

Cardiopulmonary COVID Complications

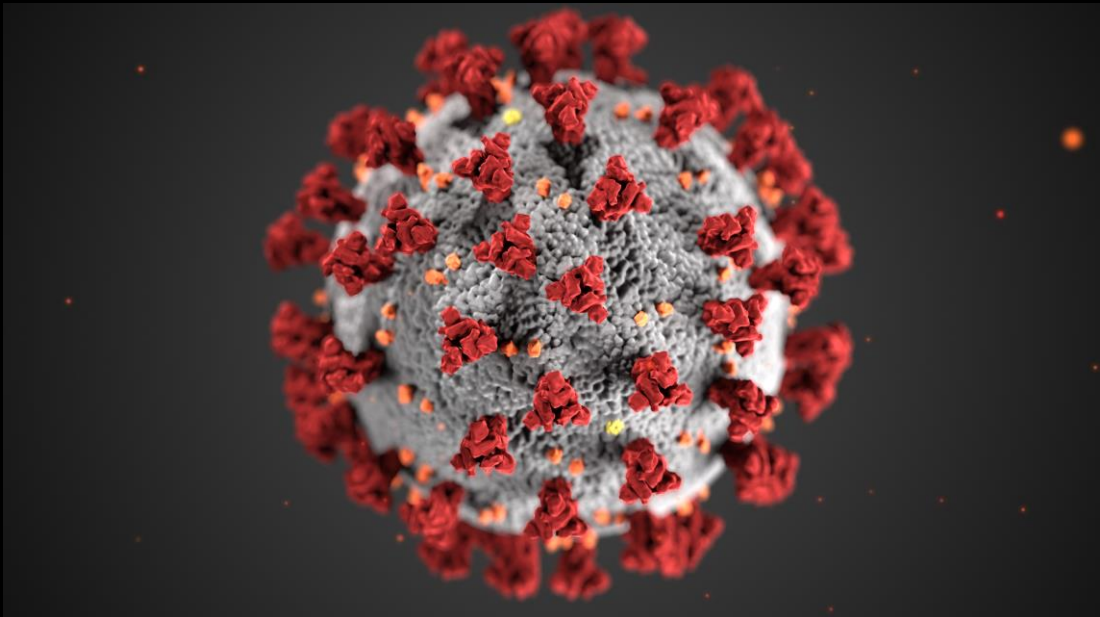
Zach Holliday

Pulmonary Complications Outline

1. Epidemiology of COVID-19
2. Symptom Presentation
3. Method of viral infection and Immune Response
4. Prognostic Factors/Serum Markers
5. Management and Treatment
6. PASC/Long Hauler Syndrome
7. Subacute and chronic Pulmonary Complications

Epidemiology (as of August 1, 2021)

- 203 million cases worldwide with 4.3 million deaths
- 36 million cases in the US with 617,000 deaths
- 51% of US population is fully vaccinated
- 704,000 cases in Missouri with 10,300 deaths



<https://coronavirus.jhu.edu/data>

<https://phil.cdc.gov/Details.aspx?pid=23311>

Common symptoms

- Fever (80.4%)
- Fatigue (46%)
- Cough (63%)
- Sputum production (42%)
- Myalgia (33%)
- Anorexia (39%)
- Chest tightness (36%)
- Shortness of breath (36%)
- N/V (10%)

SARS-CoV-2

- Infects via the angiotensin-converting enzyme 2 (ACE) receptor or the transmembrane serine protease 2 (TMPRSS2)
 - Uses spike (S) glycoprotein
 - Respiratory and intestinal epithelial cells, alveolar macrophages, olfactory sustentacular cells, bile duct, cardiocytes, testicular Sertoli cell¹
- Causes viral alveolitis and pulmonary vascular immunothrombosis
 - Clots are red (platelets) and white (NETotic neutrophils) in origin
 - In-situ thrombosis of capillary networks and microcirculation
 - Large vessel as well²
 - IL-6 driven and direct viral infection of endothelial cells^{3,4}

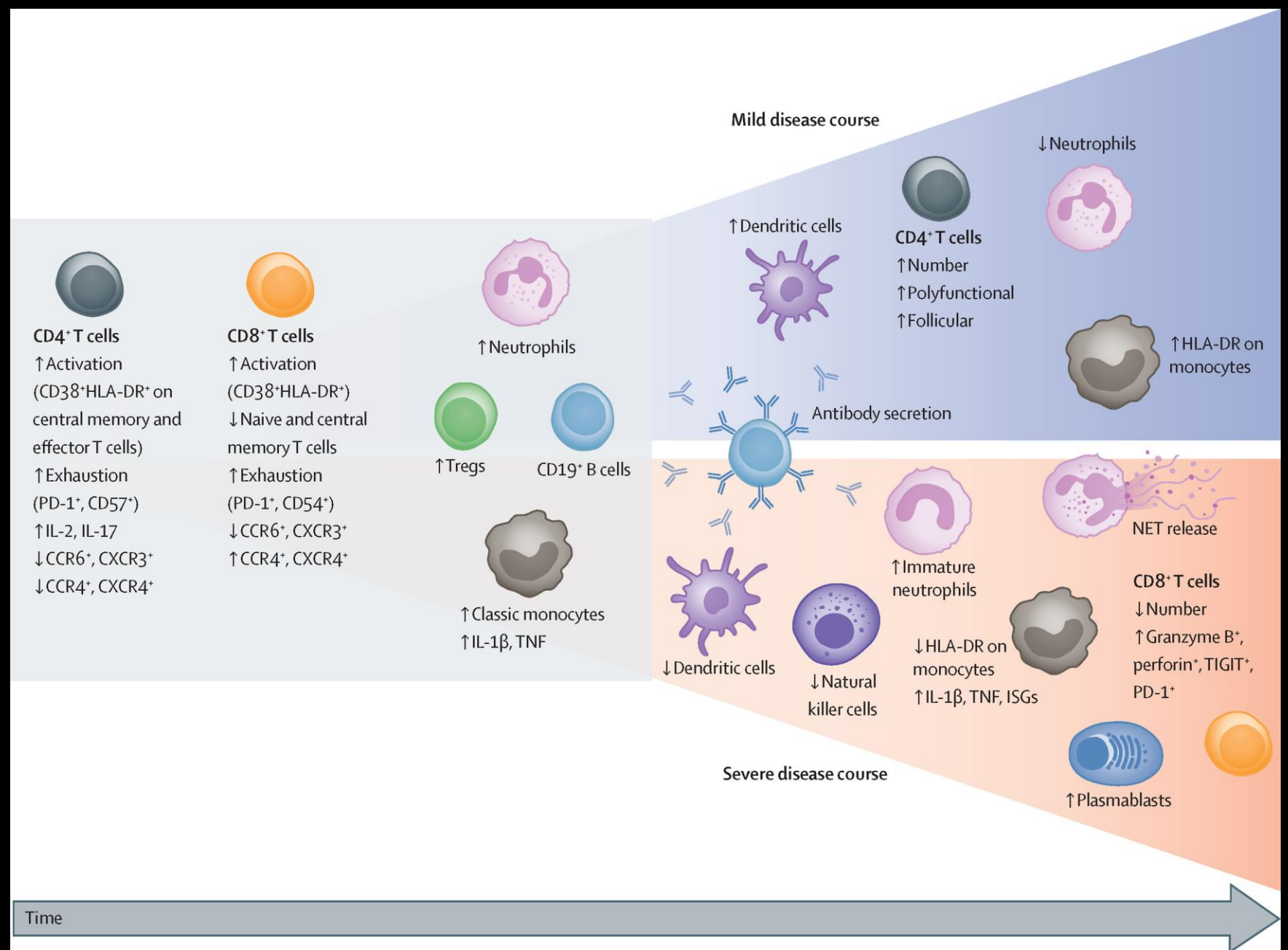
1. Marcin F Osuchowski et al. The COVID-19 puzzle deciphering pathophysiology and phenotypes of a new disease entity, *The Lancet Respiratory Medicine*, Volume 9, Issue 6, 2021: 622-642; 2213-2600.

2. McGonagle D, Bridgewood C, Meaney JFM. A tricompartamental model of lung oxygenation disruption to explain pulmonary and systemic pathology in severe COVID-19. *Lancet Respir Med*. 2021;9(6):665-672. doi:10.1016/S2213-2600(21)00213-7

3. McElvaney OJ, Curley GF, Rose-John S, McElvaney NG. Interleukin-6: obstacles to targeting a complex cytokine in critical illness. *Lancet Respir Med*. 2021;9(6):643-654. doi:10.1016/S2213-2600(21)00103-X

4. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet*. 2020;395(10234):1417-1418. doi:10.1016/S0140-6736(20)30937-5

Immune/Host Response



Prognostic factors/Serum markers

Increased Mortality

- Low pulmonary compliance
- high d-dimer
- High ferritin
- Elevated CRP
- Greater in-hospital blood glucose variability

Secondary infection

- Elevated CRP
- Elevated procalcitonin

Management and Treatment

- Anti-viral therapy (i.e., Remdesivir)
- Immunotherapy (glucocorticoids, Tocilizumab, etc.)
- Monoclonal antibody therapy
- Convalescent plasma
- Adjunct therapy (clinical trials, no evidence or evidence against)
 - Ivermectin, Hydroxychloroquine, Azithromycin, Fluroquinolones, Dornase alfa, and many more

Post-Acute Sequelae of COVID/Long hauler Syndrome

- Symptoms persisting 4 weeks after onset of illness
- Subacute (< 12 weeks)
- Chronic (> 12 weeks) and no alternative diagnosis

Subacute Complications

- Persistent dyspnea and fatigue (23-43% and 53% respectively)^{1,2}
- Cough (15-18%)³
- Venous thromboembolisms rate of 2.5% at 30 days⁴
- Supplemental oxygen at discharge
- Critical Care Weakness

1. Chopra, V., Flanders, S. A. & O'Malley, M. Sixty-day outcomes among patients hospitalized with COVID-19. *Ann. Intern. Med.* <https://doi.org/10.7326/M20-5661> (2020).

2. Nalbandian, A., Sehgal, K., Gupta, A. *et al.* Post-acute COVID-19 syndrome. *Nat Med* **27**, 601–615 (2021). <https://doi.org/10.1038/s41591-021-01283-z>

3. Carfi A, Bernabei R, Landi F; Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA*. 2020;324(6):603-605. doi:10.1001/jama.2020.12603

4. Patell, R. *et al.* Post-discharge thrombosis and hemorrhage in patients with COVID-19. *Blood* **136**, 1342–1346 (2020).

Chronic Complications

Dyspnea

- 51% at 3 months¹ and 17-18% at 6 months
- Increased risk with older age, female gender and underlying lung disease²

Reduced exercise tolerance

- More common in patients with moderate/severe disease
- Reduced 6 min walk distance
- Increased rates of desaturation during 6 min walk test³

1. Venturelli S, Benatti SV, Casati M, et al. Surviving COVID-19 in Bergamo province: a post-acute outpatient re-evaluation. *Epidemiology and Infection*. 2021;149:e32. doi:10.1017/S0950268821000145

2. Blomberg, B., Mohn, K.Gl., Brokstad, K.A. et al. Long COVID in a prospective cohort of home-isolated patients. *Nat Med* (2021). <https://doi.org/10.1038/s41591-021-01433-3>

3. Guler SA, Ebner L, Aubry-Beigelman C, et al. Pulmonary function and radiological features 4 months after COVID-19: first results from the national prospective observational Swiss COVID-19 lung study. *Eur Respir J*. 2021;57(4):2003690. Published 2021 Apr 29. doi:10.1183/13993003.03690-2020

Chronic Complications

Abnormalities in Pulmonary Function testing

- Reduced diffusion capacity for carbon monoxide (DLCO) at 3 month follow up¹
- Restrictive lung physiology²
 - Increased FEV1/FVC
 - Reduced Total lung capacity (TLC)

1. Qin W, Chen S, Zhang Y, et al. Diffusion capacity abnormalities for carbon monoxide in patients with COVID-19 at 3-month follow-up. *Eur Respir J.* 2021;58(1):2003677. Published 2021 Jul 22. doi:10.1183/13993003.03677-2020
2. Guler SA, Ebner L, Aubry-Beigelman C, et al. Pulmonary function and radiological features 4 months after COVID-19: first results from the national prospective observational Swiss COVID-19 lung study. *Eur Respir J.* 2021;57(4):2003690. Published 2021 Apr 29. doi:10.1183/13993003.03690-2020

Chronic Complications

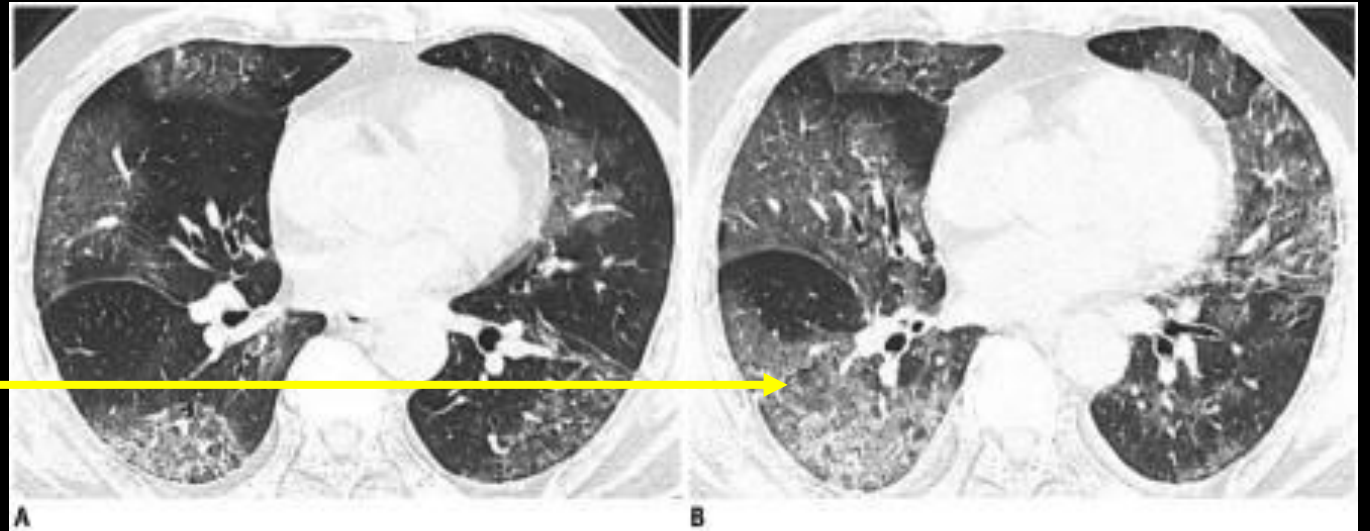
Risk of Pulmonary Fibrosis

- High TGF- β signaling¹
- Epithelial to mesenchymal transition
- Risk factors: Severe clinical picture, smoking, alcoholism, age, CT imaging of irregular interface and parenchymal band²
- Previous cases of SARS showed improvement in fibrosis over time³

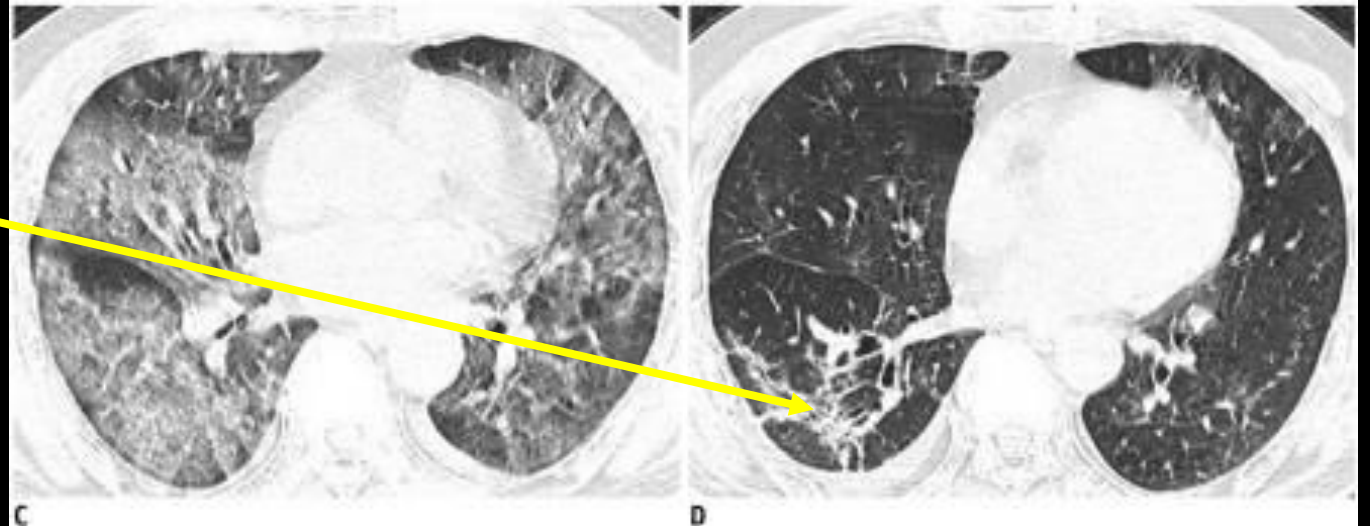
1. Marcin F Osuchowski et al. The COVID-19 puzzle deciphering pathophysiology and phenotypes of a new disease entity, *The Lancet Respiratory Medicine*, Volume 9, Issue 6, 2021: 622-642; 2213-2600.
2. Yu M, Liu Y, Xu D, Zhang R, Lan L, Xu H. Prediction of the Development of Pulmonary Fibrosis Using Serial Thin-Section CT and Clinical Features in Patients Discharged after Treatment for COVID-19 Pneumonia. *Korean J Radiol.* 2020;21(6):746-755. doi:10.3348/kjr.2020.0215
3. Ojo AS, Balogun SA, Williams OT, Ojo OS. Pulmonary Fibrosis in COVID-19 Survivors: Predictive Factors and Risk Reduction Strategies. *Pulm Med.* 2020;2020:6175964. Published 2020 Aug 10. doi:10.1155/2020/6175964

Chronic Complications

Ground glass opacities



Parenchymal bands



Chronic Complications

Are there lung parenchyma changes?

- Maybe (see slide before) but....
- Compared 11 patients' histopathological examination after elective lung resection
- Asymptomatic to severe disease cases
- Surgery was average of 69 days after diagnosis
- No difference noted in lung parenchyma of COVID-19 survivors¹

1. Díaz A, Bujnowski D, McMullen P, et al. Pulmonary parenchymal changes in COVID-19 survivors [published online ahead of print, 2021 Jul 31]. *Ann Thorac Surg*. 2021;S0003-4975(21)01307-2. doi:10.1016/j.athoracsur.2021.06.076

Post COVID Respiratory Evaluation

- Start with easy to perform tests
 - 6 min walk test
 - Pulmonary Function Testing
- Consider if symptoms persist or abnormalities note with above testing
 - Chest imaging (chest x-ray, HRCT)
 - PE work up
 - CPET
 - Echocardiogram
 - Sub-specialty referral

Thank you.

Questions?