Low-dose Radiation Therapy and Severe COVID-19-Related Pneumonia

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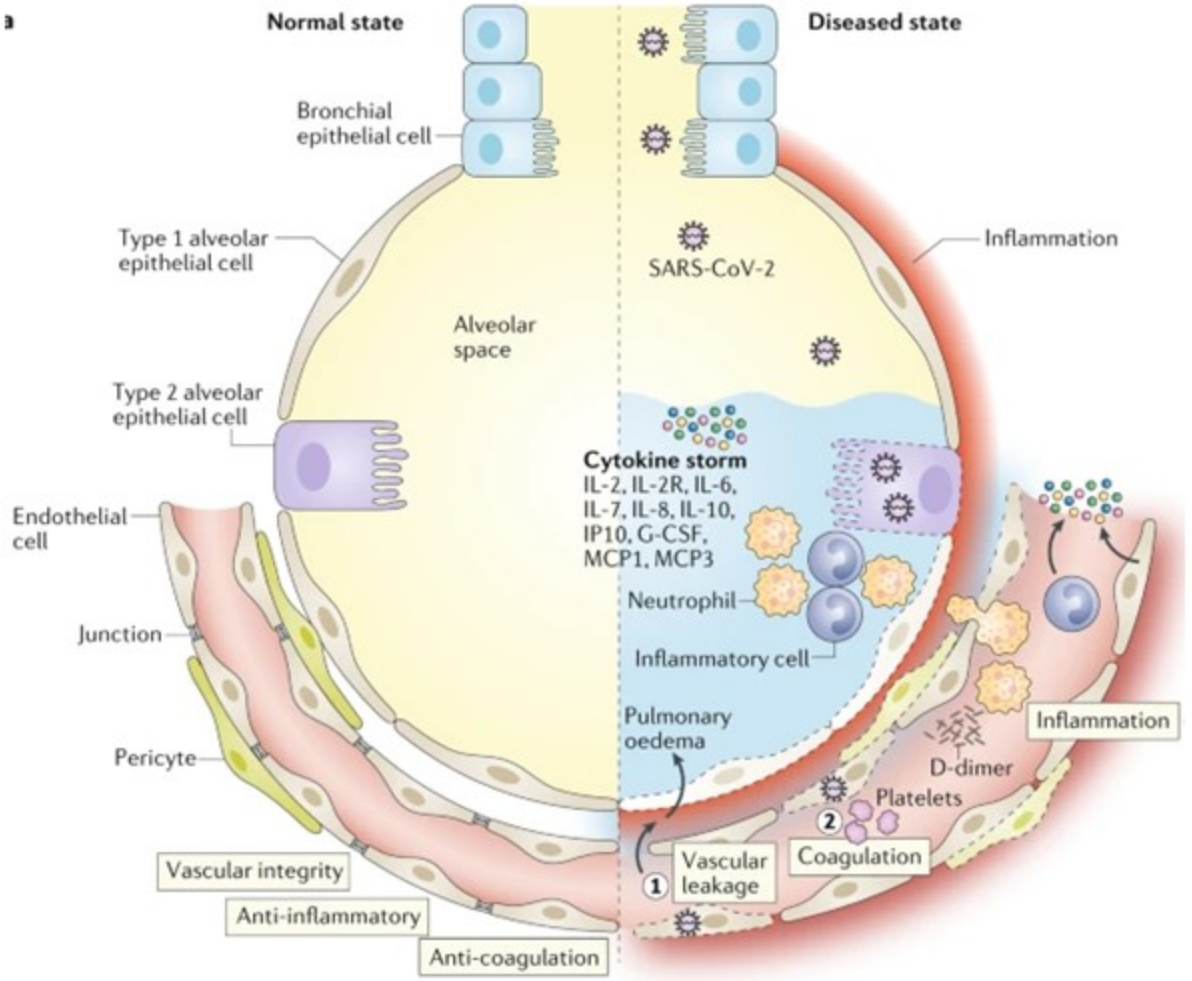
Disclosures

- I have no conflicts of interest to disclose

Biologic Rationale: COVID-19 pneumonia

- Accumulation of macrophages in the alveolus, lymphocytes in the interstitium, and a diffuse alveolar damage[1]
- Cytokine storm is the result of activated immune cells producing large amounts of cytokines that in turn leads to hyperinflammation
  - Macrophage activation implicated as a key component of cytokine storm[2]
  - Immune suppression (dexamethasone) has proven useful in severe COVID-19



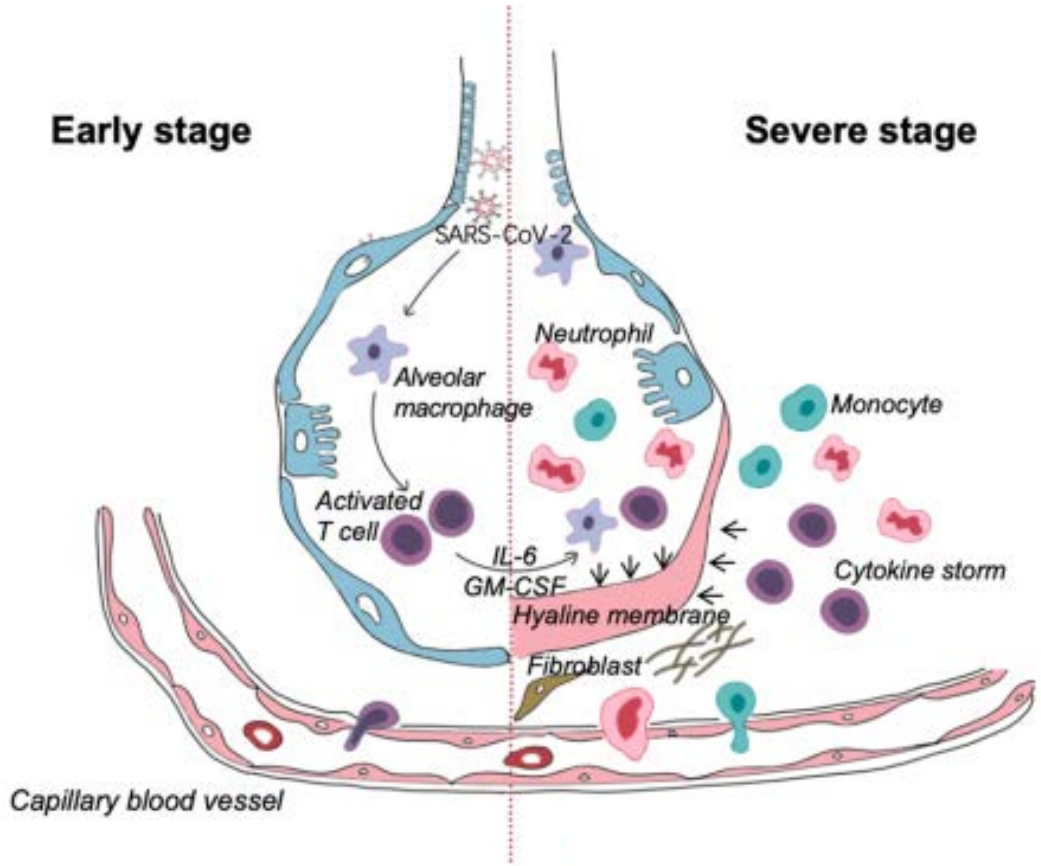
Nat Rev Immunol. 20: 389-391, 2020.

1. Carsana L et al. Lancet Infect Dis 2020; 20: 1135-40.
2. Merad, M and J Martin. Nat Rev Immunol. 20, 355-362 (2020).

•. 2002 Jul;78(7):567-76.

Why might this work?

- Cells of different types have varying sensitivity to radiation
  - Immune cells – relatively sensitive
  - Other lung cells - relatively resistant
- Low dose radiation (< 1 Gy)
  - can reduce the oxidative burst and NO· production from macrophages[1,2]
  - can cause fibrocytes to differentiate, reducing proliferation and eventual fibrosis[3]
  - may reduce leukocyte adhesion to endothelial cells

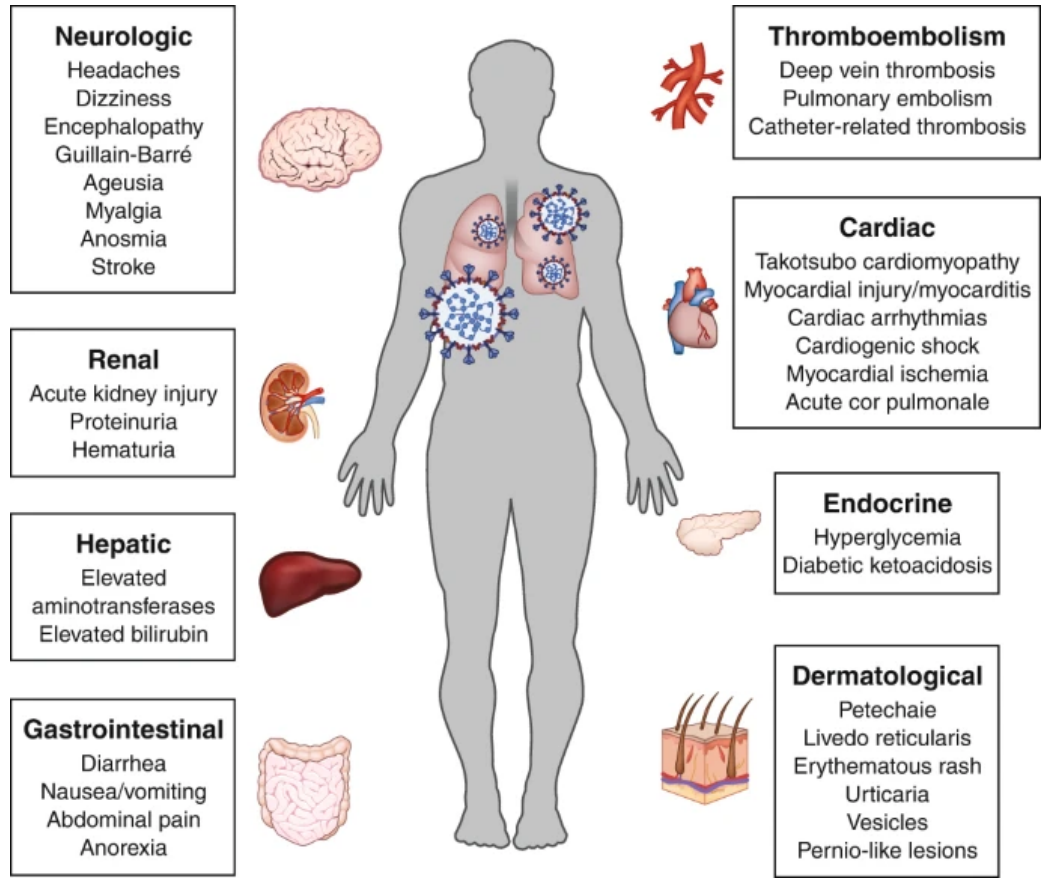


Cell Death & Differentiation. 27: 1451–1454(2020)

1. Schaue, D et al. Int J Radiat Biol. 78(7): 567-576, 2002.
2. Hildebrandt G, et al. Int J Rad Biol, 74(1998): 367-378.
3. Bumann, J. et al. Strahlenther Onkol. 171(1995), pp 35-41.

Cytokines/Correlatives

- Inflammation
  - IL-6
  - **CRP**
  - LDH
  - Ferritin
  - ESR
- Kidney injury
  - Creatinine
- Liver injury
  - *AST*
  - **ALT**



- Clotting
  - D-Dimer
- Cardiac injury
  - *Creatine Kinase*
  - Troponin-1
  - Myoglobin
- Immune cells
  - **White blood count**
  - *Neutrophil/WBC ratio*
  - *Monocyte count*

Bold: p<0.05; *italics*: trend

Nature Medicine. 26: 1017–1032, 2020.

What are some concerns?

- Risk of long-term toxicity
  - Risk of cancer or cardiac damage is well documented from similar radiation doses in long term atomic bomb survivors
- Reducing long term toxicity
  - Determining whether there is a benefit that outweighs risks
  - Treating patients at lower risk of cancers (shorter overall life expectancy)
  - The lowest dose that achieves successful outcomes will reduce long term risks
  - Fractionated versus single dose (safety of patients and caregivers)
- Low dose is variably defined
- Lymphocytes more sensitive than macrophages – can this impact immunity or clearance?