



# Fisiopatologia da COVID-19

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Faculdade de Odontologia de Bauru – Curso de Medicina



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# Autópsia como Ferramenta!



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51

Laboratório Multiusuário



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VIRTÓPSIA

# Autópsia como Ferramenta!

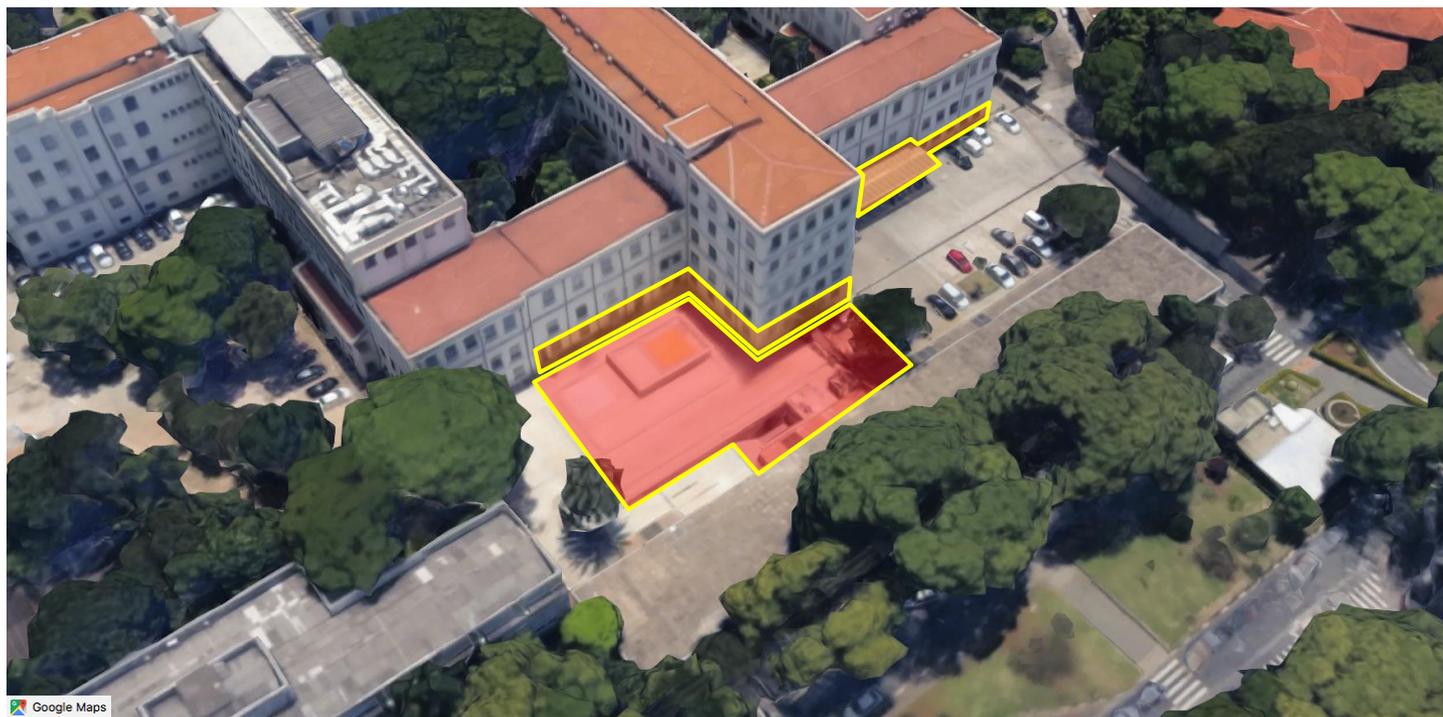
## Plataforma de Imagem na Sala de Autópsia



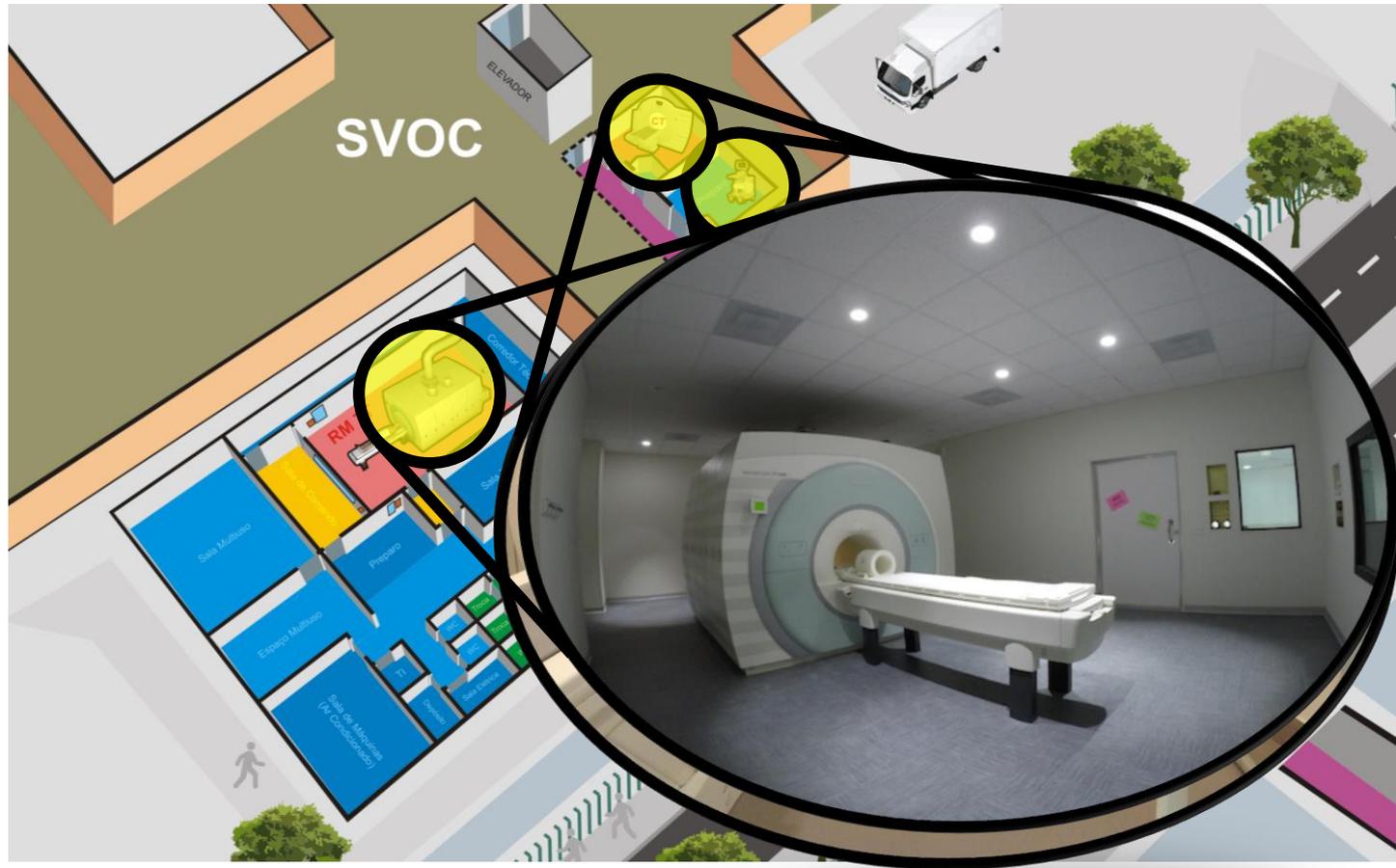
Dep. **Patologia**  
Dep. **Radiologia**  
**SVOC** (Serv. Verif. Óbitos)



# Autópsia como Ferramenta!



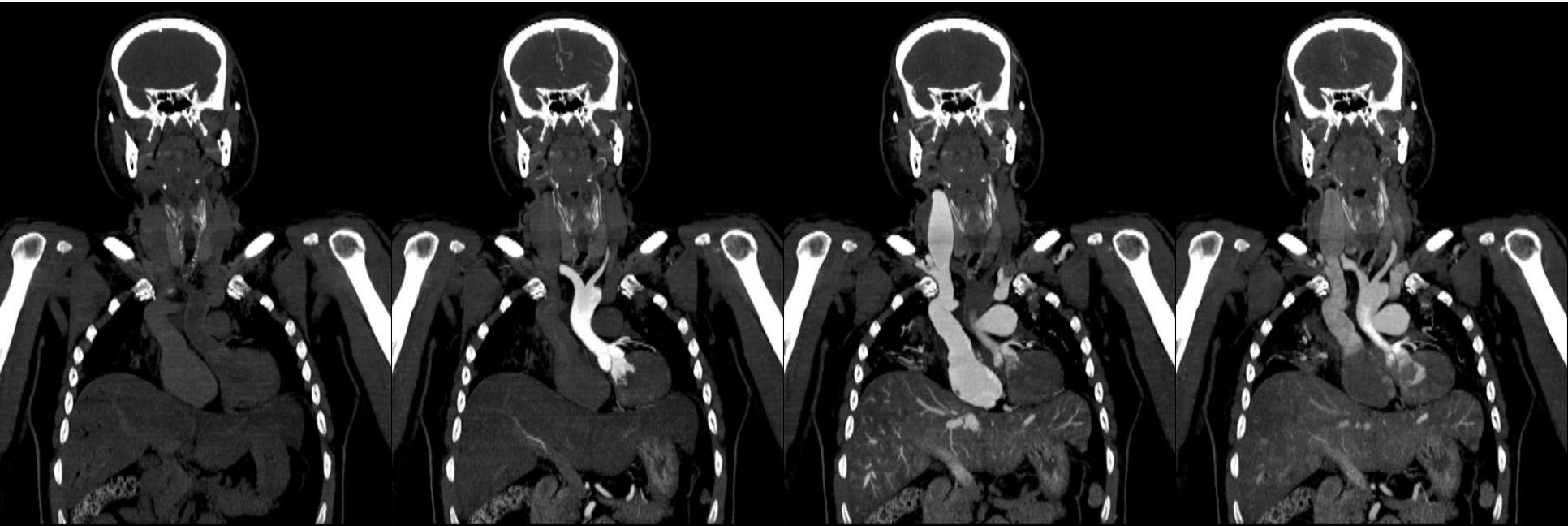
# Autópsia como Ferramenta!



# Autópsia como Ferramenta!



# Autópsia como Ferramenta!



PRE

ARTERIAL

VENOUS

DINAMIC

# Autópsia Minimamente Invasiva - AMI

**Conceito:** Diagnóstico post-mortem pouco invasivo, que combina informações de história clínica, exames de imagem, e coleta de tecido por agulha dirigida a órgãos-alvo.

## Métodos possíveis:

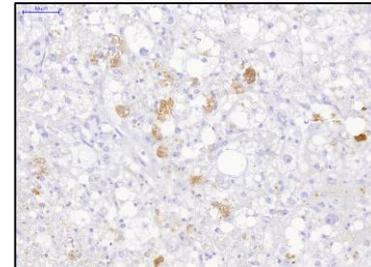
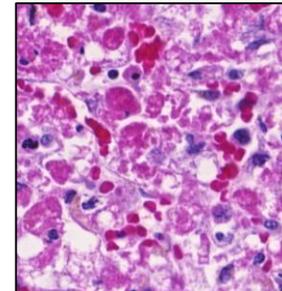
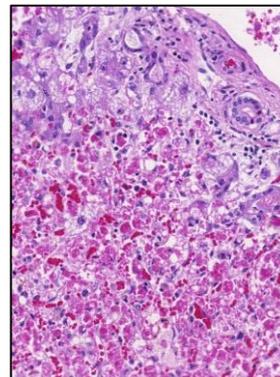
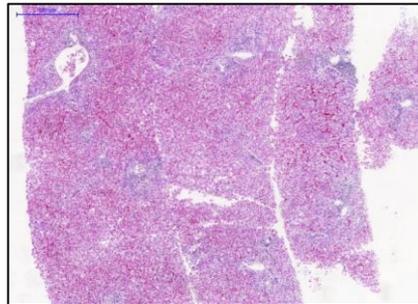
- Exames de imagem exclusivamente (Autópsia Virtual)
- Associação de imagens e análise de tecido coletado por agulhas (biópsias post-mortem)
  - TC, US, RNM, angiografia
- Biópsias post-mortem sem o uso de exames de imagem

# Autópsia Minimamente Invasiva - AMI

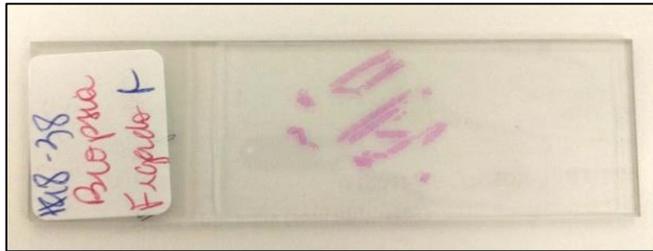
Ultrasound-guided minimally invasive autopsy as a tool for rapid post-mortem diagnosis in the 2018 Sao Paulo yellow fever epidemic: Correlation with conventional autopsy

Amaro Nunes Duarte-Neto<sup>1</sup>, Renata Aparecida de Almeida Monteiro<sup>1</sup>, Janaina Johnsson<sup>2</sup>, Marielton dos Passos Cunha<sup>3</sup>, Shahab Zaki Pour<sup>3</sup>, Amanda Cartagenes Saraiva<sup>1</sup>, Yeh-Li Ho<sup>4</sup>, Luiz Fernando Ferraz da Silva<sup>1</sup>, Thais Mauad<sup>1</sup>, Paolo Marinho de Andrade Zanotto<sup>3</sup>, Paulo Hilário Nascimento Saldiva<sup>1</sup>, Ilka Regina Souza de Oliveira<sup>5</sup>, Marisa Dolhnikoff<sup>1\*</sup>

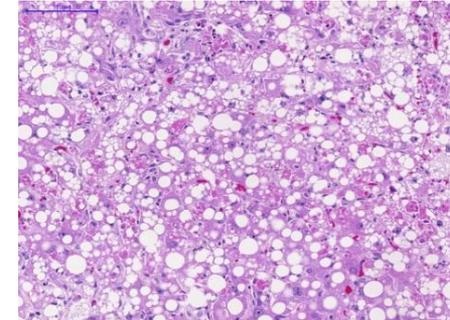
PLOS Neglected Tropical Diseases | <https://doi.org/10.1371/journal.pntd.0007625> July 22, 2019



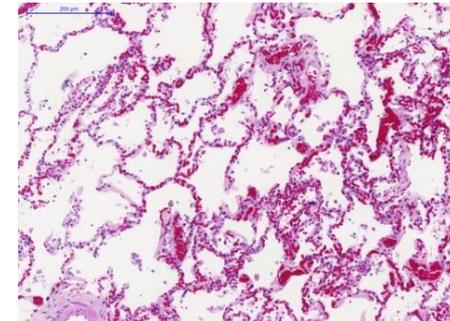
# AMI na COVID-19



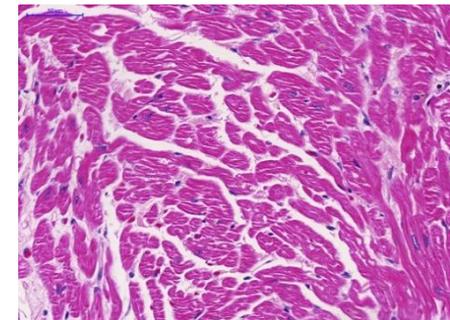
Fígado



Pulmão



Coração



# AMI na COVID-19



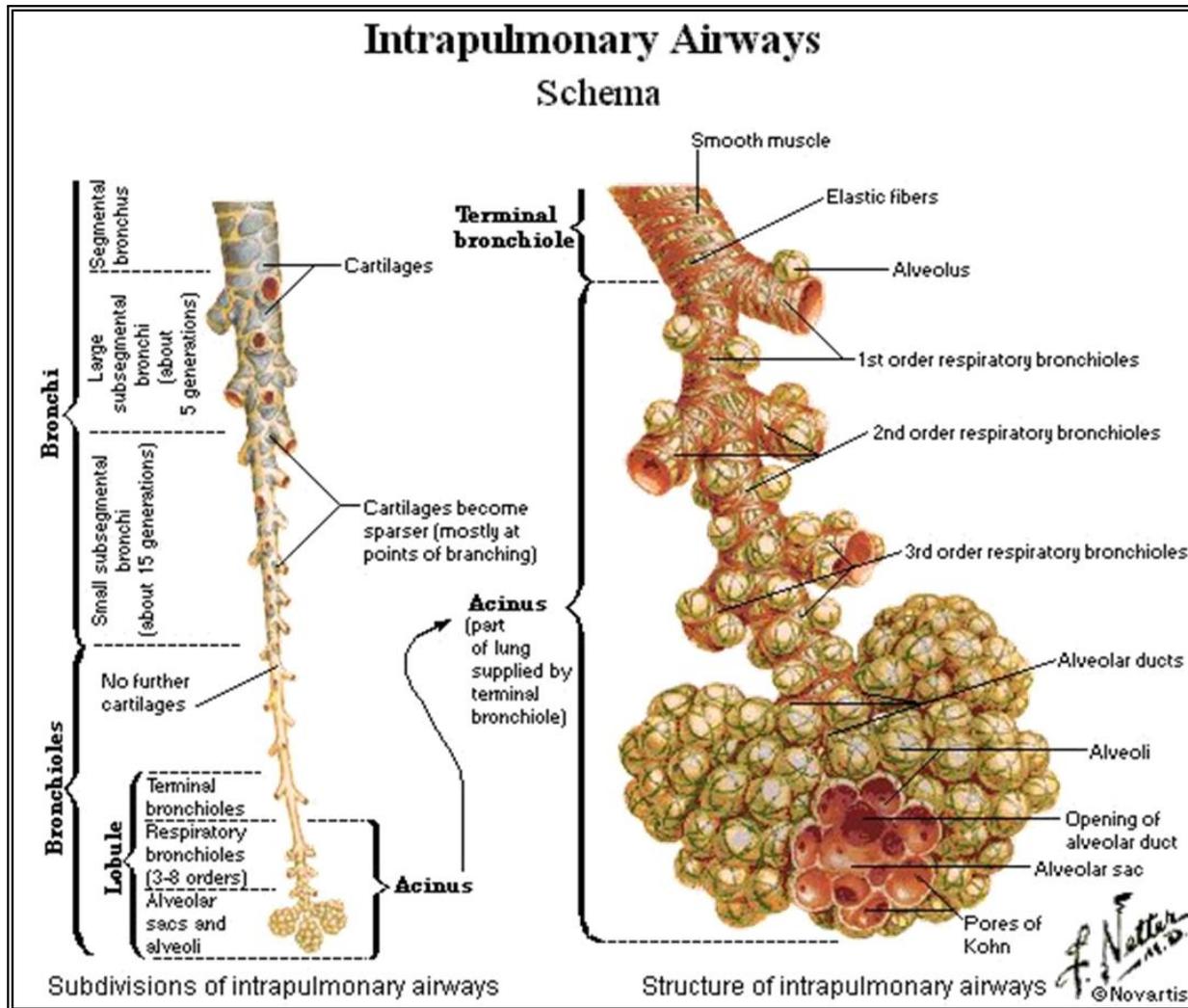
# AMI na COVID-19

- 61 pacientes
- 0 a 91 anos
- 65% homens / 35% mulheres
- Comorbidades
  - DM, HAS, cardiopatia isquêmica, DPOC
- 0 a 42 dias de internação

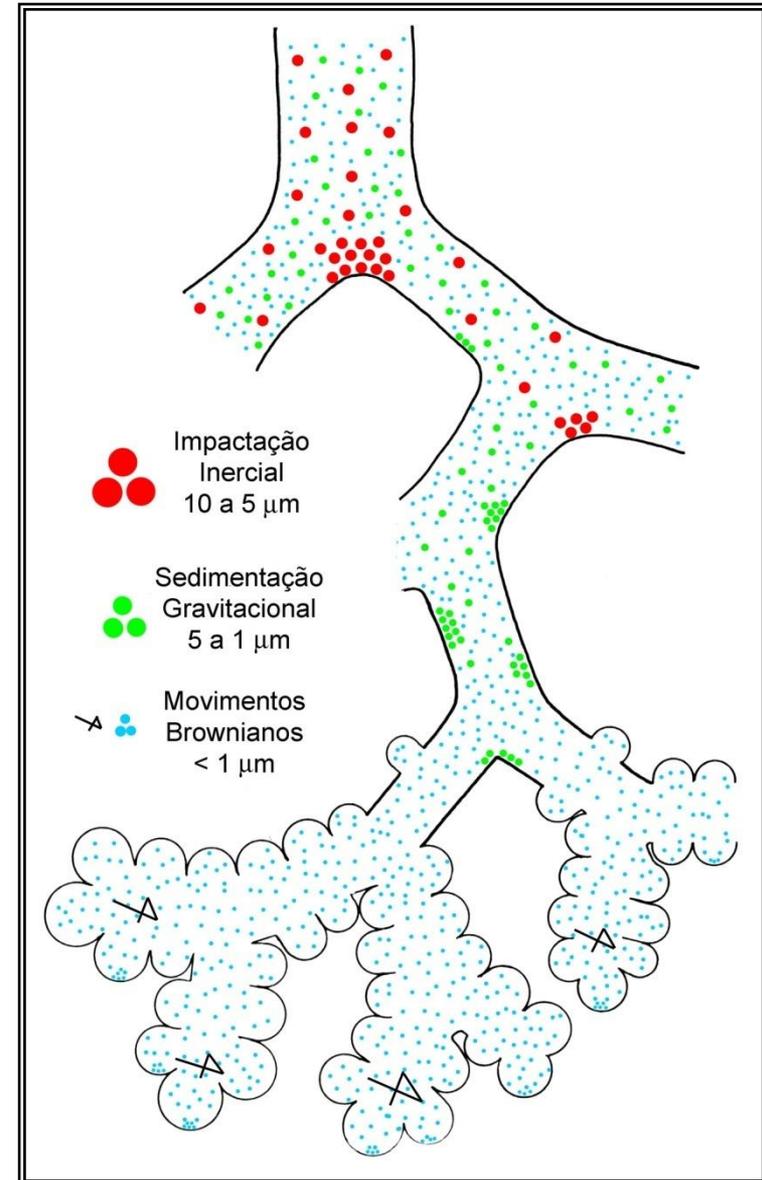
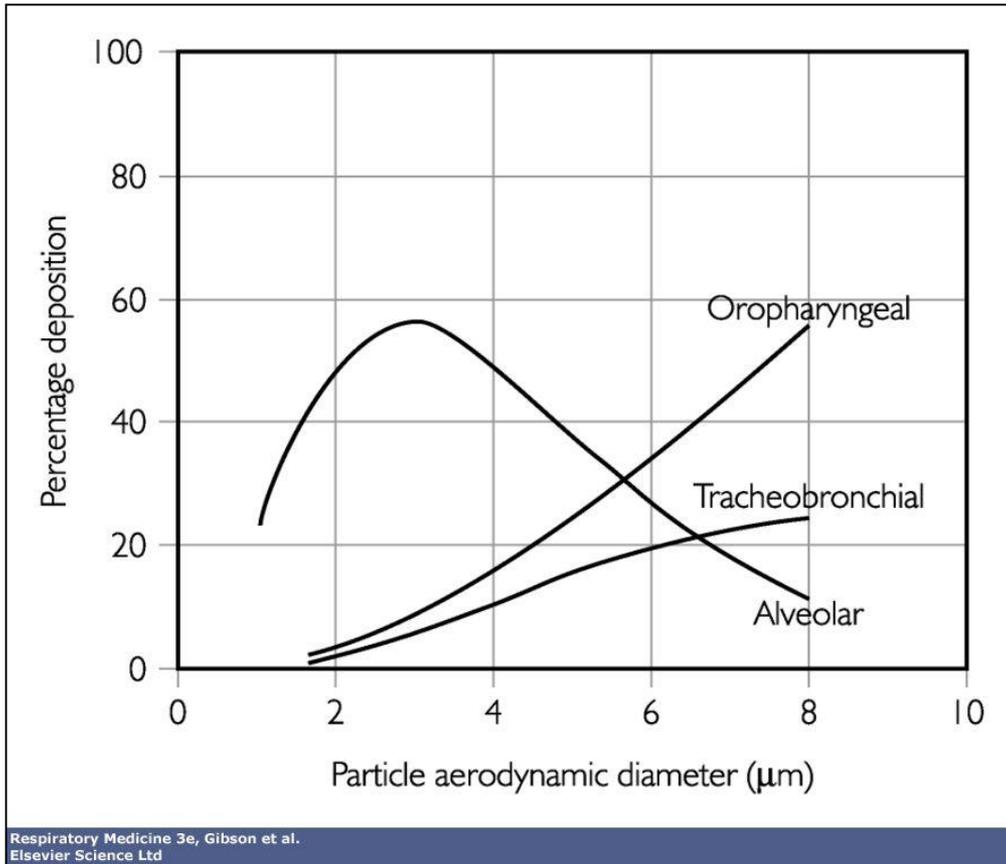
# Componentes do Sistema Respiratório



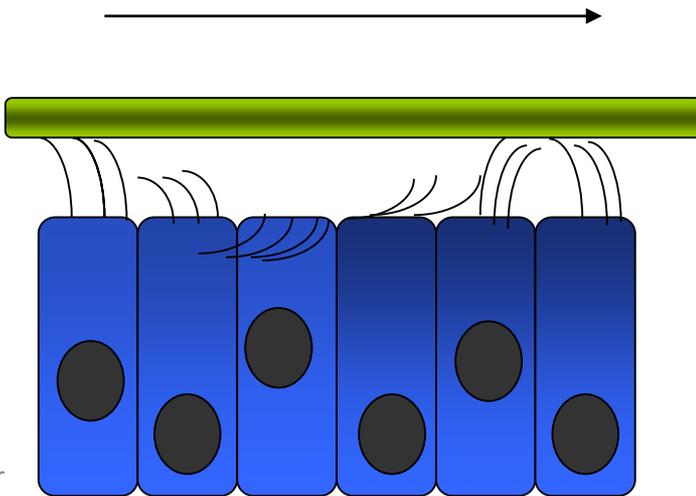
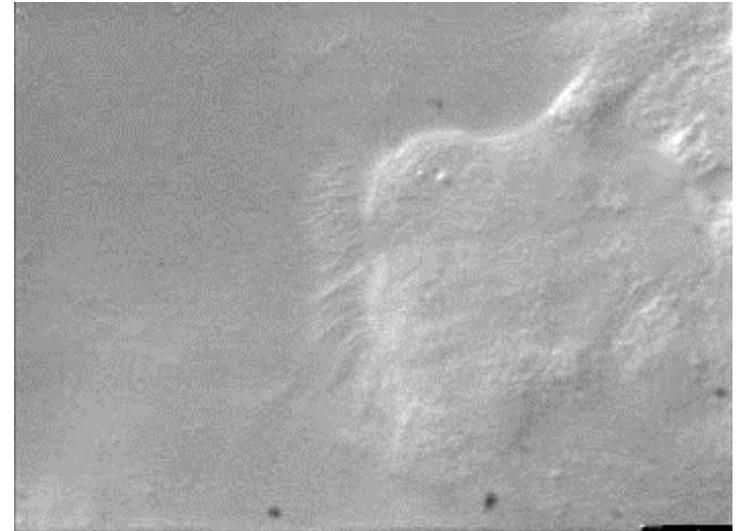
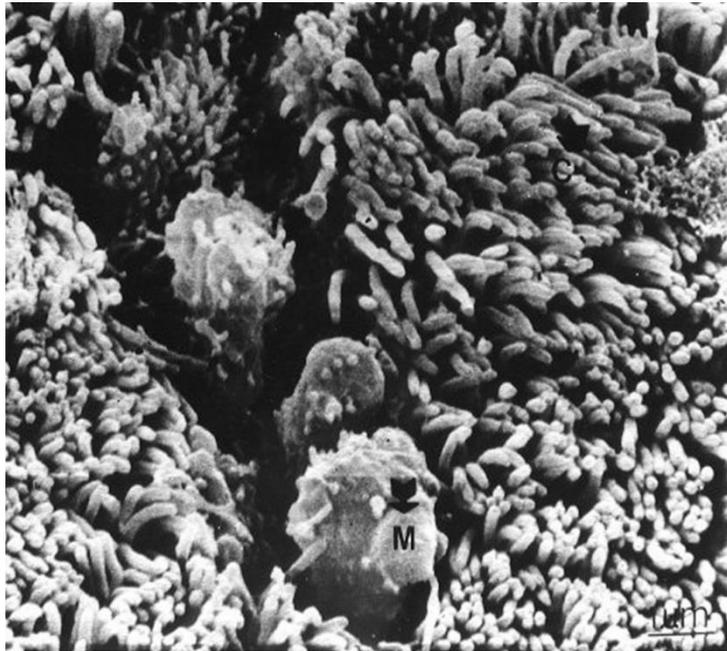
# Arvore Traqueobrônquica



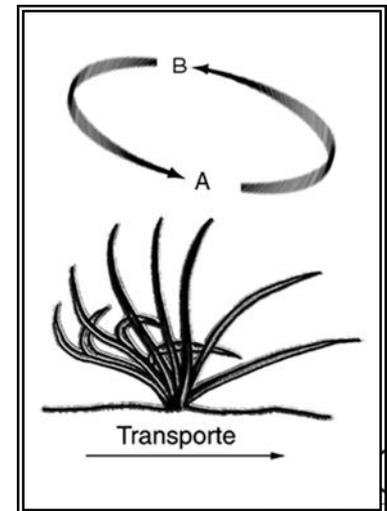
# Componentes da Parede Brônquica



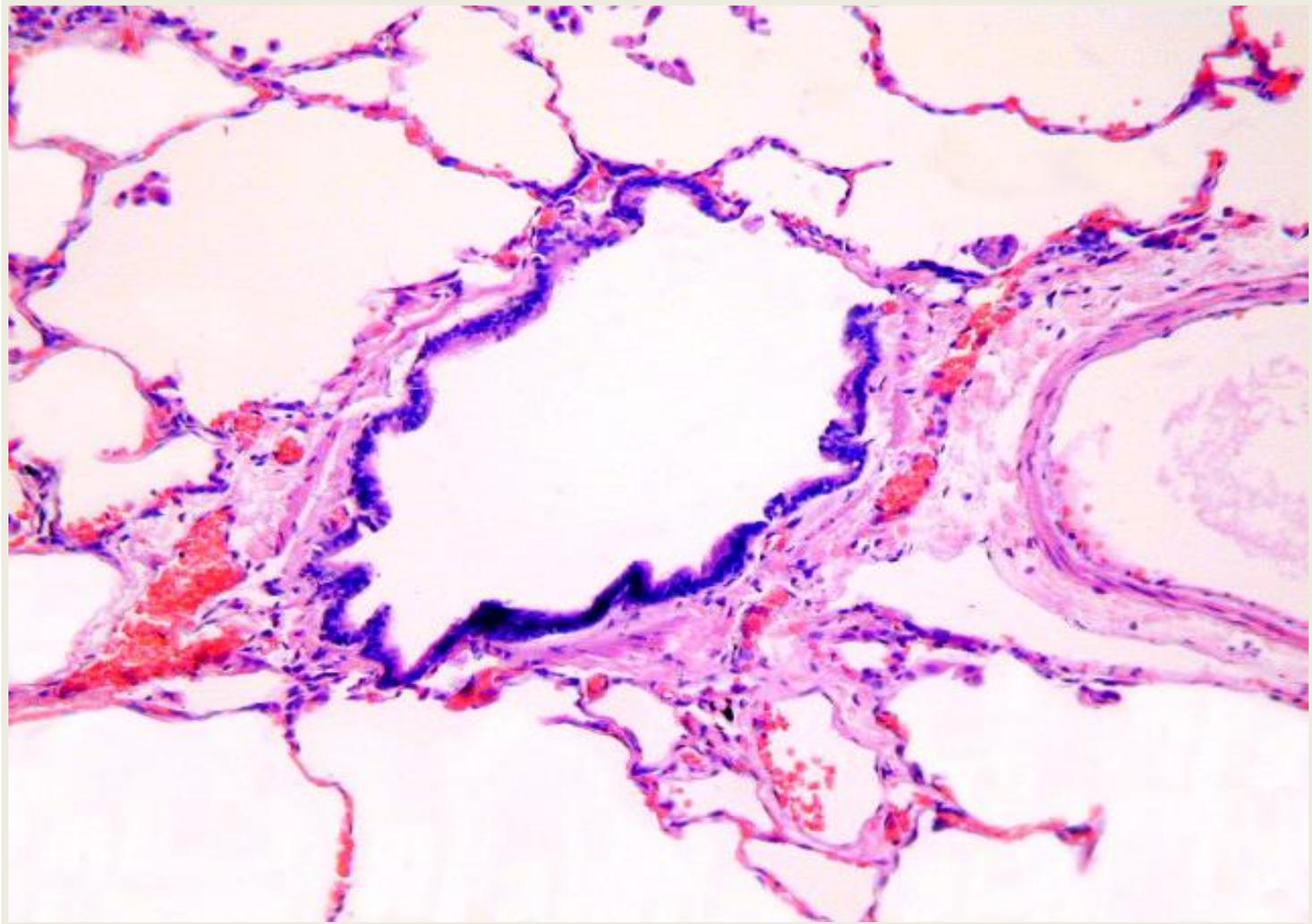
# Aparelho Muco-ciliar



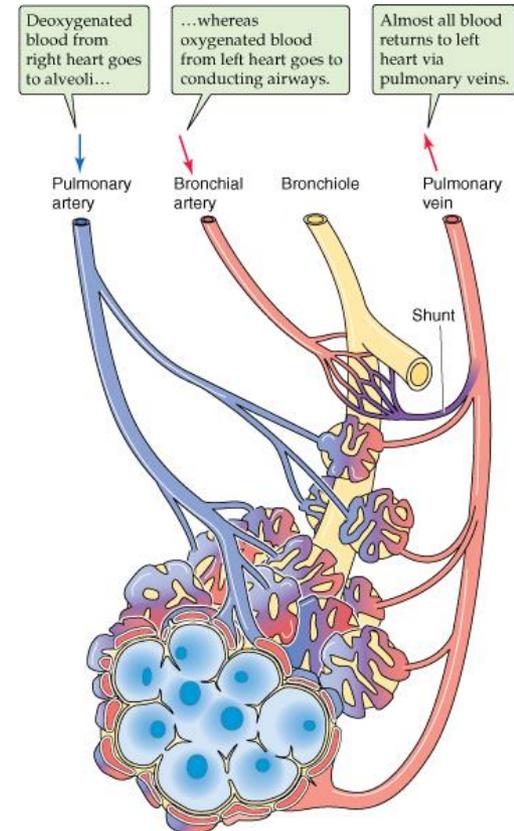
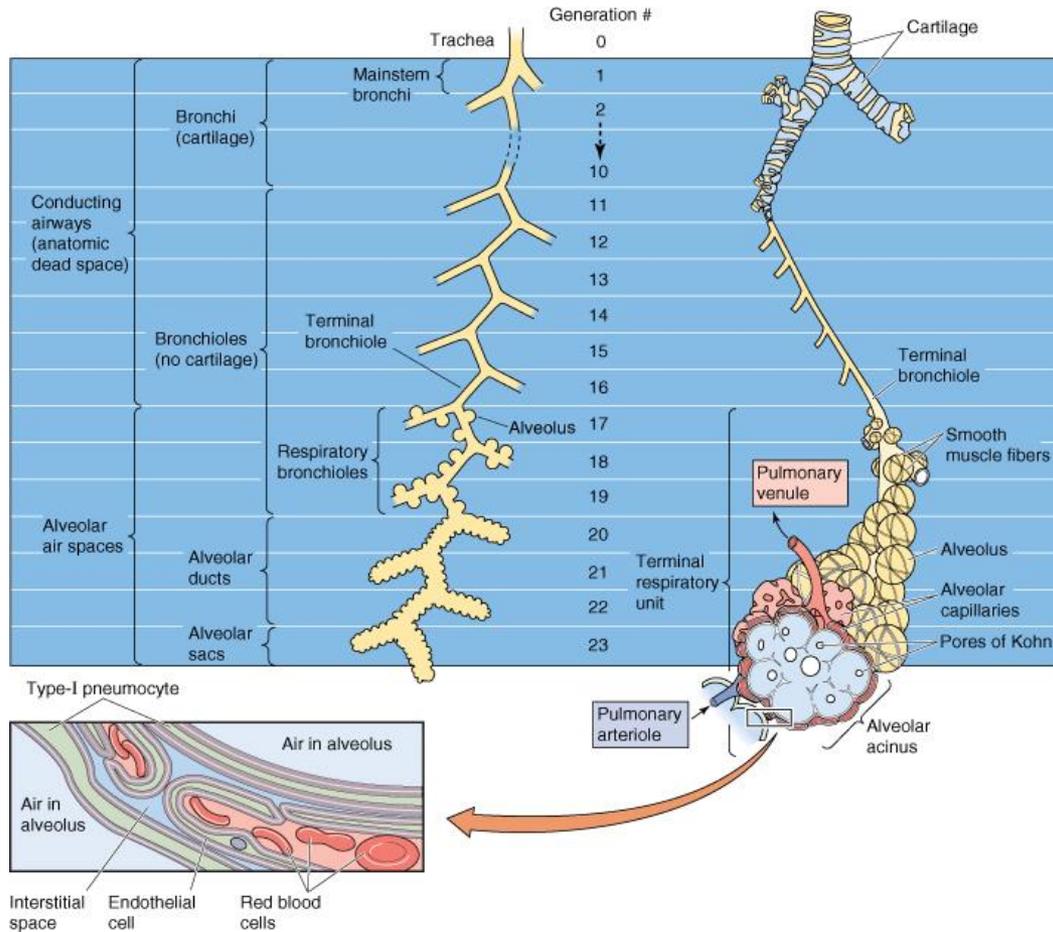
gel
sol



# Pequenas Vias Aéreas



# Circulação Pulmonar

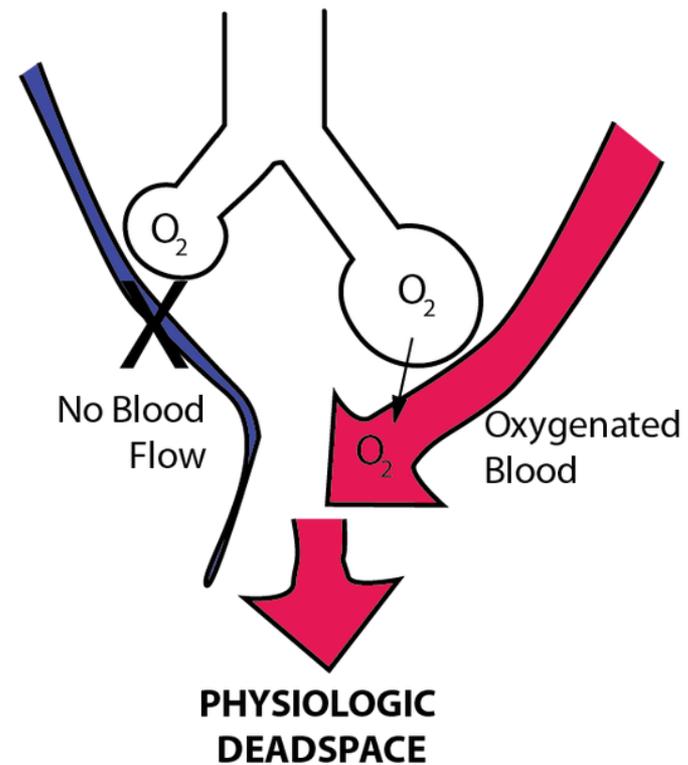
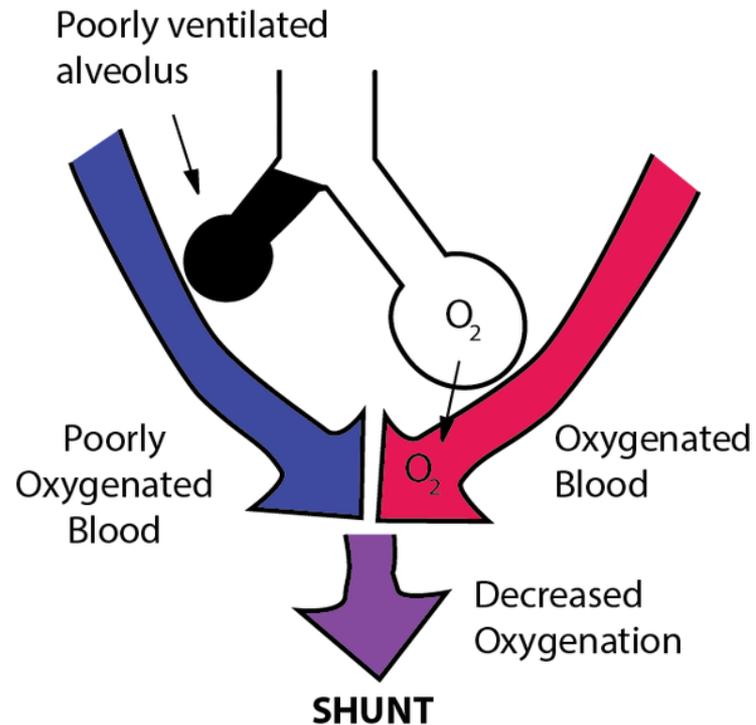


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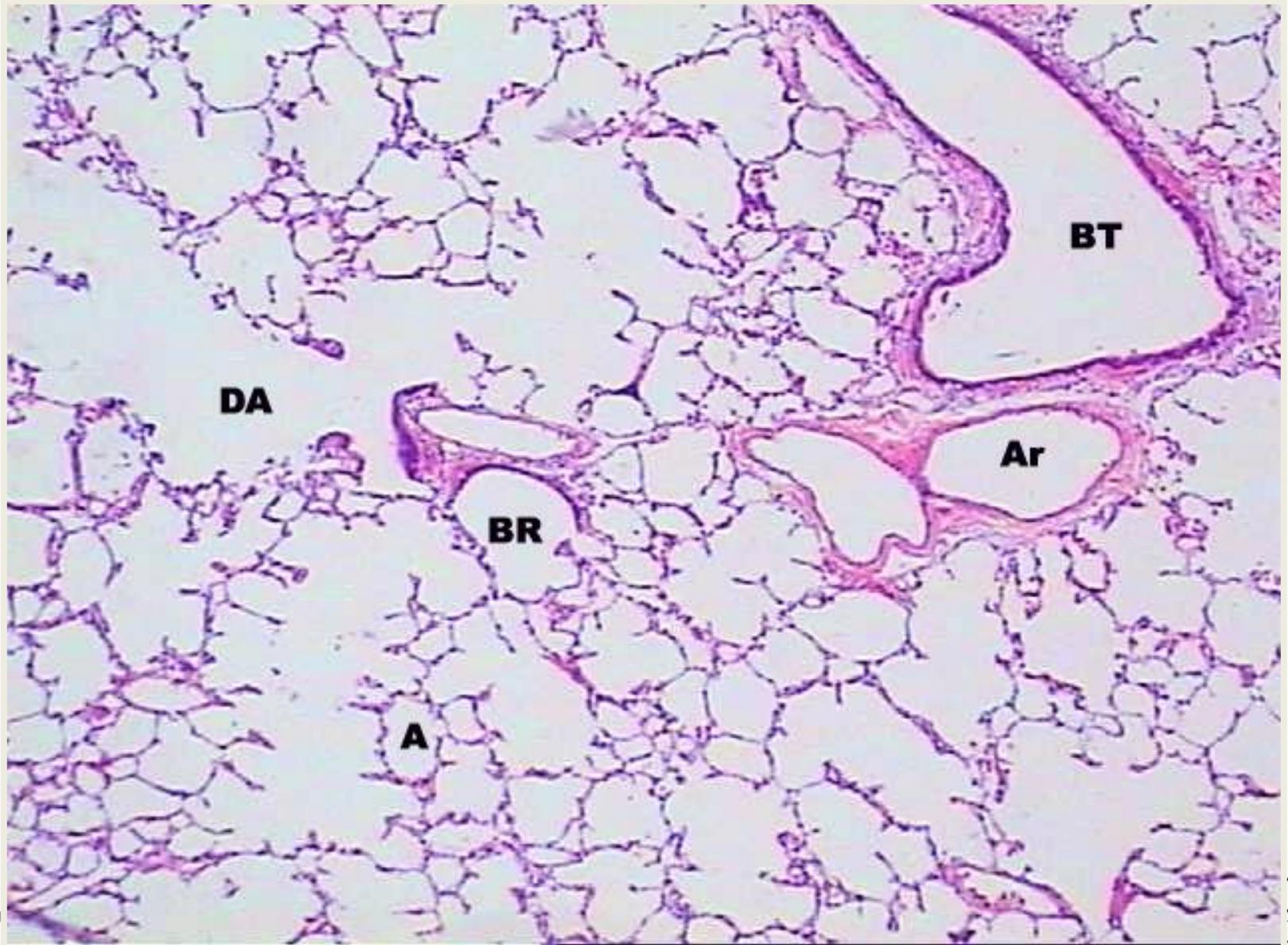
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# Relação Ventilação-Perfusão

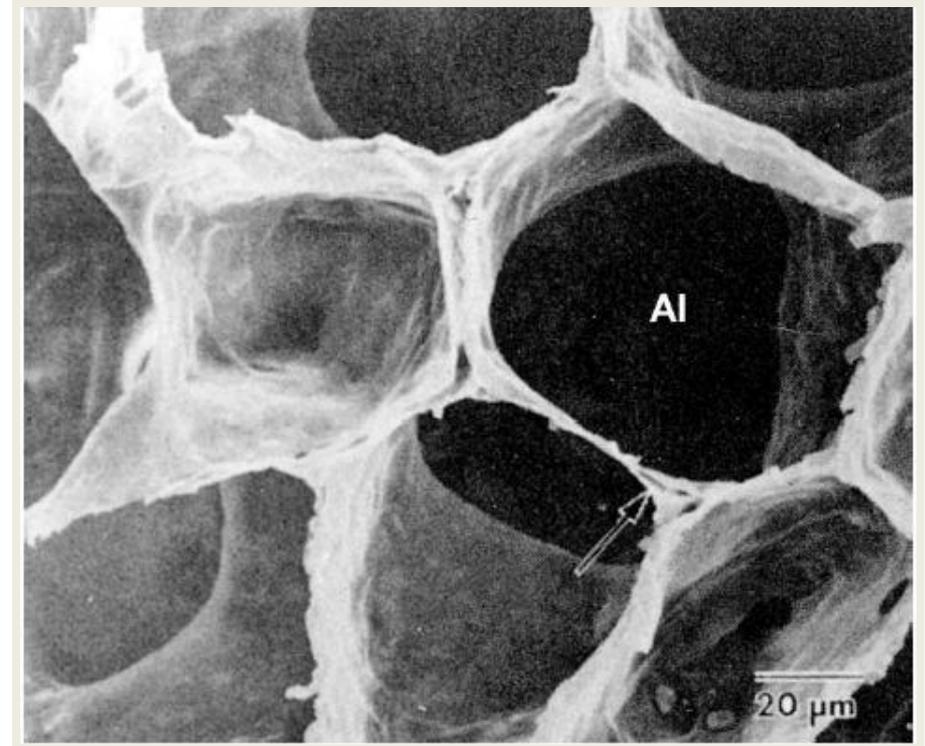
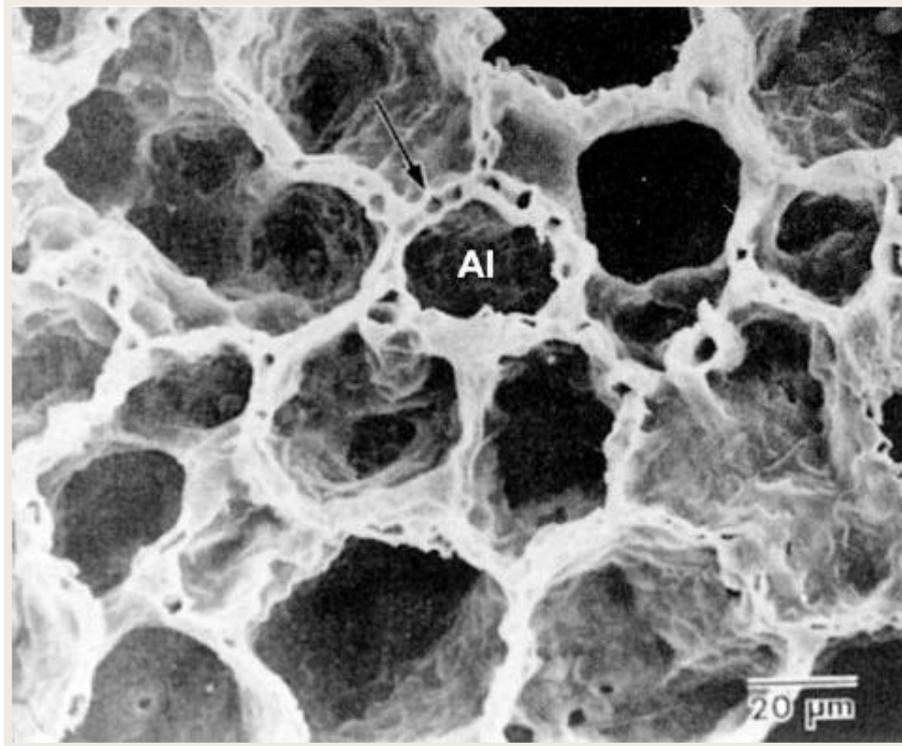
- Efeito Shunt e Espaço Morto



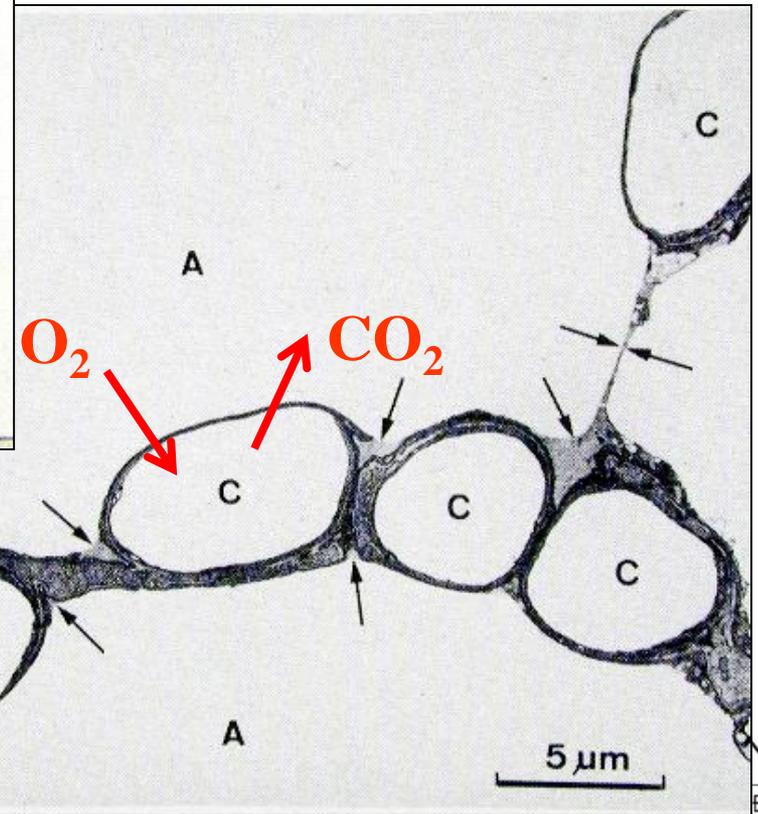
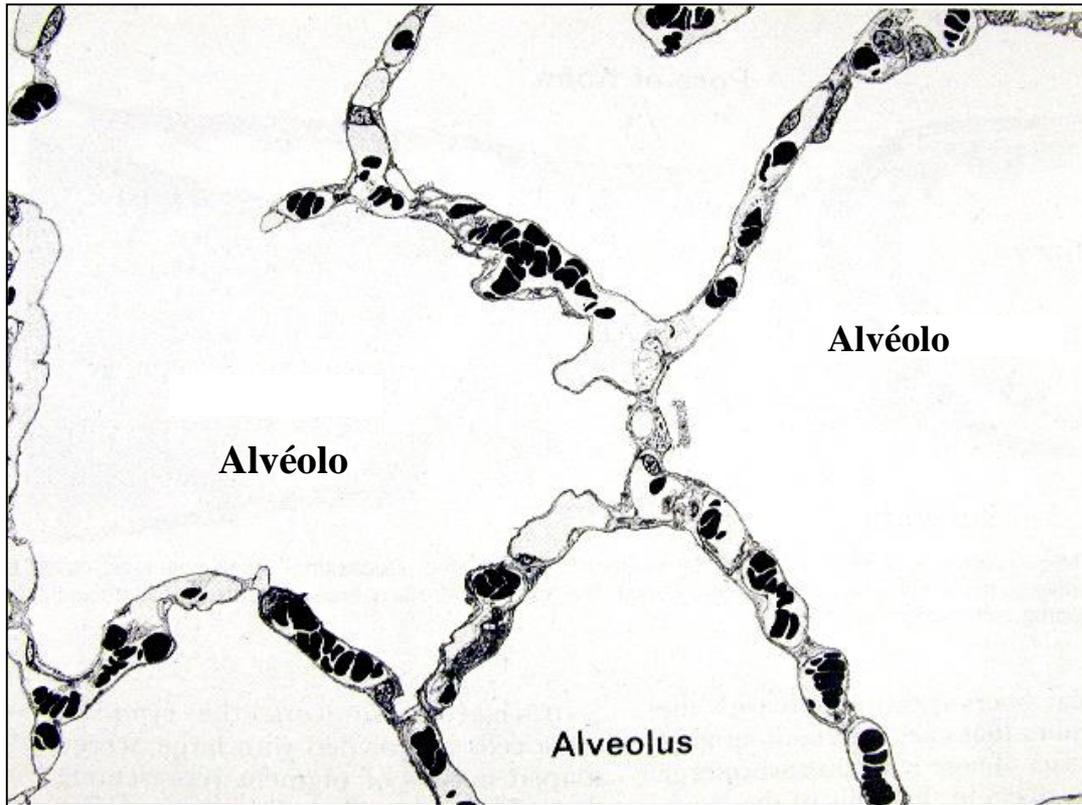
# Alveolos



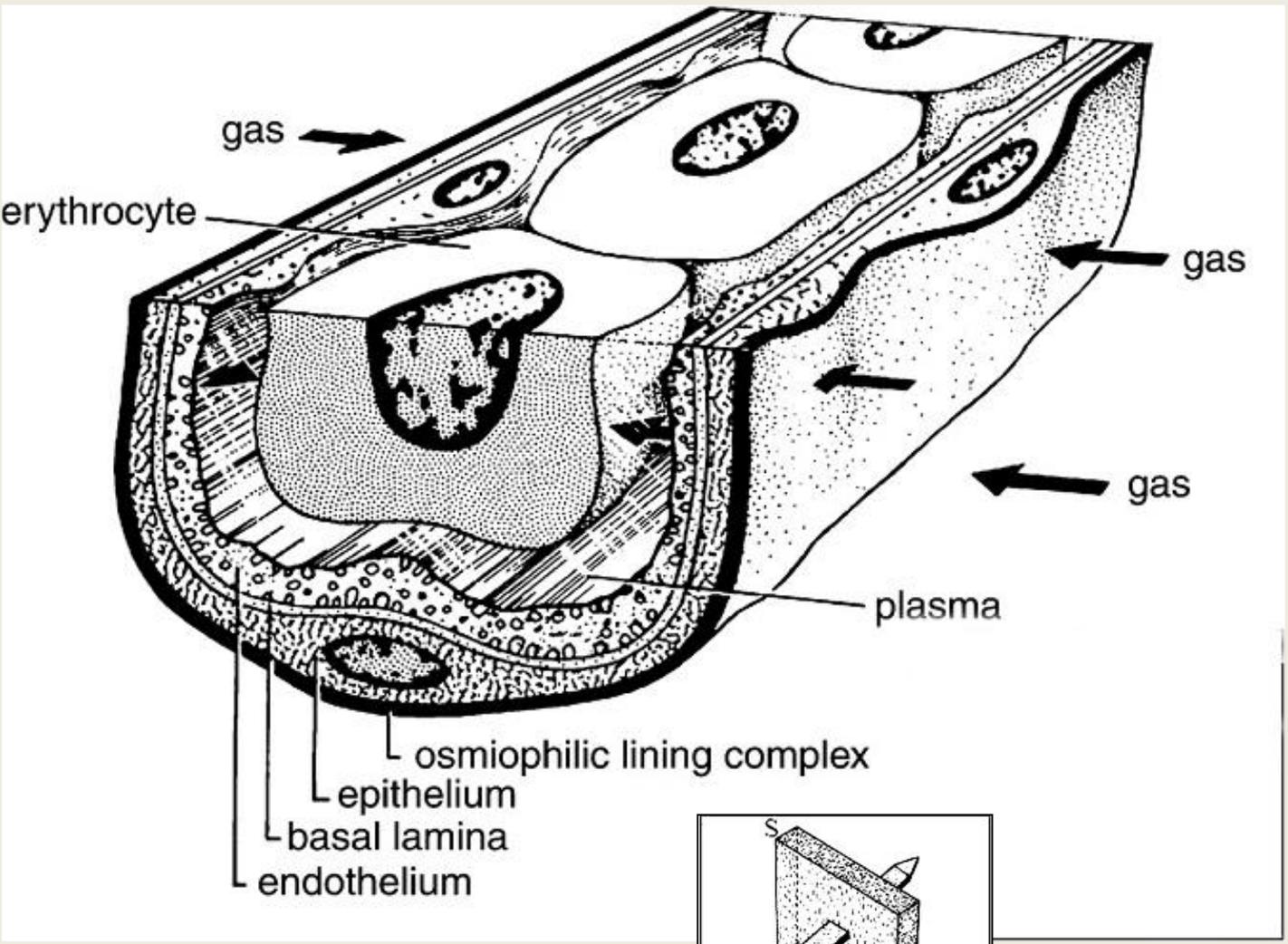
# Alveolos



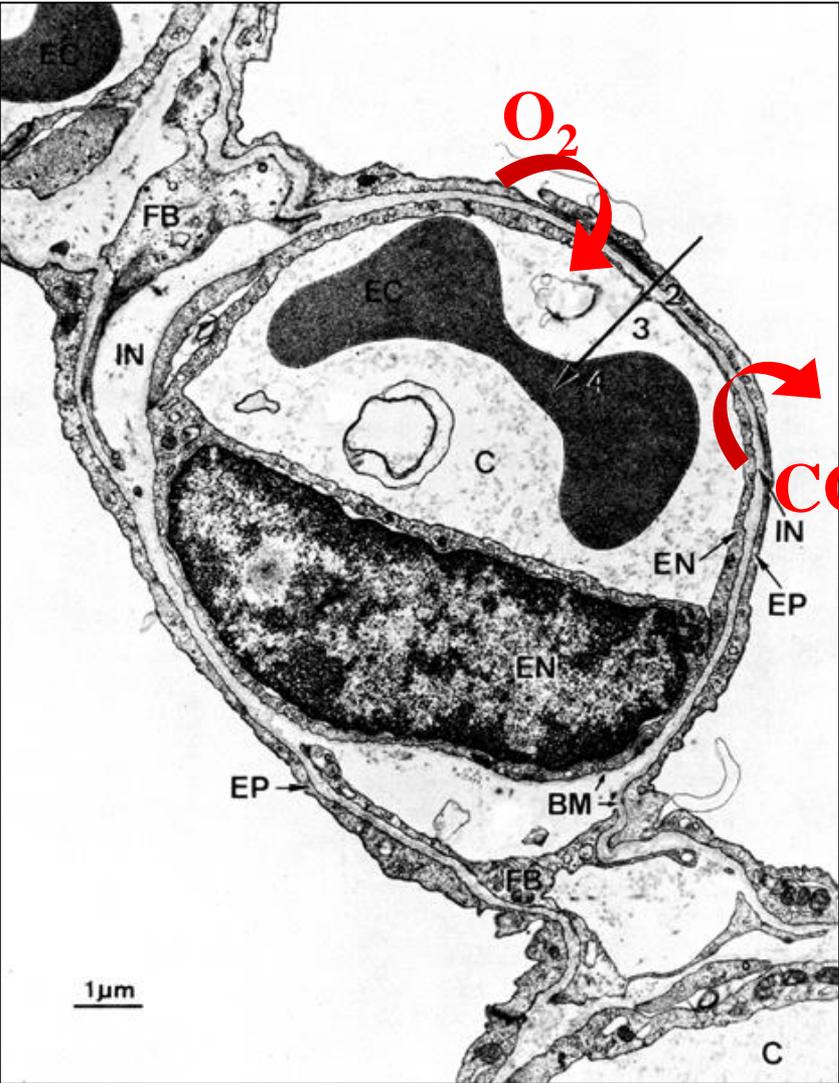
# Alveolos



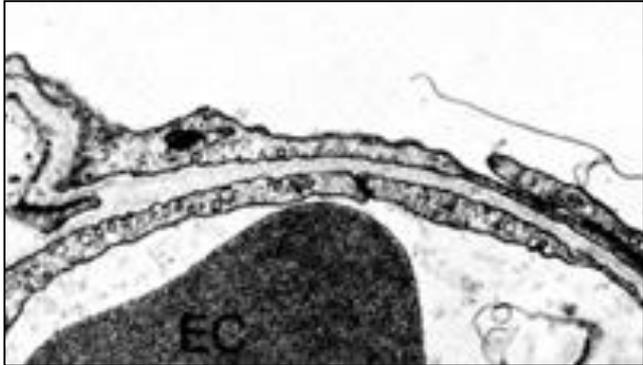
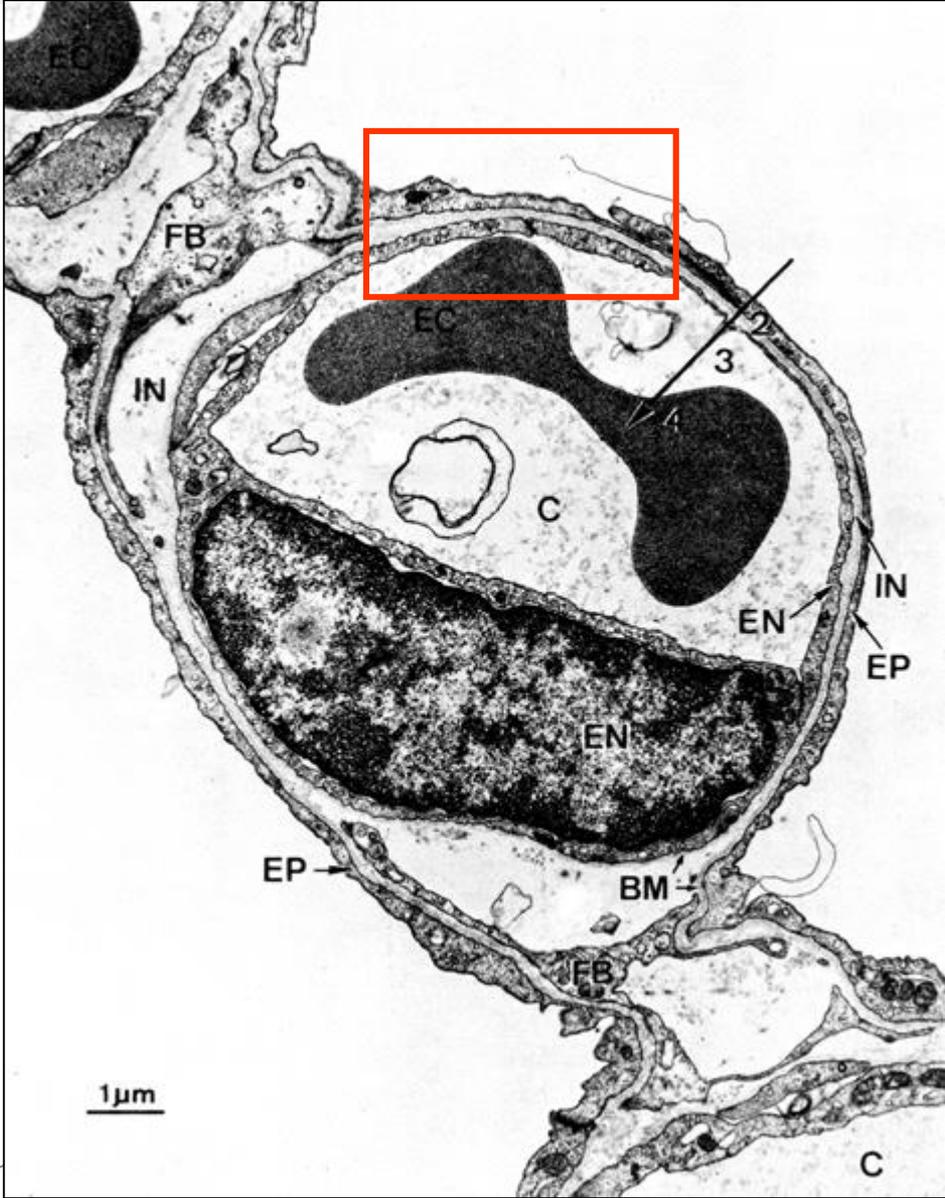
# Alveolos



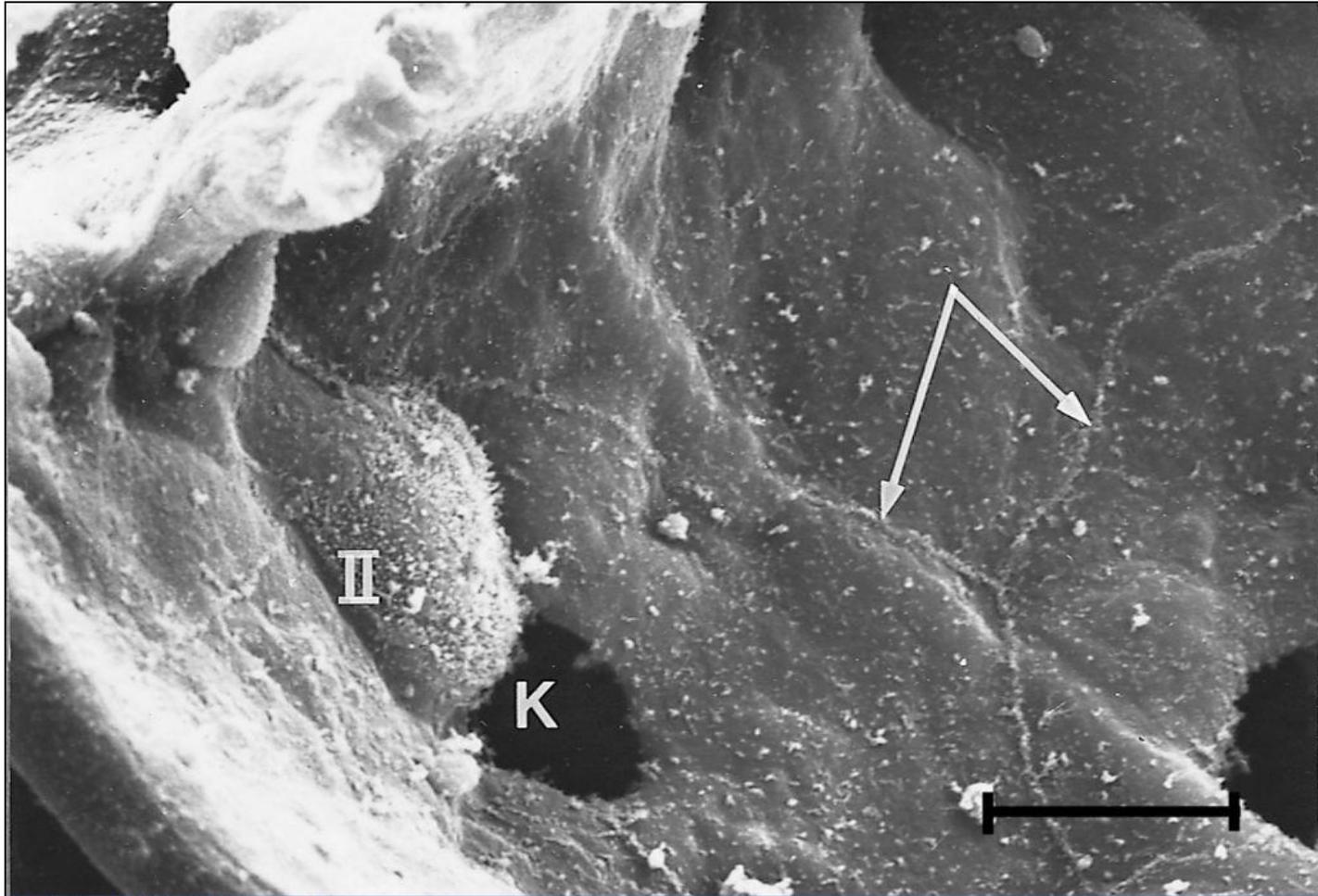
# Alveolos



# Alveolus

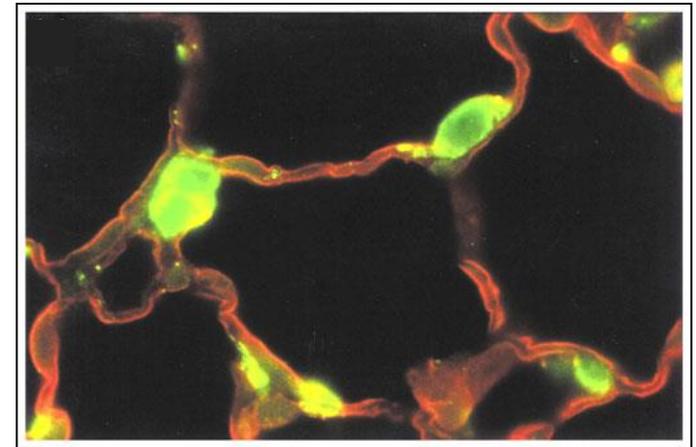
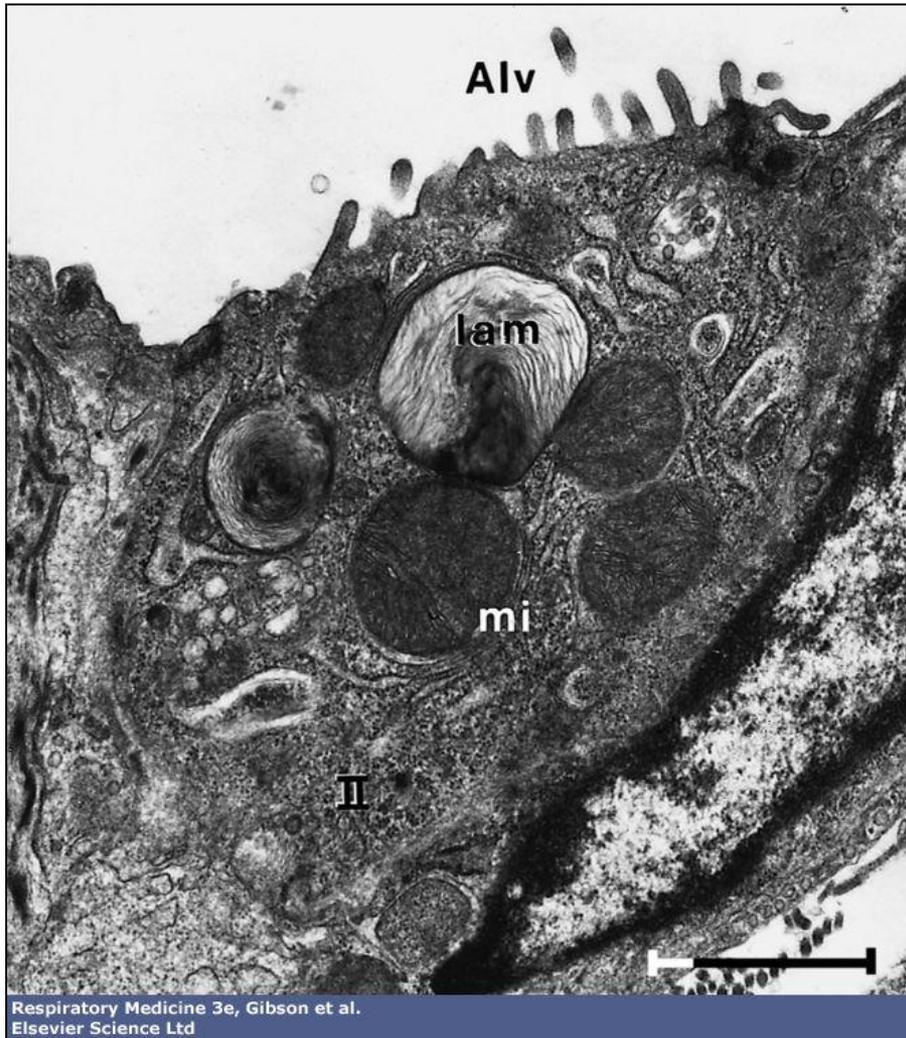


# Pneumócitos I e II

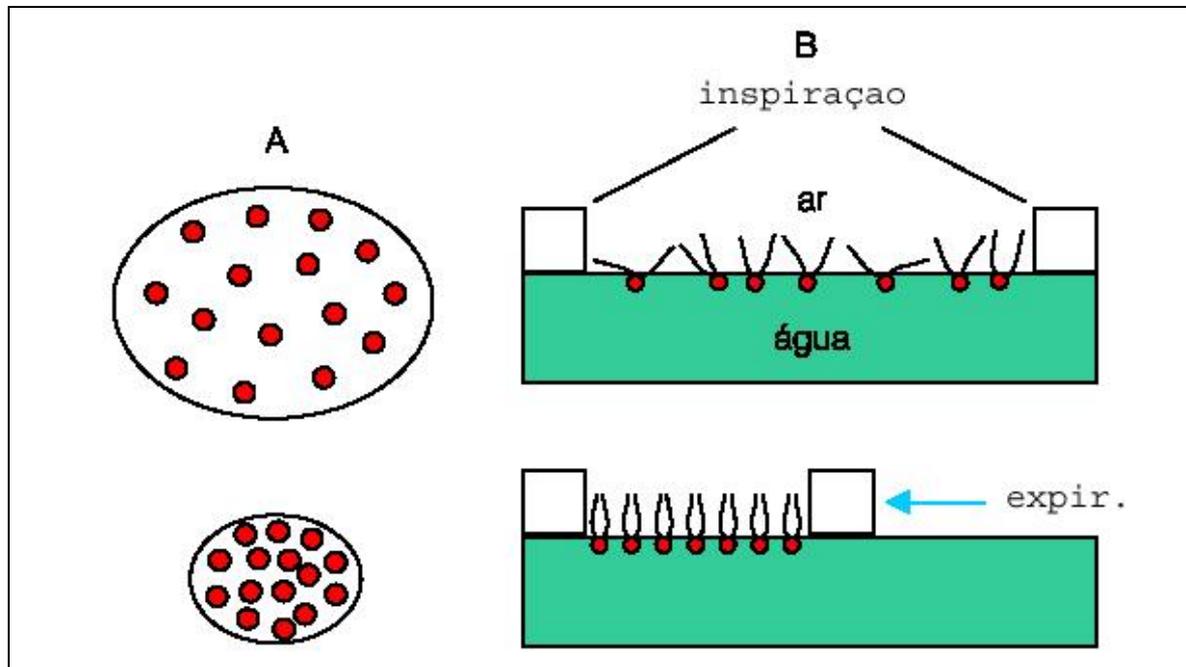
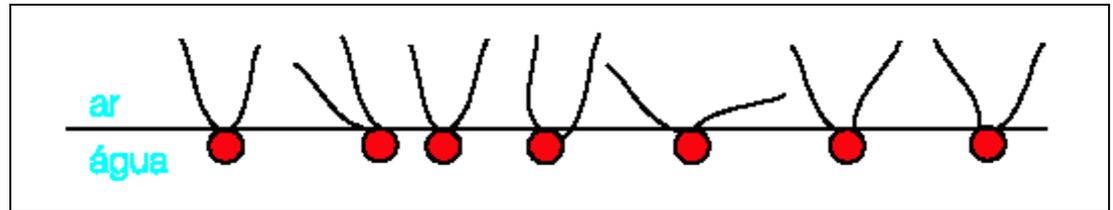
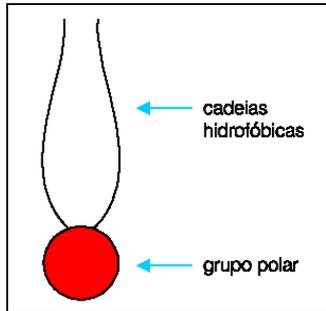


Respiratory Medicine 3e, Gibson et al.  
Elsevier Science Ltd

# Pneumócito II

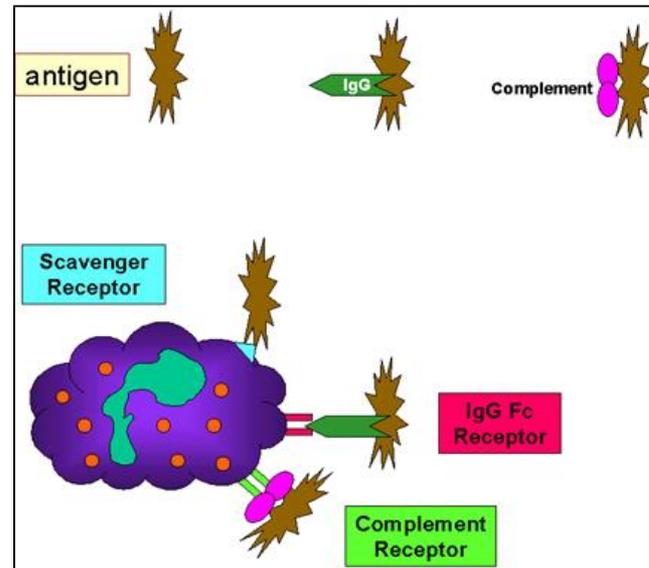


# Surfactante



# Macrófago Alveolar

- Célula residente do espaço alveolar
- Origem – monócitos circulantes
- Detecção de microorganismos patogênicos
  - Fc da IgG
  - Complemento
  - TLR

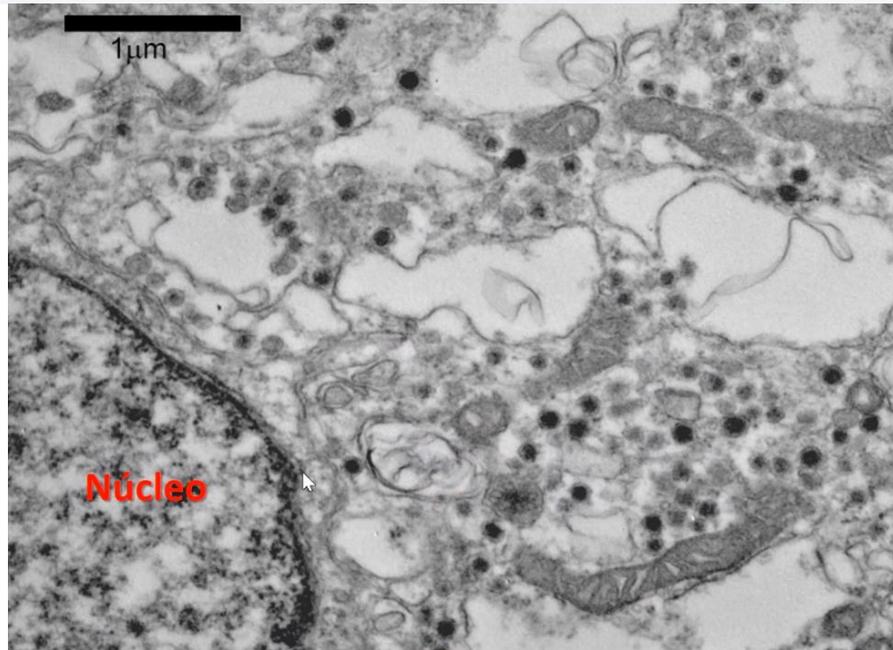
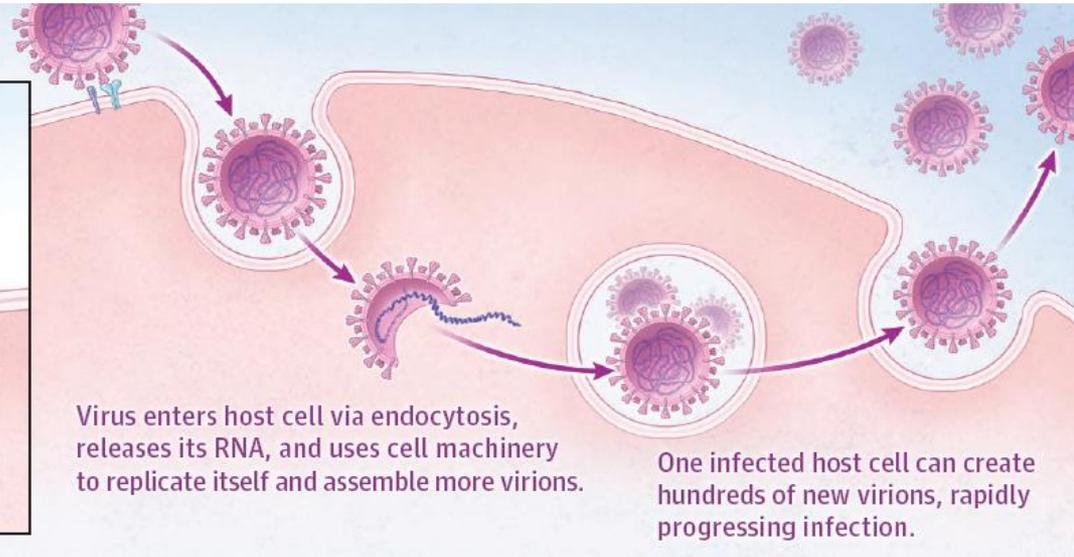
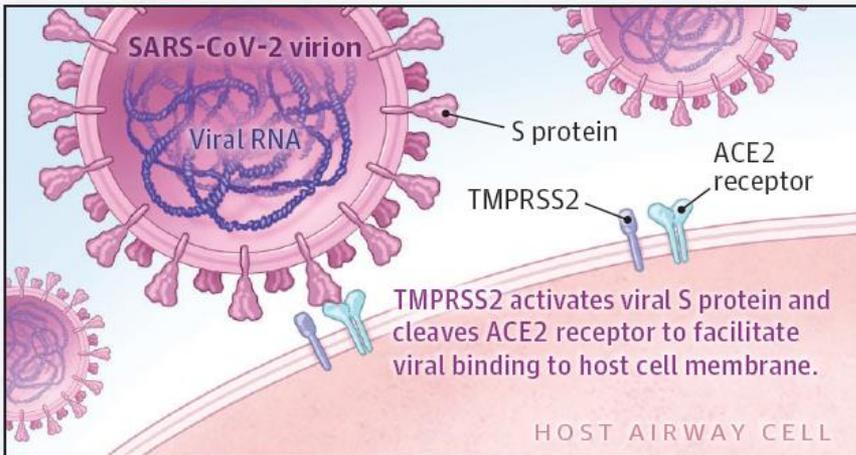


# COVID-19 – Visão Integrada

- Entrada → Vias aéreas superiores e inferiores
  - Destruição do epitélio das vias aéreas
  - Comprometimento do clearance muco-ciliar
- Atinge alvéolos
  - Destruição de pneumócitos tipo 1
    - Alteração da barreira alvéolo-capilar
    - Estímulo à inflamação
    - Edema com espessamento do septo
  - Destruição endotelial
    - Distúrbios da coagulação → trombooses
    - Disseminação → comprometimento sistêmico

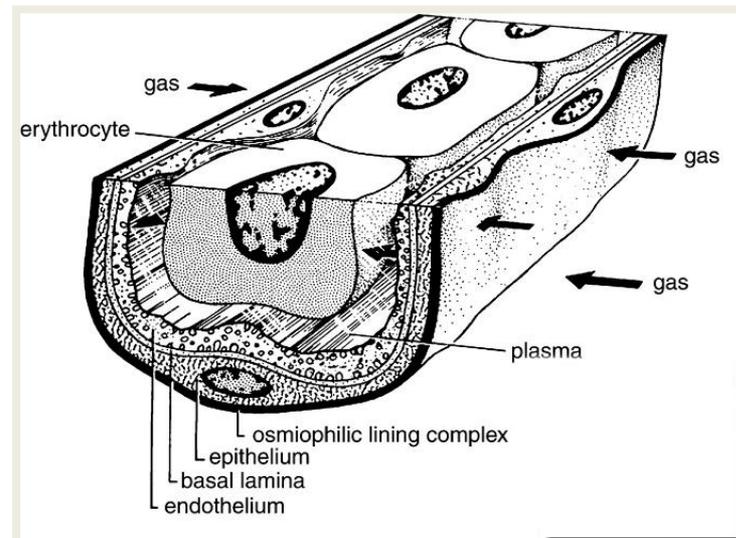
# COVID-19 – Infecção

A SARS-CoV-2 viral infection of host airway cells

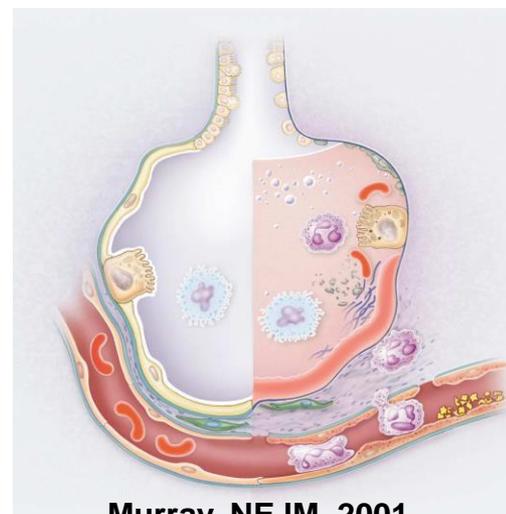


# COVID-19 – Visão Integrada

- Inflamação
  - Tempestade Inflamatória
  - Regulação do Sistema Imune
- Lesão Epitelial
  - Dano Alveolar Difuso
- Lesão Endotelial
  - Trombose



Maina et al. *Physiol. Rev.*, 2005



Murray, *NEJM*, 2001

# COVID-19 – Dano Epitelial – Pneumócitos

- Pneumócitos Tipo 1
  - Perda da proteção mecânica
  - Alteração da Barreira Alvéolo-Capilar
  - Dano Alveolar Difuso – Fase Exsudativa

## Histopathology



*Histopathology* 2020, 77, 186–197. DOI: 10.1111/his.14160

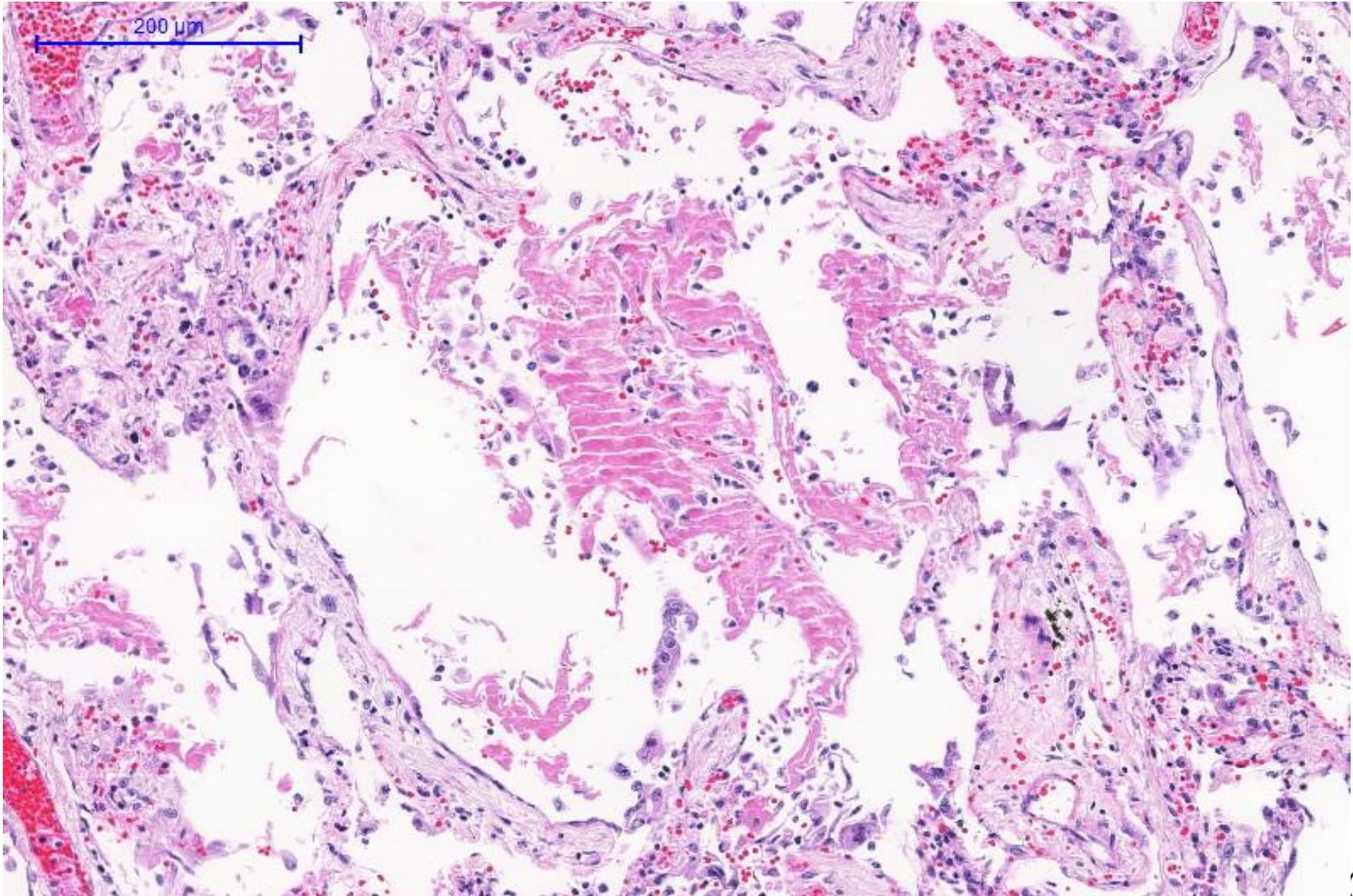
### Pulmonary and systemic involvement in COVID-19 patients assessed with ultrasound-guided minimally invasive autopsy

Amaro N Duarte-Neto,<sup>1</sup>  Renata A A Monteiro,<sup>1</sup> Luiz F F da Silva,<sup>1,2</sup> Denise M A C Malheiros,<sup>1</sup> Ellen P de Oliveira,<sup>3</sup> Jair Theodoro-Filho,<sup>1</sup> João R R Pinho,<sup>4</sup> Michele S Gomes-Gouvêa,<sup>4</sup> Ana P M Salles,<sup>4</sup> Ilka R S de Oliveira,<sup>5</sup> Thais Mauad,<sup>1</sup> Paulo H N Saldiva<sup>1</sup> & Marisa Dolhnikoff<sup>1</sup> 

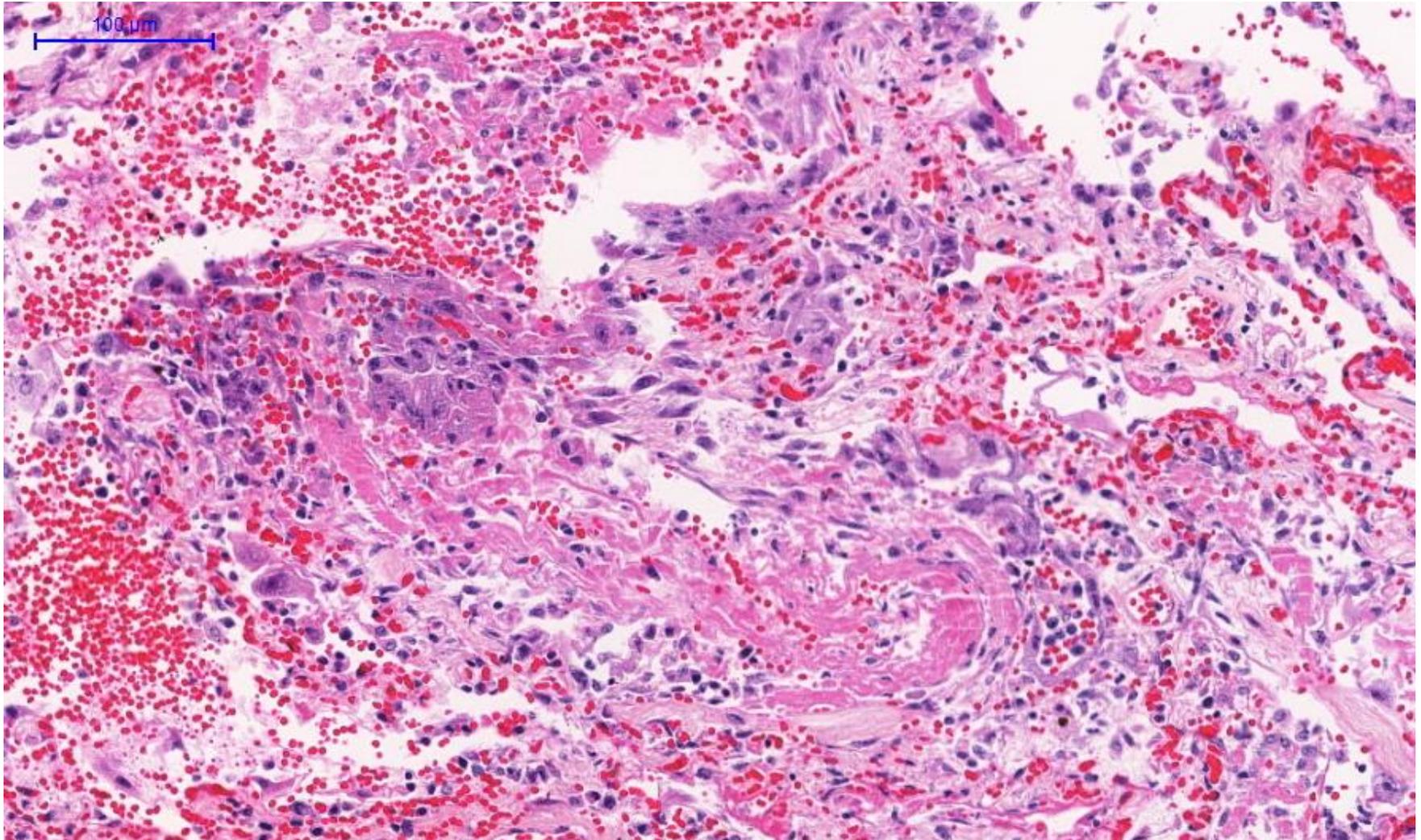
<sup>1</sup>BIAS—Brazilian Image Autopsy Study Group, Departamento de Patologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, <sup>2</sup>Serviço de Verificação de Óbitos da Capital, Universidade de São Paulo, São Paulo, Brazil, <sup>3</sup>Departamento de Cardiopneumologia, Instituto do Coração, São Paulo, Brazil, <sup>4</sup>Departamento de Gastroenterologia, LIM-07, São Paulo, Brazil, and <sup>5</sup>Departamento de Radiologia e Oncologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Date of submission 1 May 2020  
Accepted for publication 18 May 2020  
Published online Article Accepted 22 May 2020

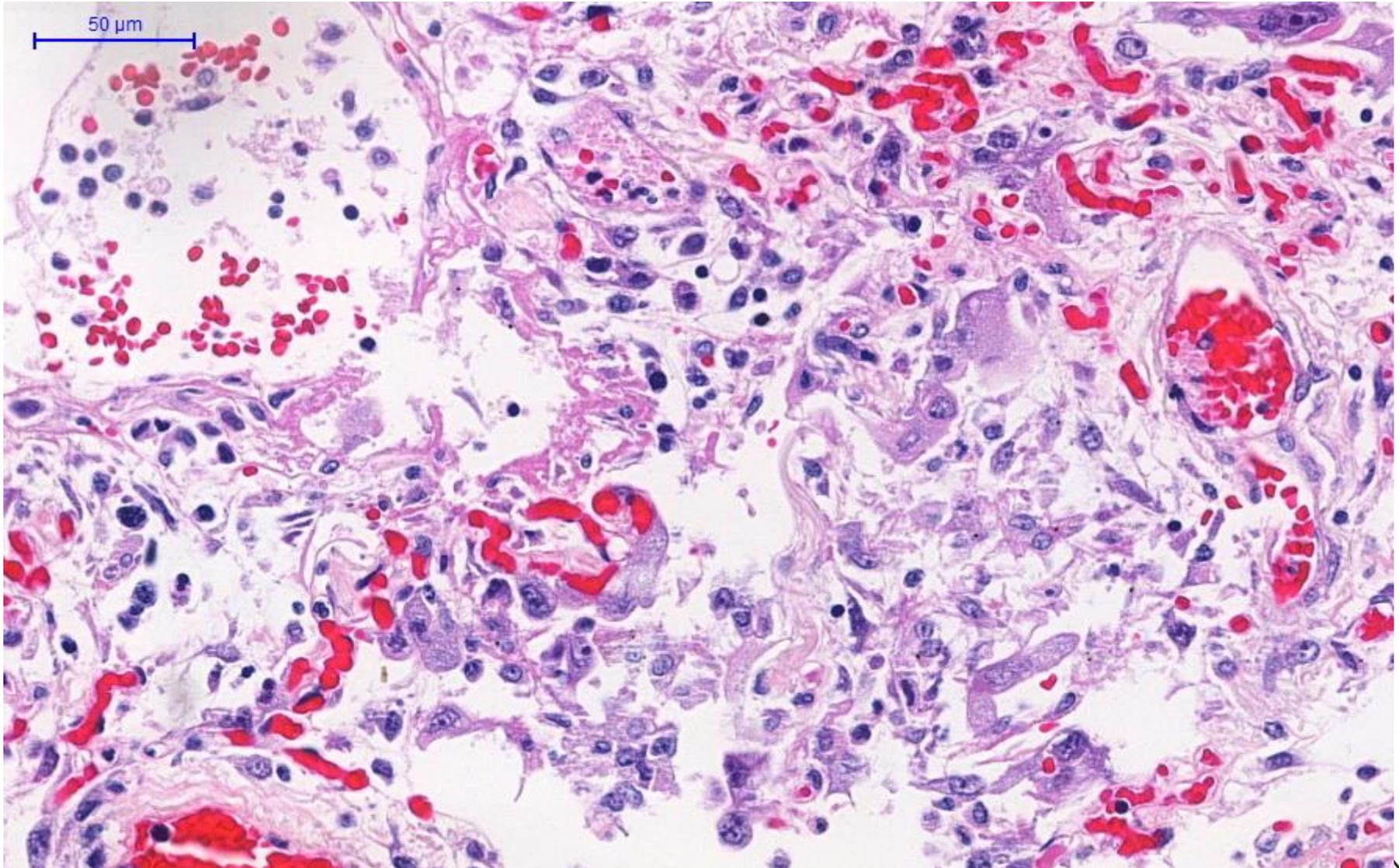
# COVID-19 – Dano Epitelial – Pneumócitos



# COVID-19 – Dano Epitelial – Pneumócitos



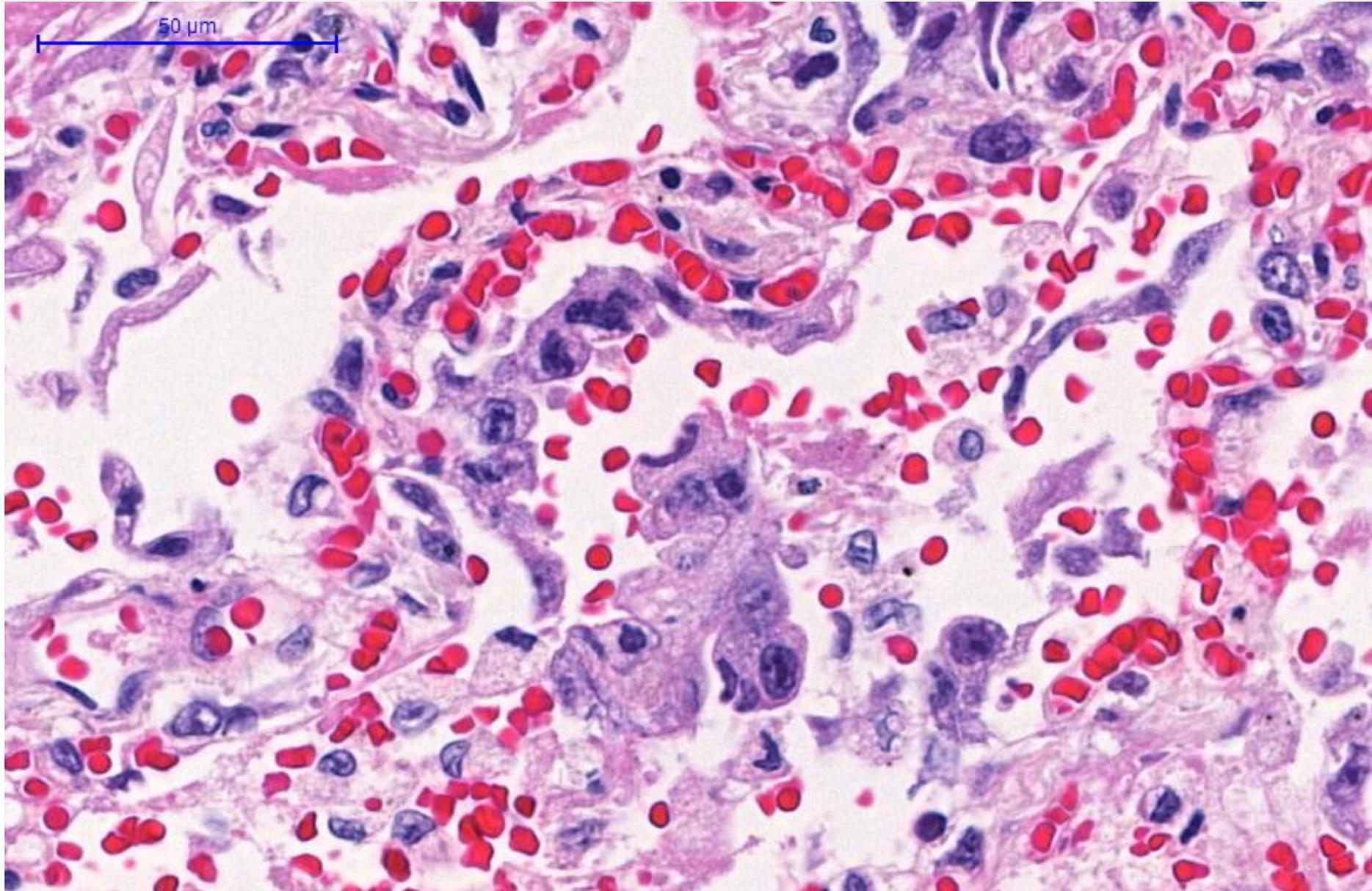
# COVID-19 – Dano Epitelial – Pneumócitos



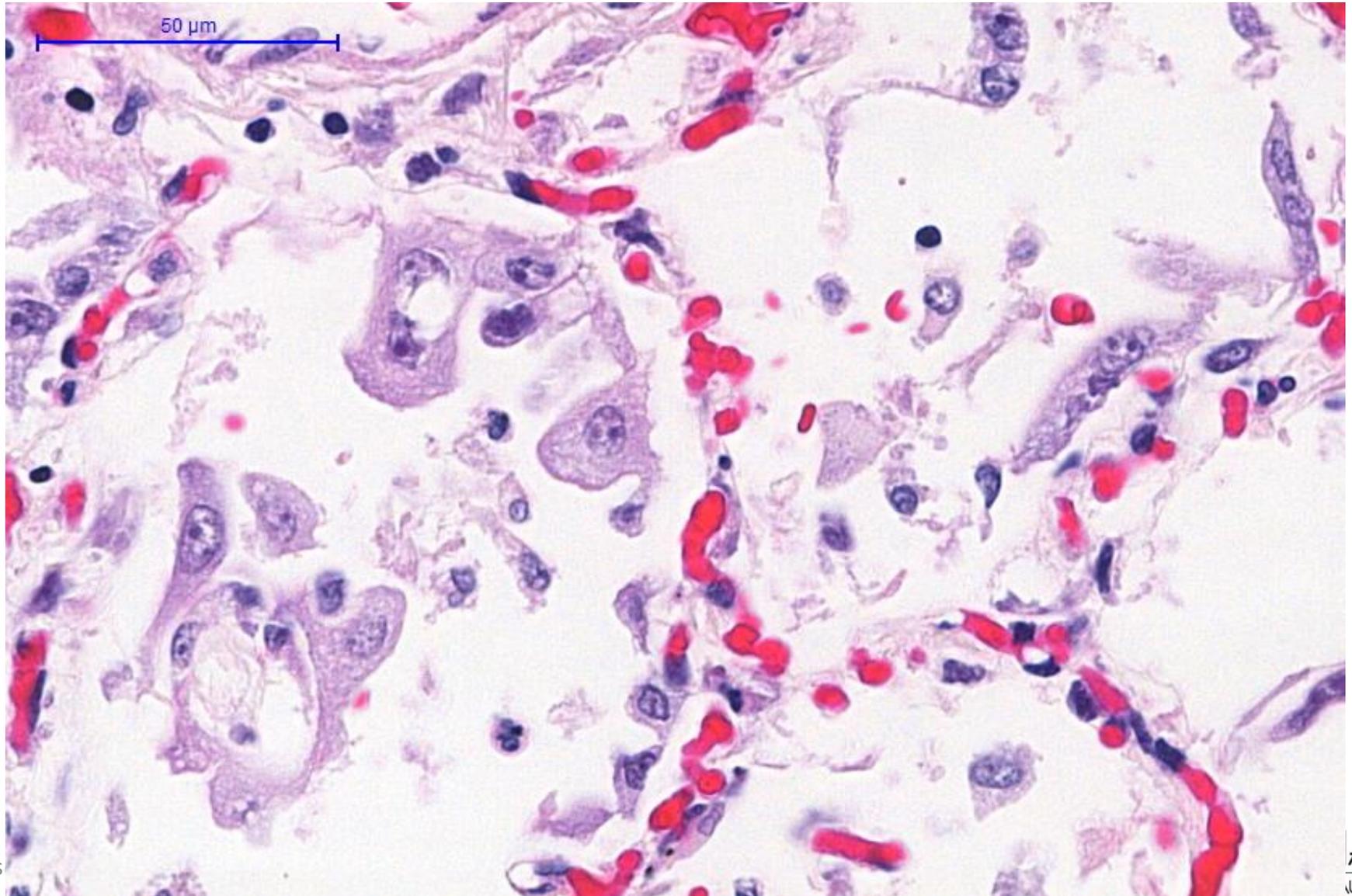
# COVID-19 – Dano Epitelial – Pneumócitos

- Pneumócitos Tipo 2
  - Alteração da Produção de Surfactante
  - Proliferação reacional / Reatividade
  - Efeitos citopáticos

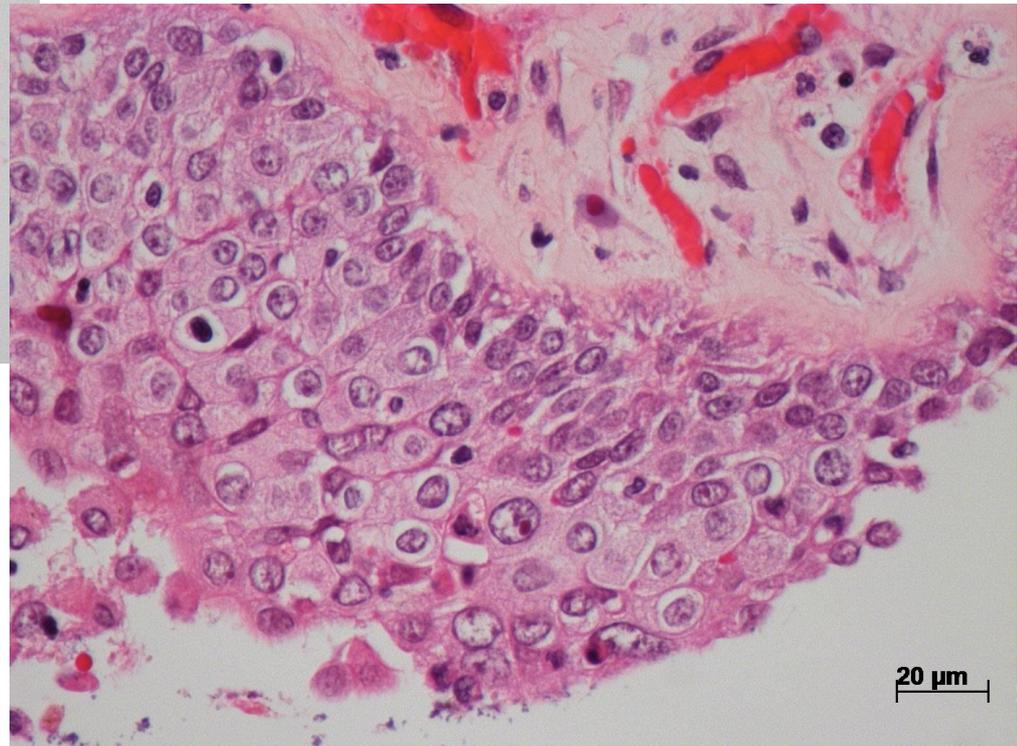
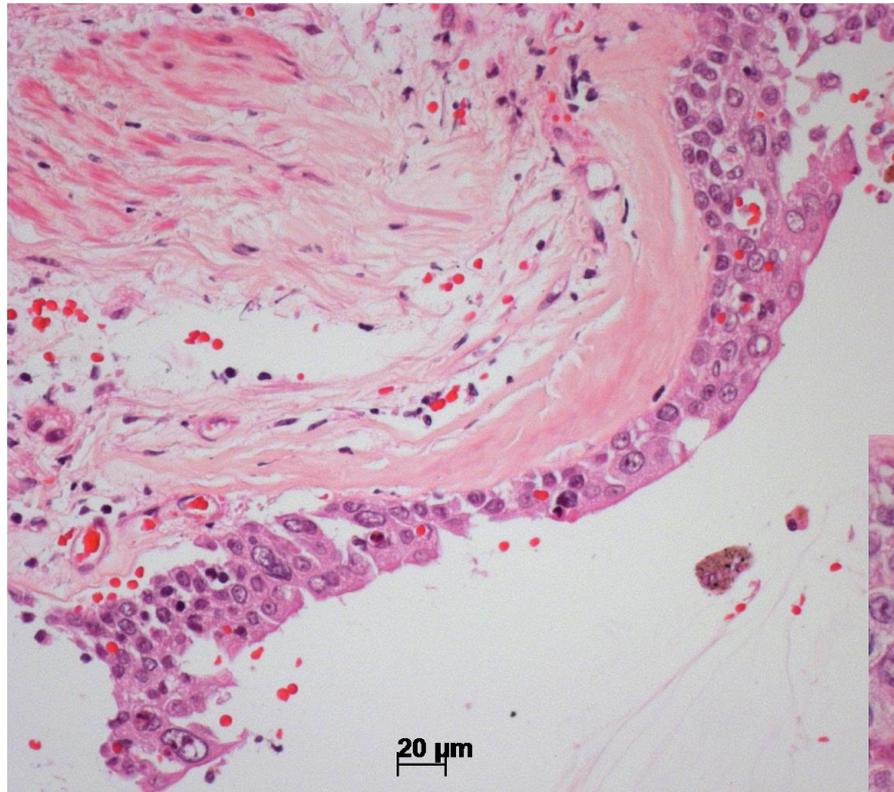
# COVID-19 – Dano Epitelial – Pneumócitos



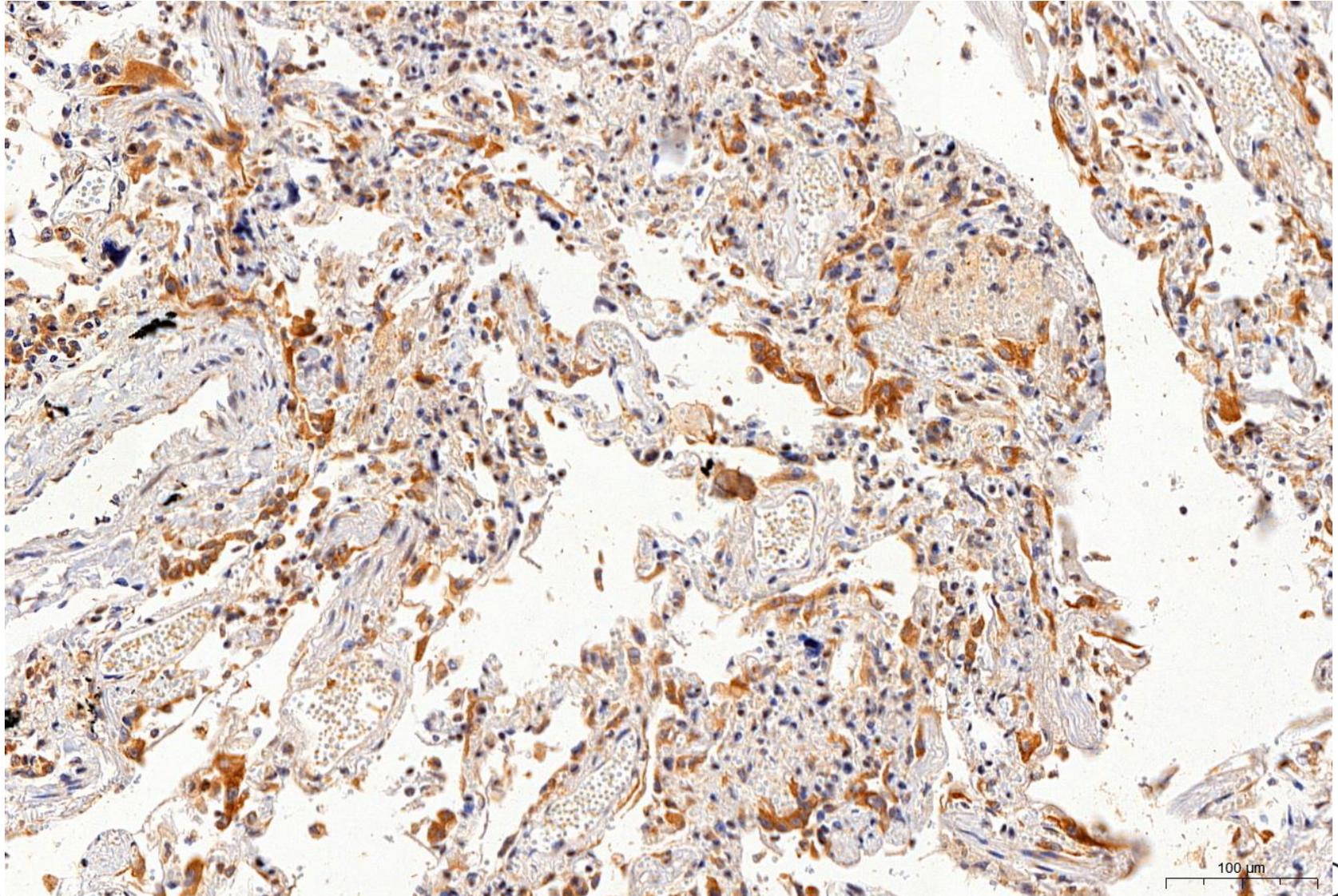
# COVID-19 – Dano Epitelial – Pneumócitos



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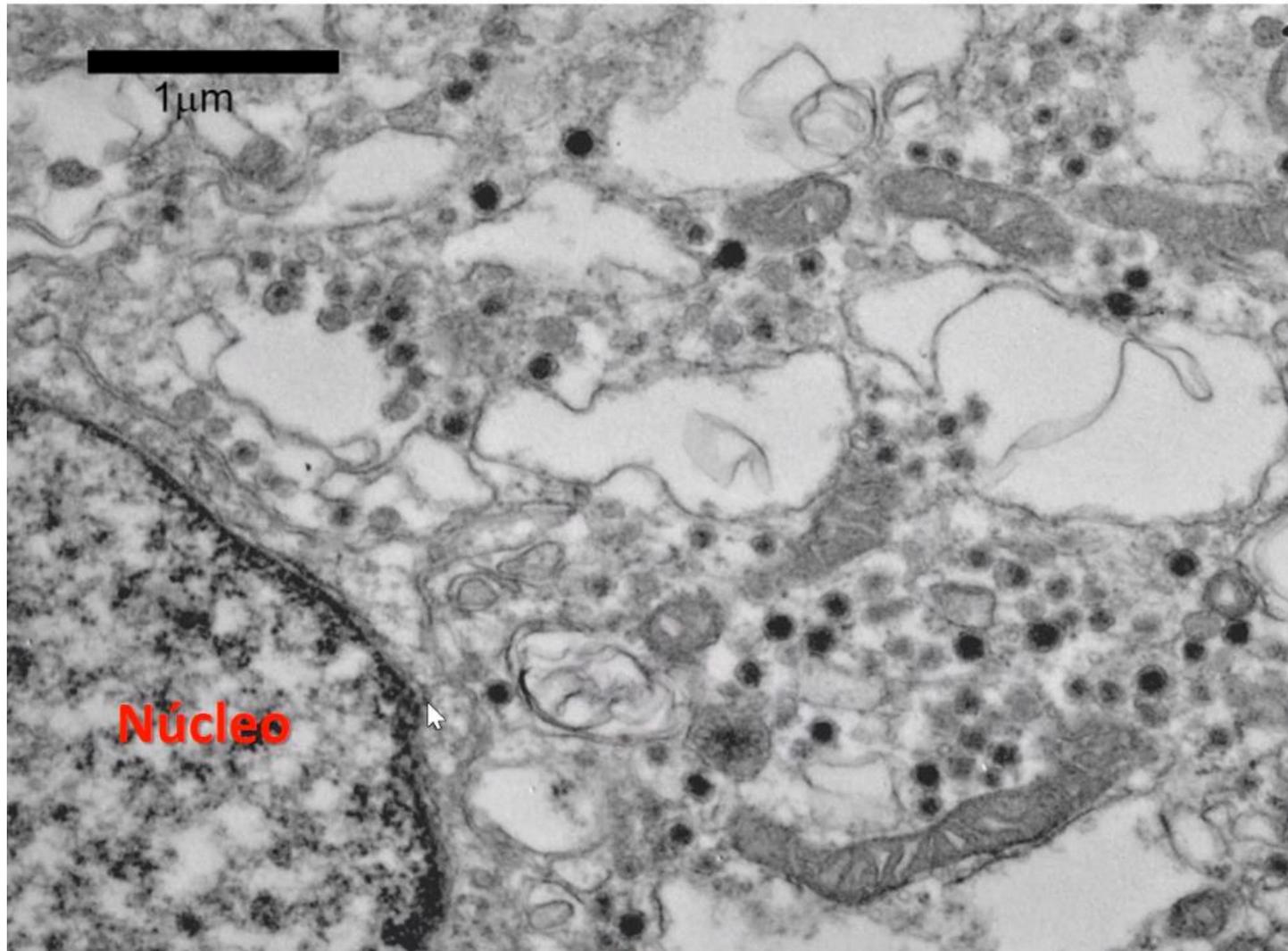


# COVID-19 – Dano Epitelial – Pneumócitos

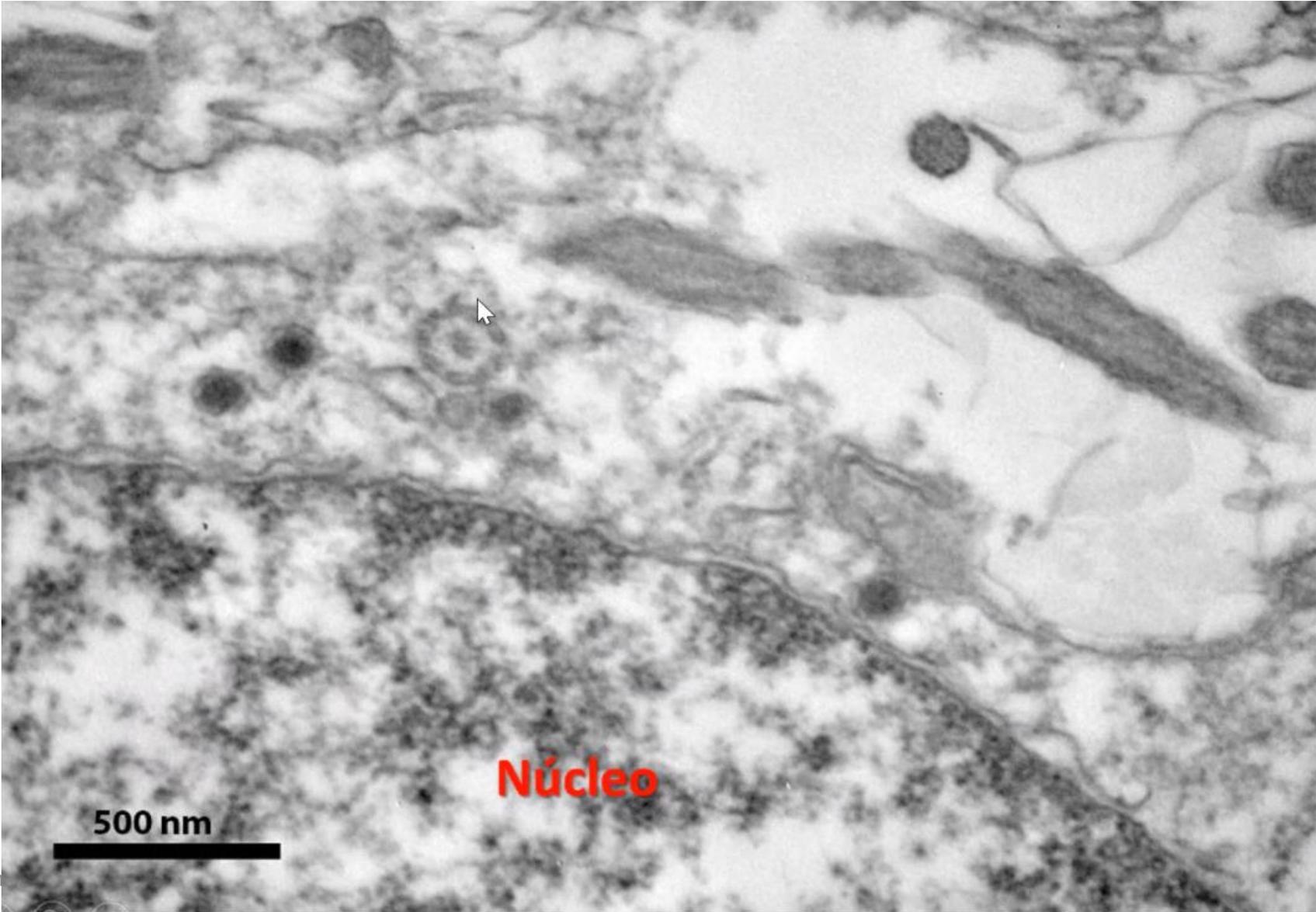


# COVID-19 – Dano Epitelial – Ultraestrutura

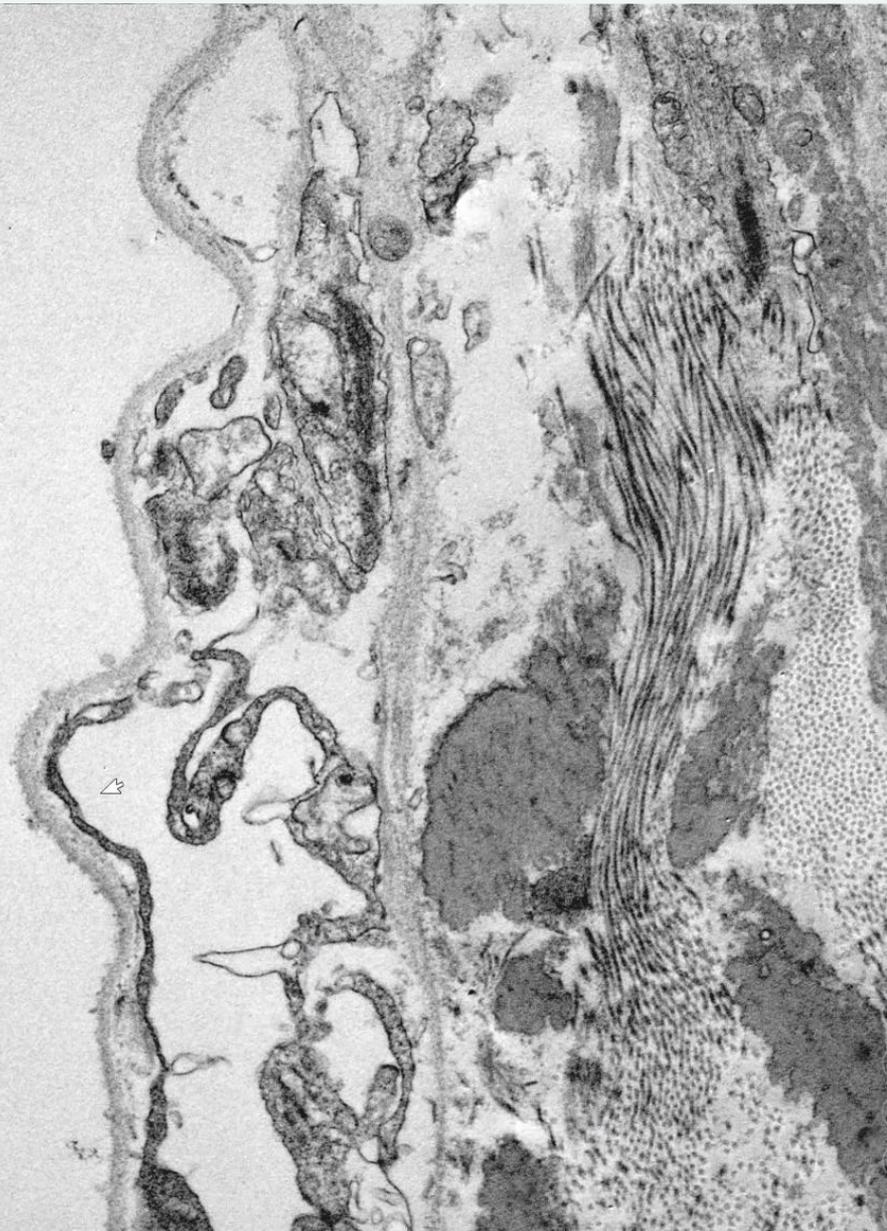
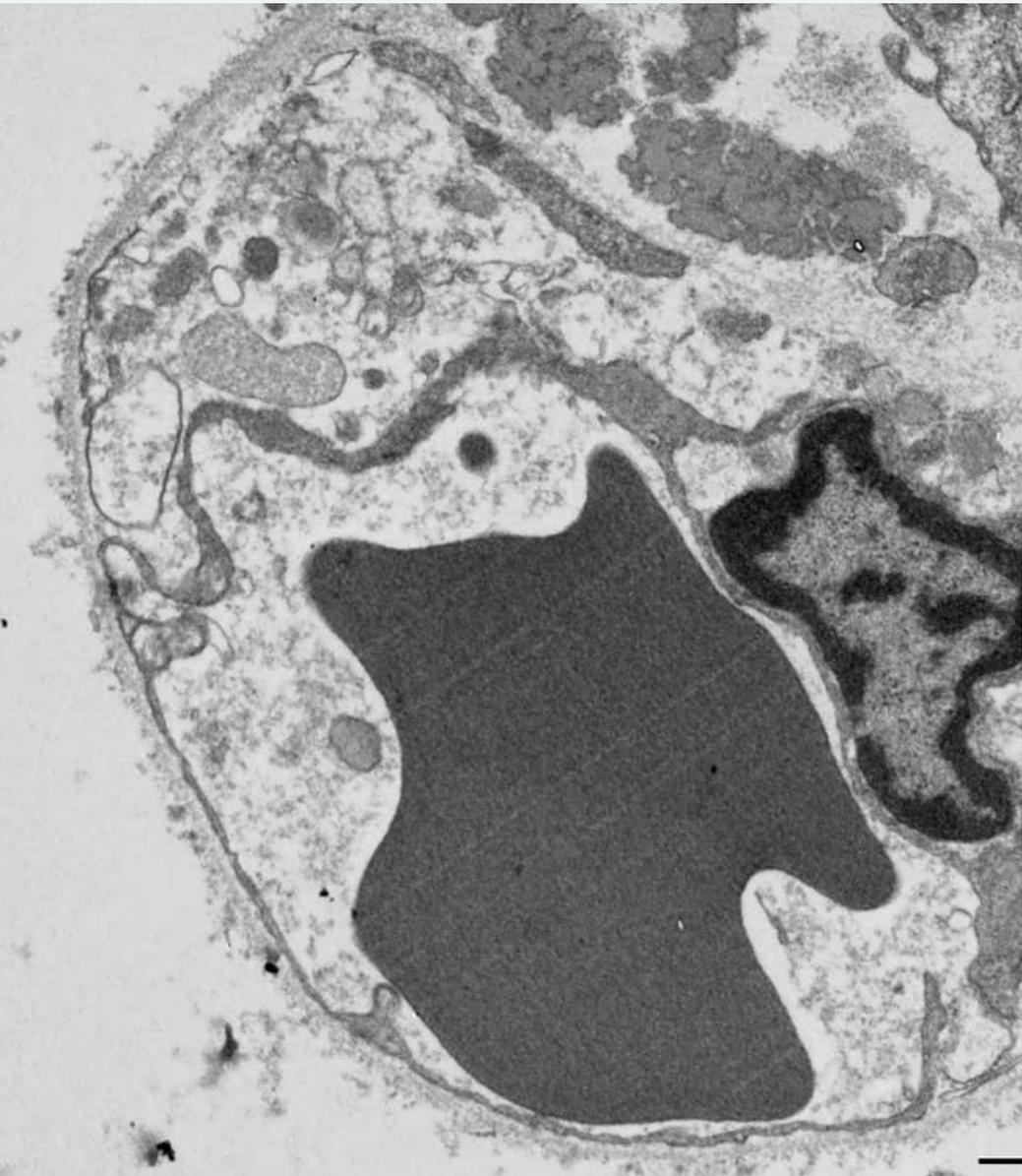
## Célula caliciforme



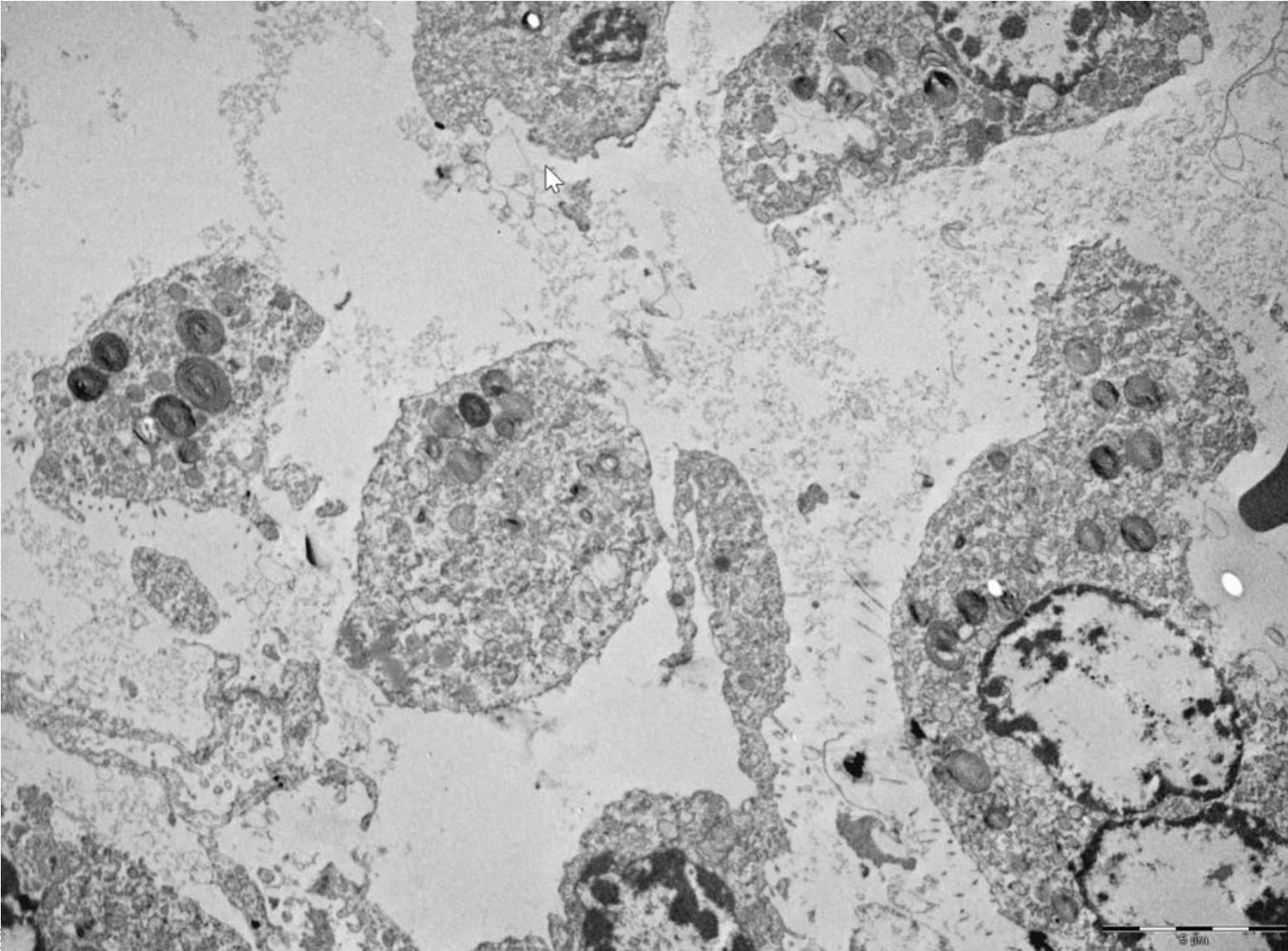
# COVID-19 – Dano Epitelial – Ultraestrutura



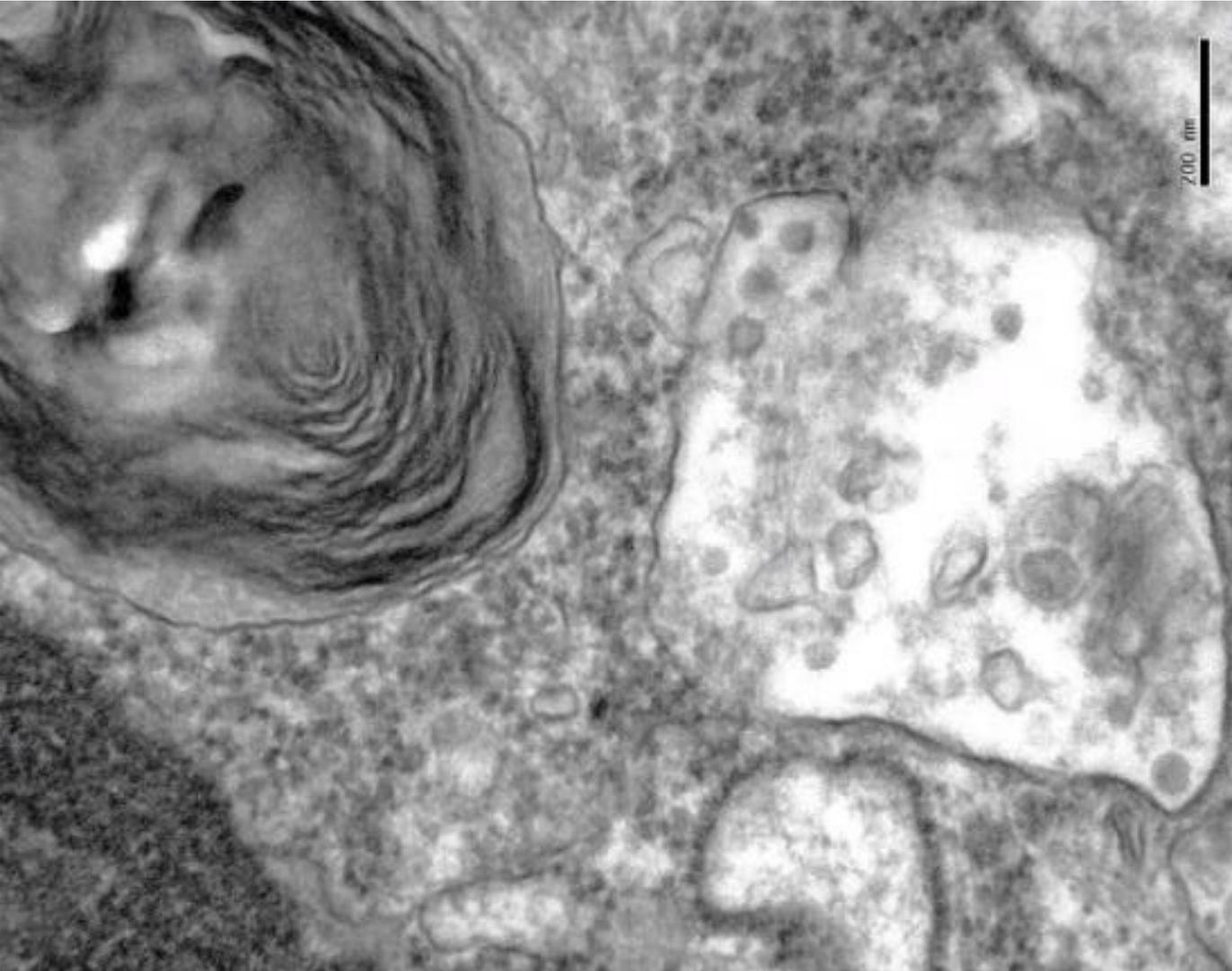
# COVID-19 – Dano Epitelial – Ultraestrutura



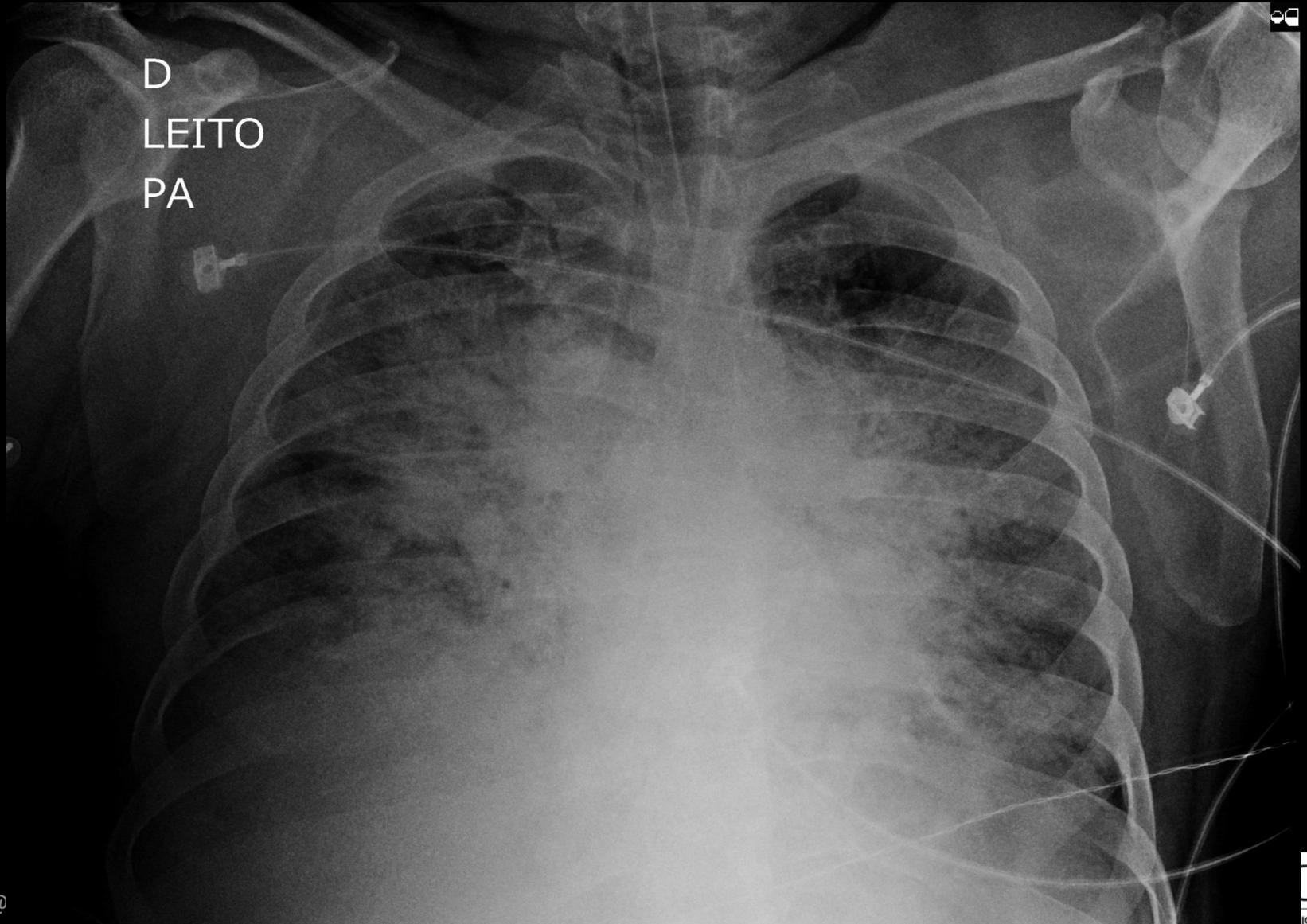
# COVID-19 – Dano Epitelial – Ultraestrutura



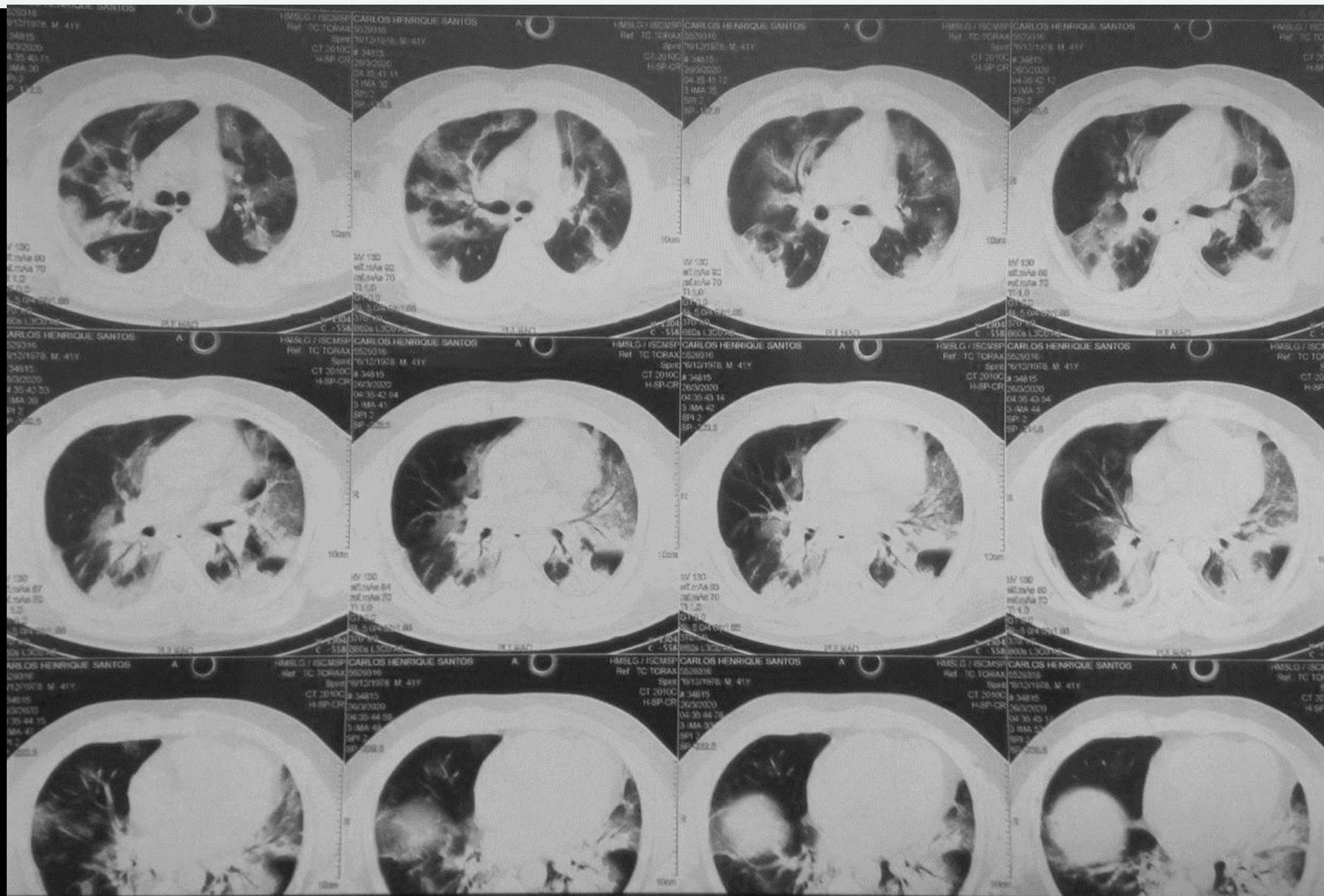
# COVID-19 – Dano Epitelial – Ultraestrutura



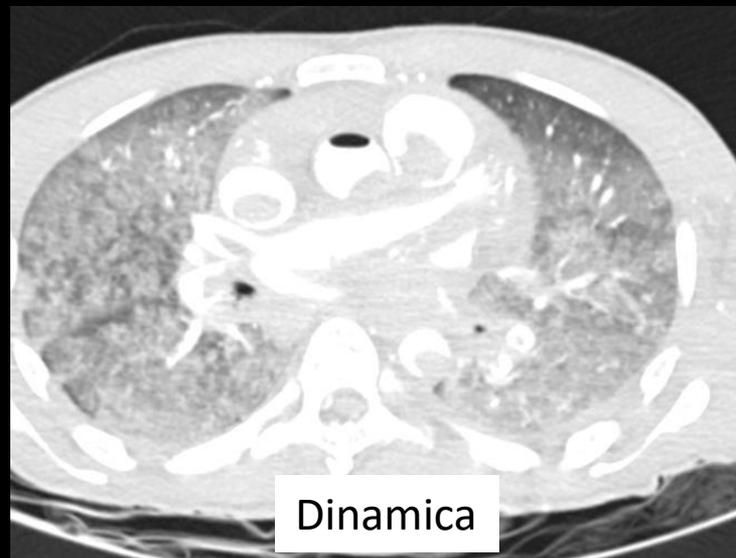
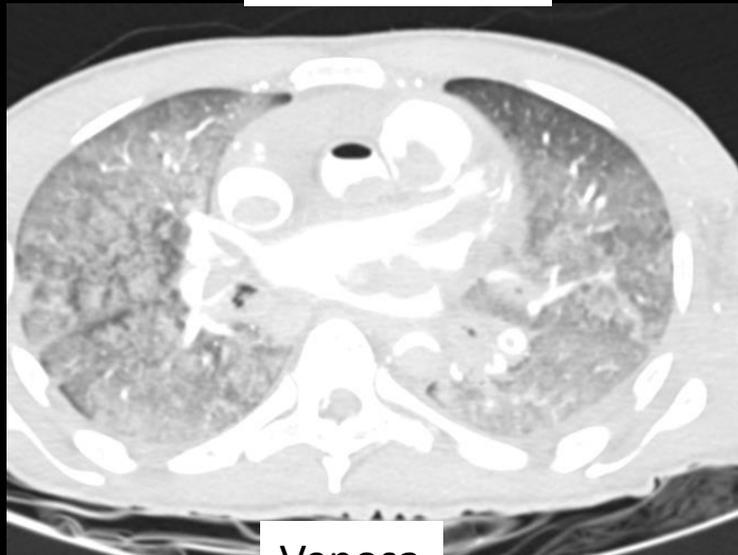
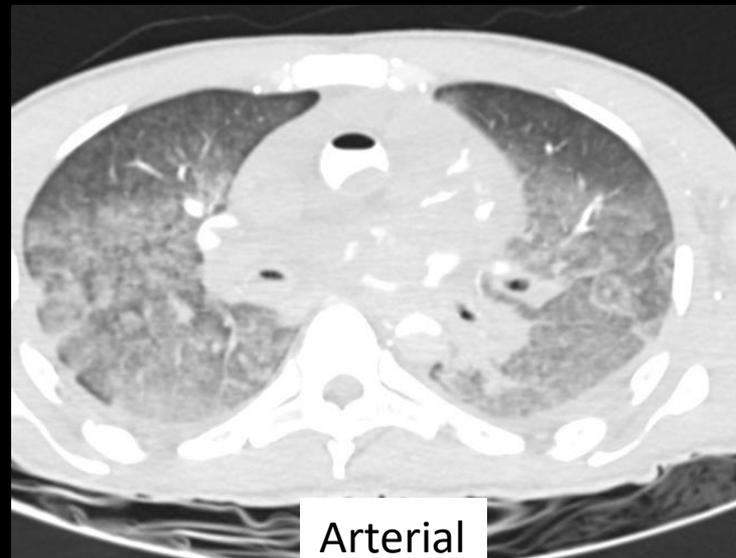
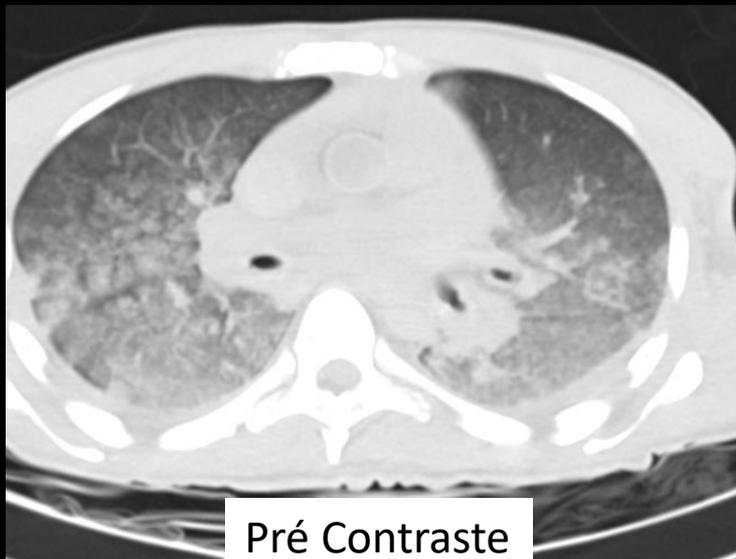
# COVID-19 – Dano Epitelial – Como isso aparece?



# COVID-19 – Dano Epitelial – Como isso aparece?

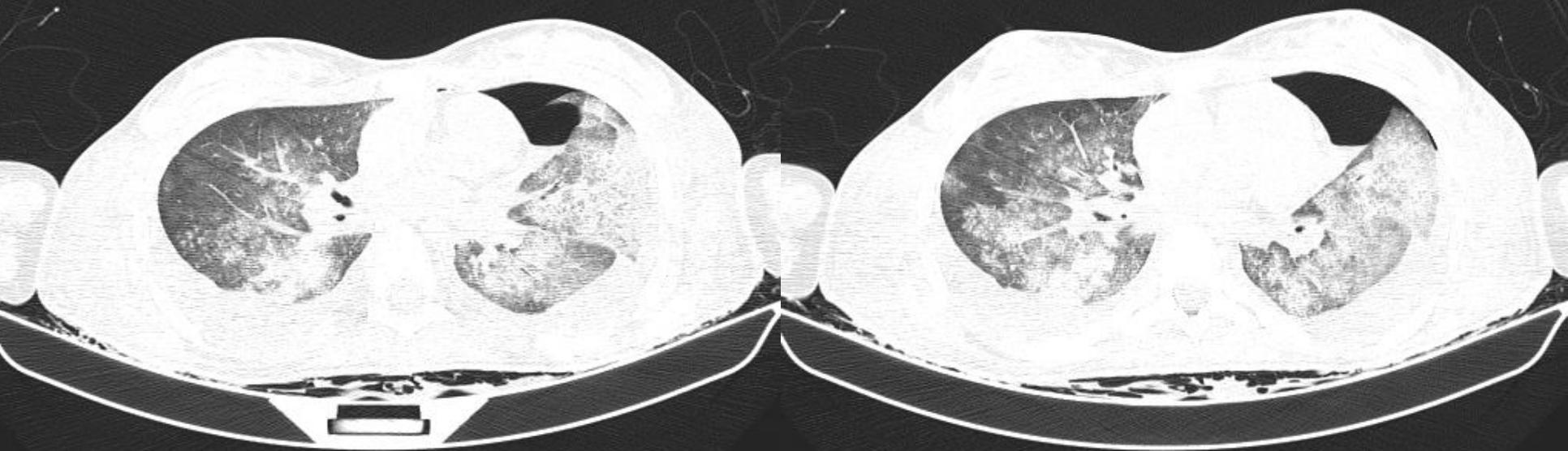


# COVID-19 – Dano Epitelial – Como isso aparece?



# COVID-19 – Dano Epitelial – Como isso aparece?

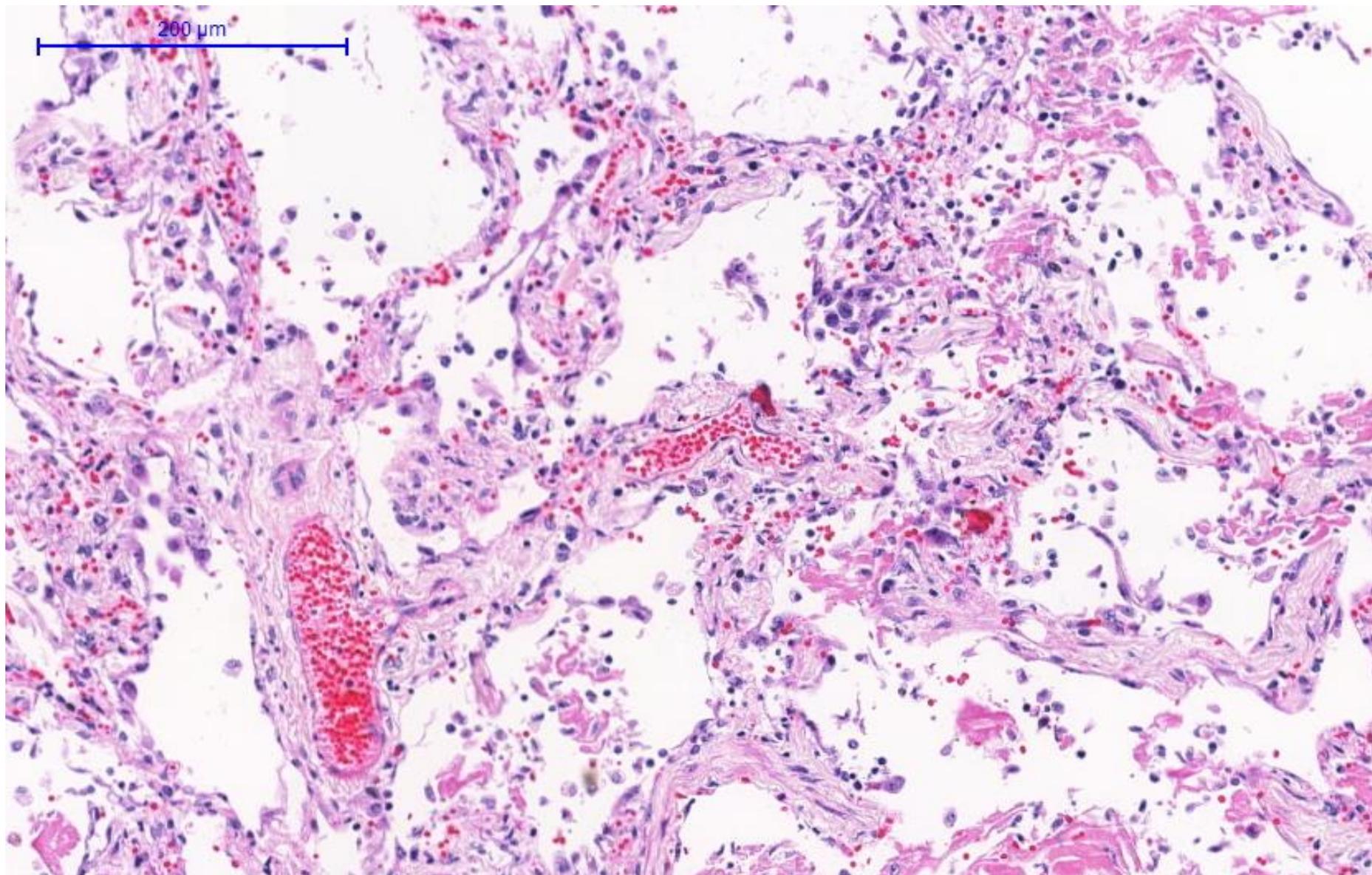
TC pós morte



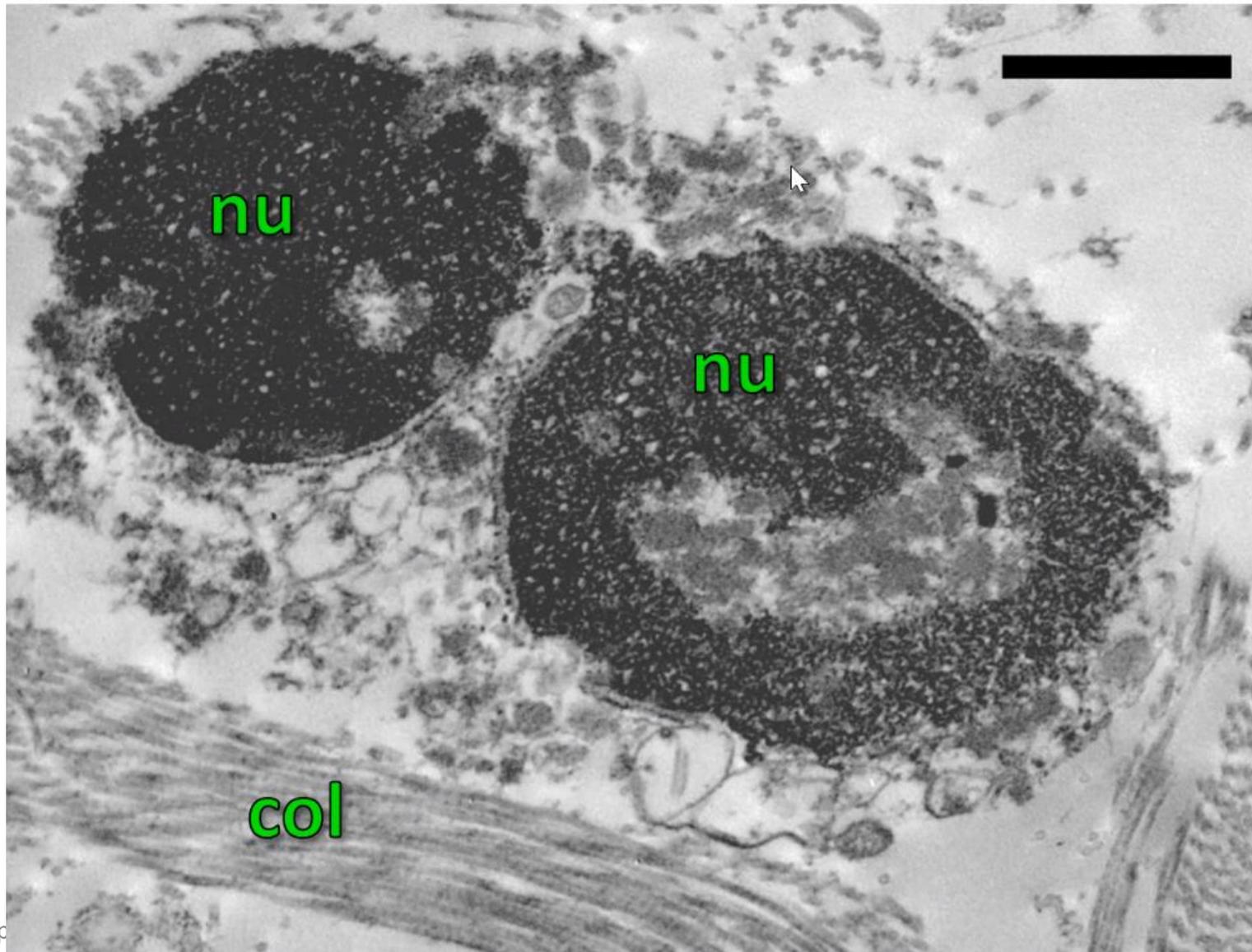
# COVID-19 – Inflamação

- Padrão de resposta a infecções virais
  - Fase Inicial – Imunidade Inata –
    - Citocinas e Neutrófilos
    - NET (Neutrophyl Extracellular Trap)
  - Desenvolvimento da Imunidade Adaptativa
    - Resposta de células T
    - Infiltrado de polimorfonucleares
  - Regulação do Sistema Imune
  - Reparo Tecidual

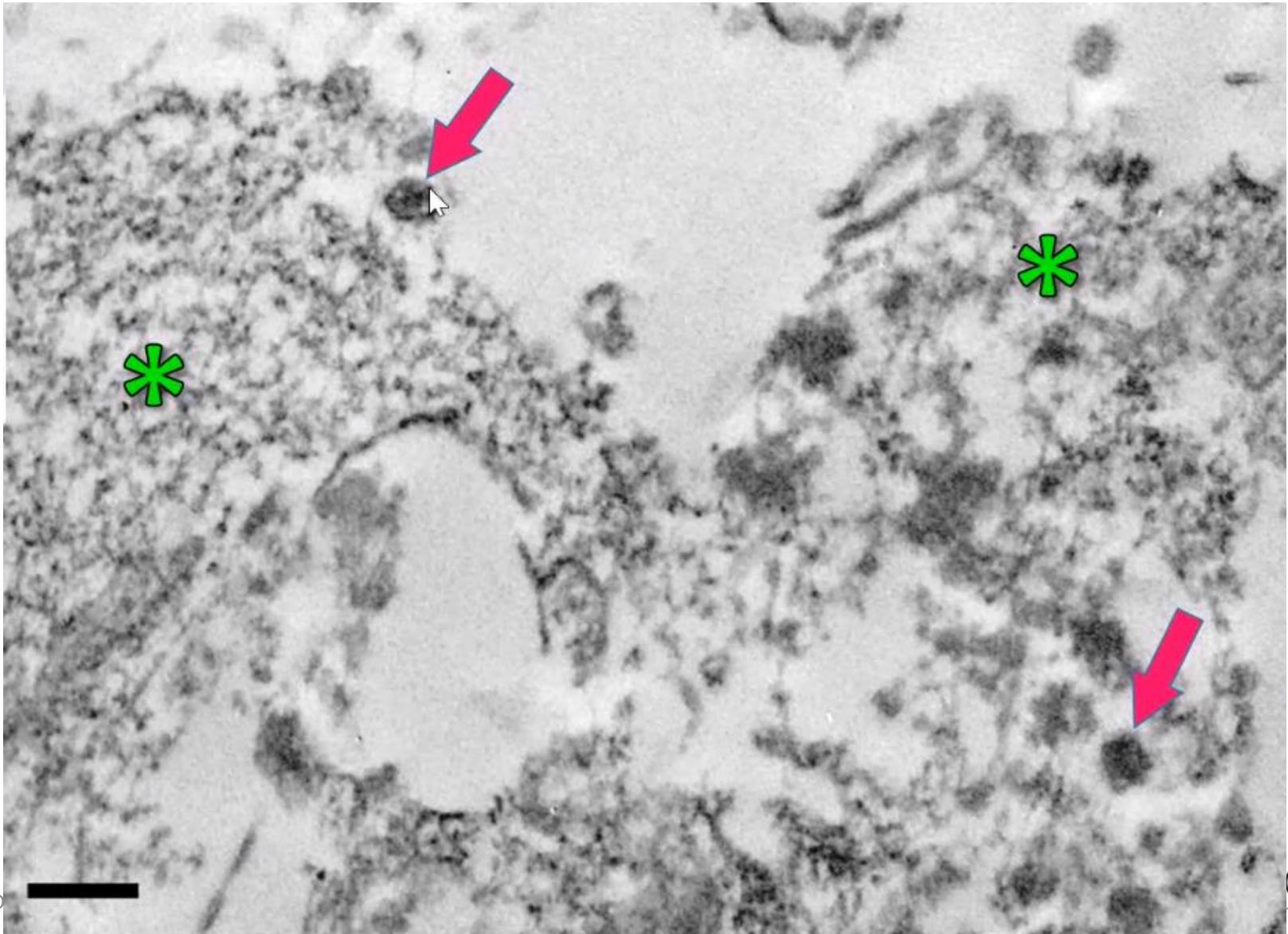
# COVID-19 – Inflamação



# COVID-19 – Inflamação – Ultraestrutura



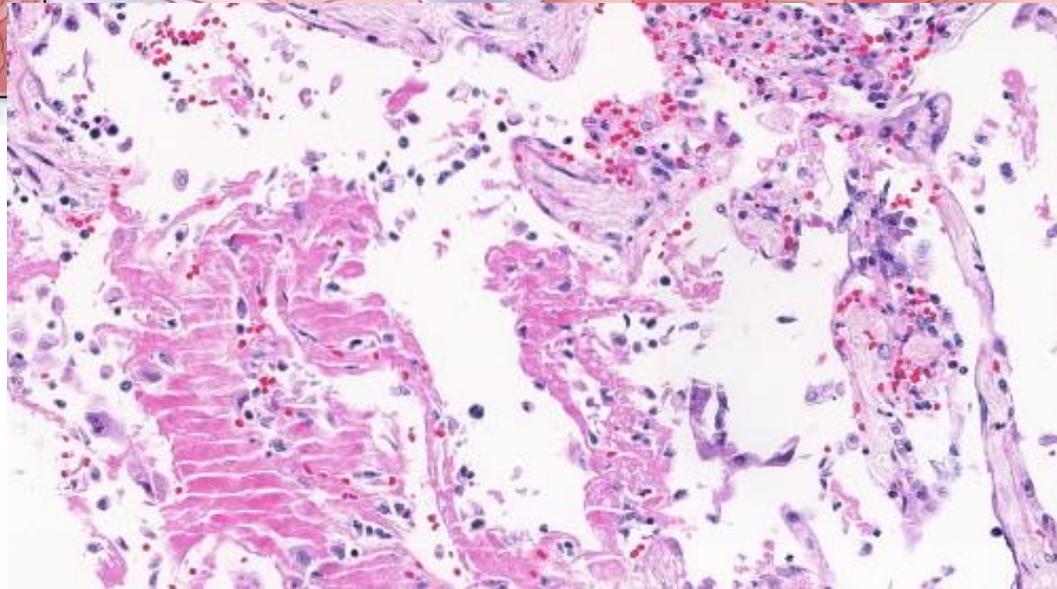
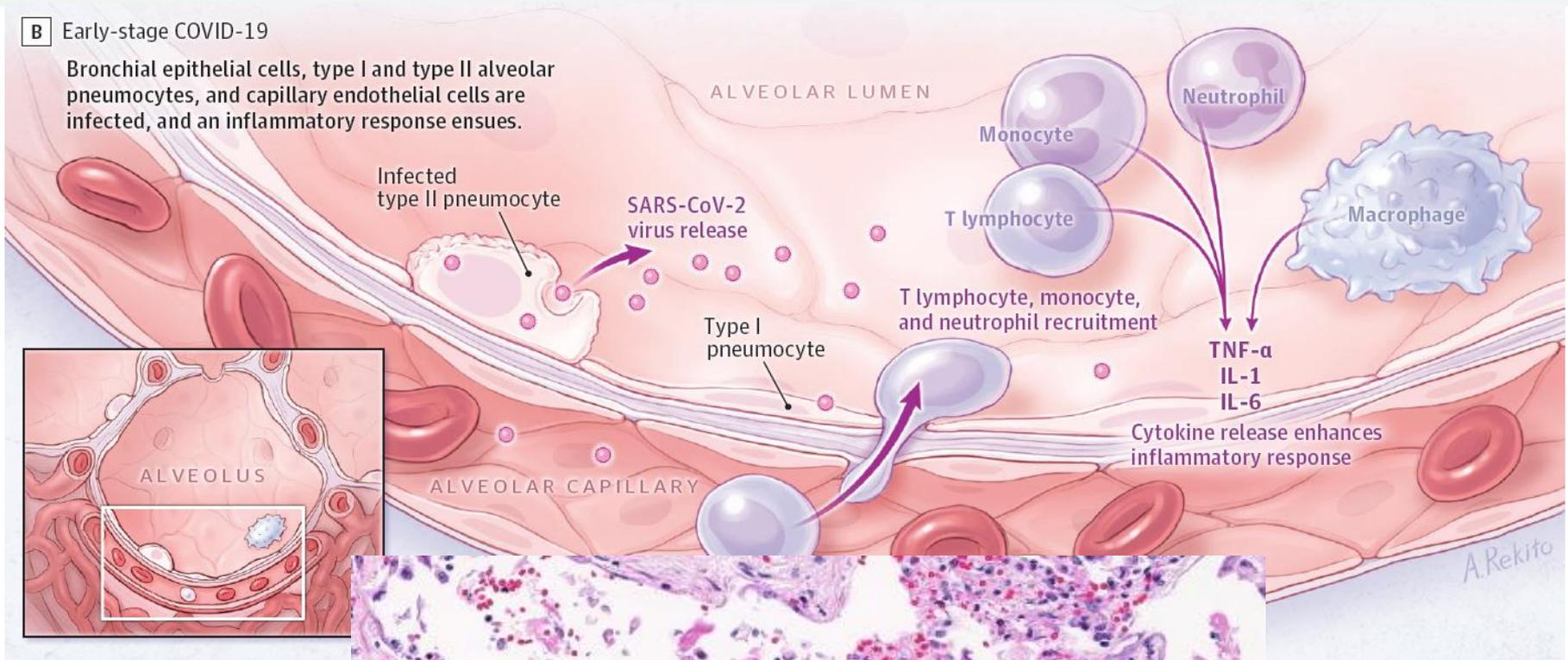
# COVID-19 – Inflamação – Ultraestrutura



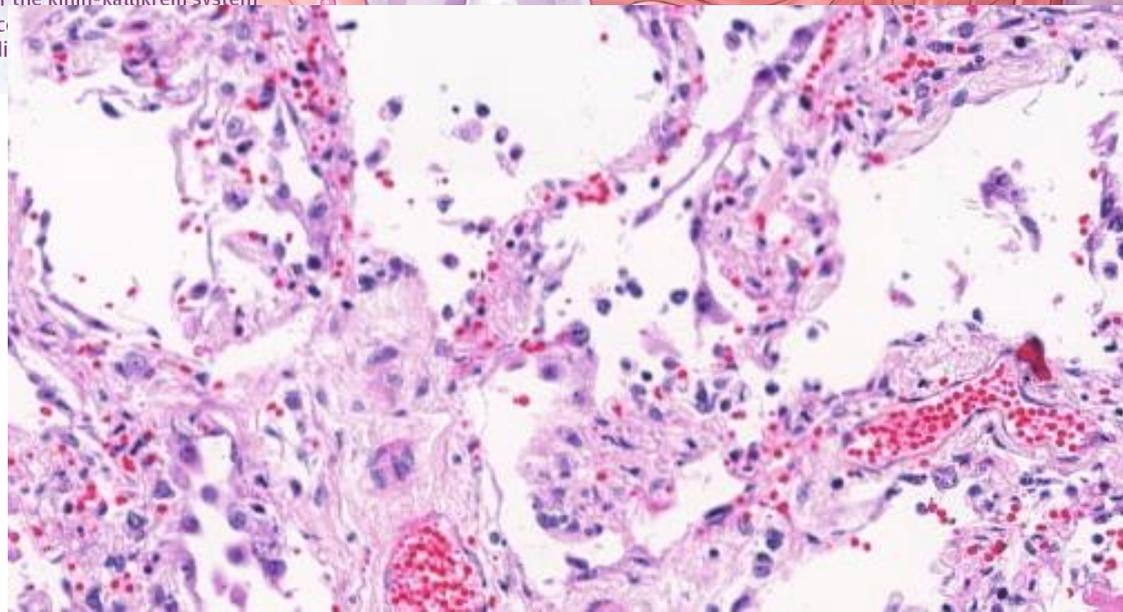
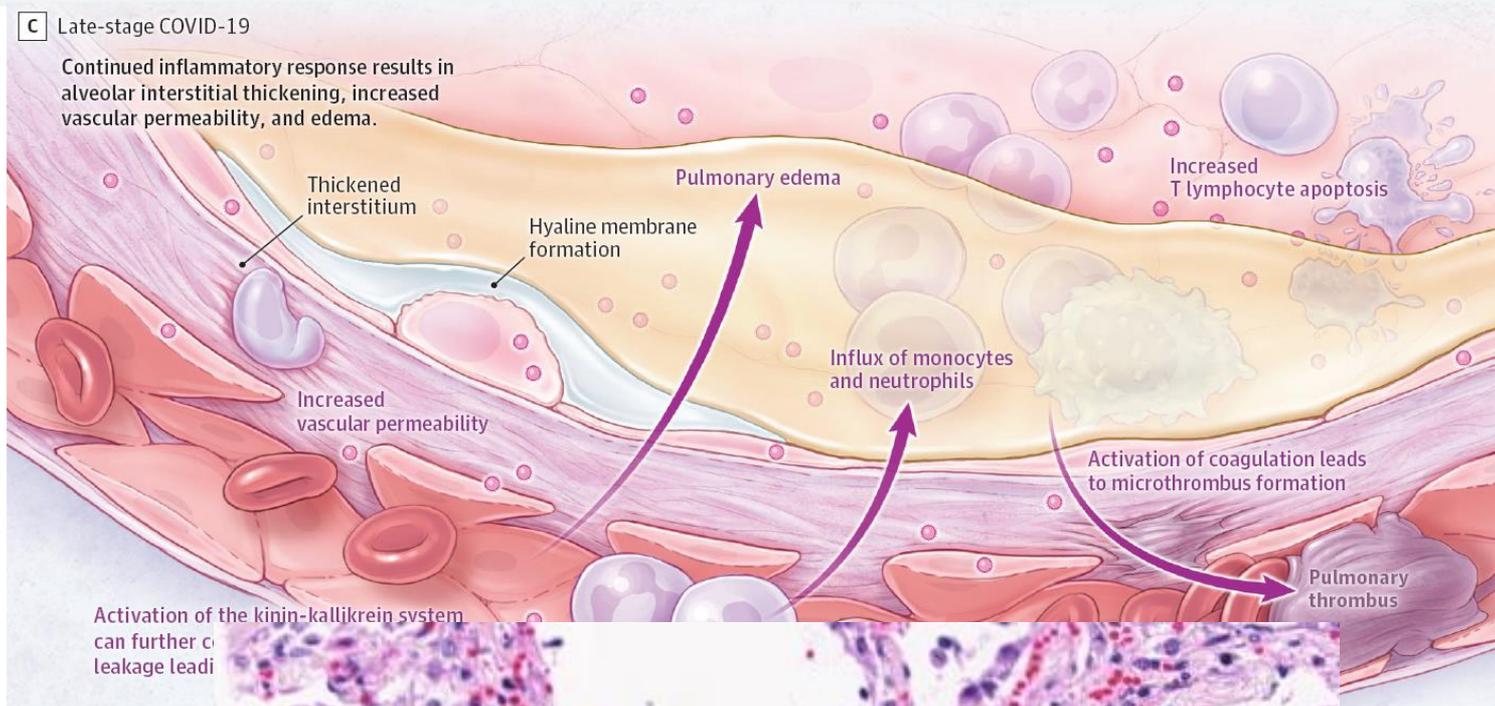
# COVID-19 – Fase Exsudativa – Inicial

## B Early-stage COVID-19

Bronchial epithelial cells, type I and type II alveolar pneumocytes, and capillary endothelial cells are infected, and an inflammatory response ensues.



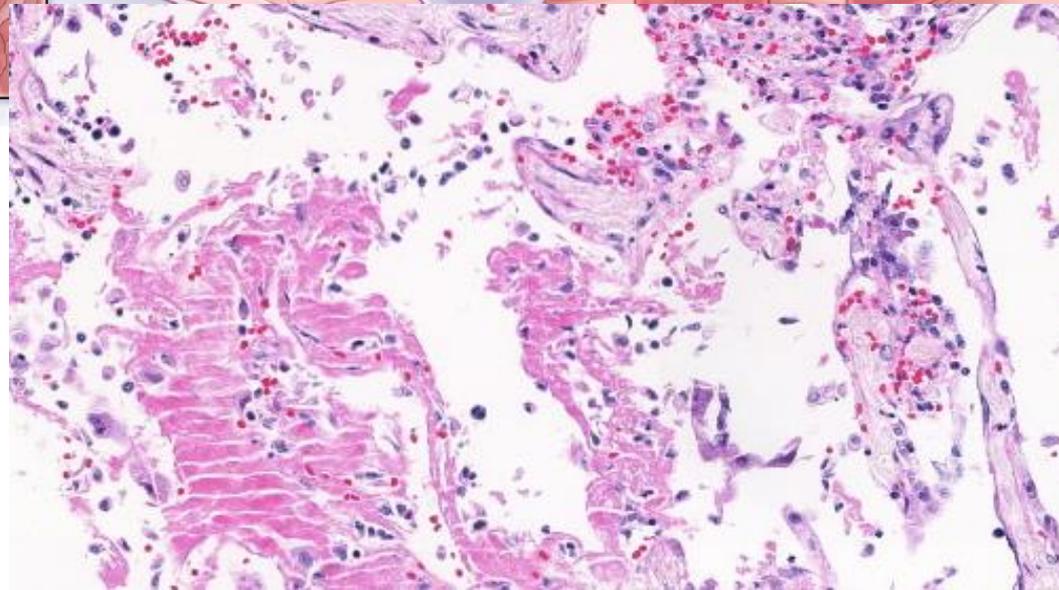
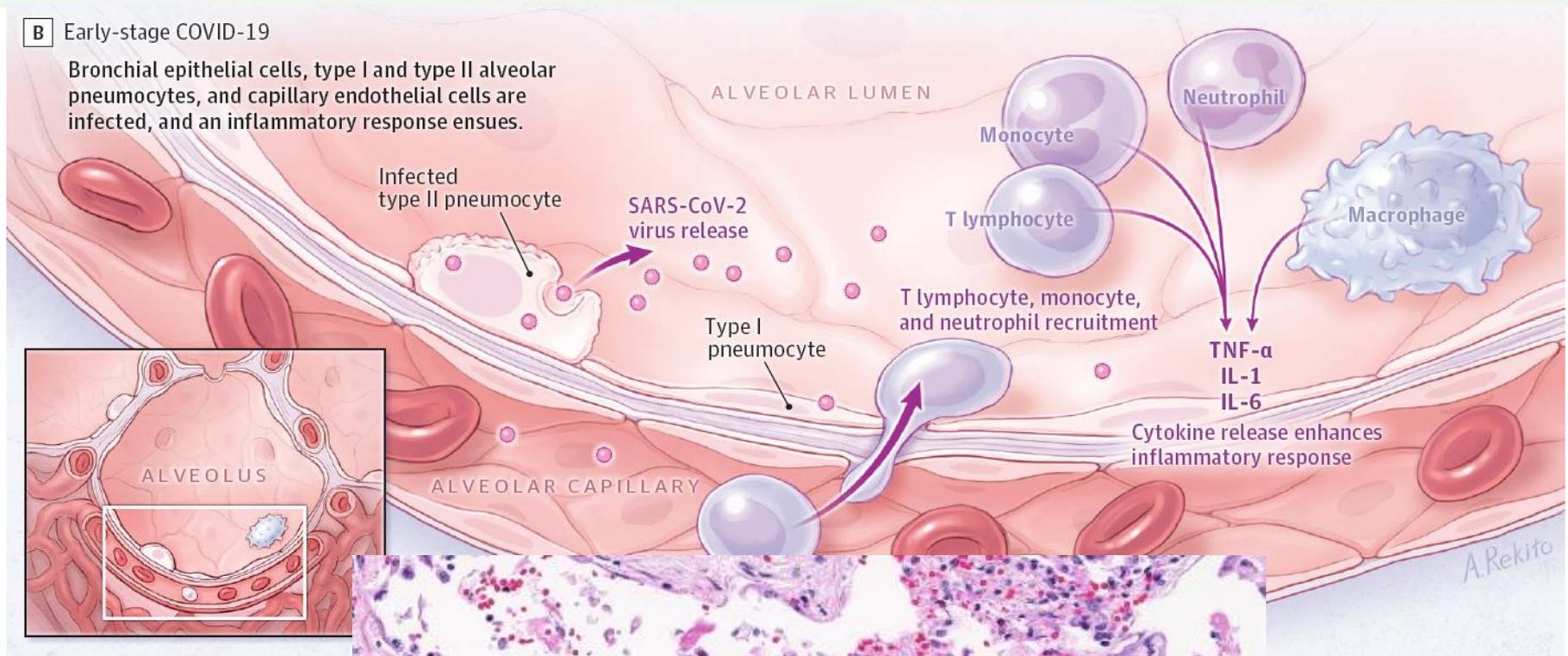
# COVID-19 – Fase Exsudativa - Evolução



# COVID-19 – Fase Exudativa – Inicial

## B Early-stage COVID-19

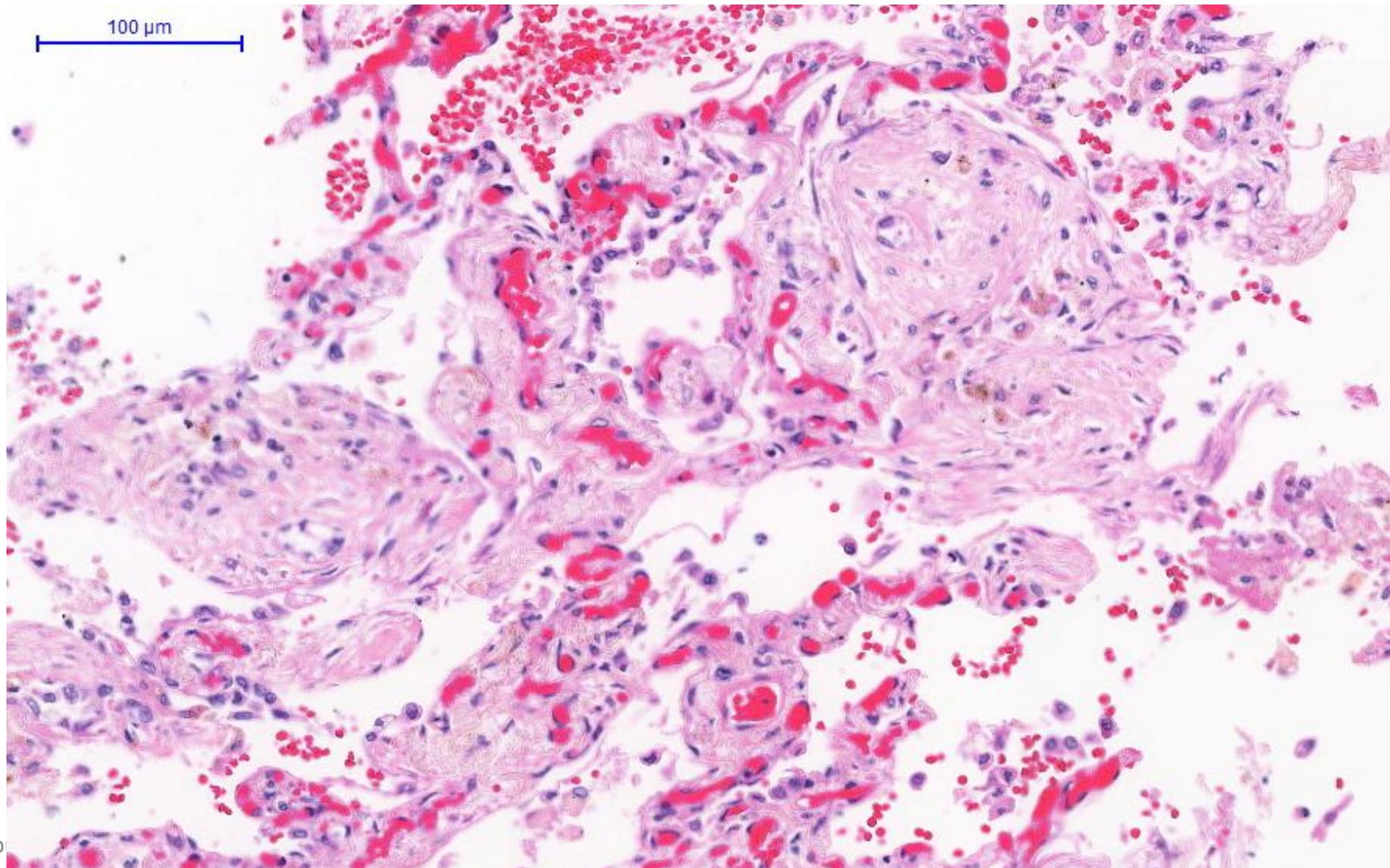
Bronchial epithelial cells, type I and type II alveolar pneumocytes, and capillary endothelial cells are infected, and an inflammatory response ensues.



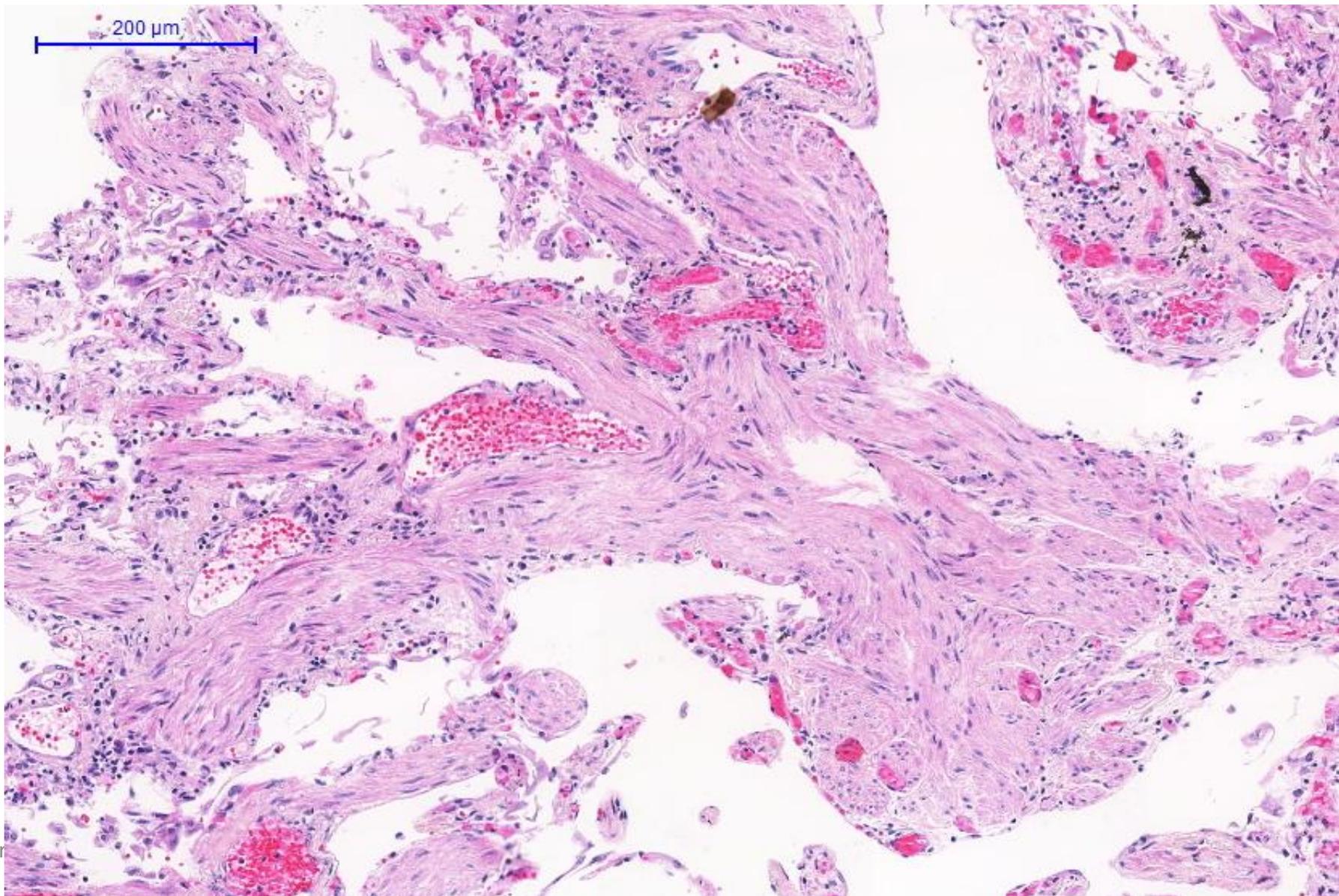
# COVID-19 – Evolução e Fibrose

- Dano Alveolar Agudo – Fase Proliferativa
  - Ativação dos mecanismos de reparo
  - Destrução alveolar impede reposição completa
  - FIBROSE

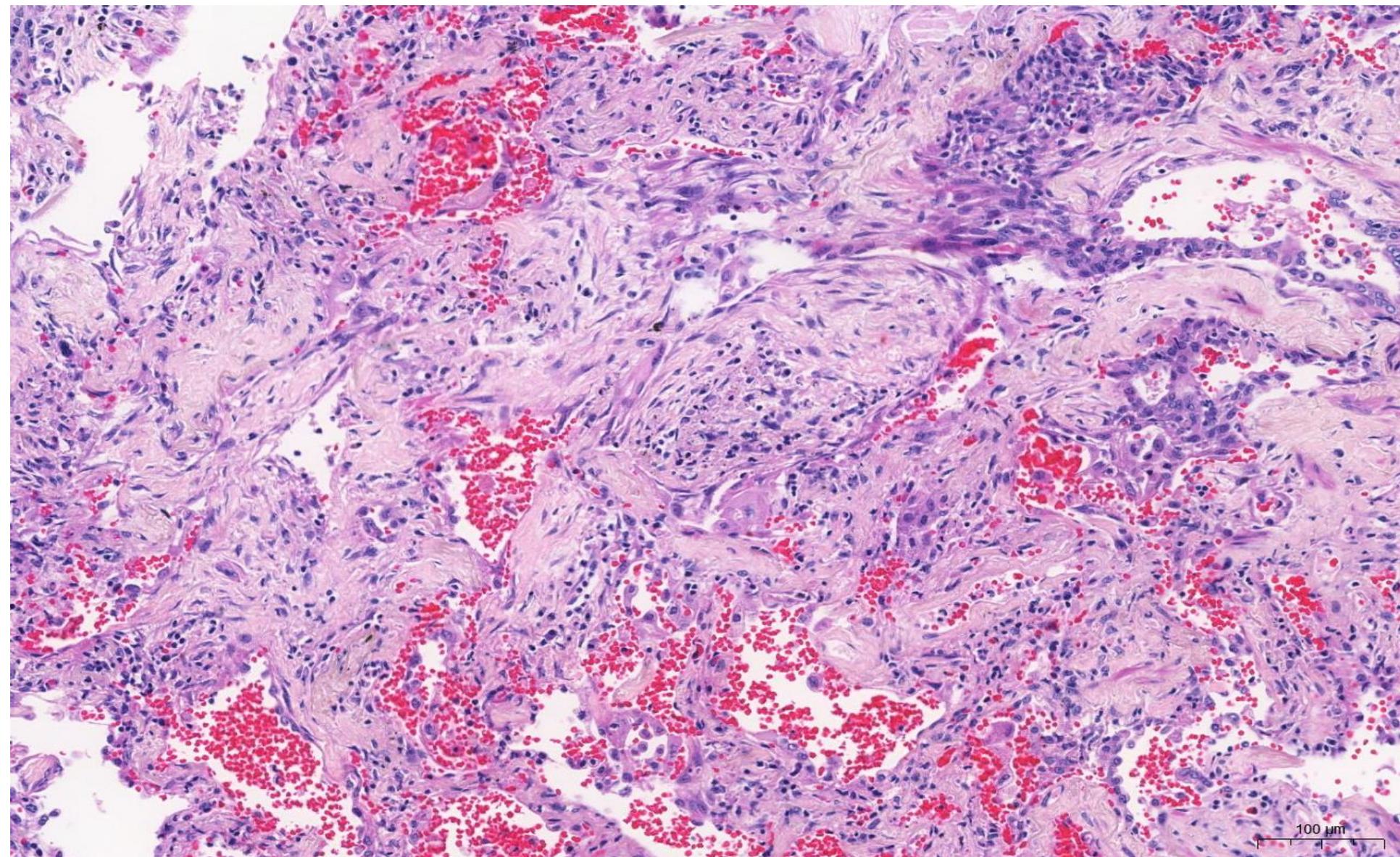
# COVID-19 – Evolução e Fibrose



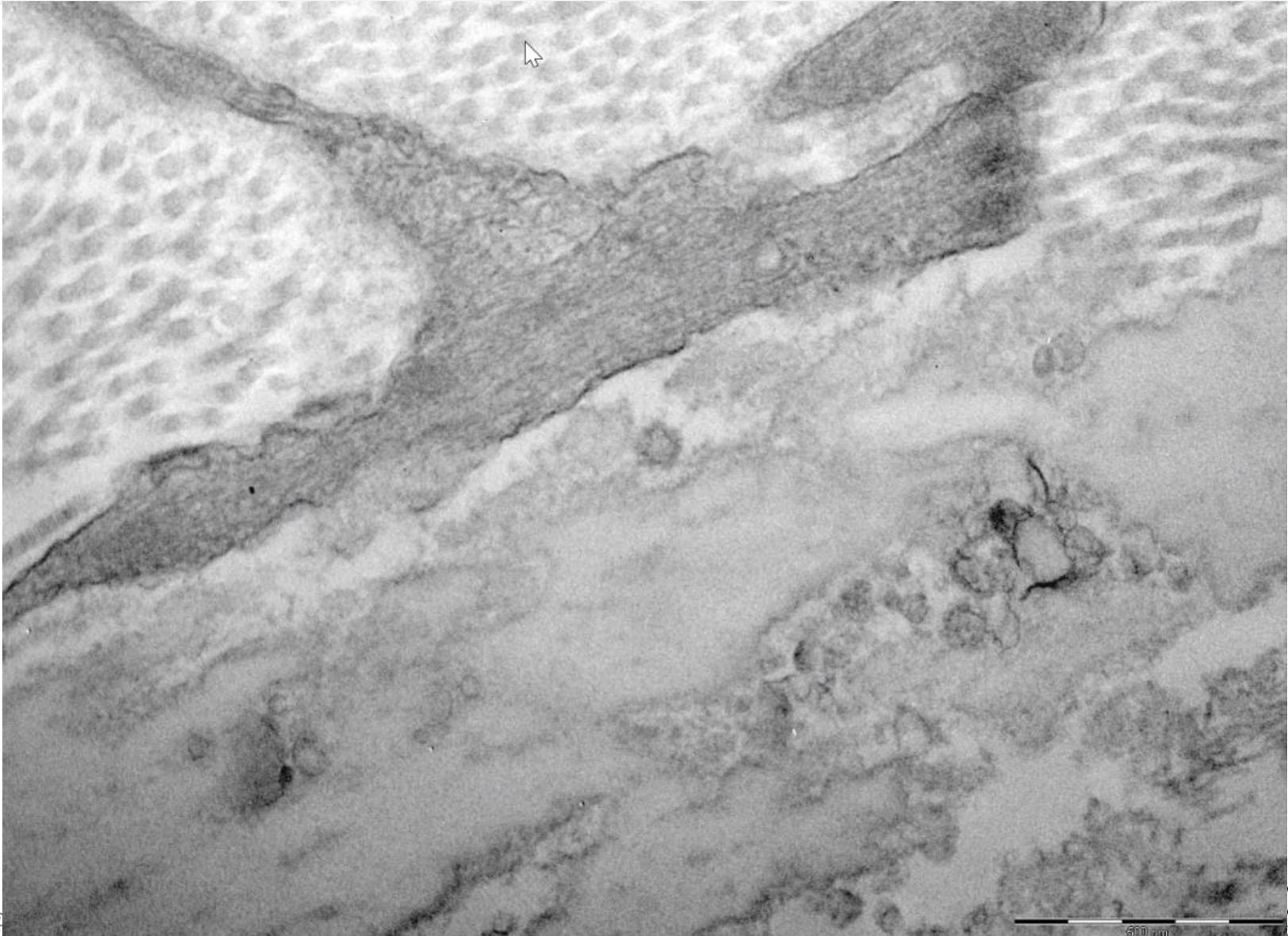
# COVID-19 – Evolução e Fibrose



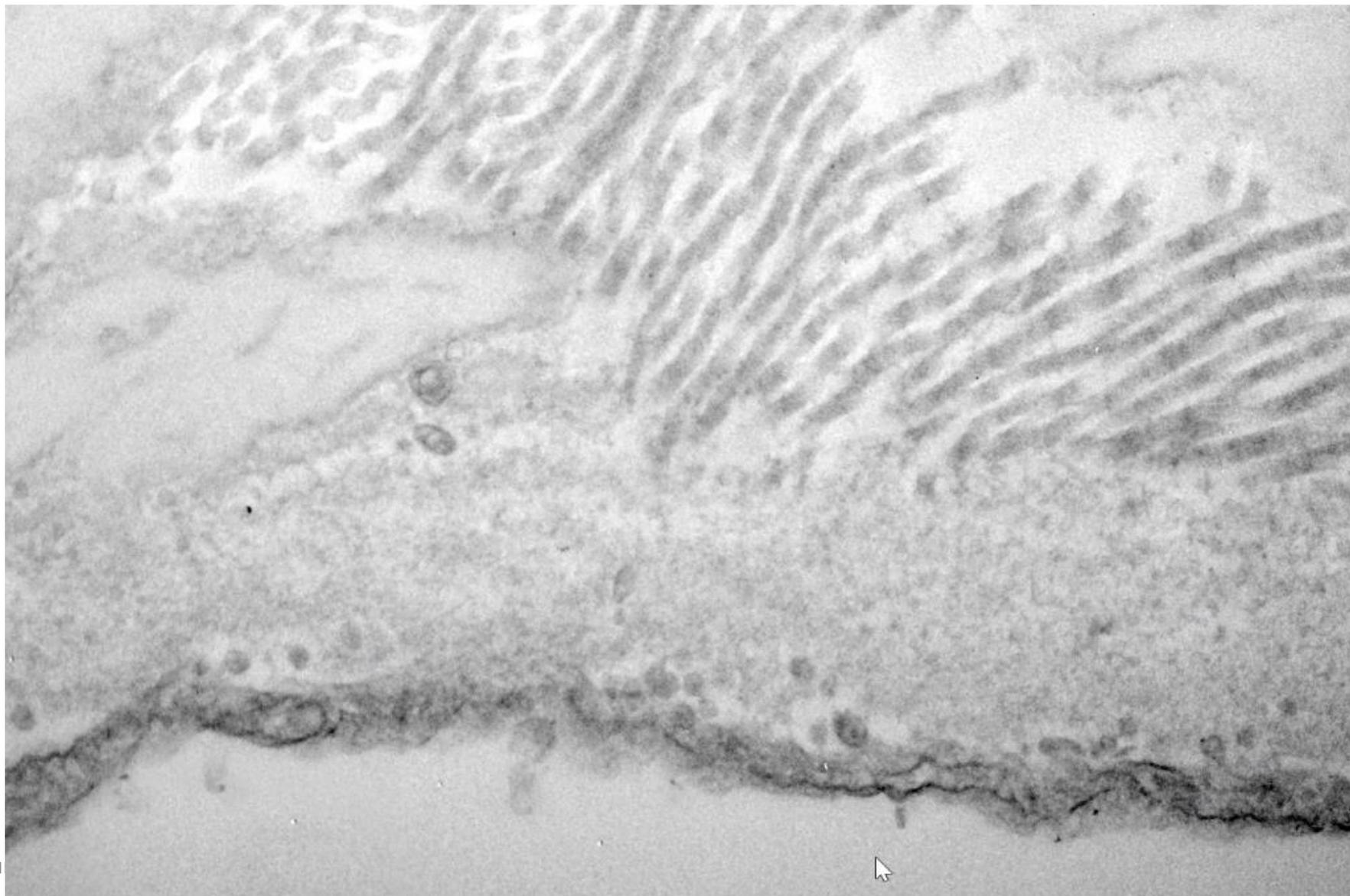
# COVID-19 – Evolução e Fibrose



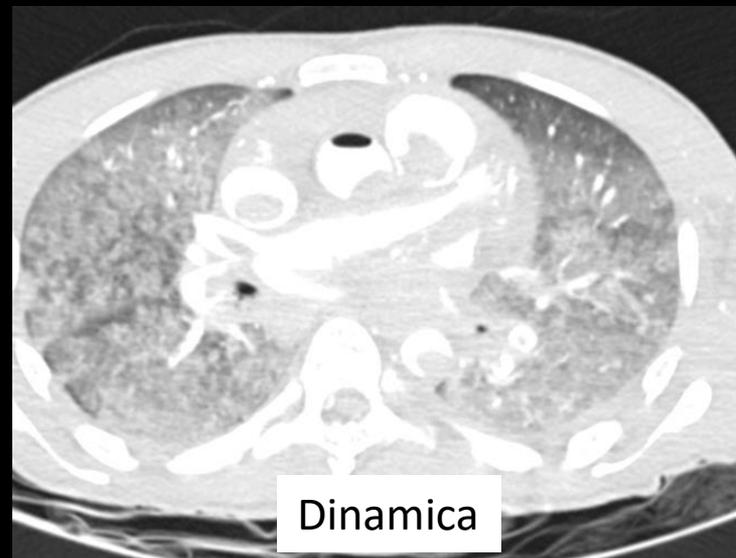
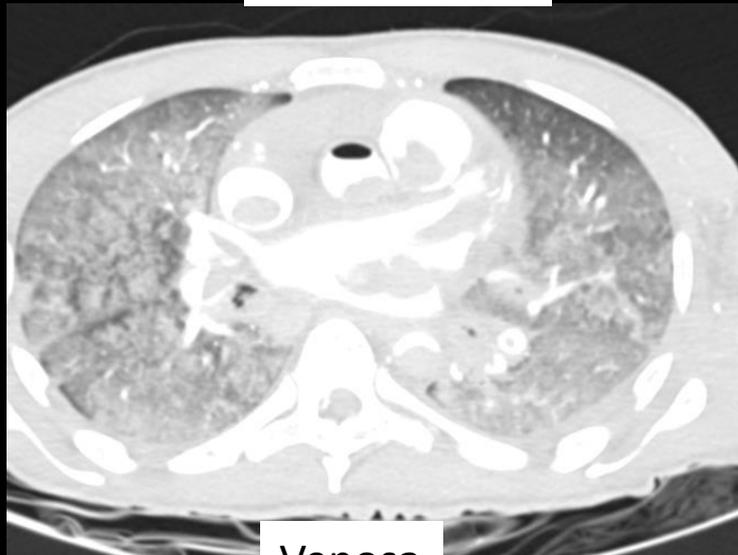
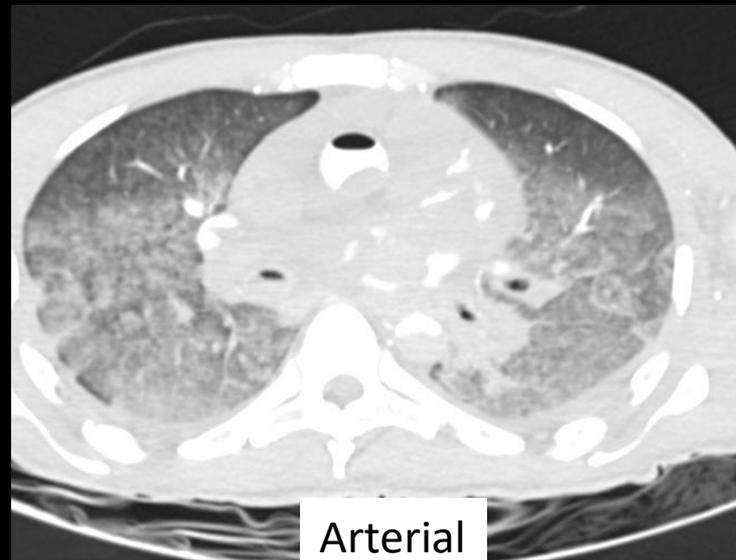
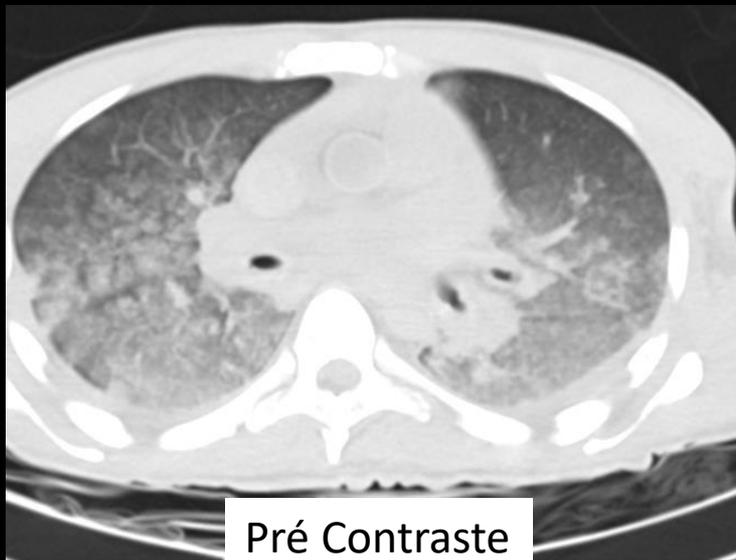
# COVID-19 – Evolução e Fibrose - Ultraestrutura



# COVID-19 – Evolução e Fibrose - Ultraestrutura

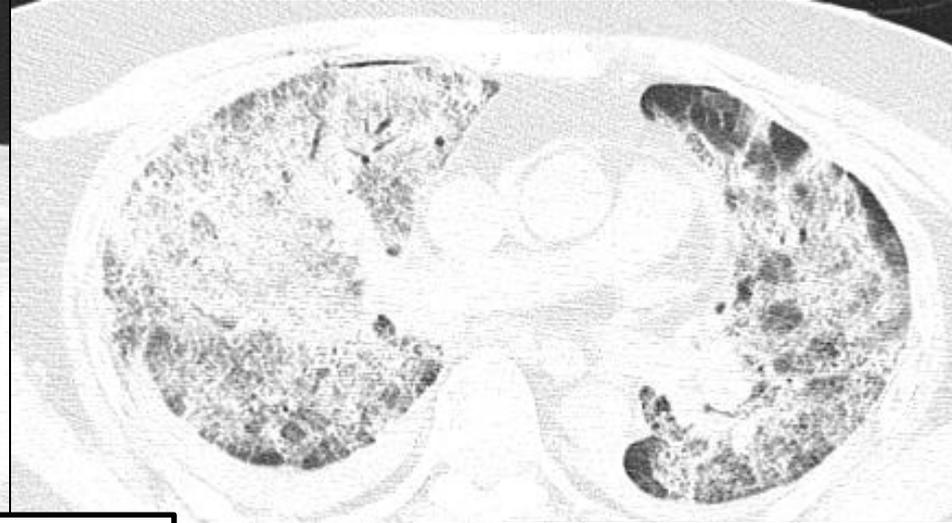
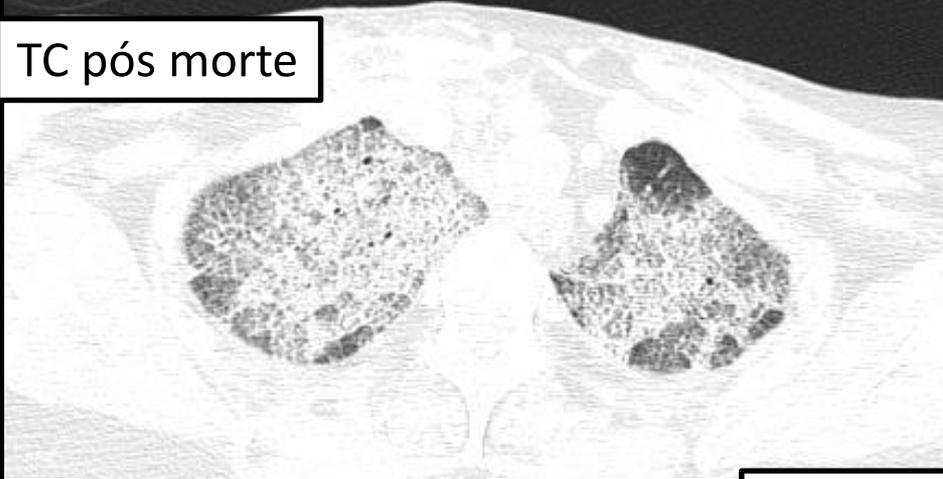


# COVID-19 – Dano Epitelial – Como isso aparece?

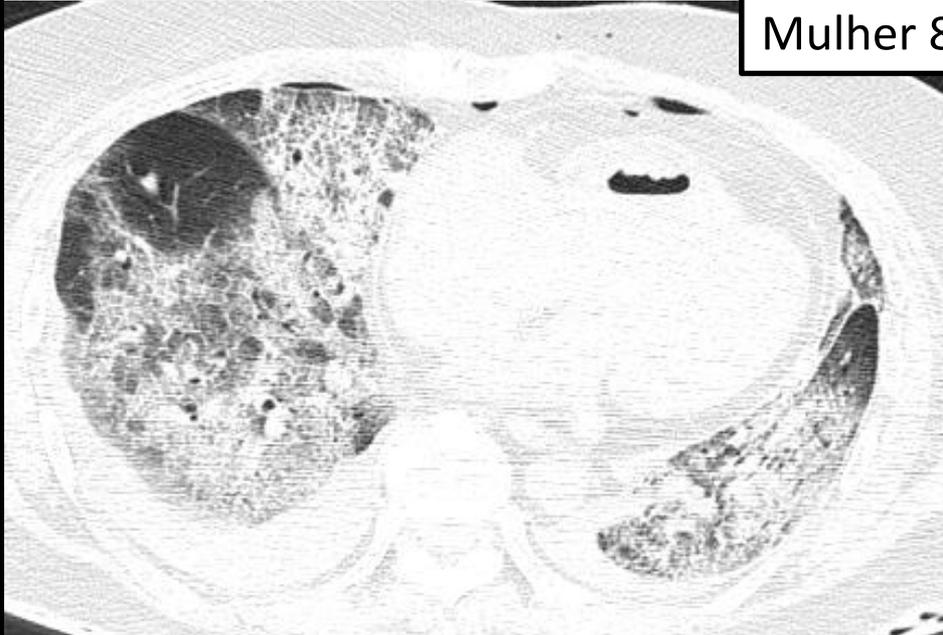


# COVID-19 – Evolução e Fibrose – Como isso aparece?

TC pós morte



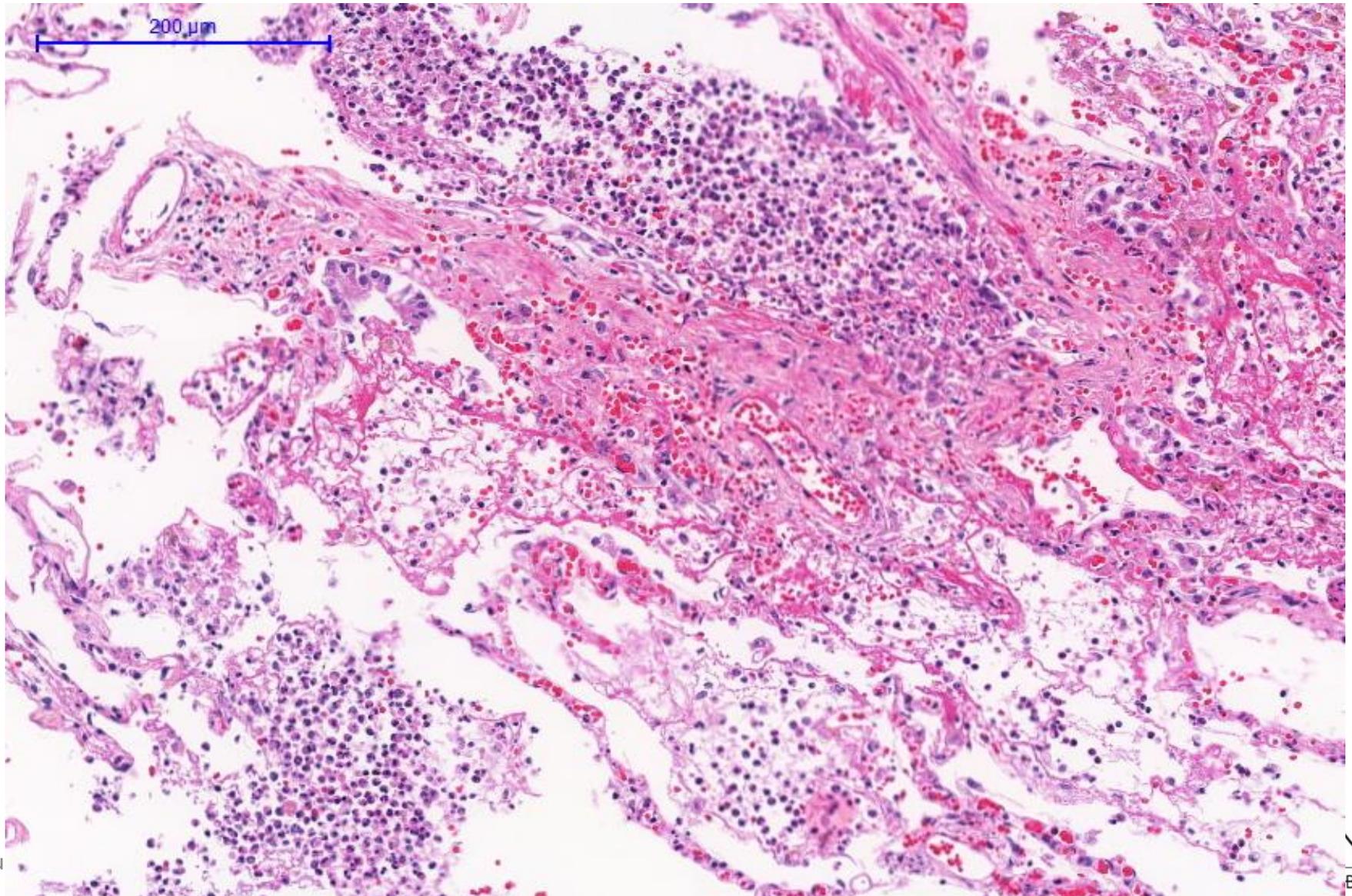
Mulher 83 anos



# COVID-19 – E os mecanismos de defesa?

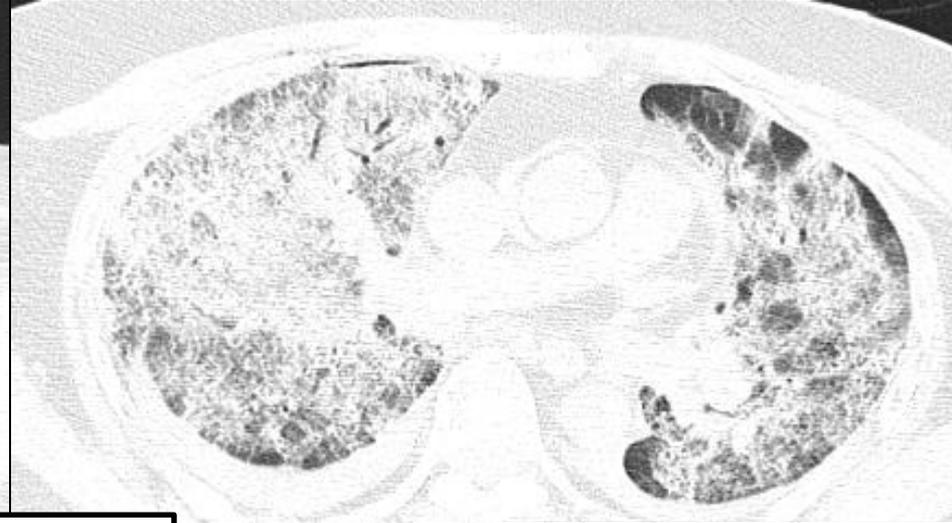
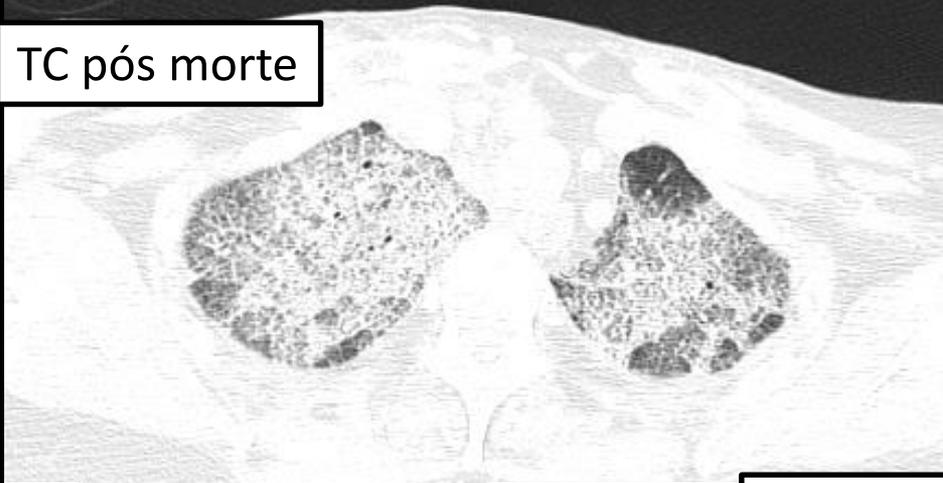
- Mecanismos de Defesa Pulmonar
  - Reflexo de Tosse → Comprometido pela IOT
  - Barreira mecânica – Epitélio → Comprometido pela lesão
  - Clearance Muco-Ciliar → Alteração das propriedades e quantidades de muco
  - Efeitos imunológicos locais → Comprometidos pela inflamação local

# COVID-19 – O que acontece então?

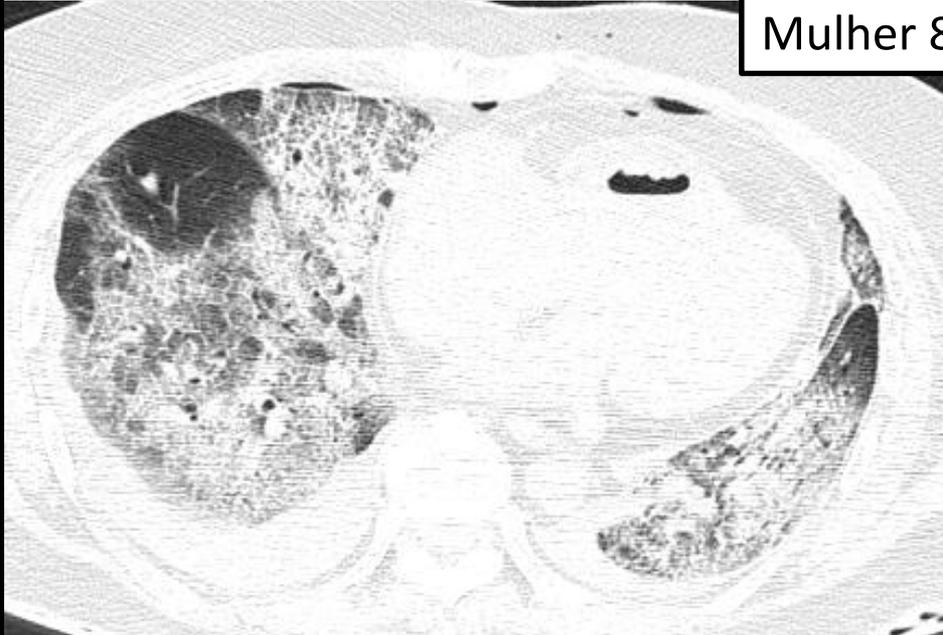


# COVID-19 – Evolução e Fibrose – Como isso aparece?

TC pós morte

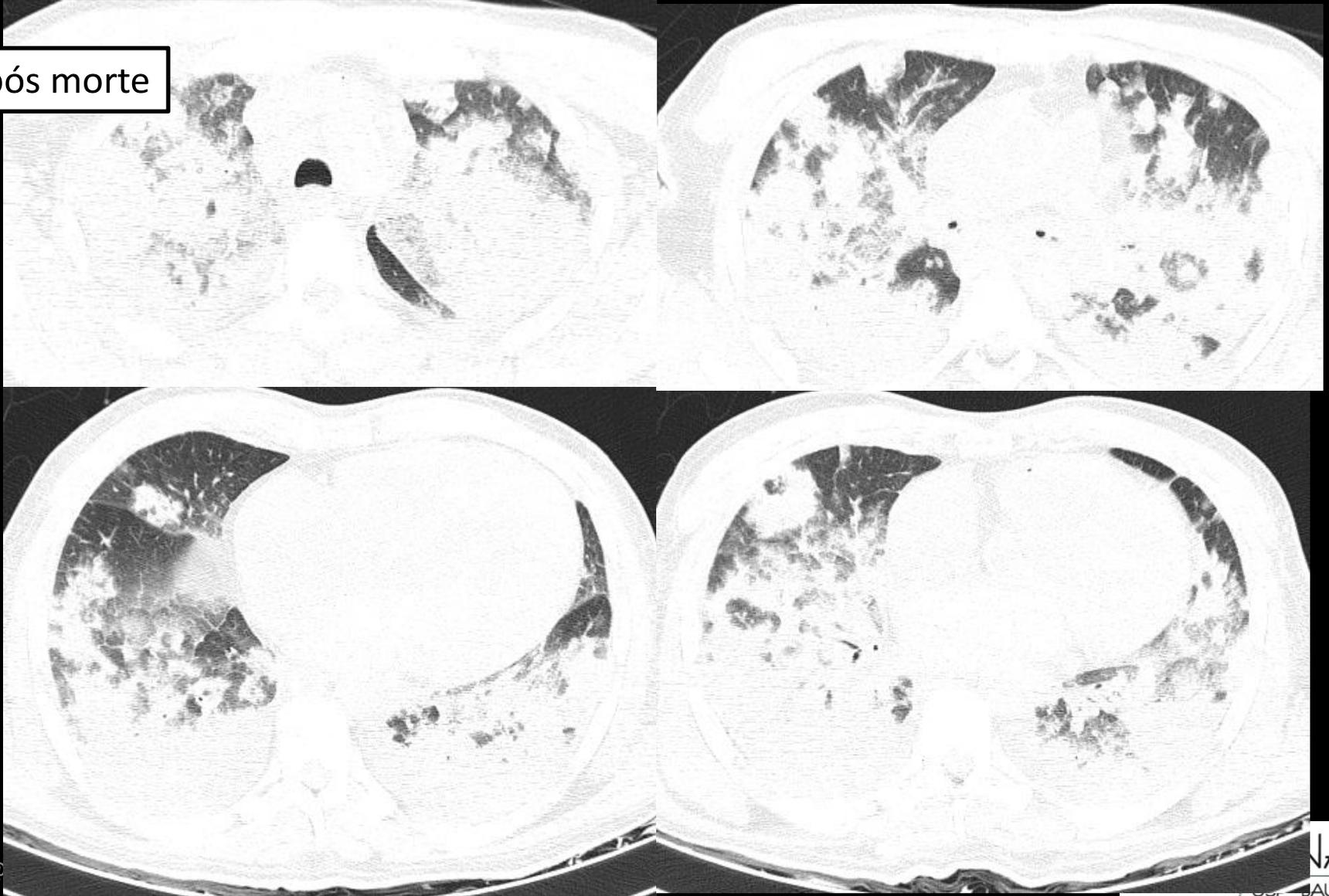


Mulher 83 anos



# COVID-19 – O que acontece então e como aparece?

TC pós morte



# COVID-19 – Dano Endotelial – Vasos Pulmonares

- Dano Endotelial
  - Efeitos pró-trombóticos
  - Comprometimento Sistêmico



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DOI: 10.1111/jth.14844

**Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19**

Marisa Dolhnikoff<sup>1</sup>   
Amaro Nunes Duarte-Neto<sup>2</sup>  
Renata Aparecida de Almeida Monteiro<sup>2</sup>  
Luiz Fernando Ferraz da Silva<sup>2,3</sup>  
Ellen Pierre de Oliveira<sup>3</sup>  
Paulo Hilário Nascimento Saldiva<sup>3</sup>  
Thais Mauad<sup>3</sup>  
Elnara Marcia Negri<sup>4</sup>

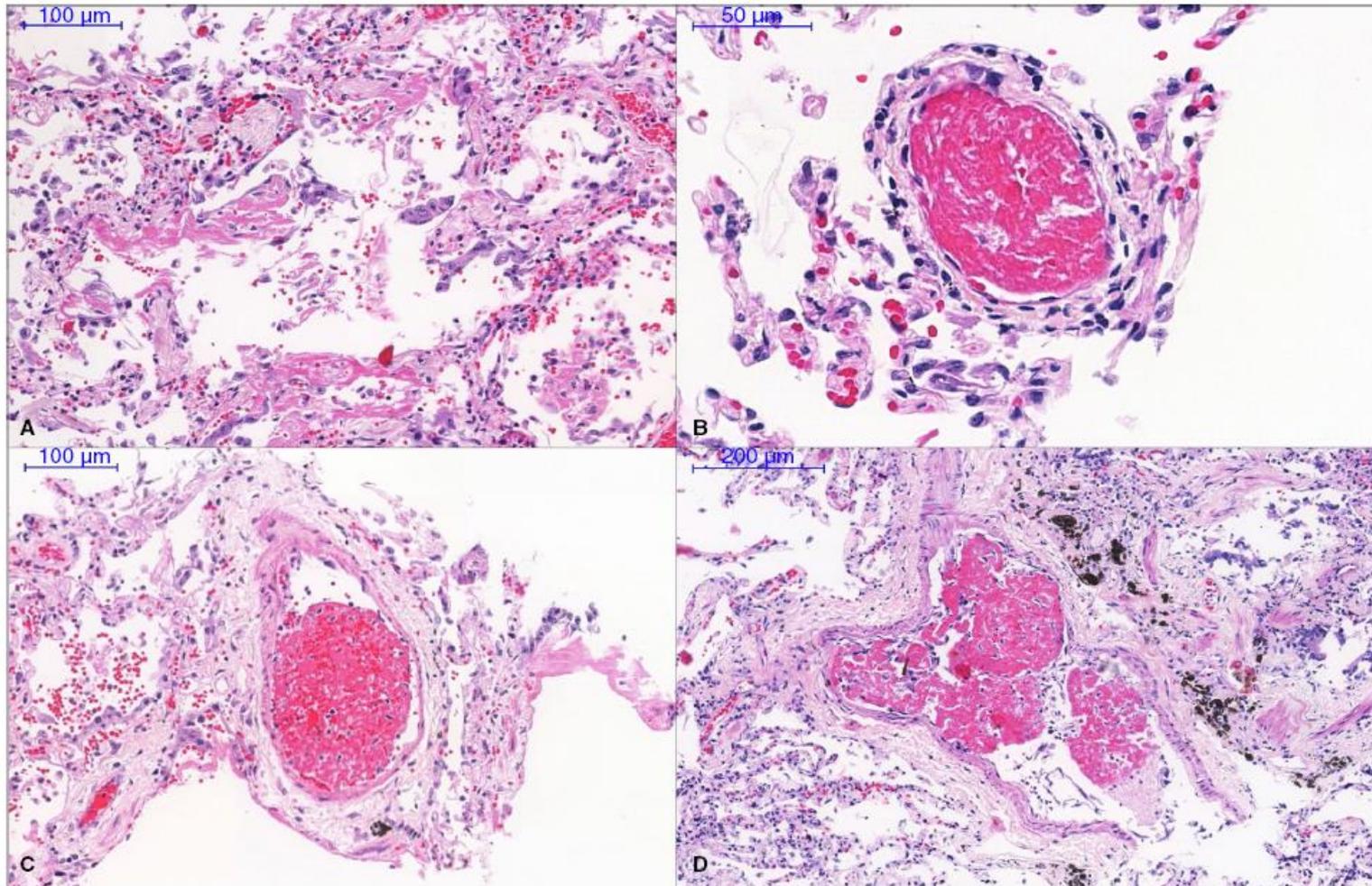
<sup>1</sup>Departamento de Patologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

<sup>2</sup>Serviço de Verificação de Óbitos da Capital, Universidade de São Paulo, São Paulo, Brazil

<sup>3</sup>Departamento de Cardiopneumologia, Instituto do Coração, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

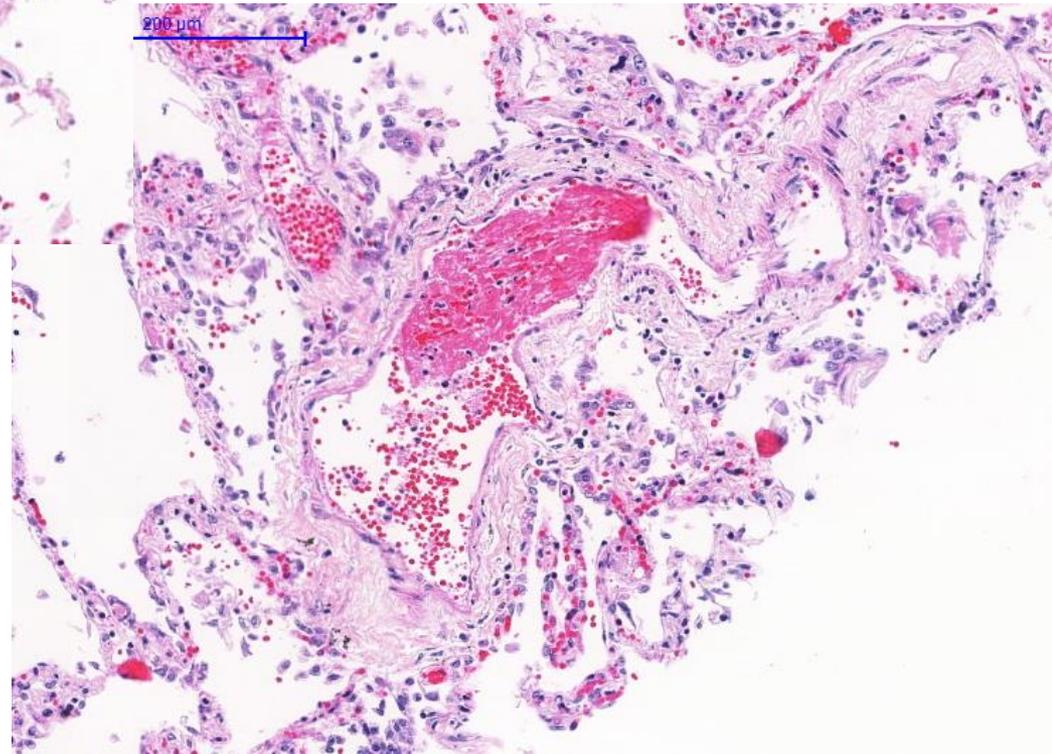
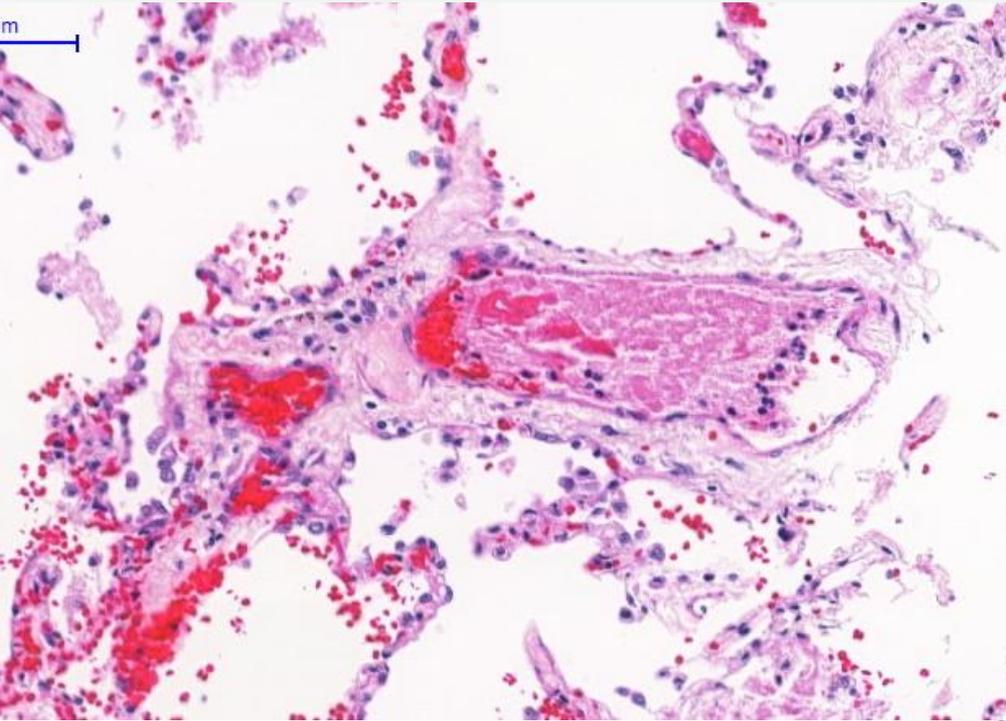
<sup>4</sup>LIM-59, Biologia Celular, Departamento de Patologia, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

# COVID-19 – Dano Endotelial – Vasos Pulmonares

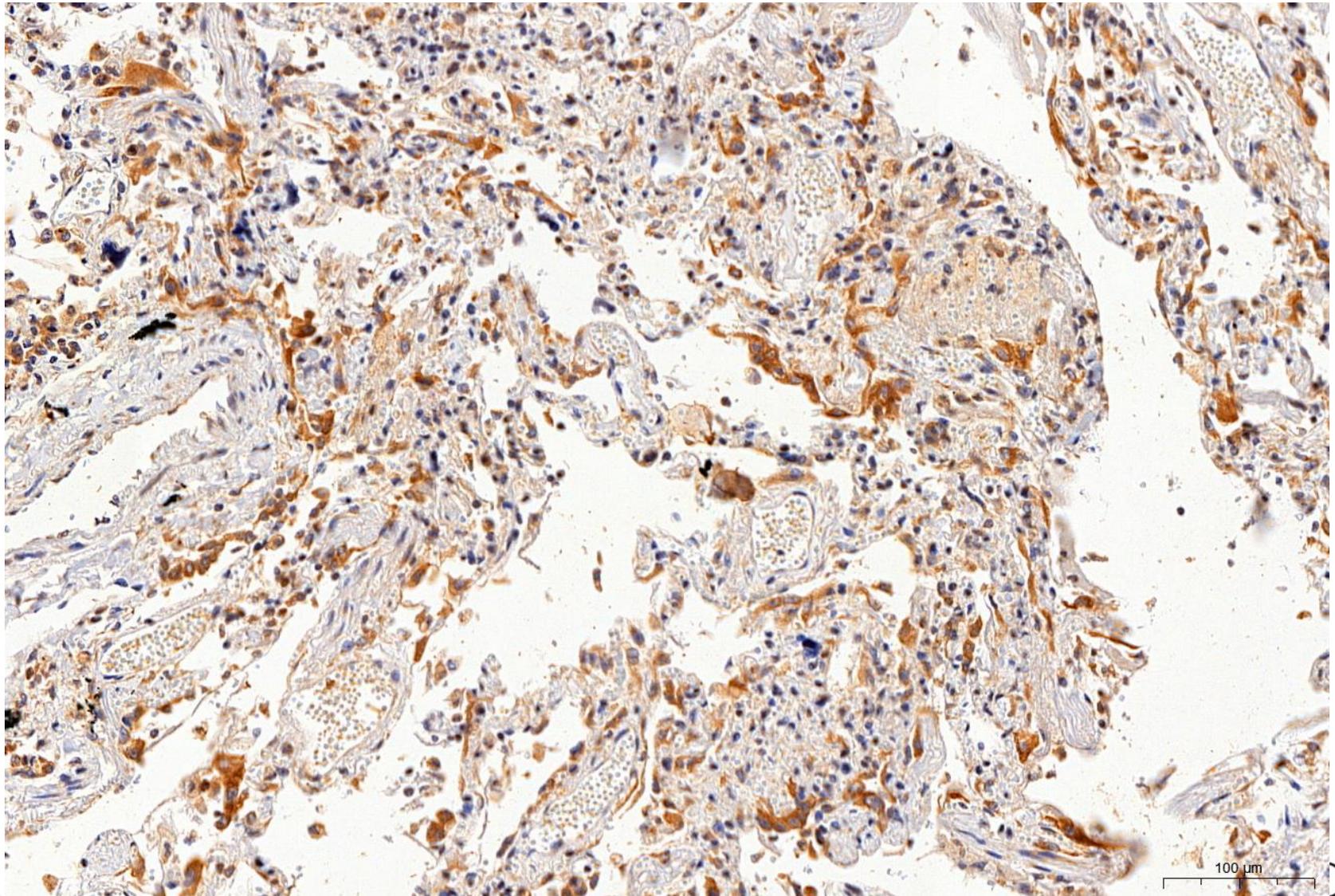


**FIGURE 1(A)** Diffuse alveolar damage in fatal COVID-19. (B-D) Fibrinous microthrombi in small-sized pulmonary arterioles, observed in 8 of 10 patients.

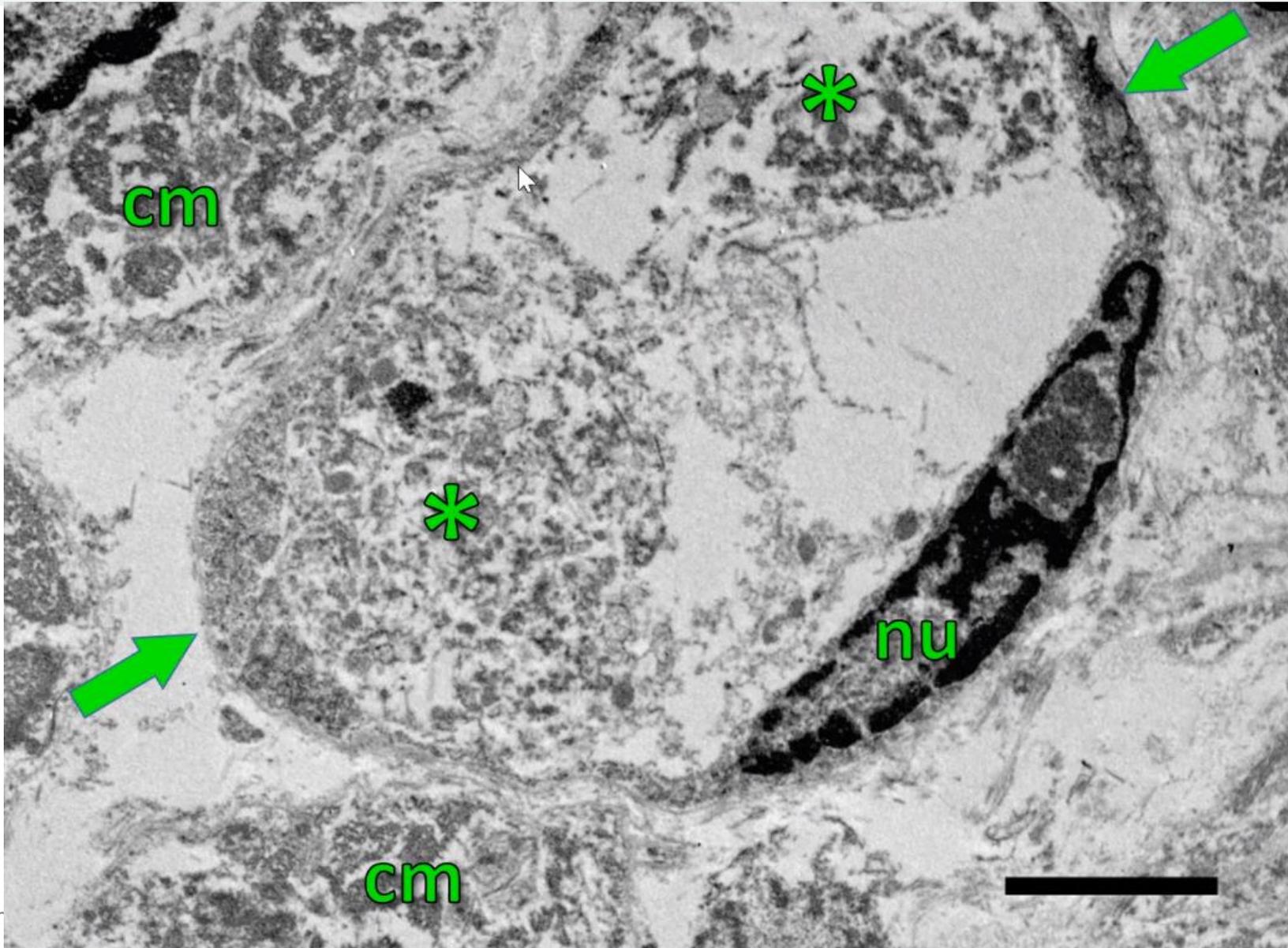
# COVID-19 – Dano Endotelial – Vasos Pulmonares



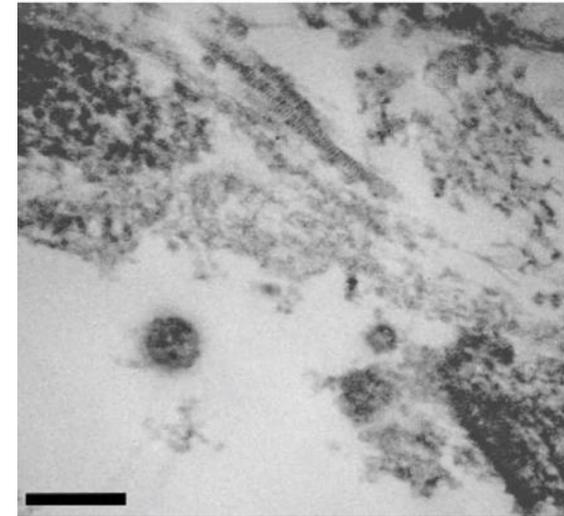
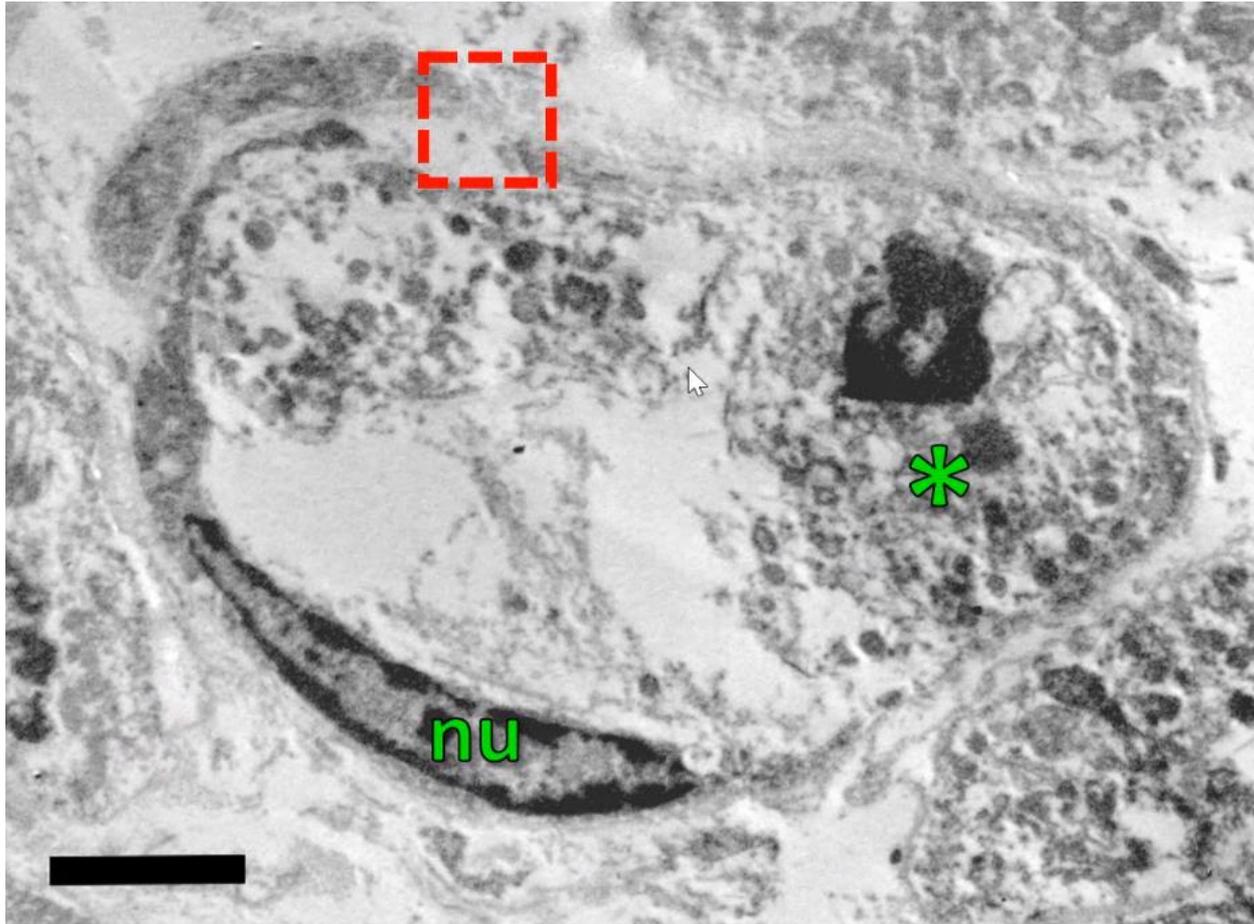
# COVID-19 – Dano Endotelial – Vasos Pulmonares



# COVID-19 – Dano Endotelial – Ultraestrutura



# COVID-19 – Dano Endotelial – Ultraestrutura



# COVID-19 – Efeitos Sistêmicos – Coração

- Efeitos Cardiovasculares
  - Efeitos pró-trombóticos
  - Pancardite Viral

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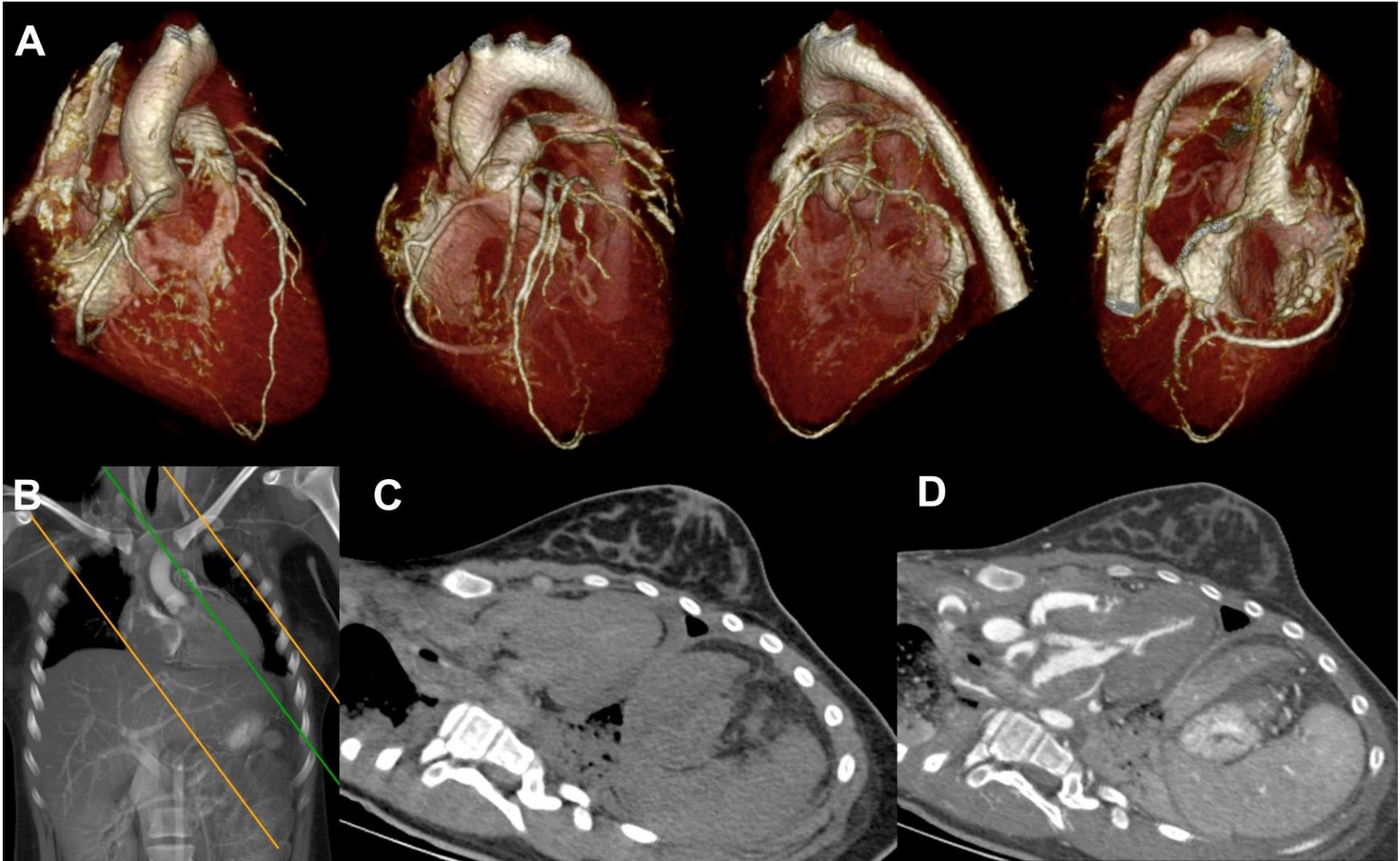
## SARS-CoV-2 in cardiac tissue of a child with COVID-19-related multisystem inflammatory syndrome

Marisa Dolhnikoff, MD   • Juliana Ferreira Ferranti, MD  • Renata Aparecida de Almeida Monteiro, MD • Amaro Nunes Duarte-Neto, MD • Michele Soares Gomes-Gouvêa, PhD • Natália Víu Degaspere, MD • Artur Figueiredo Delgado, MD • Carolina Montanari Fiorita, MD • Gabriela Nunes Leal, MD • Regina Maria Rodrigues, MD • Khalil Taverna Chaim, MSc • João Renato Rebello Pinho, MD • Prof Magda Carneiro-Sampaio, MD • Thais Mauad, MD • Luiz Fernando Ferraz da Silva, MD • Prof Werther Brunow de Carvalho, MD • Prof Paulo Hilario Nascimento Saldiva, MD • Elia Garcia Caldini, PhD • [Show less](#) • [Show footnotes](#)

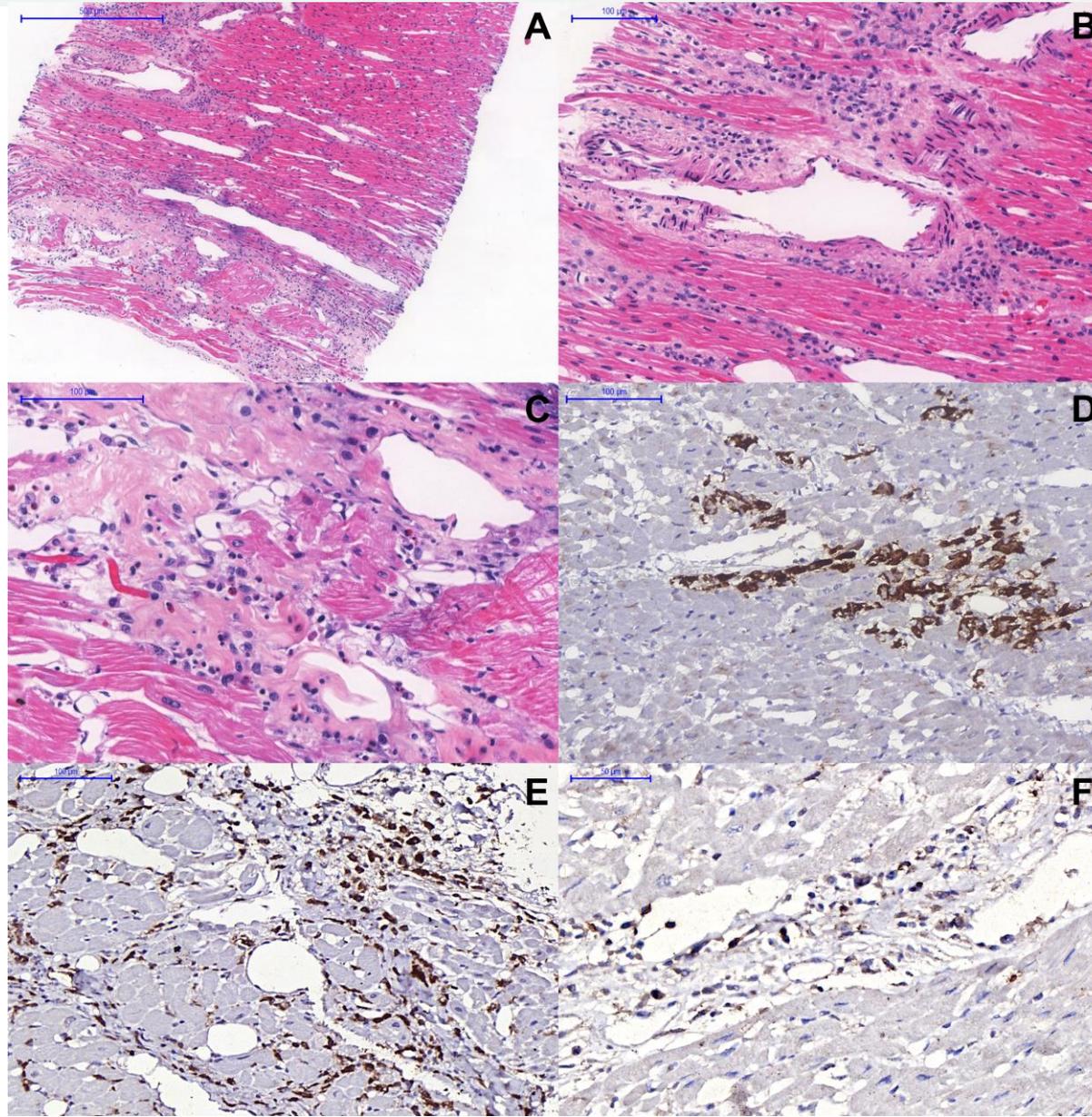
Published: August 20, 2020 • DOI: [https://doi.org/10.1016/S2352-4642\(20\)30257-1](https://doi.org/10.1016/S2352-4642(20)30257-1)



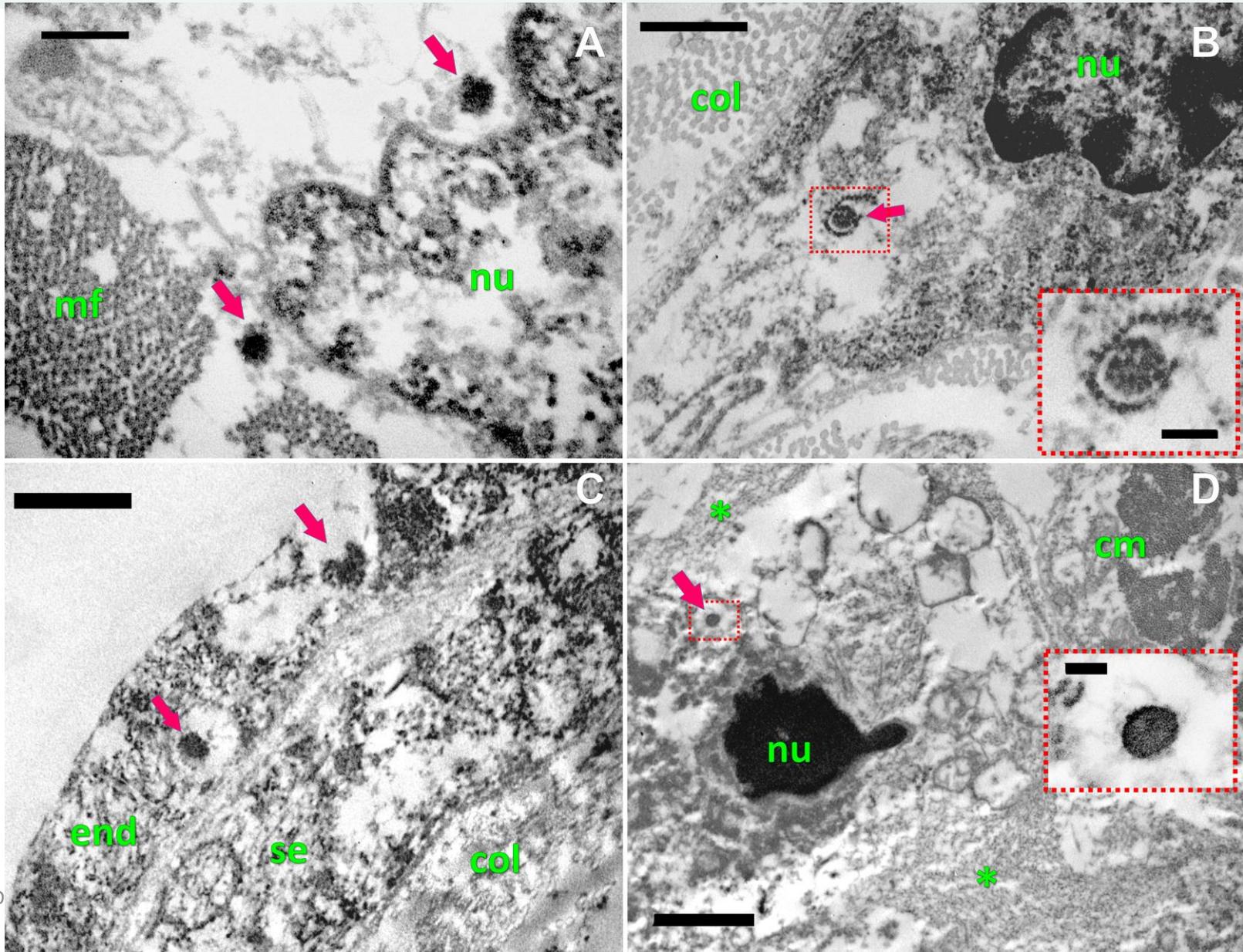
# COVID-19 – Efeitos Sistêmicos – Coração



# COVID-19 – Efeitos Sistêmicos – Coração



# COVID-19 – Efeitos Sistêmicos – Coração

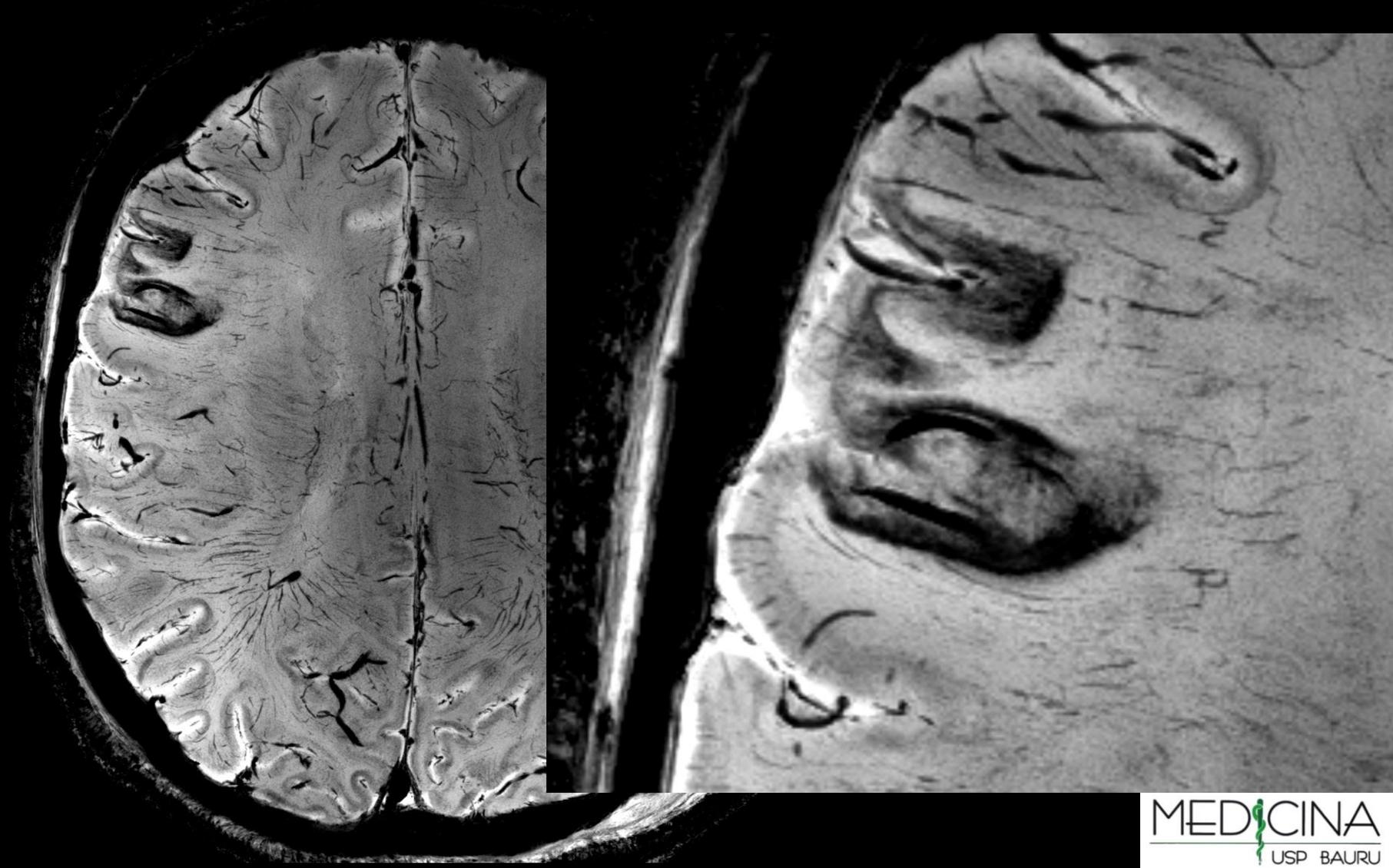


# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso

- Efeitos Neurológicos
  - Obstruções vasculares
  - Hemorragias
  - Encefalites focais
  - Reatividade glial

Artigo em breve!!! =)

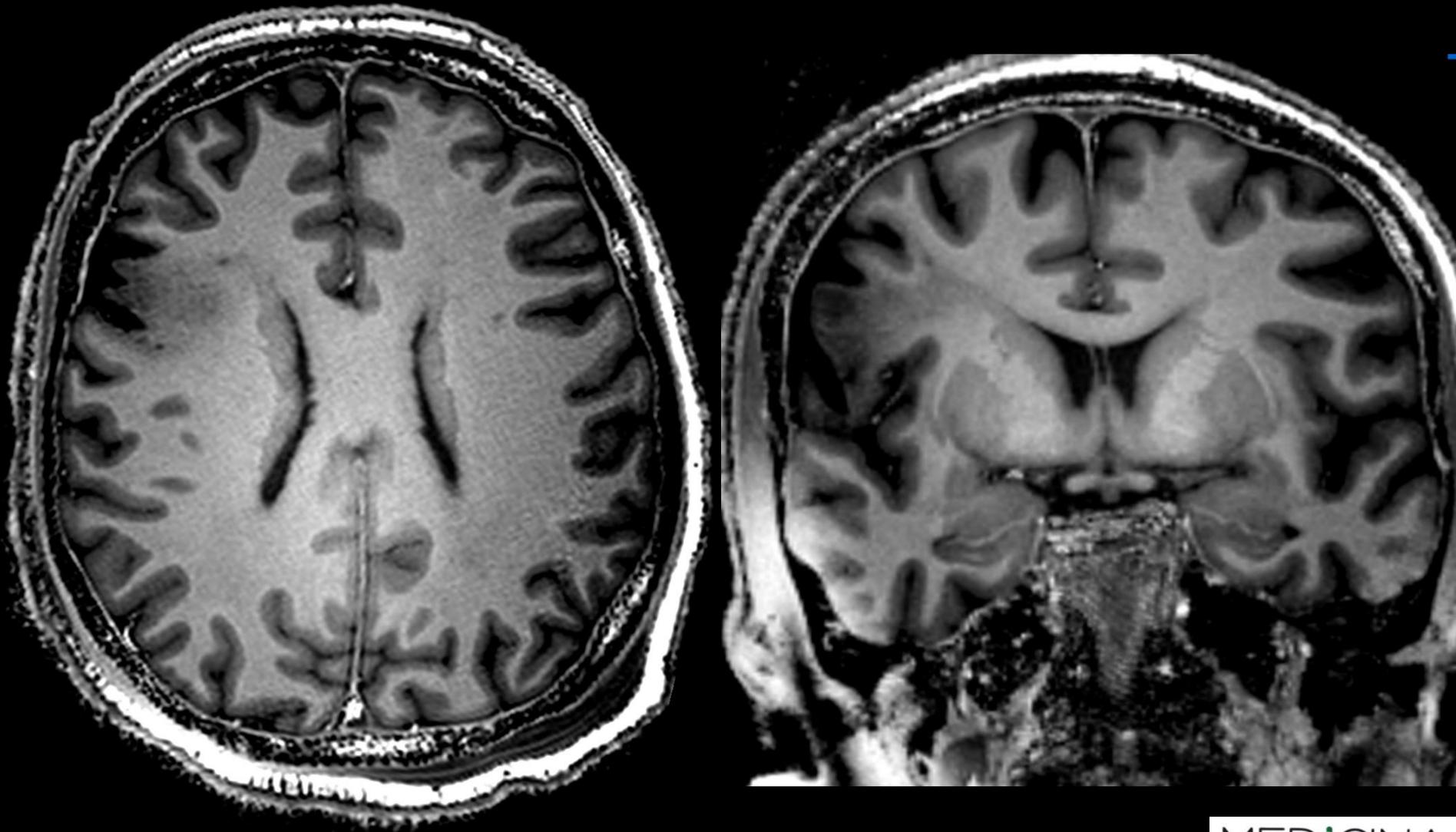
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



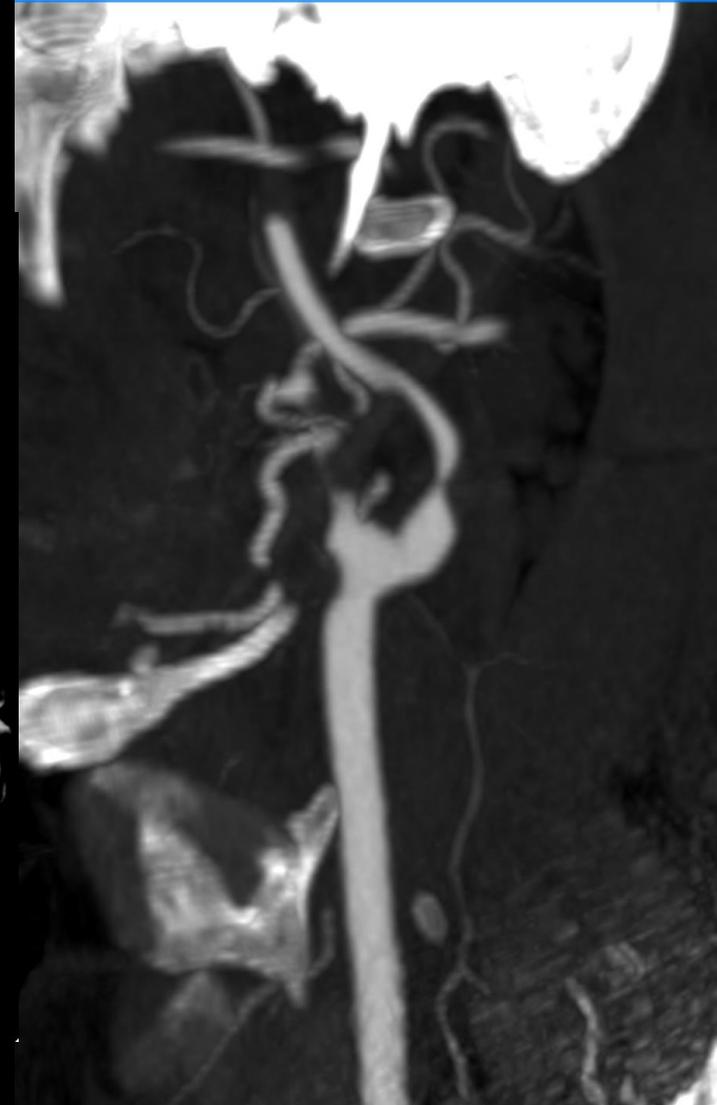
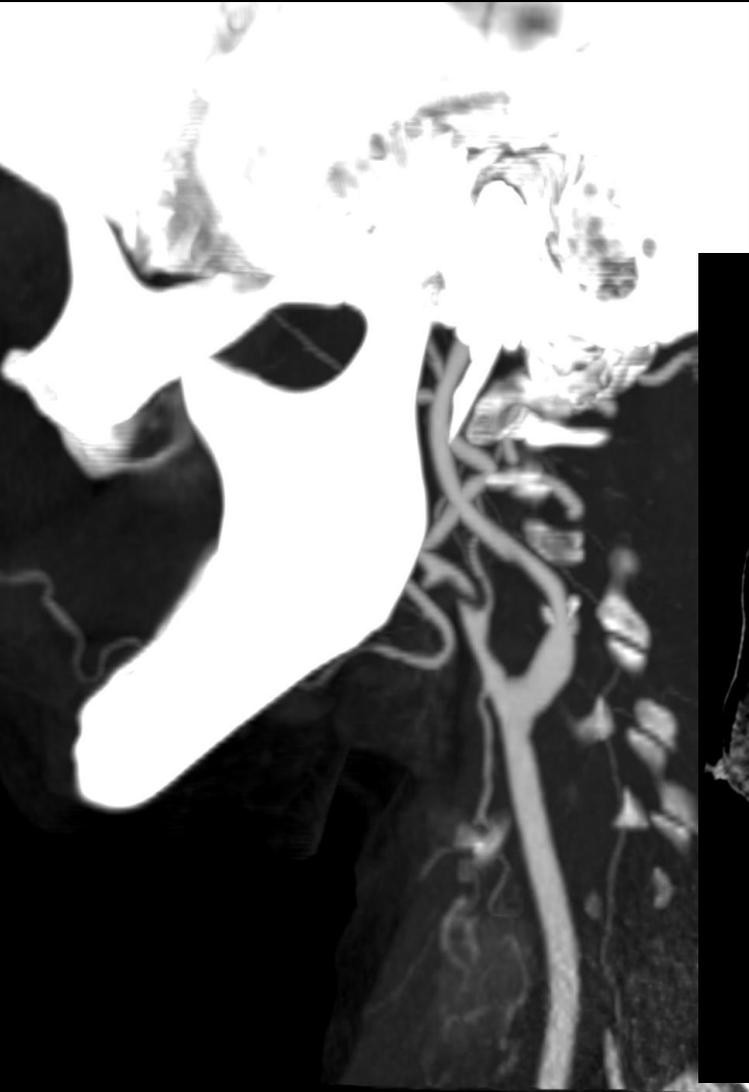
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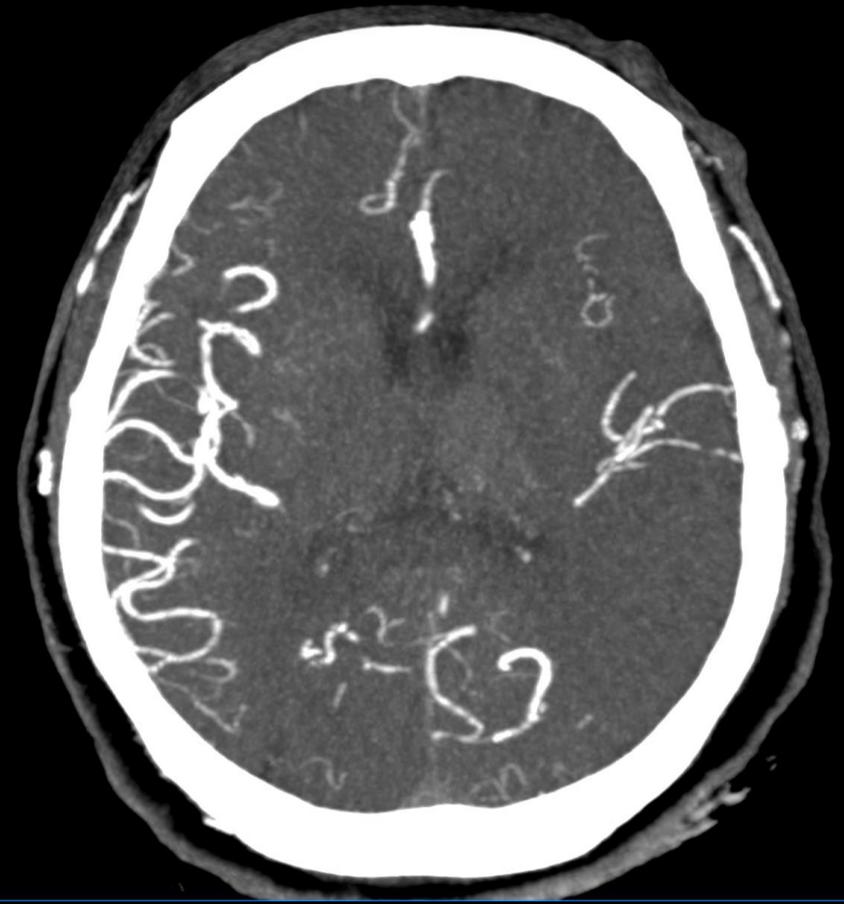
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



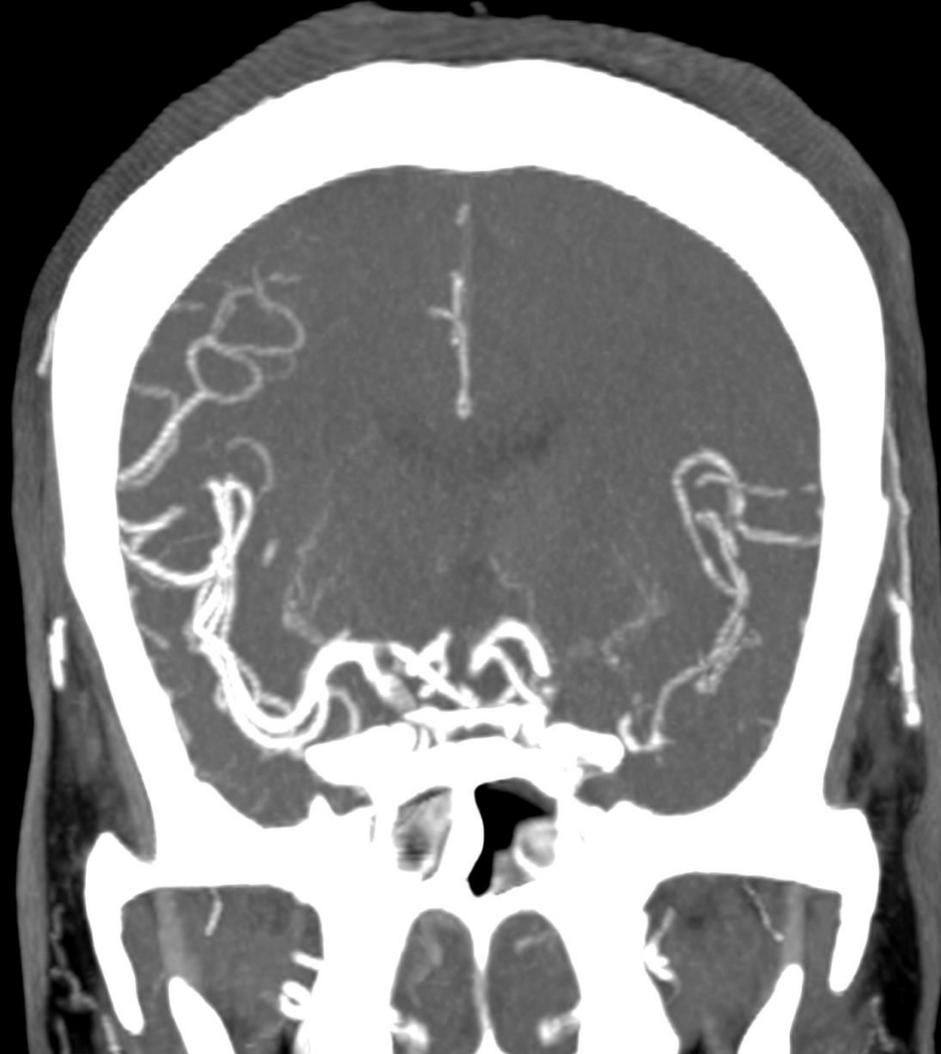
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



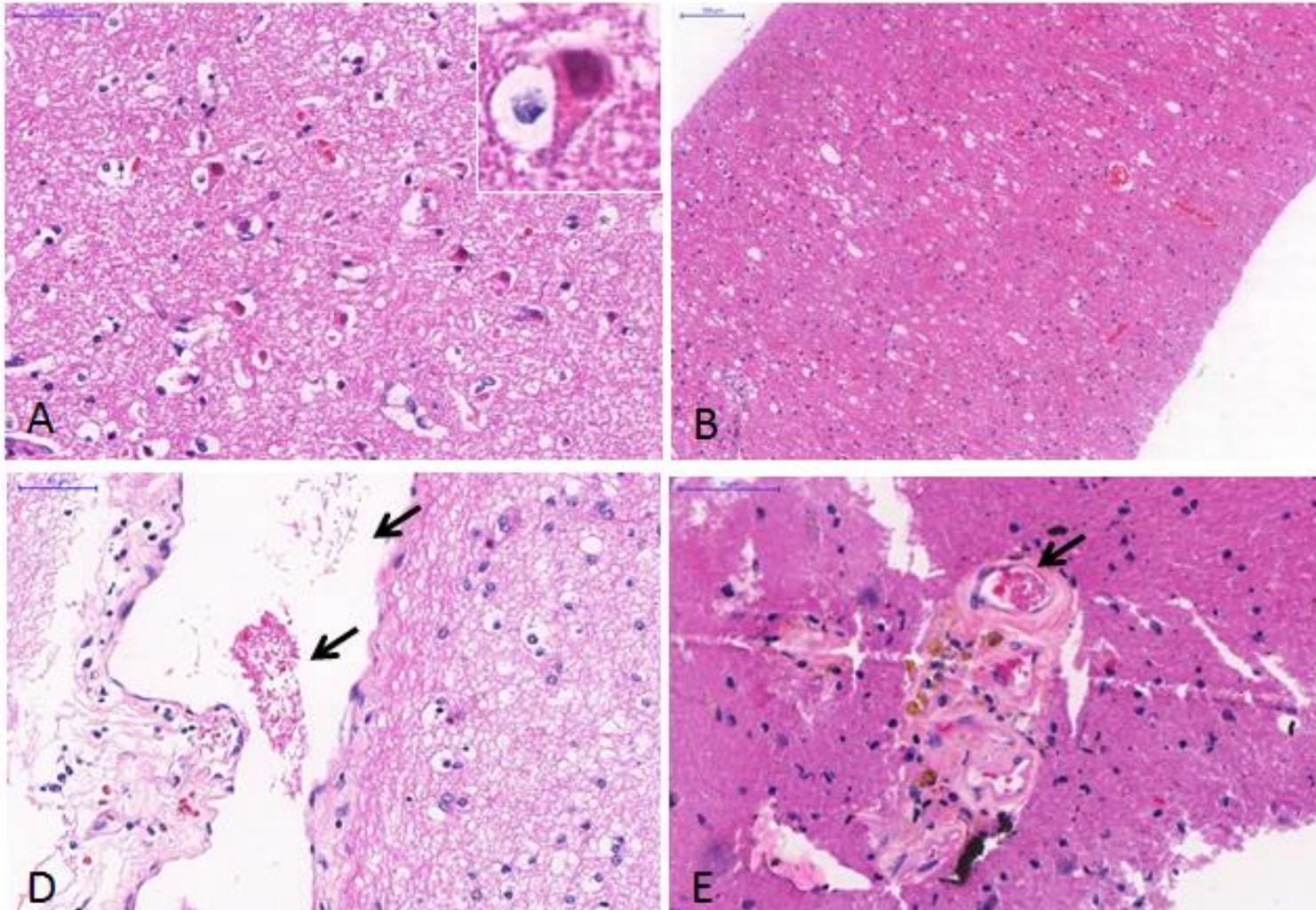
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



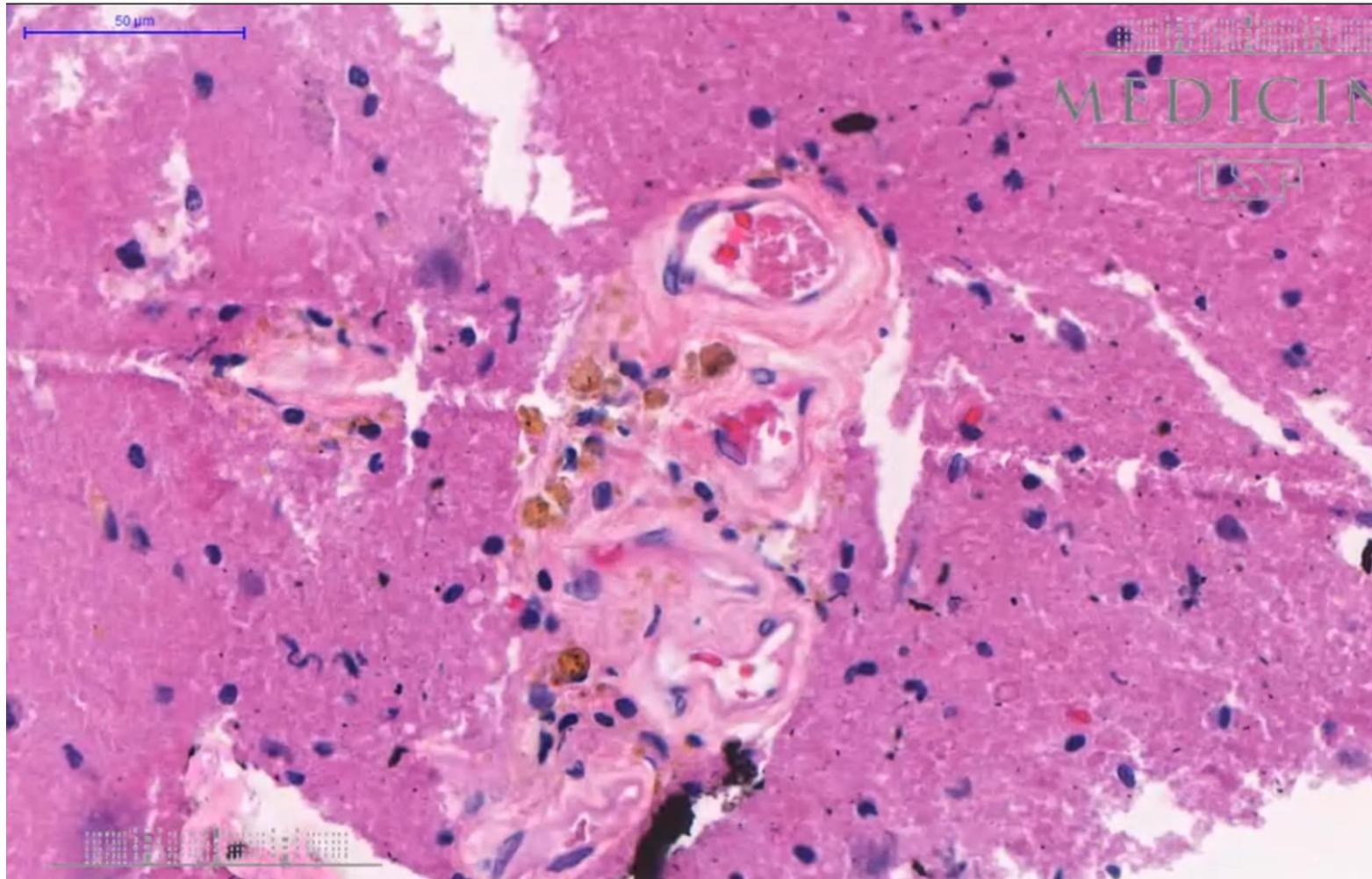
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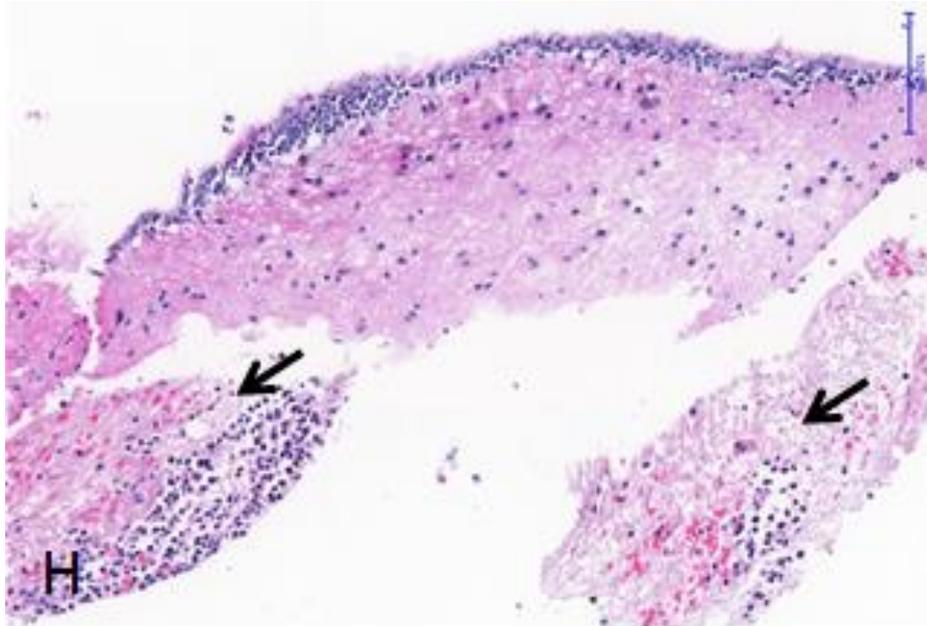
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



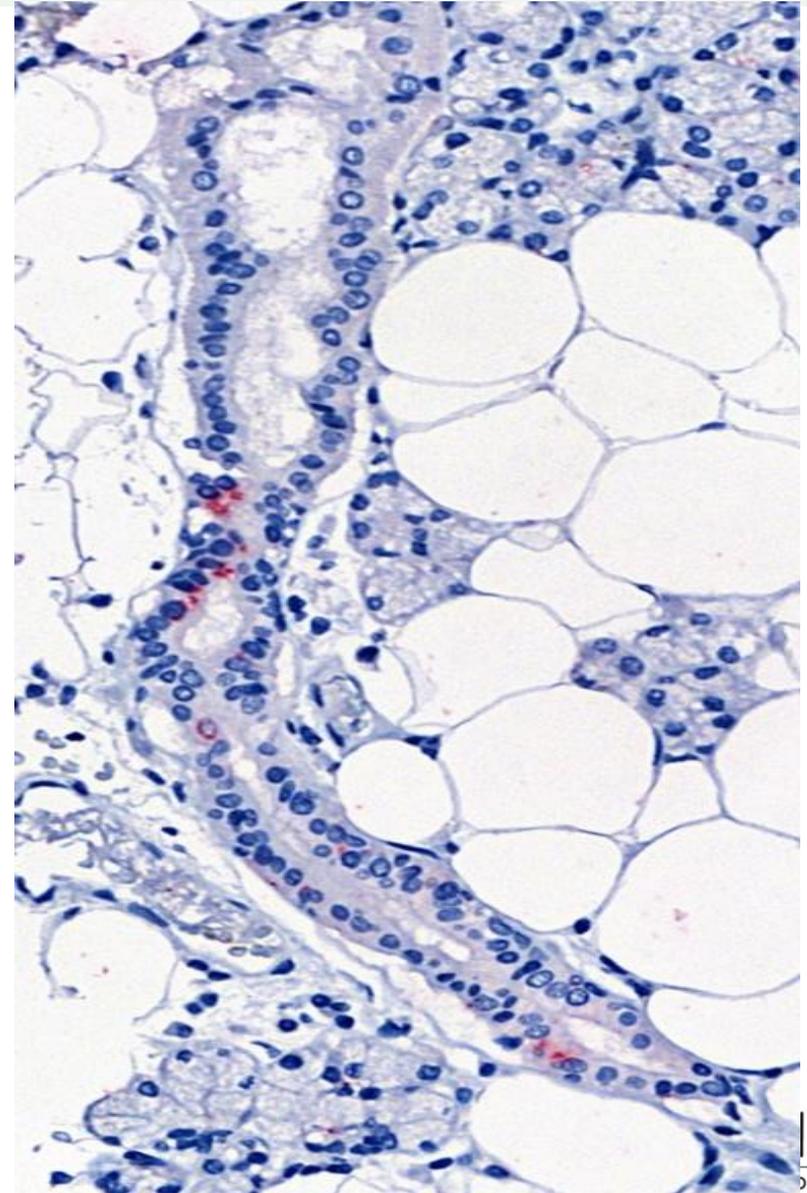
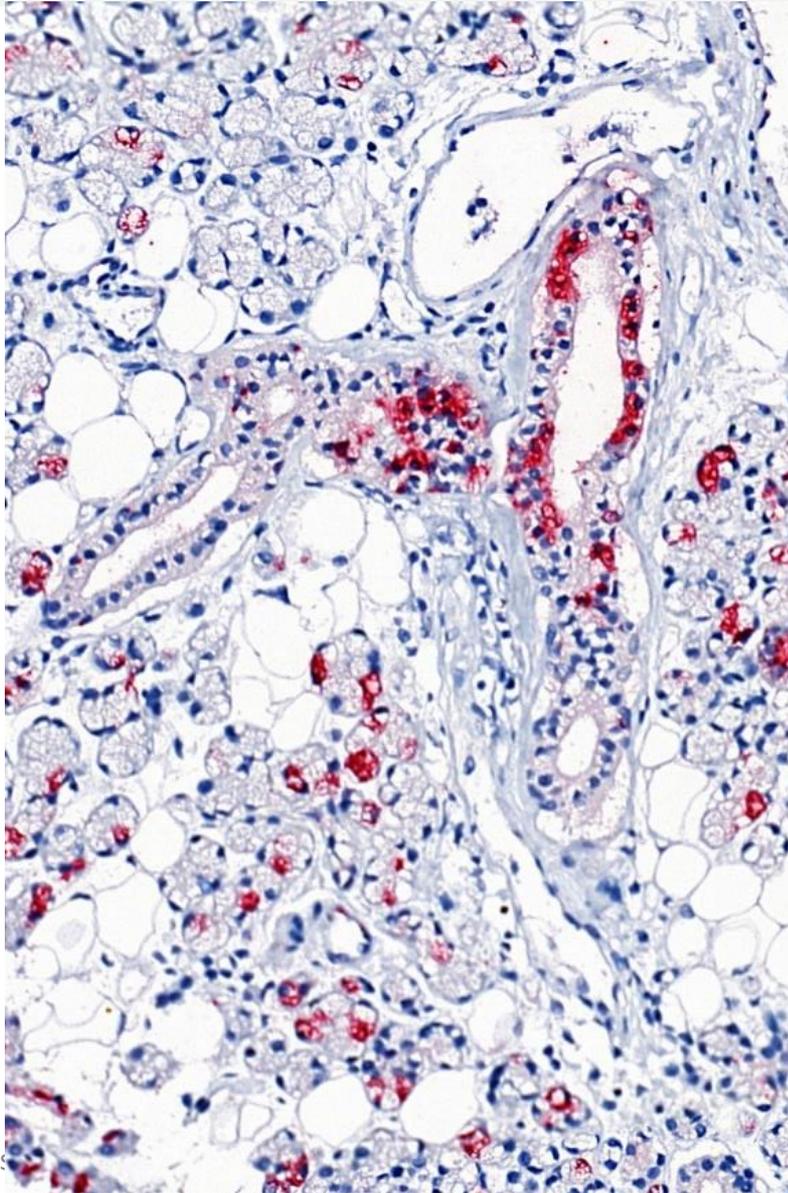
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



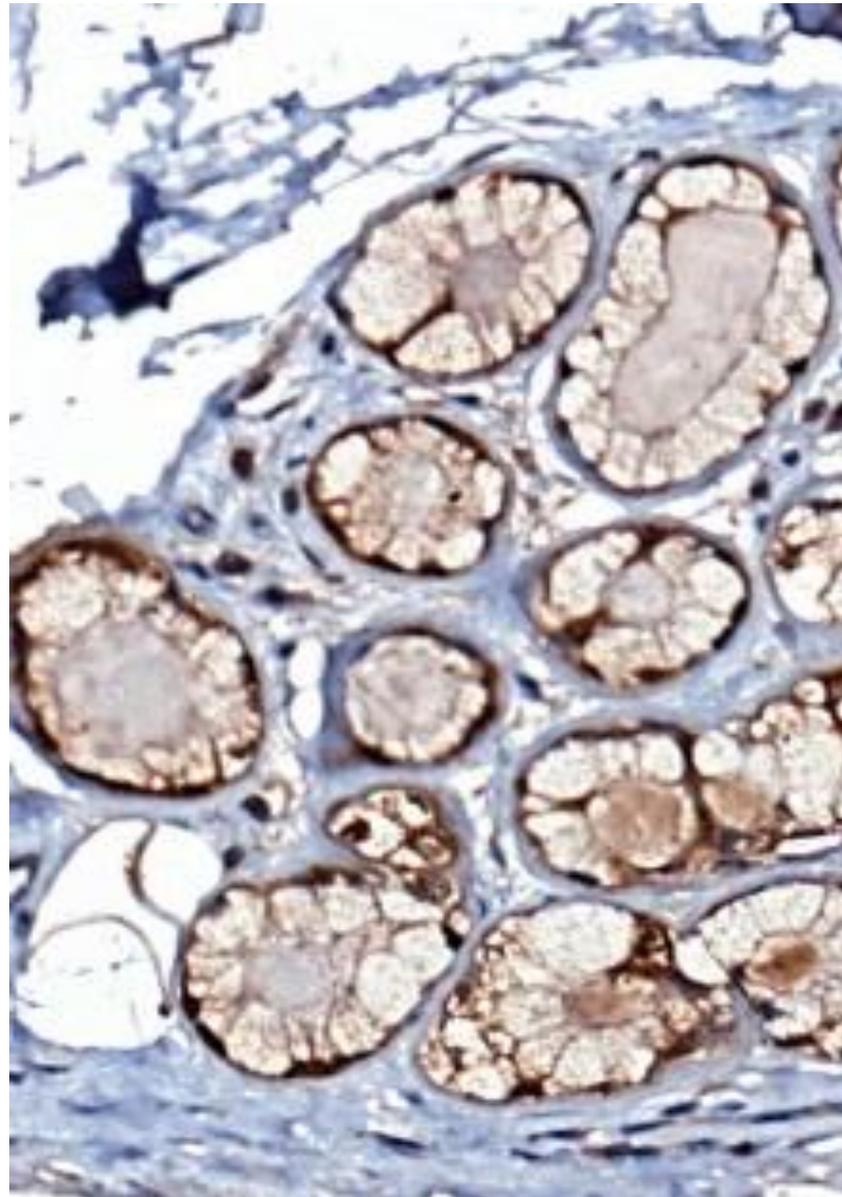
# COVID-19 – Efeitos Sistêmicos – Sist. Nervoso



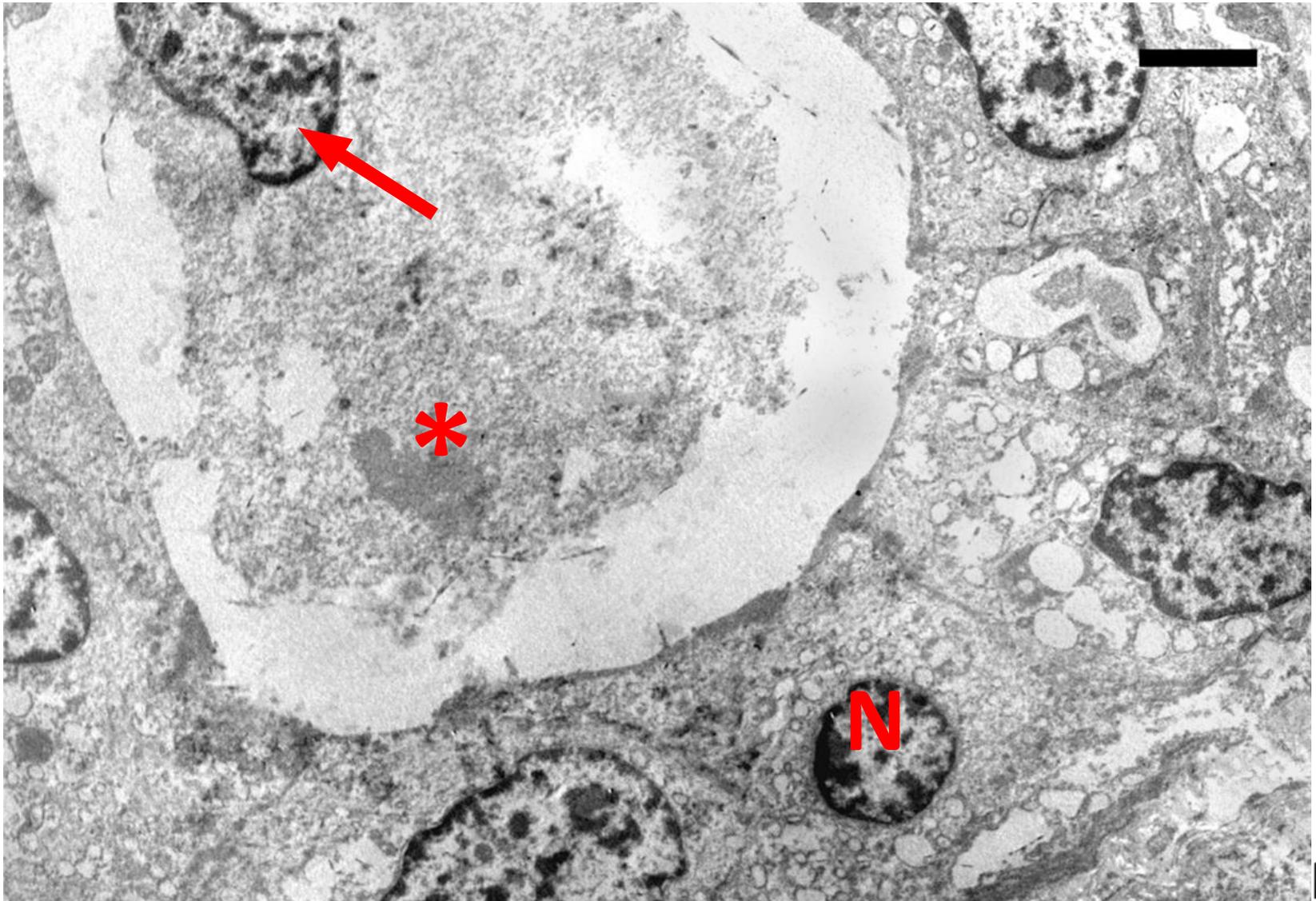
# COVID-19 – Efeitos Sistêmicos – Glândula Salivar



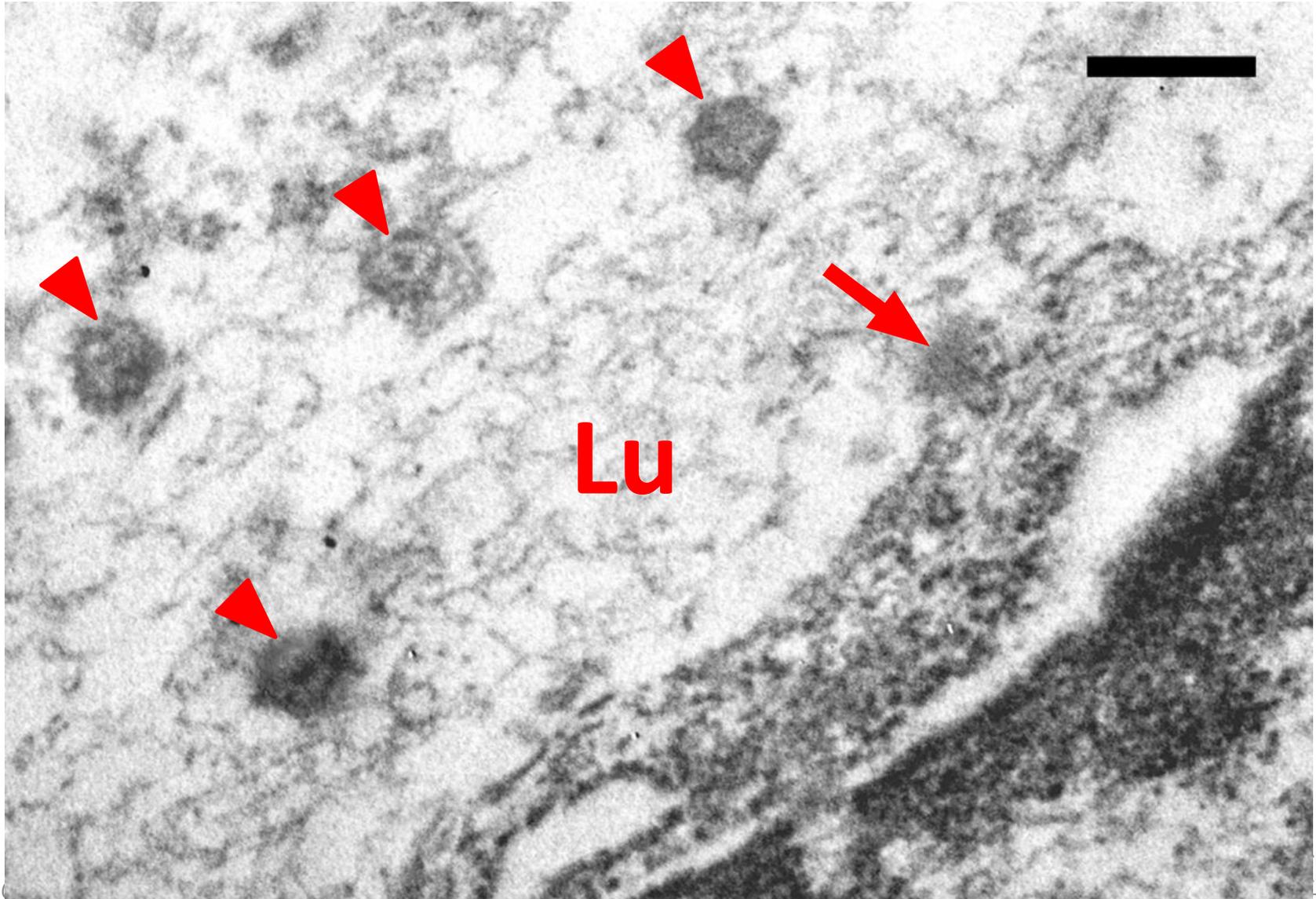
# COVID-19 – Efeitos Sistêmicos – Glândula Salivar



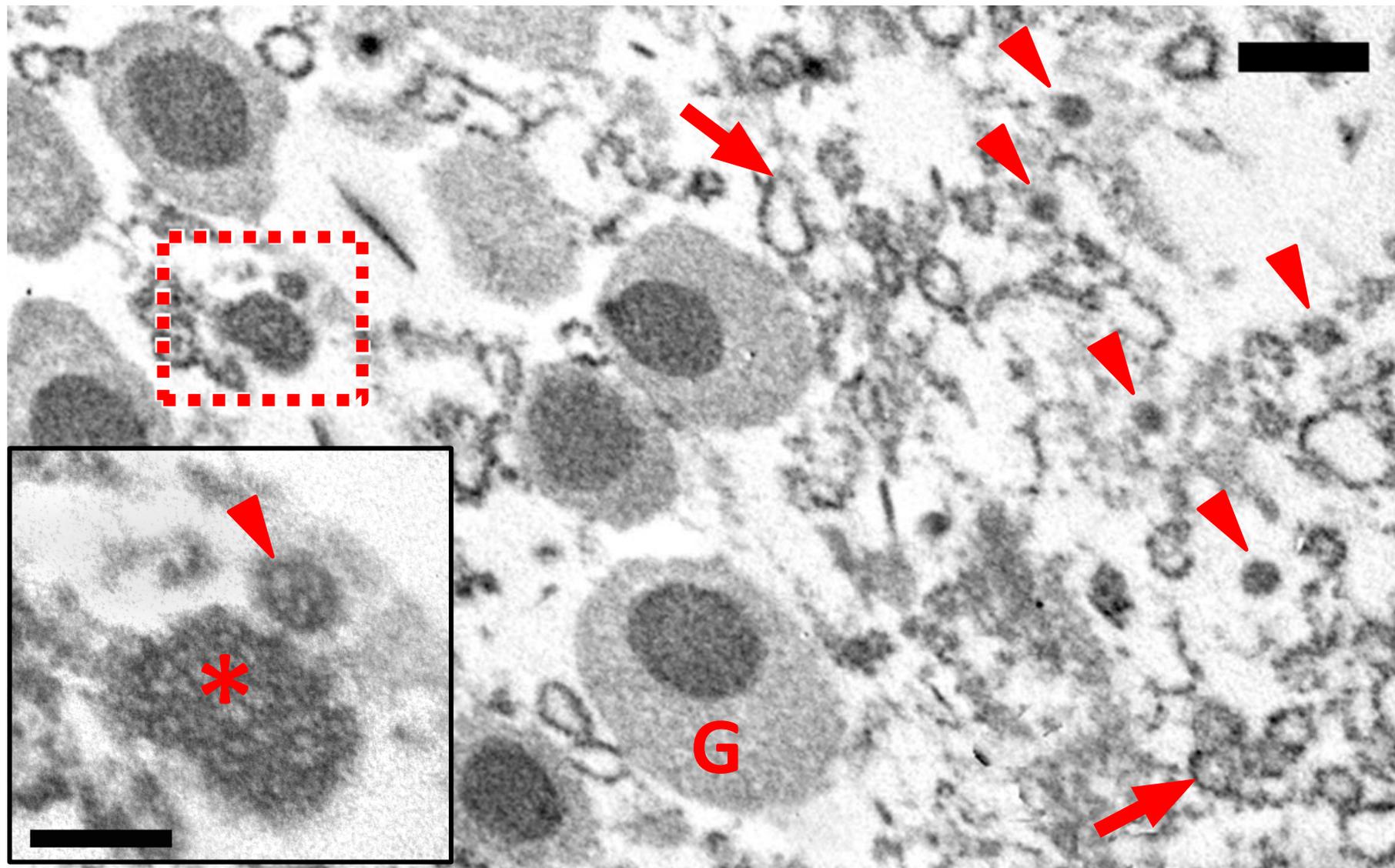
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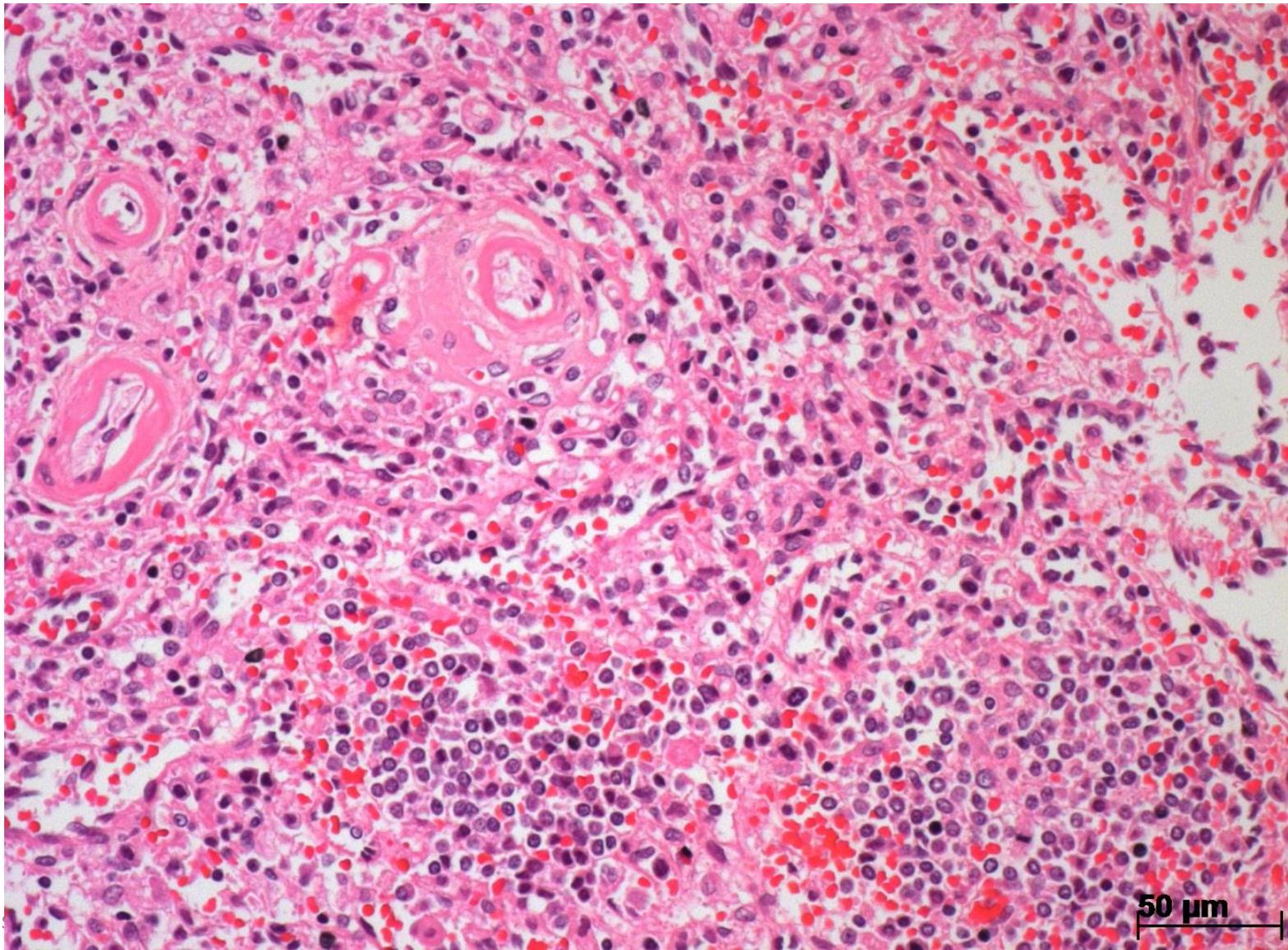
# COVID-19 – Efeitos Sistêmicos – Glândula Salivar



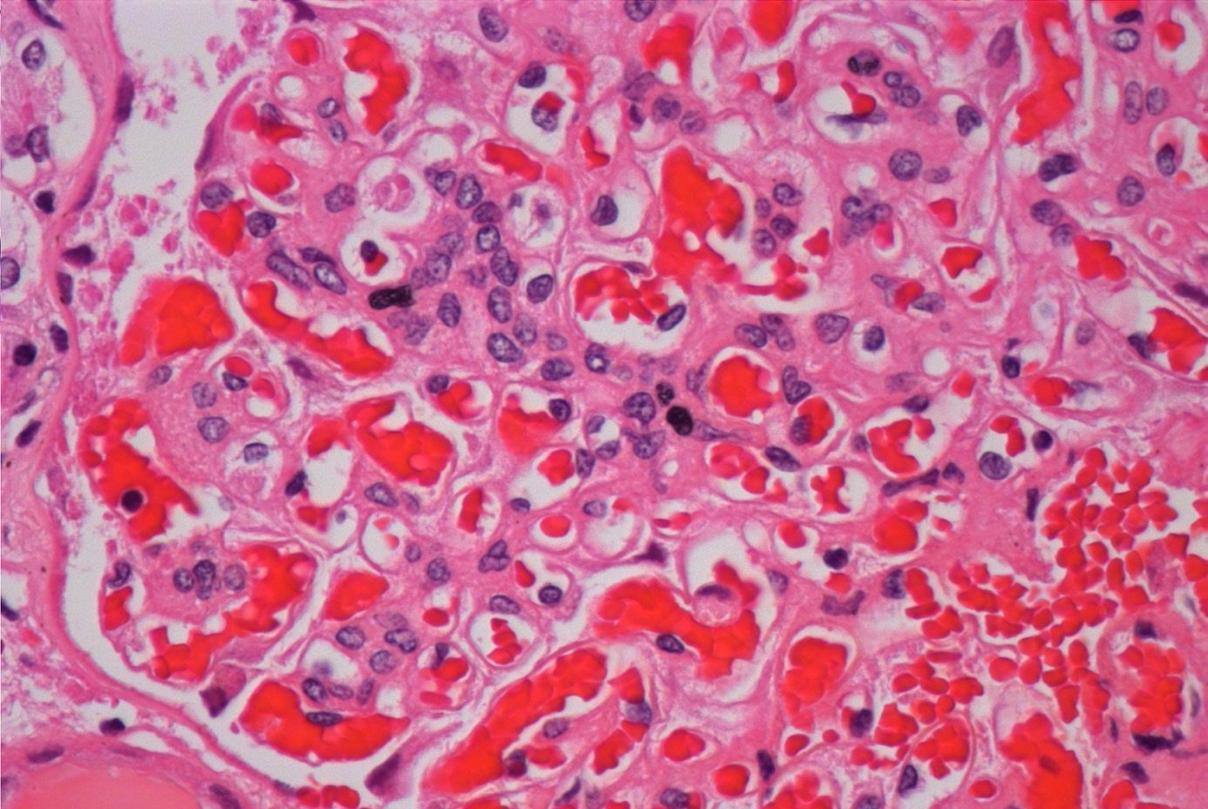
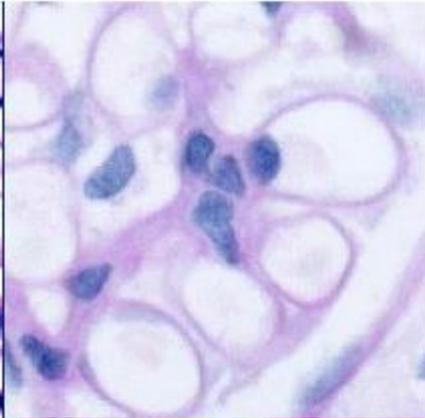
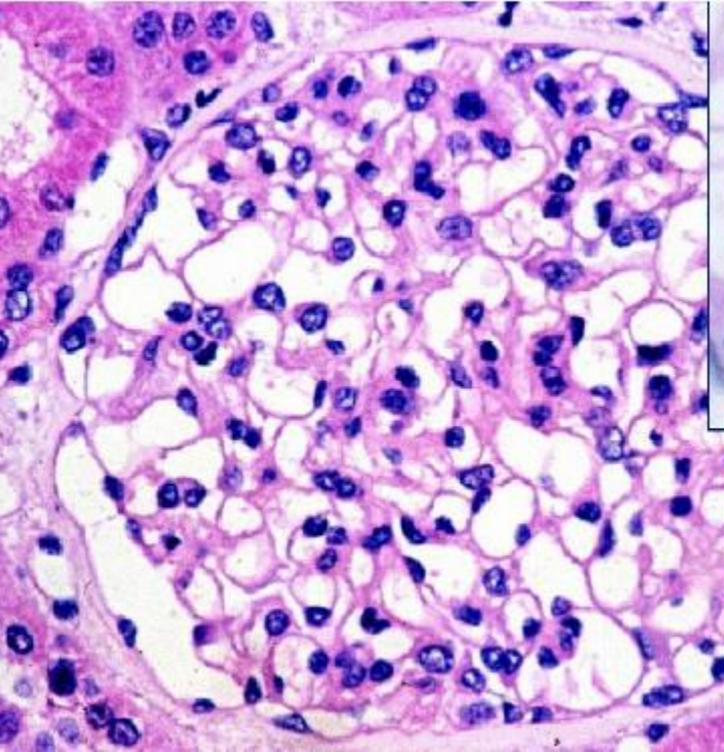
# COVID-19 – Efeitos Sistêmicos – Glândula Salivar



# COVID-19 – Efeitos Sistêmicos – Baço



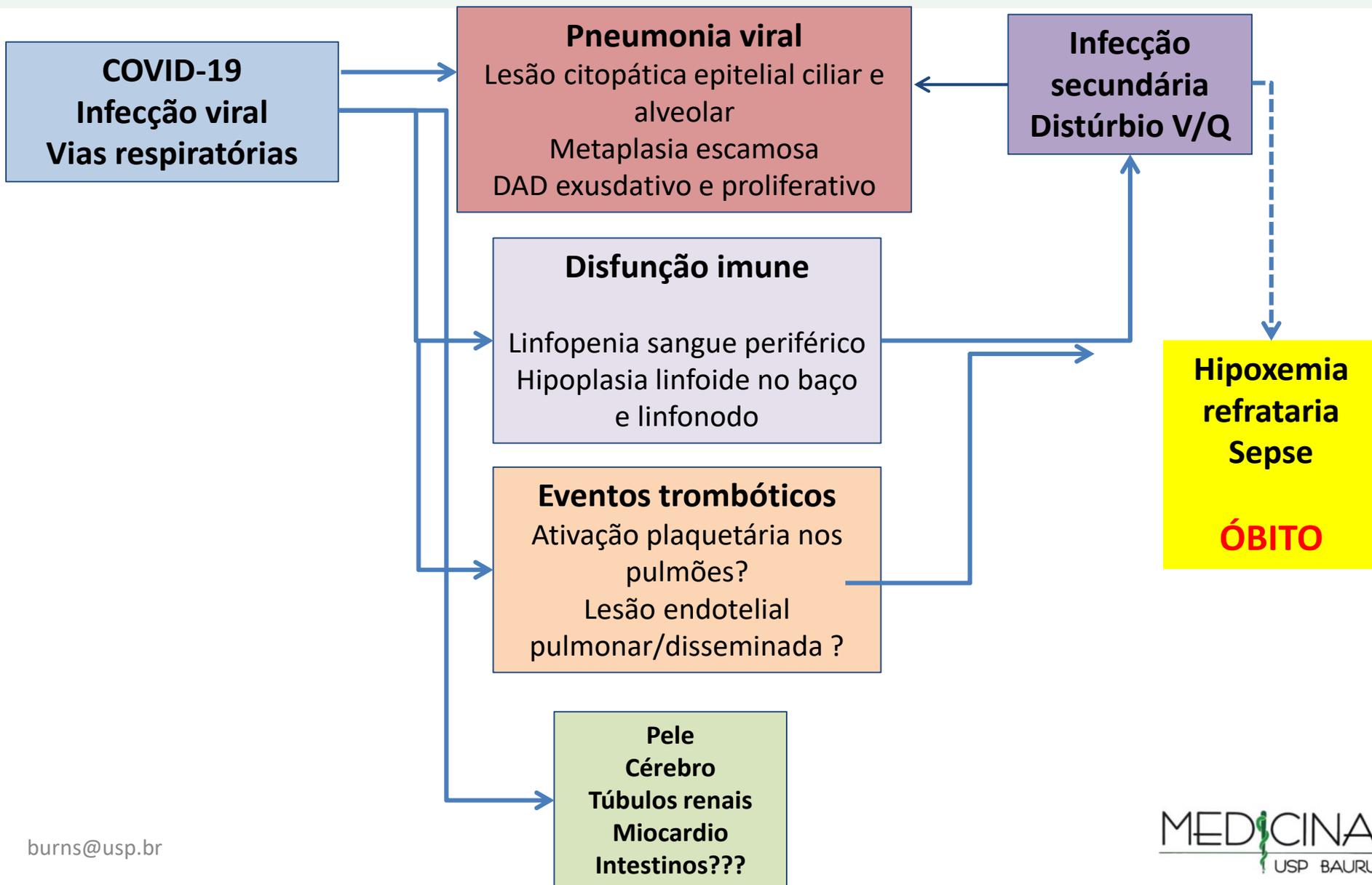
# COVID-19 – Efeitos Sistêmicos – Rins



# COVID-19 – Efeitos Sistêmicos – Outros

- Lesão muscular esquelética
- Comprometimento do epitélio olfatório
- Comprometimento de glândulas salivares
- Retardo maturativo da medula óssea
- Adrenalite focal
- Edema testicular e orquite focal
- Dermatite com infiltrado linfomononuclear perivascular

# COVID-19 – Visão Integrada



# Finalmente!!!

