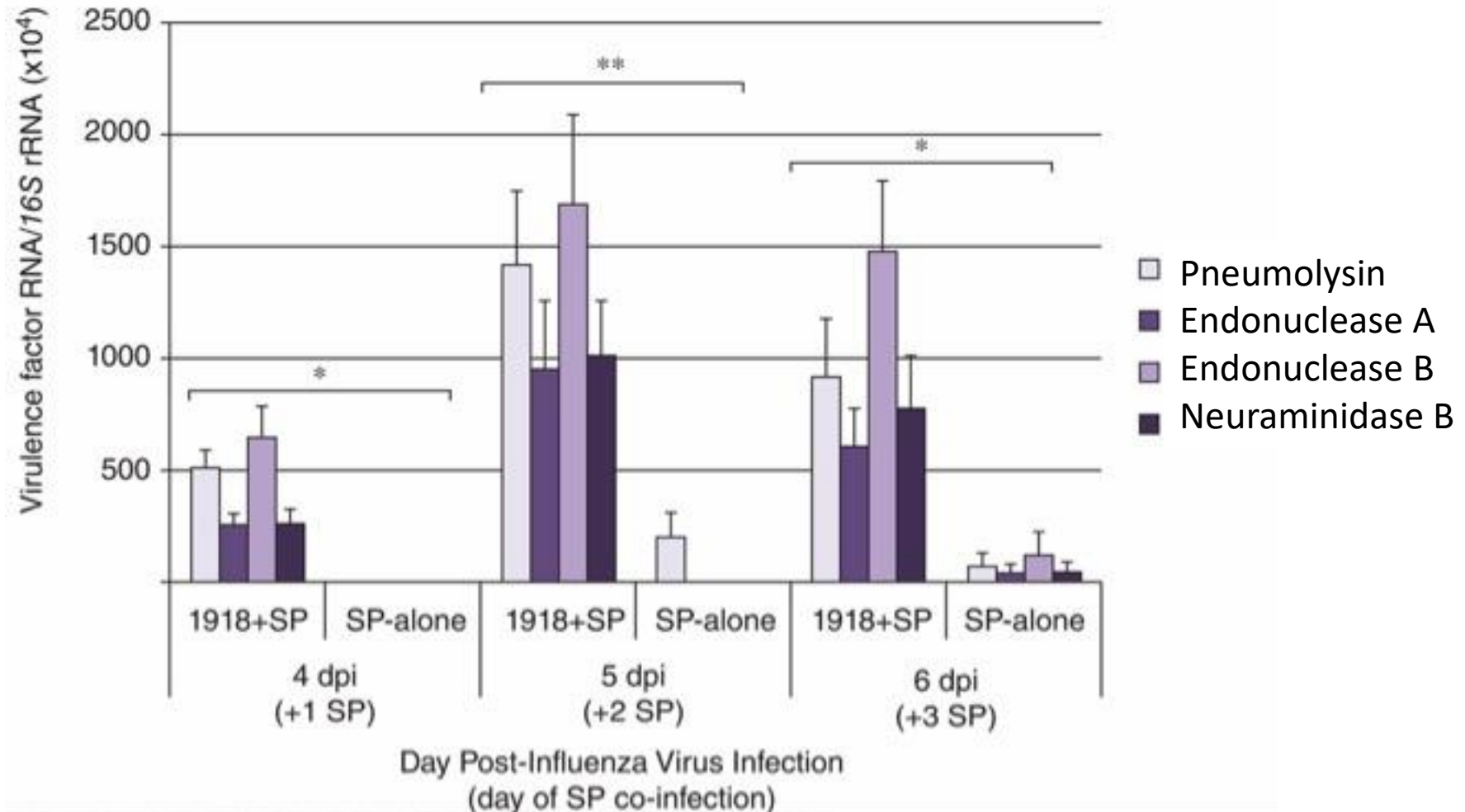


Viral damage to and loss of airway epithelial cells may expose basal epithelial cells to bacteria leading to the death of these progenitor cells, limiting re-proliferation

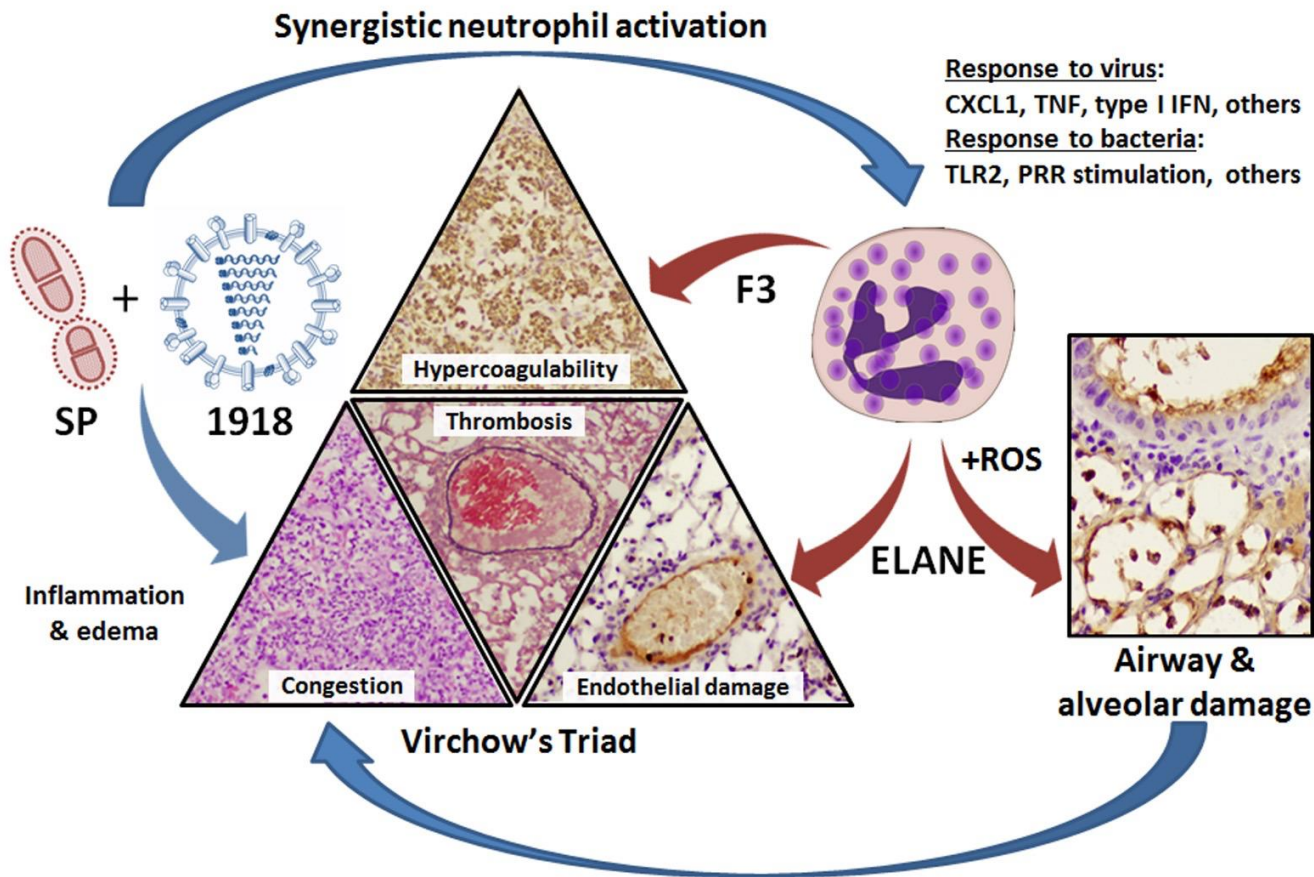
Massive infiltration of activated neutrophils in 1918 viral/Strep pneumoniae co-infection



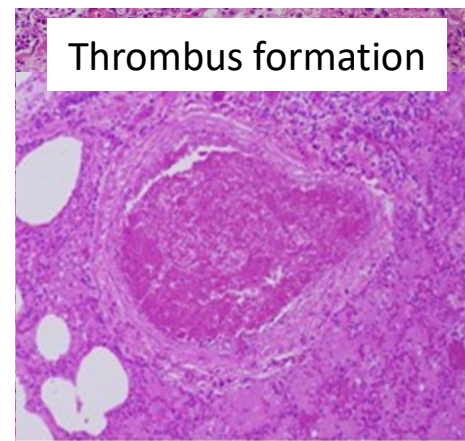
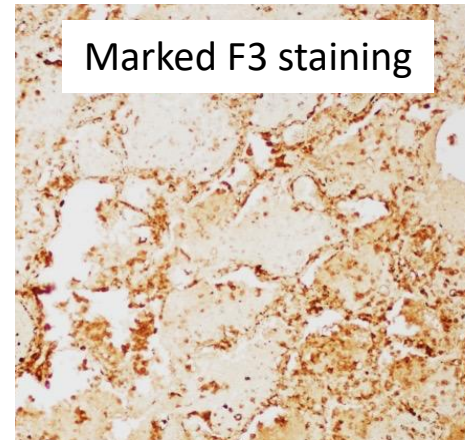
Changes in Bacterial Virulence in the Influenza/Inflammatory milieu



Model of Inflammation and Pulmonary Thrombosis during 1918 & SP Co-Infection



1918 autopsies



Widespread Thrombosis in SARS-CoV-2: Are Mechanisms of Thrombogenesis in 1918 and SARS-CoV-2 Related?

