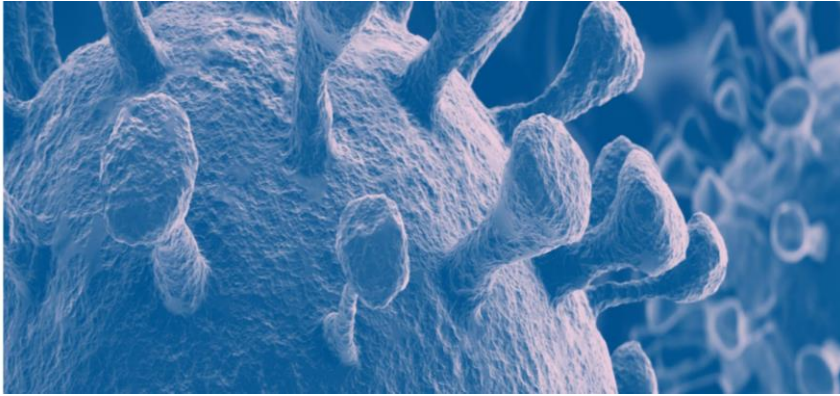


# Insuficiencia Respiratoria y COVID



Dr. Agustín Acuña Izcaray

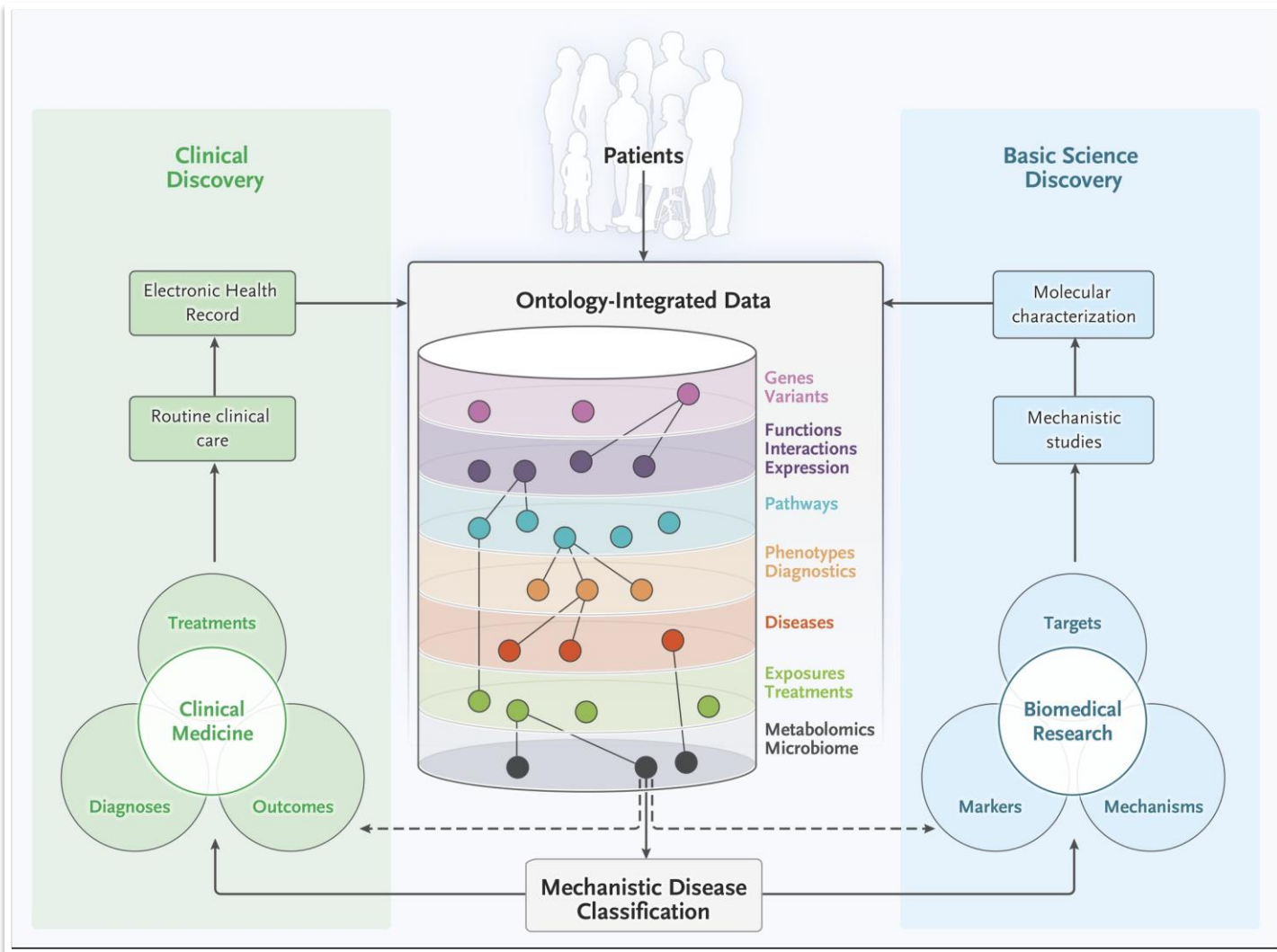


# Agenda

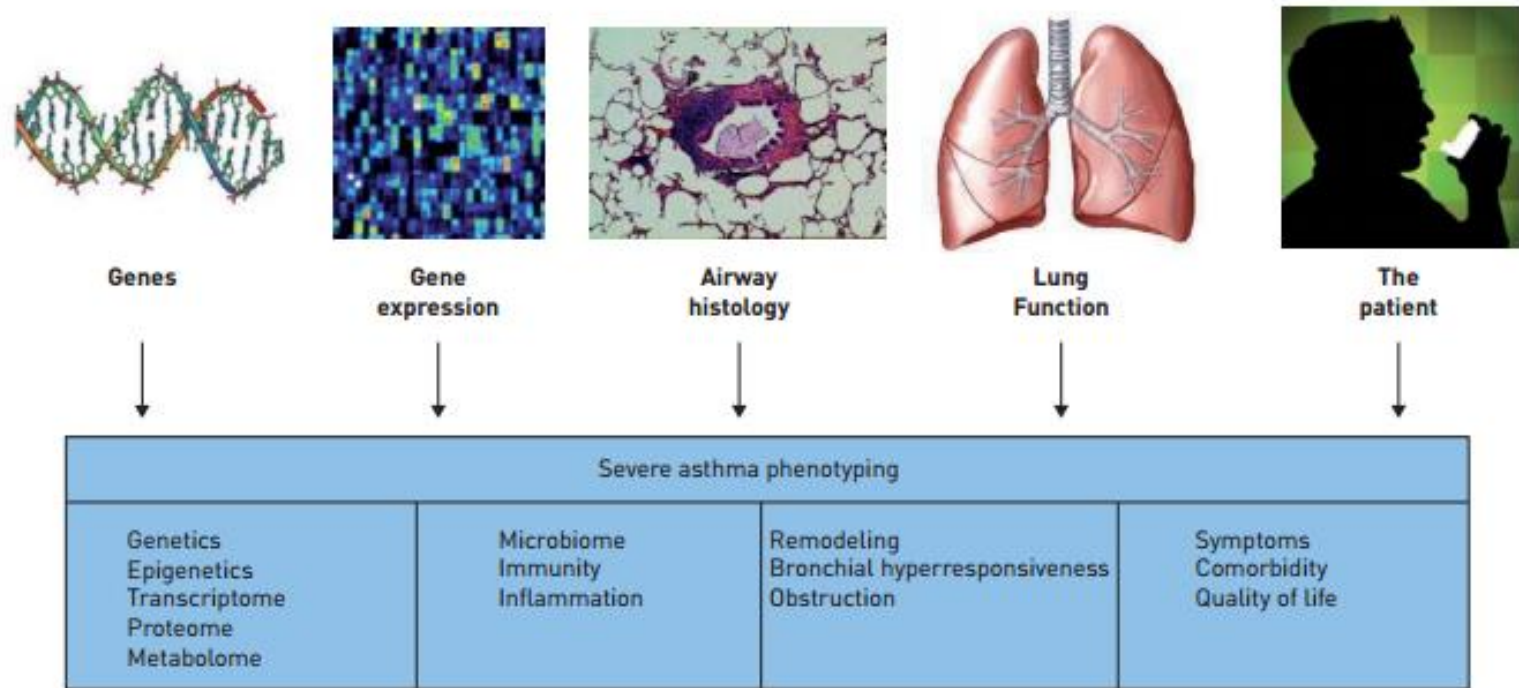
---

- **Epidemiología y características clínicas.**
- **Patogenia de la IRA en la infección por SARS CoV2**
- **Mecanismos fisiopatológicos de la IRA**

# SARS COV-2 / COVID-19. Desafío para describir una nueva enfermedad

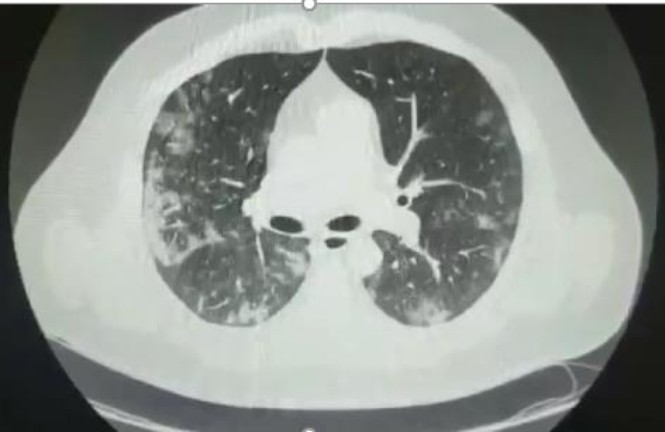


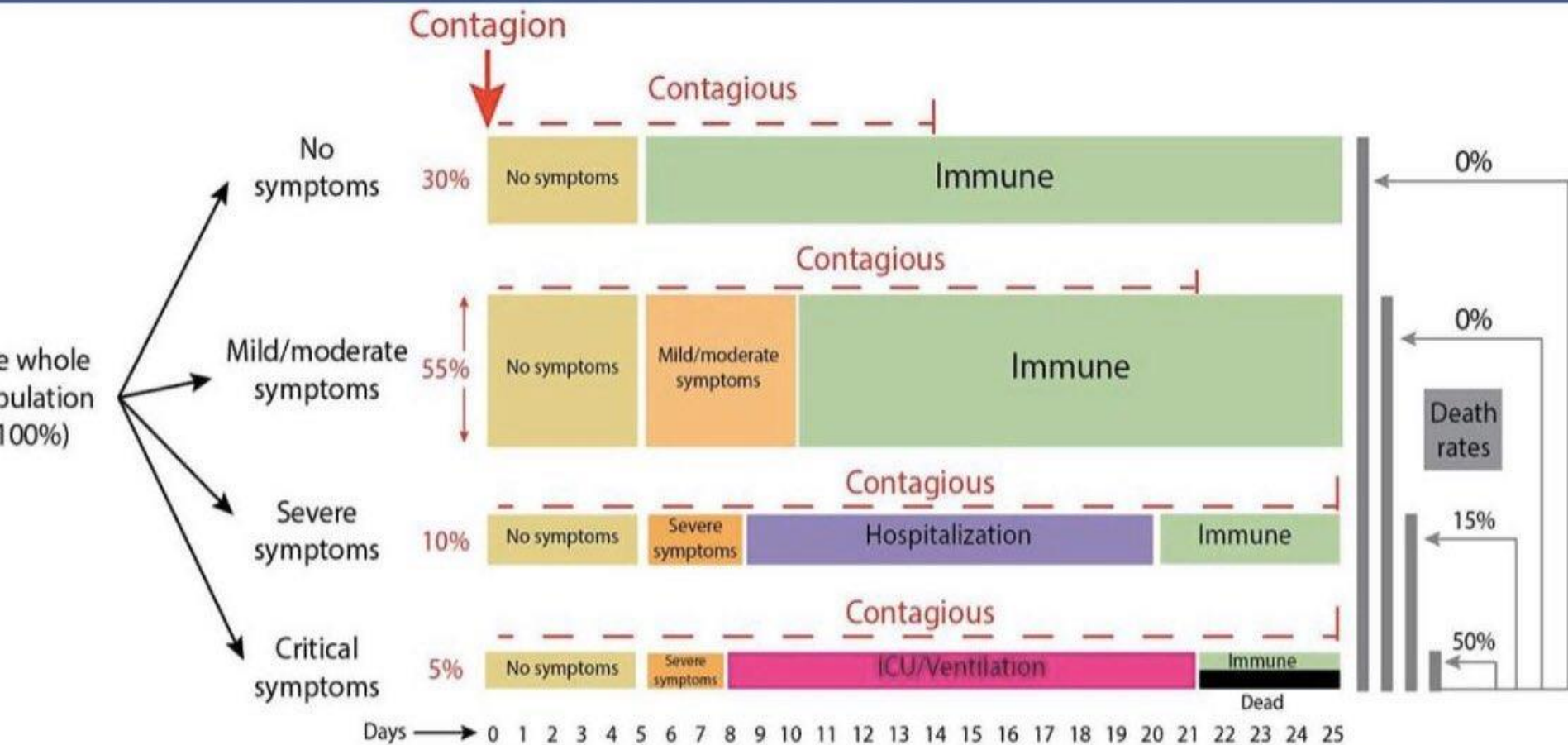
# De los Endotipos a los Fenotipos



# Espectro clínico del COVID-19

N=1



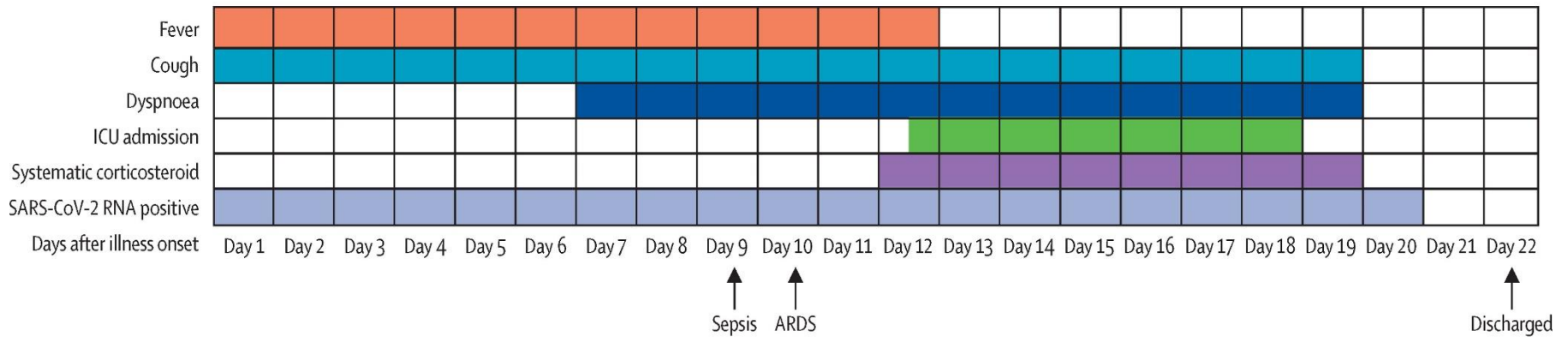


References:

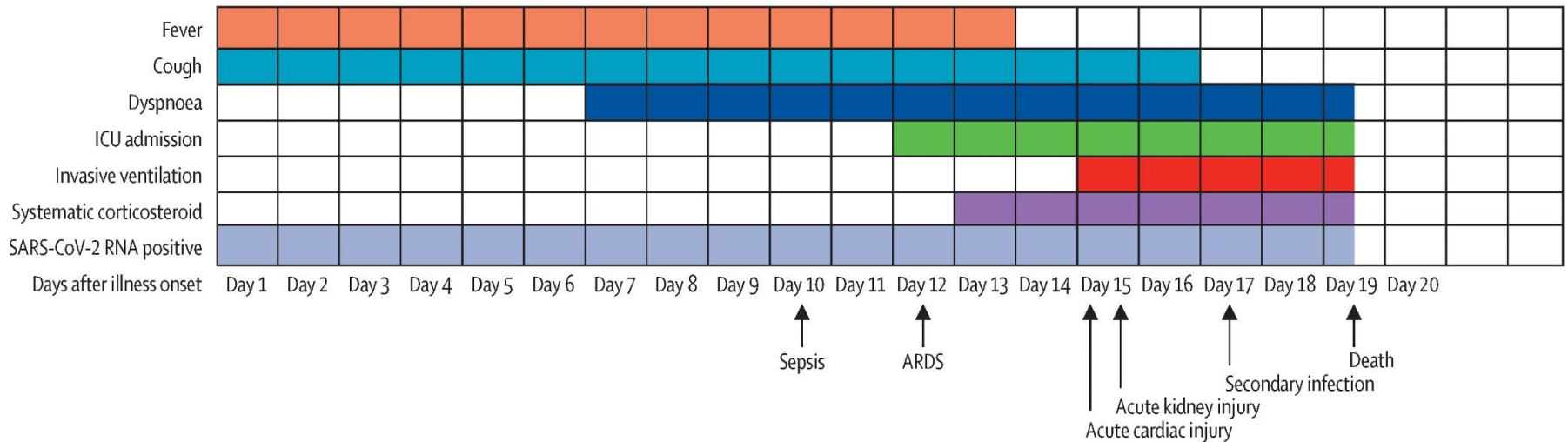
1. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. Lauer SA et al. Ann Intern Med. 2020 Mar 10.
2. Impact of non-pharmaceutical interventions (NPIs) to reduce COVID19 mortality and healthcare demand. Neil M Ferguson et al. Imperial College COVID-19 Response Team. 16 March 2020.
3. Viral dynamics in mild and severe cases of Covid-19. Yang Liu et al. The Lancet, March 19, 2020.

# Curso clínico y factores de riesgo

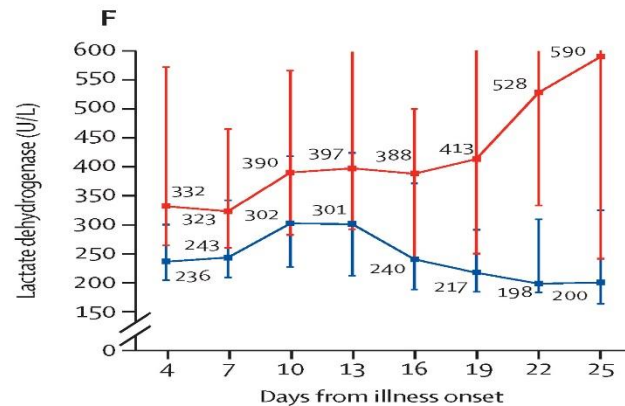
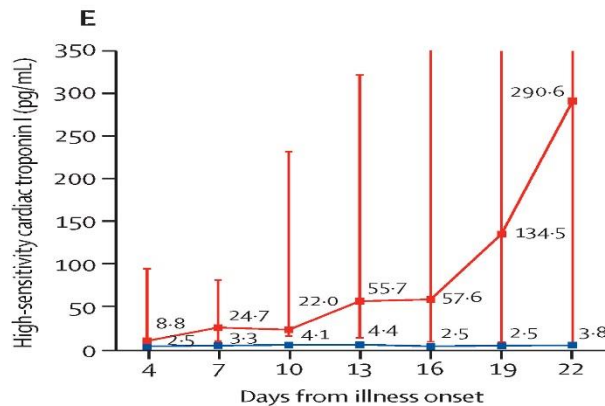
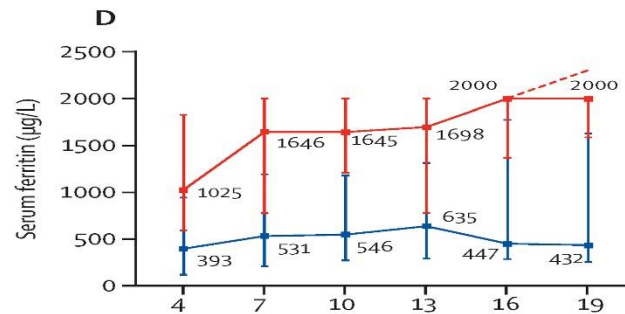
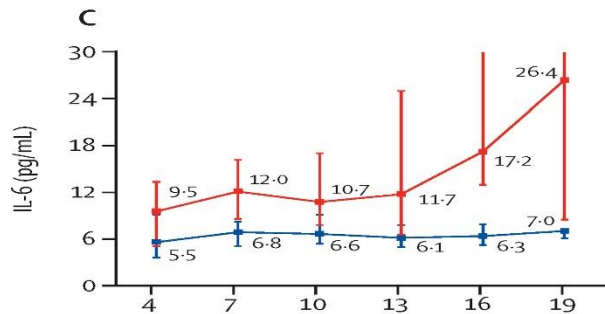
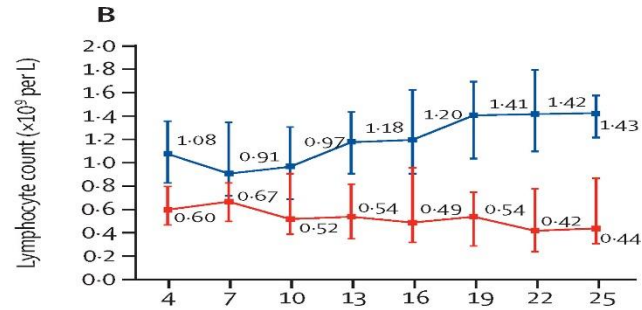
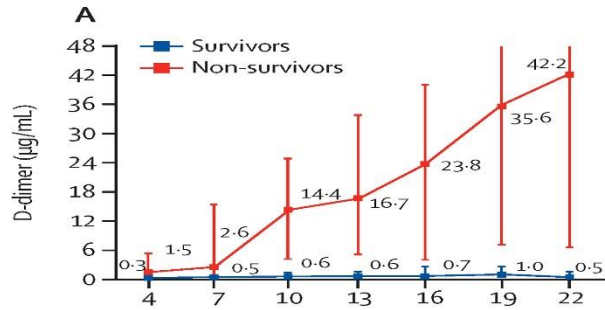
## Survivors



## Non-survivors

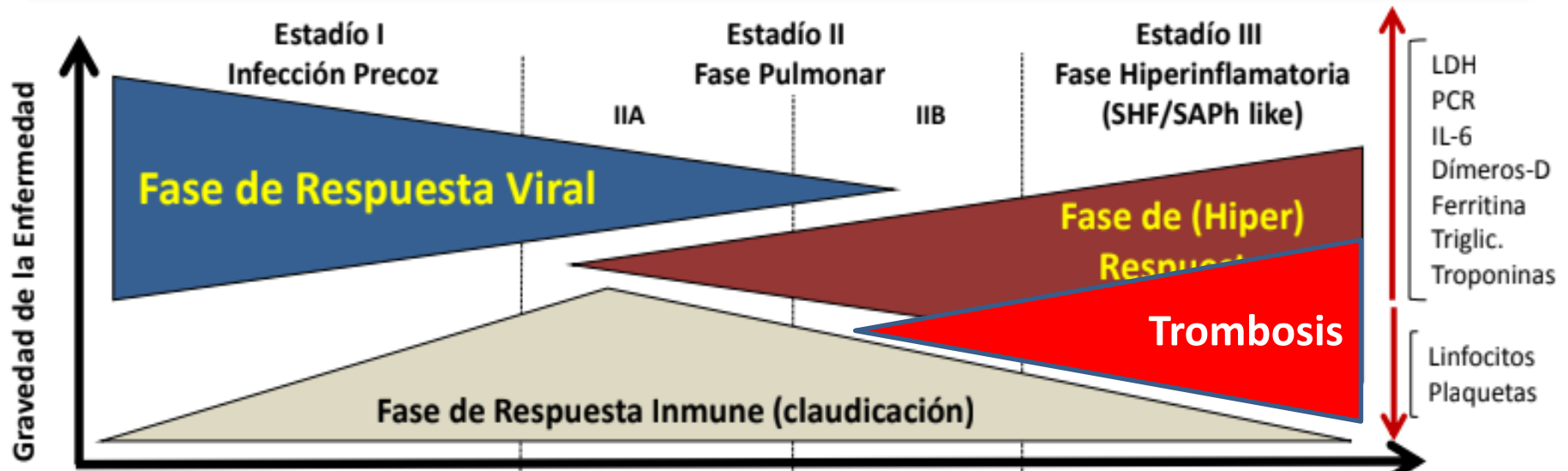


# Curso clínico y factores de riesgo





## Esquema fisiopatogénico de SARS-CoV-2 y estrategia terapéutica múltiple



Neumonía Leve-Moderada      Neumonía grave

Curso evolutivo

Semiología

Sintomatología constitucional, Fiebre, tos seca, diarrea, cefalea, alteraciones gusto y olfato

Disnea, Hipoxemia (PaO<sub>2</sub>/FiO<sub>2</sub> ≤ 300 mmHg)

SHF reactivo, SAPH-like, SDRA, Sepsis/Shock, Fallo cardiaco

Laboratorio

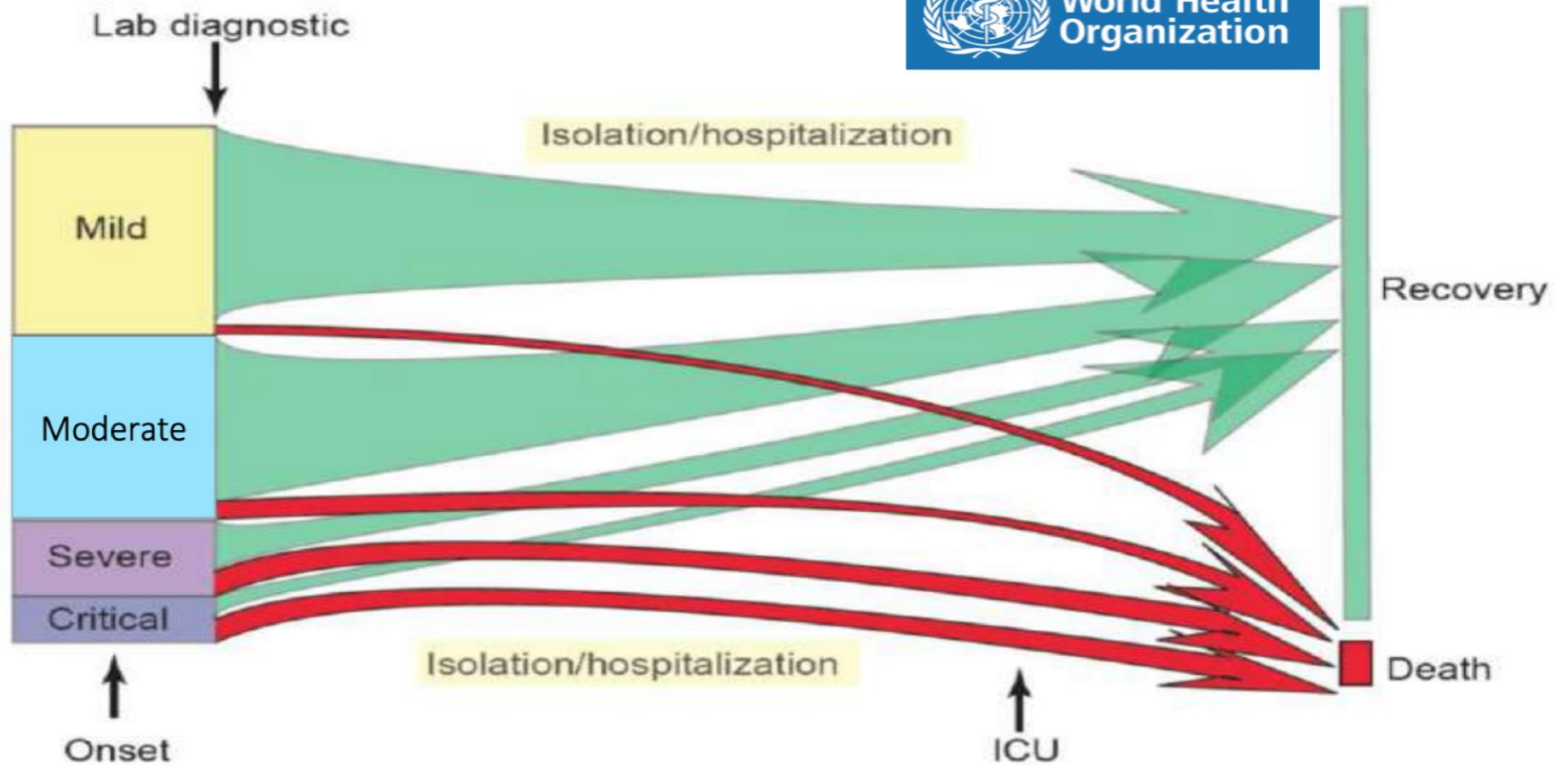
Linfocitosis o inicio linfopenia, aumento de PCR, tiempo de protrombina, Dímeros-D y LDH

Infiltrados pulmonares (bilaterales) Elevación de transaminasas, PCT normal o baja, Linfopenia creciente

Elevación de marcadores inflamatorios y de disfunción endotelial o coagulación (LDH, Ferritina, PCR, IL-6, Dímeros-D), Aumento de troponina y pro-BNP

Modificado de Siddiqqi et al JHLT 2020.

Protocolo de Hospital Universitario y politecnico.La Fe , Valencia- España.



Immediate Goals	Intermediate Goals	Long-term goals
<b>Diagnostics:</b> RNA assays, antibody & antigen assays, point of care detection	Diagnostics: Multiplex diagnostic platforms	Diagnostics: Prognostic markers
<b>Therapeutics:</b> Remdesivir, favipiravir, chloroquine, plasma, TCM	Therapeutics: intravenous immunoglobulin (IVIg)	Therapeutics: Innovative approaches (CRISPR-CAS; RNAi; Cell-based; positive hits from library screening)
<b>Vaccines:</b> Development of animal models	Vaccines: mRNA candidates and candidate viral vectors	Vaccines: inactivated candidates and subunit candidates

# Agenda

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- Epidemiología y características clínicas.
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- Mecanismos fisiopatológicos de la IRA

# ACE 2. La Protagonista

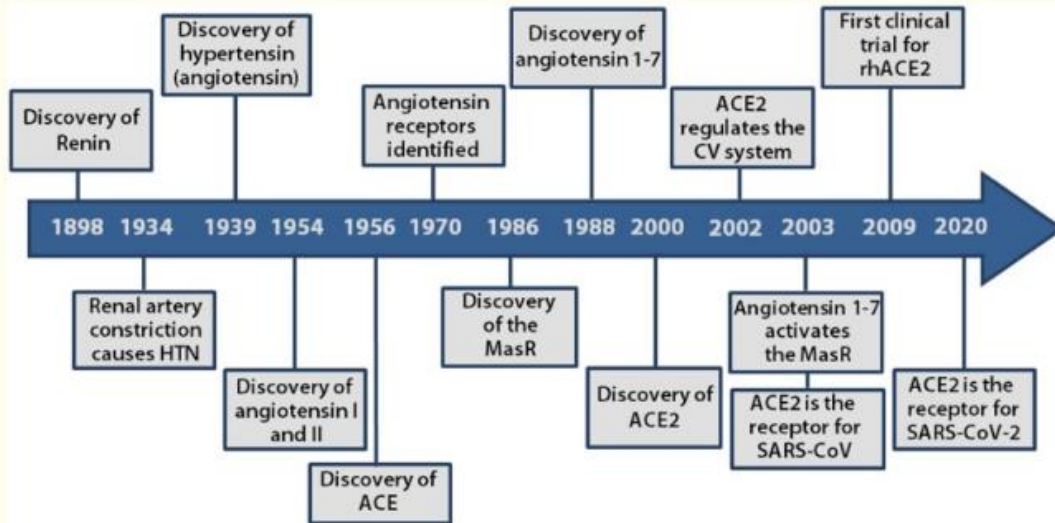
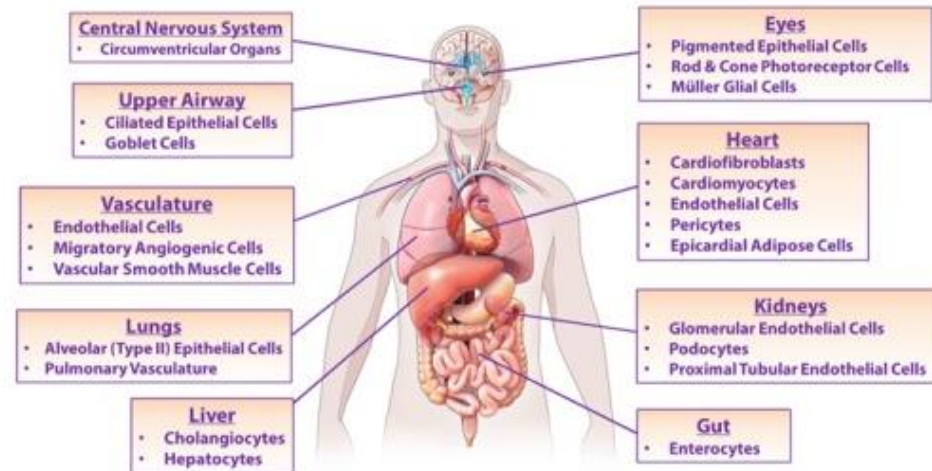


Figure 1

## ACE2 Expression



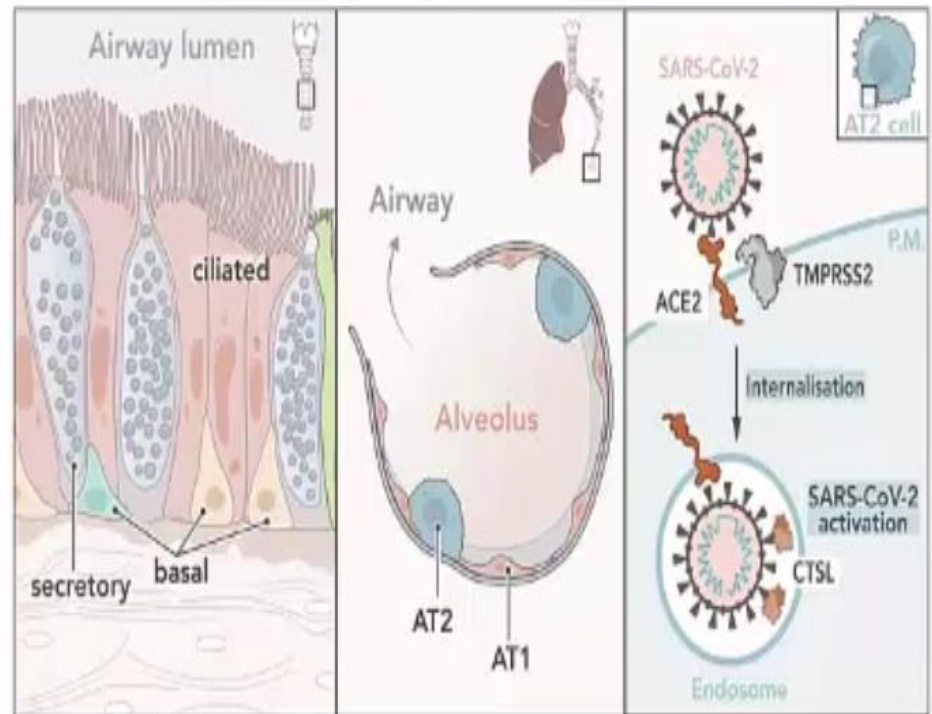
[Circ Res. 2020 May 8; 126\(10\): 10.1161/CIRCRESAHA.120.317015.](https://doi.org/10.1161/CIRCRESAHA.120.317015)

SARS-CoV-2 entry factors are highly expressed  
in nasal epithelial  
immune genes

Cell

Article

**SARS-CoV-2 Receptor ACE2 Is an Interferon-Stimulated Gene in Human Airway Epithelial Cells and Is Detected in Specific Cell Subsets across Tissues**

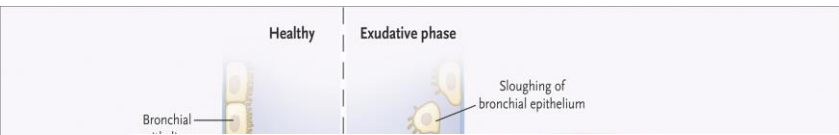


Yu Zhao *et al.*, BioRxiv, Jan 2020  
doi: <https://doi.org/10.1101/2020.01.26.919985>

Sungnak *et al.*, Nat Med (2020)

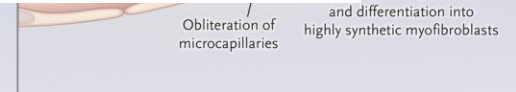
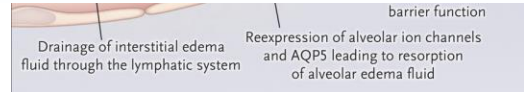
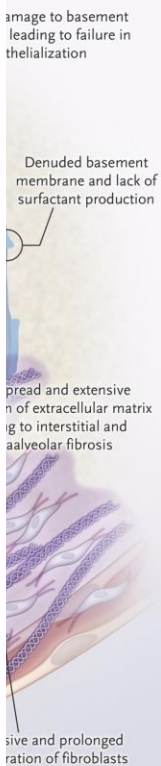
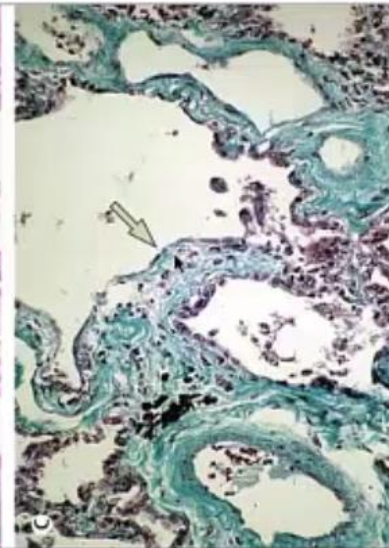
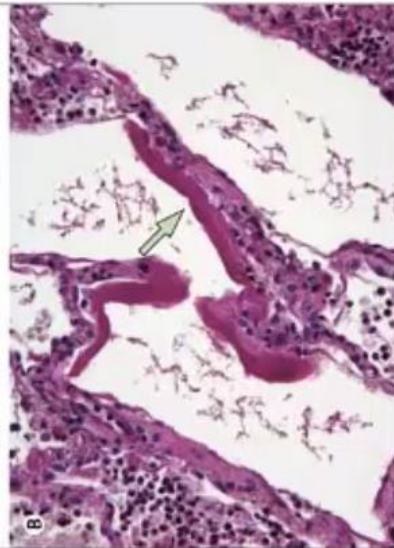
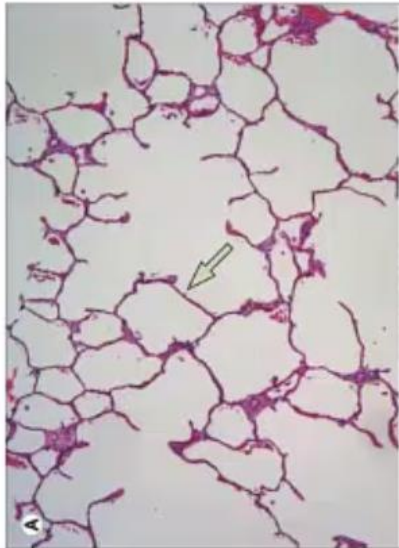
Ziegler *et al.*, Cell (2020)

# Inmunopatología del SDRA

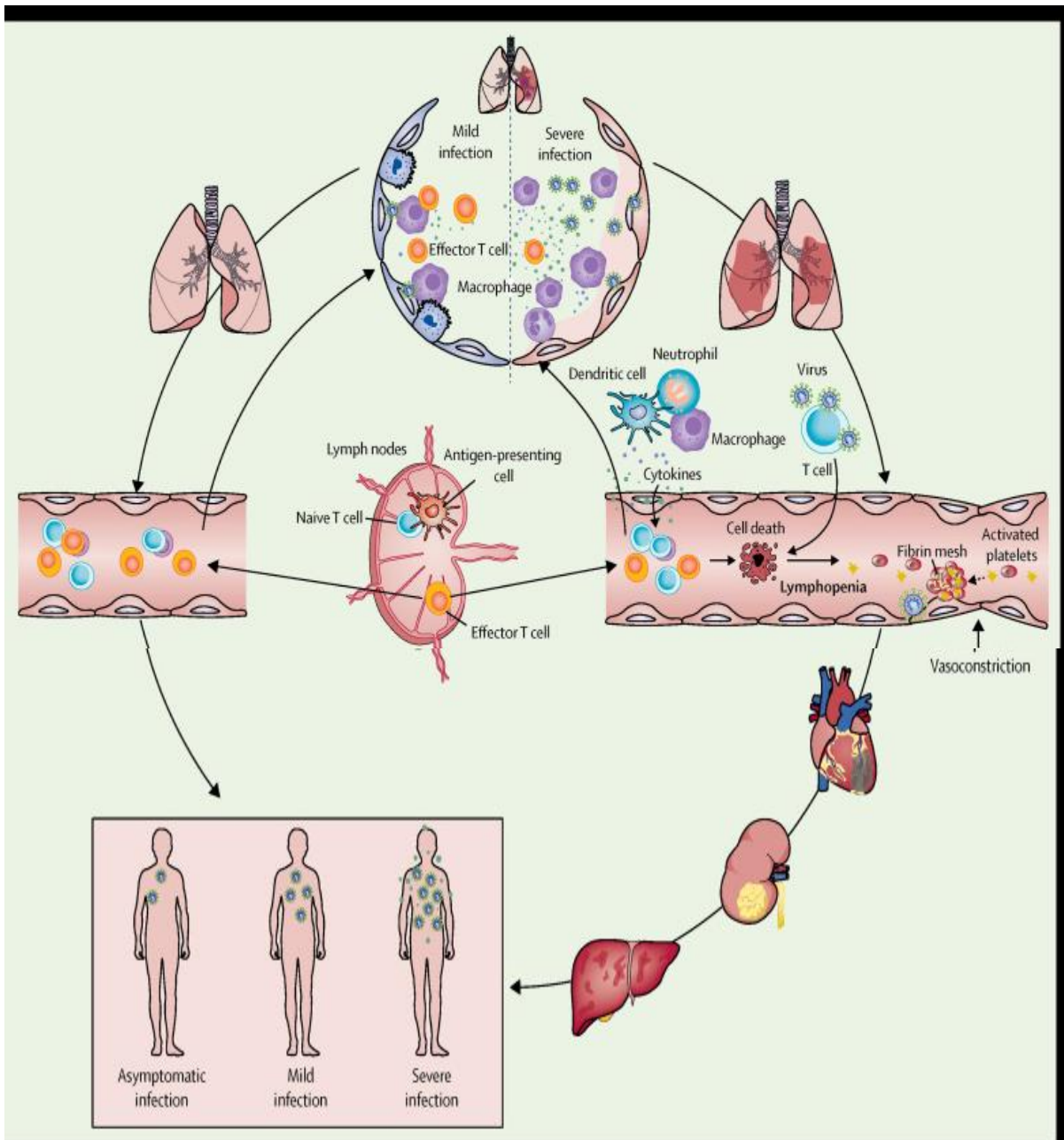


## ARDS.....

- Thille *et al Lancet RM* 2013



# SARS COV 2 y Sepsis viral





# PROGRESS

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## Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages

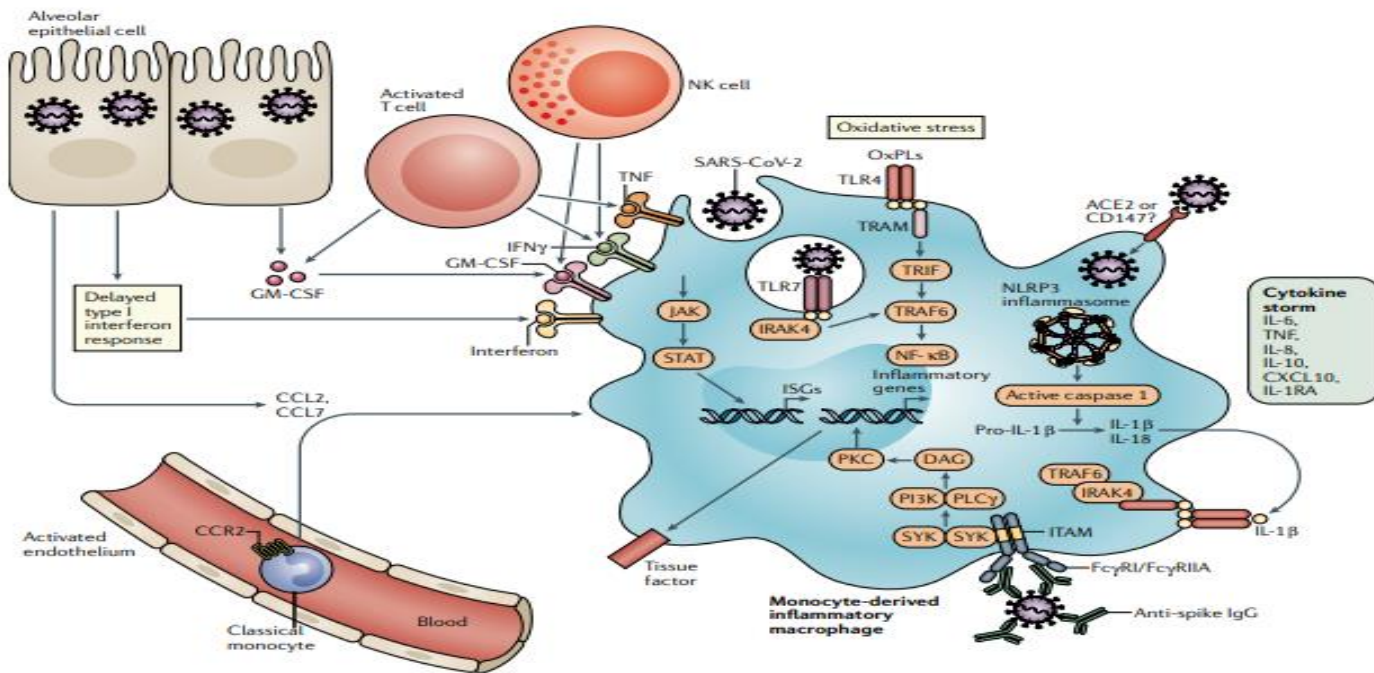
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Miriam Merad and Jerome C. Martin 

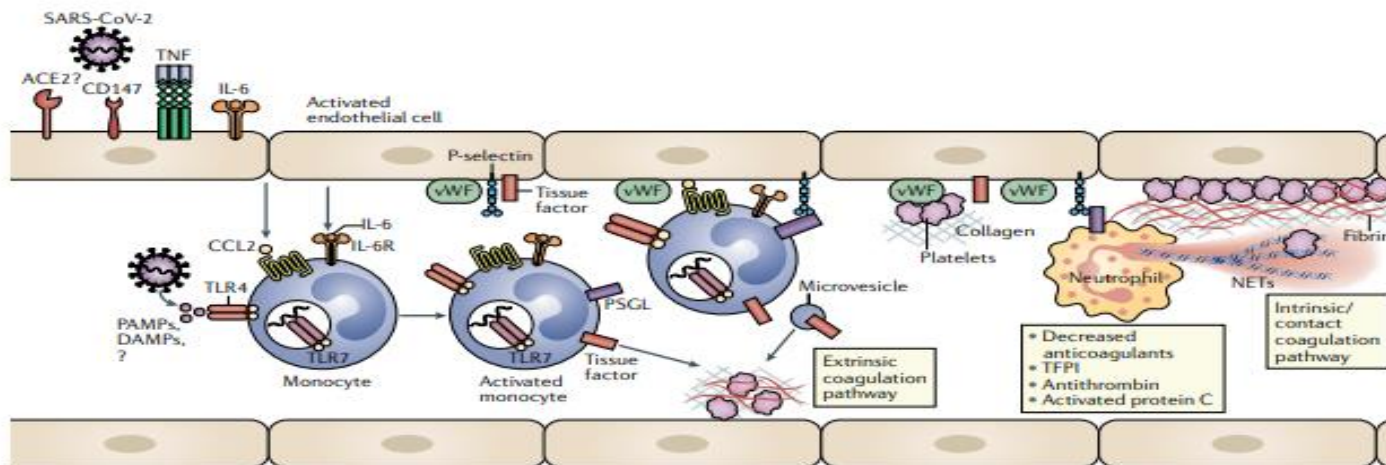
lymph nodes and kidney<sup>10,11</sup>, as observed in post-mortem analysis.

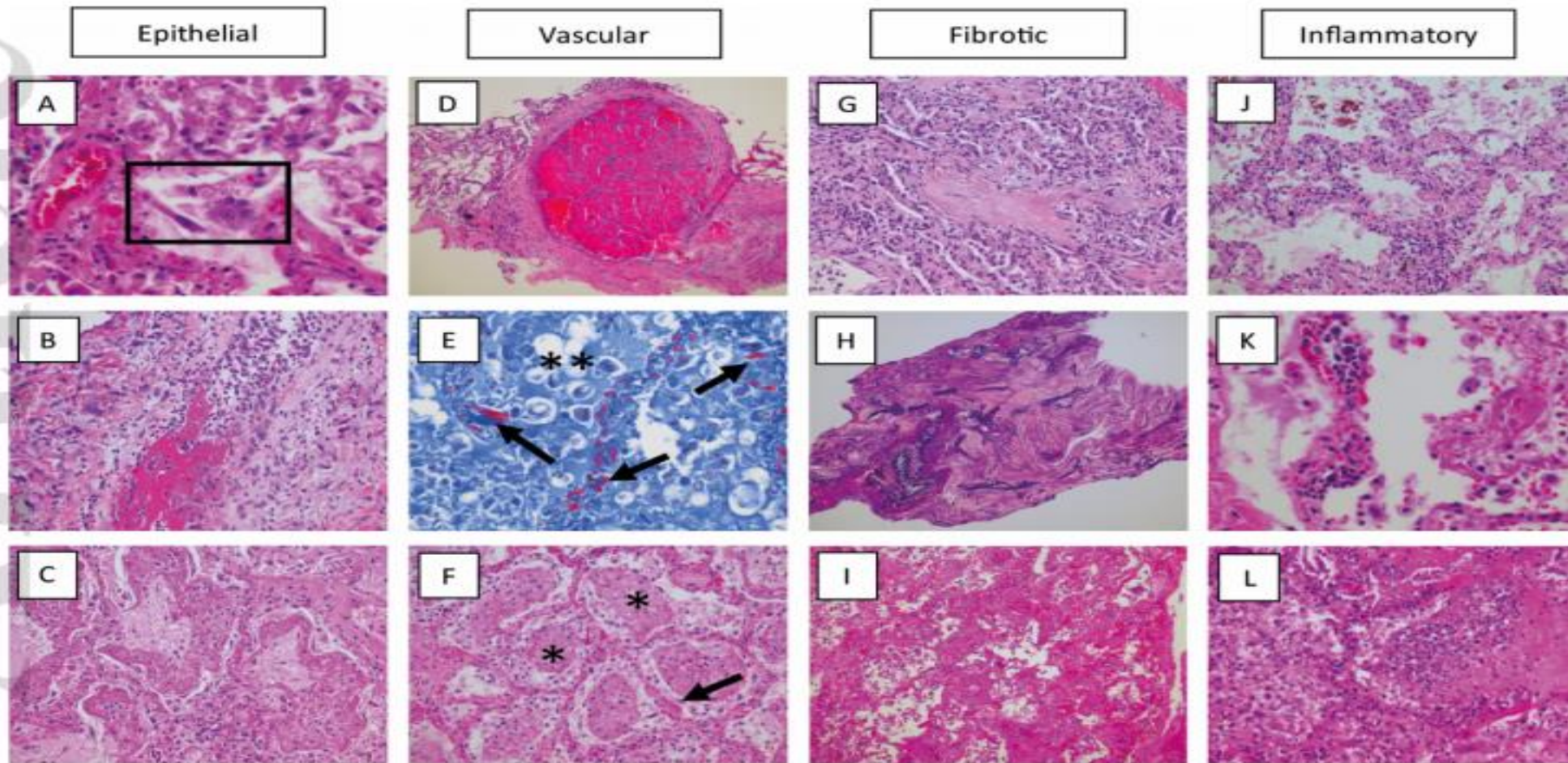
Given that the morbidity and mortality seen in COVID-19 is associated with excessive inflammation, a better understanding of the immunological underpinnings of the differential responses seen in patients infected with SARS-CoV-2 is necessary to better identify therapeutic targets. Dozens of immunomodulatory agents are rapidly going





## PROGRESS





Jan von der Thüsen, Menno van der Eerden. Histopathology and Genetic Susceptibility in COVID-19 Pneumonia.

Eur J Clin Invest. 2020 Apr 30. doi: 10.1111/eci.13259

# Agenda

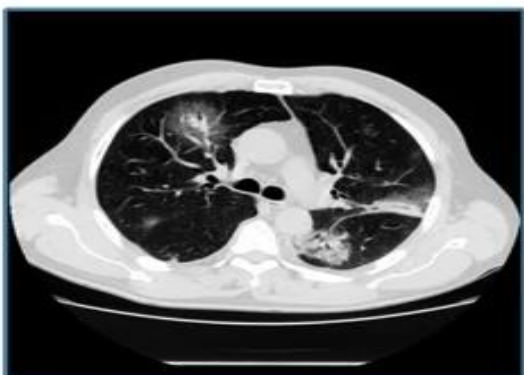
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- Epidemiología y características clínicas.
- Patogenia de la IRA en la infección SARS CoV2
- **Mecanismos fisiopatológicos de la IRA**

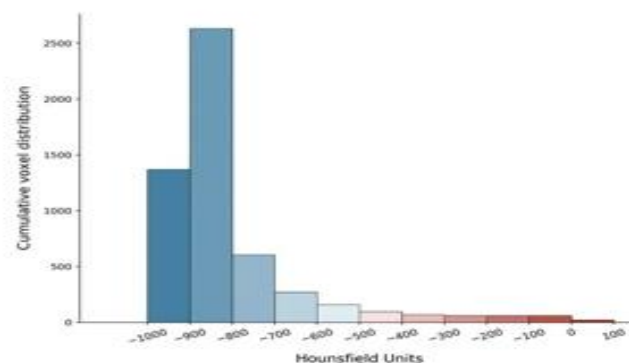
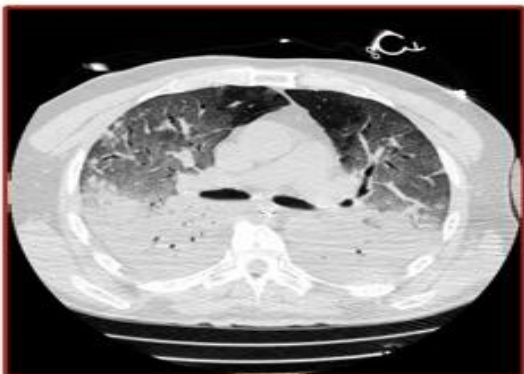


# COVID-19 pneumonia: different respiratory treatments for different phenotypes?

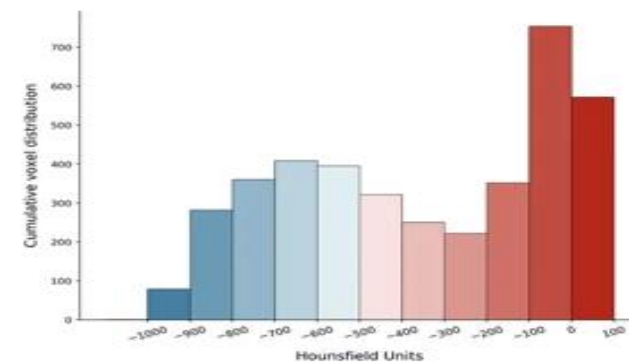
Luciano Gattinoni<sup>1\*</sup>, Davide Chiumello<sup>2</sup>, Pietro Caironi<sup>3,4</sup>, Mattia Busana<sup>1</sup>, Federica Romitti<sup>1</sup>, Luca Brazzi<sup>5</sup> and Luigi Camporota<sup>6</sup>

**A**

$\text{PaO}_2/\text{FiO}_2$   
95 mmHg

**B**

$\text{PaO}_2/\text{FiO}_2$   
84 mmHg

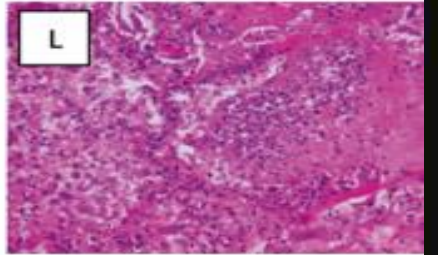
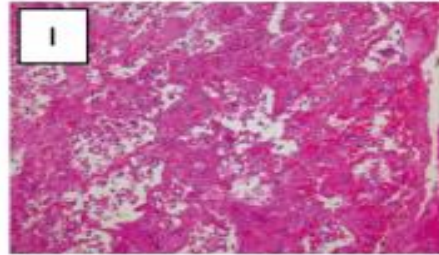
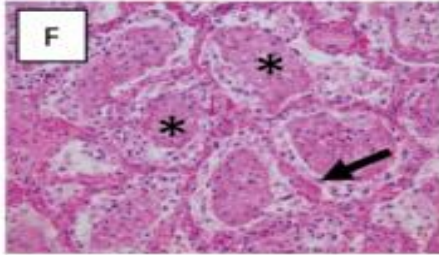
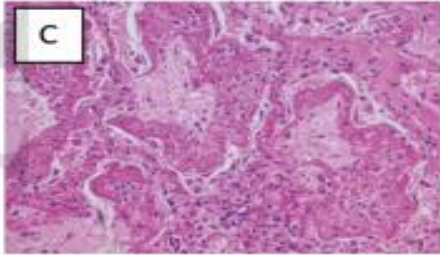
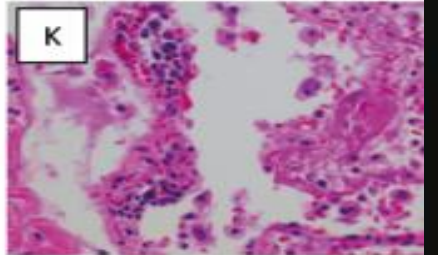
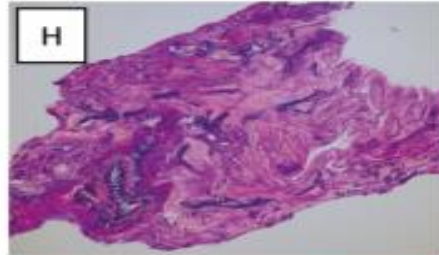
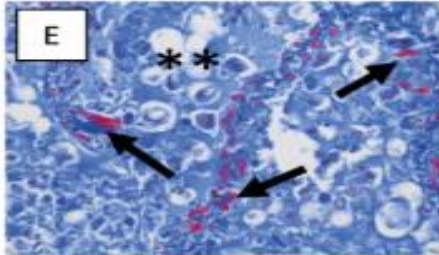
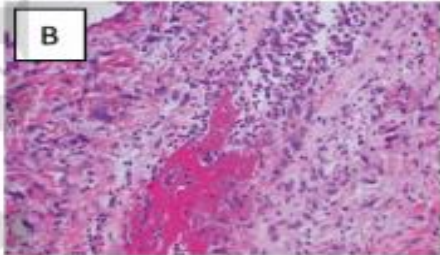
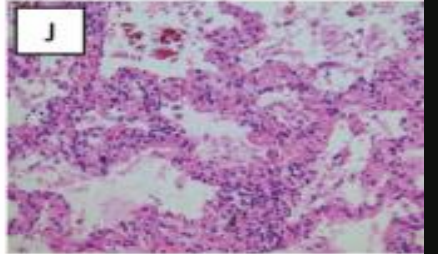
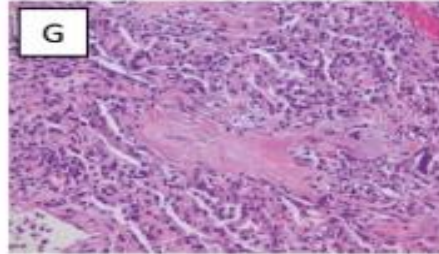
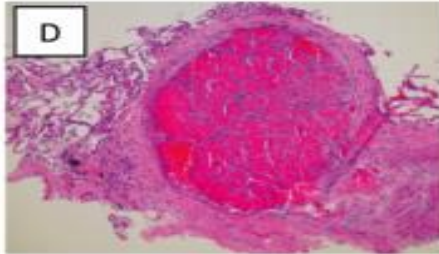
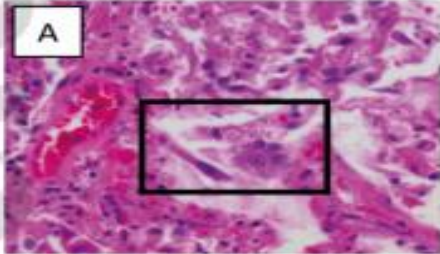


Epithelial

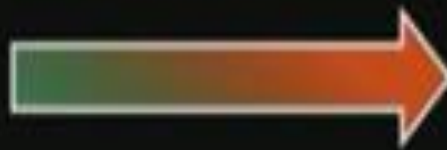
Vascular

Fibrotic

Inflammatory

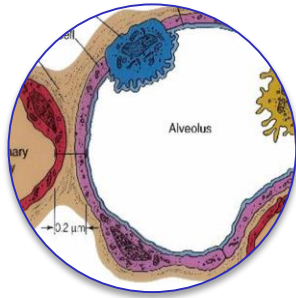


Phenotype L



Phenotype H

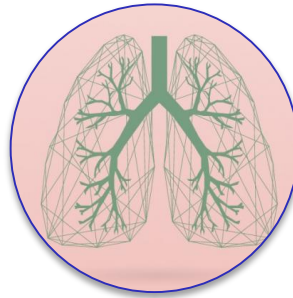
# Compromiso Respiratorio. Epectros o Dominios



Intersticio

**Trastorno de difusión**

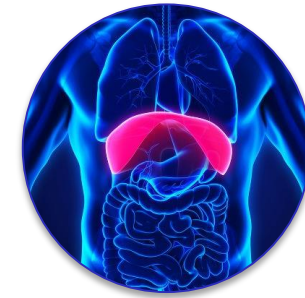
Sind de llenado alveolar  
SDRA/neumonitis/alveolitis



Vías Aéreas

**V/Q bajo**

Hipoventilación



Circulación  
pulmonar o  
neuromuscular

**V/Q alto**

Respuesta inmuntrombótica



# COCLUSIONES

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- **La COVID 19 tiene un espectro clínico amplio.**
- **La patogenia de la IRA por infección por SARS Cov -2 no es igual a un a la del SDRA**
- **Los mecanismos de hipoxemia pueden ser múltiples y su evaluación temprana permitirá mejorar nuestra aproximación terapéutica.**