

# **COVID-19**

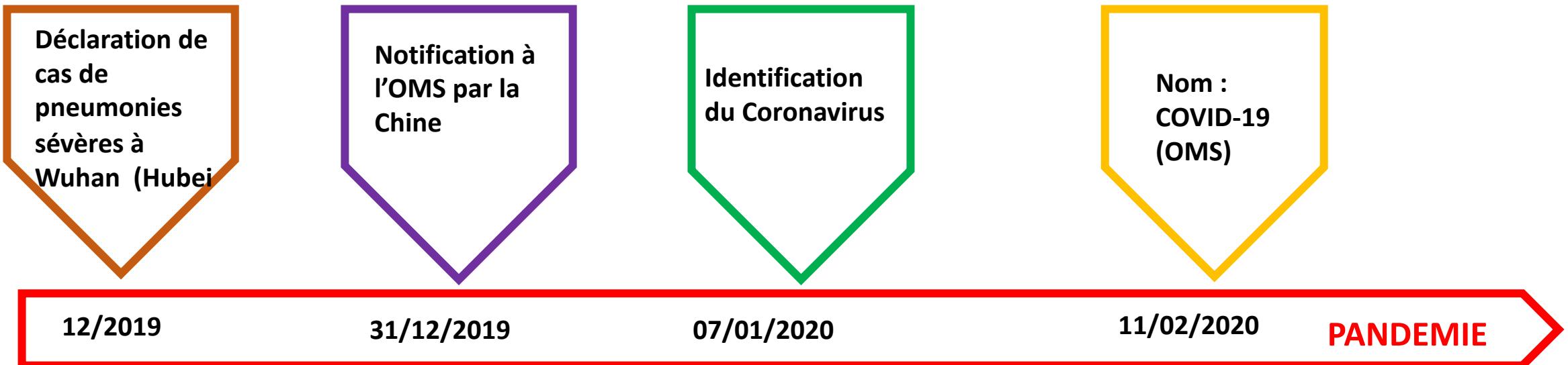
## **MÉCANISMES PHYSIOPATHOLOGIQUES IMPLIQUÉS**

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**UFR SANTE Université de Thiès**

**PTR Santé du CAMES**

# QUELQUES DATES CLÉS



# Case Comparison

## WHO Regions

### Americas



**4,370,519**

confirmed cases

### Europe



**2,543,778**

confirmed cases

### Eastern Mediterranean



**914,518**

confirmed cases

### South-East Asia



**600,191**

confirmed cases

### Africa



**224,673**

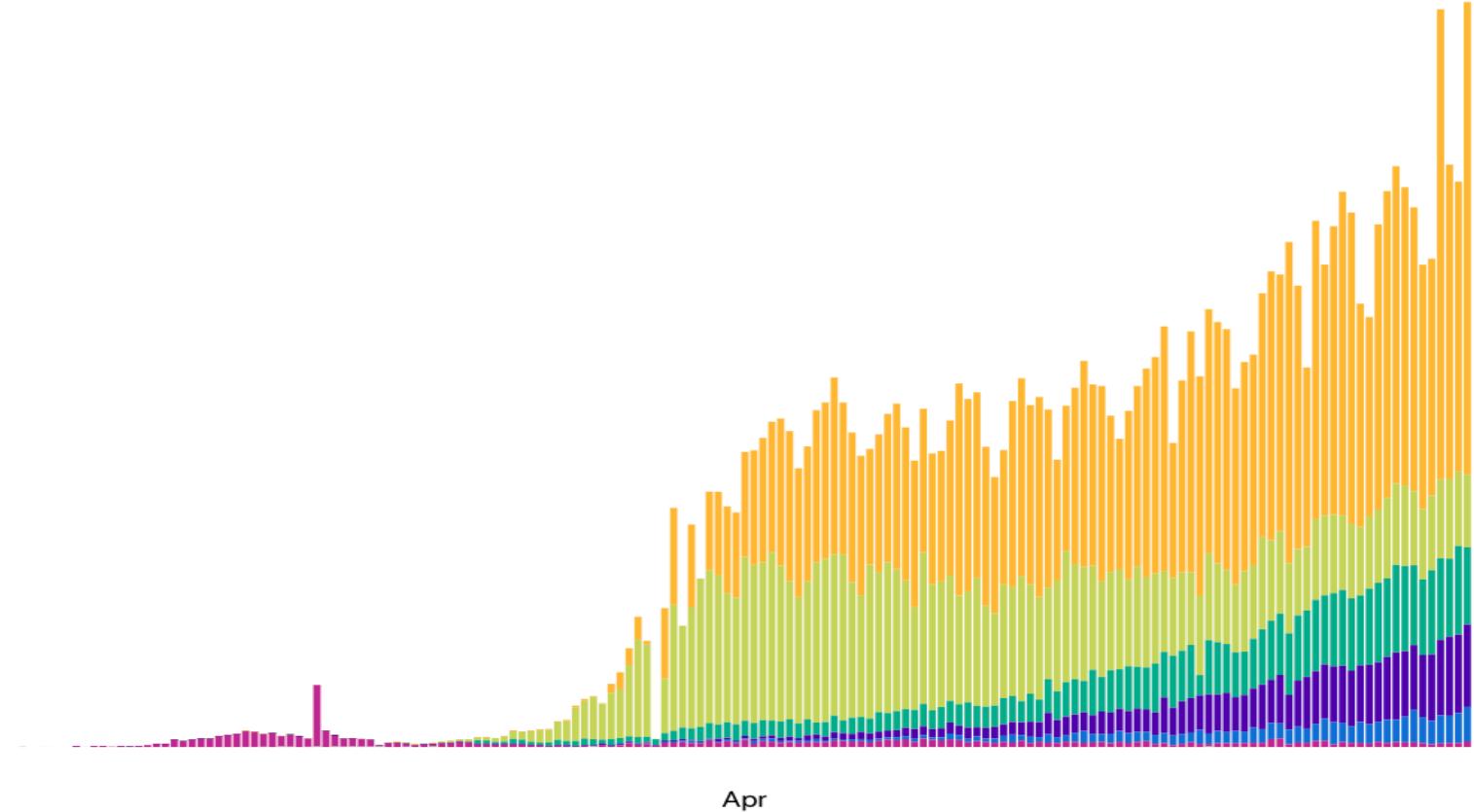
confirmed cases

### Western Pacific



**205,911**

confirmed cases

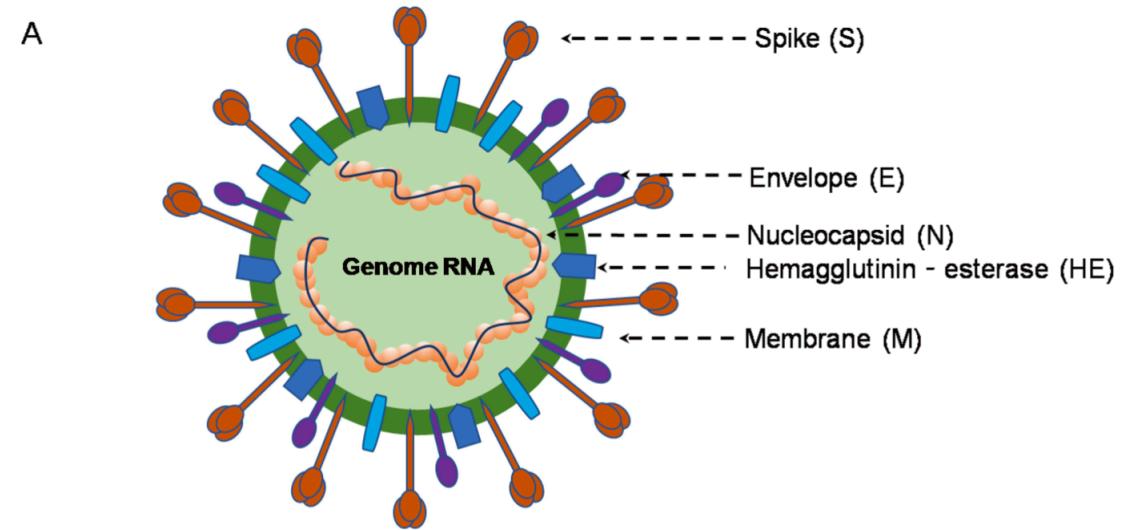


Source: World Health Organization

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# PATHOGENE

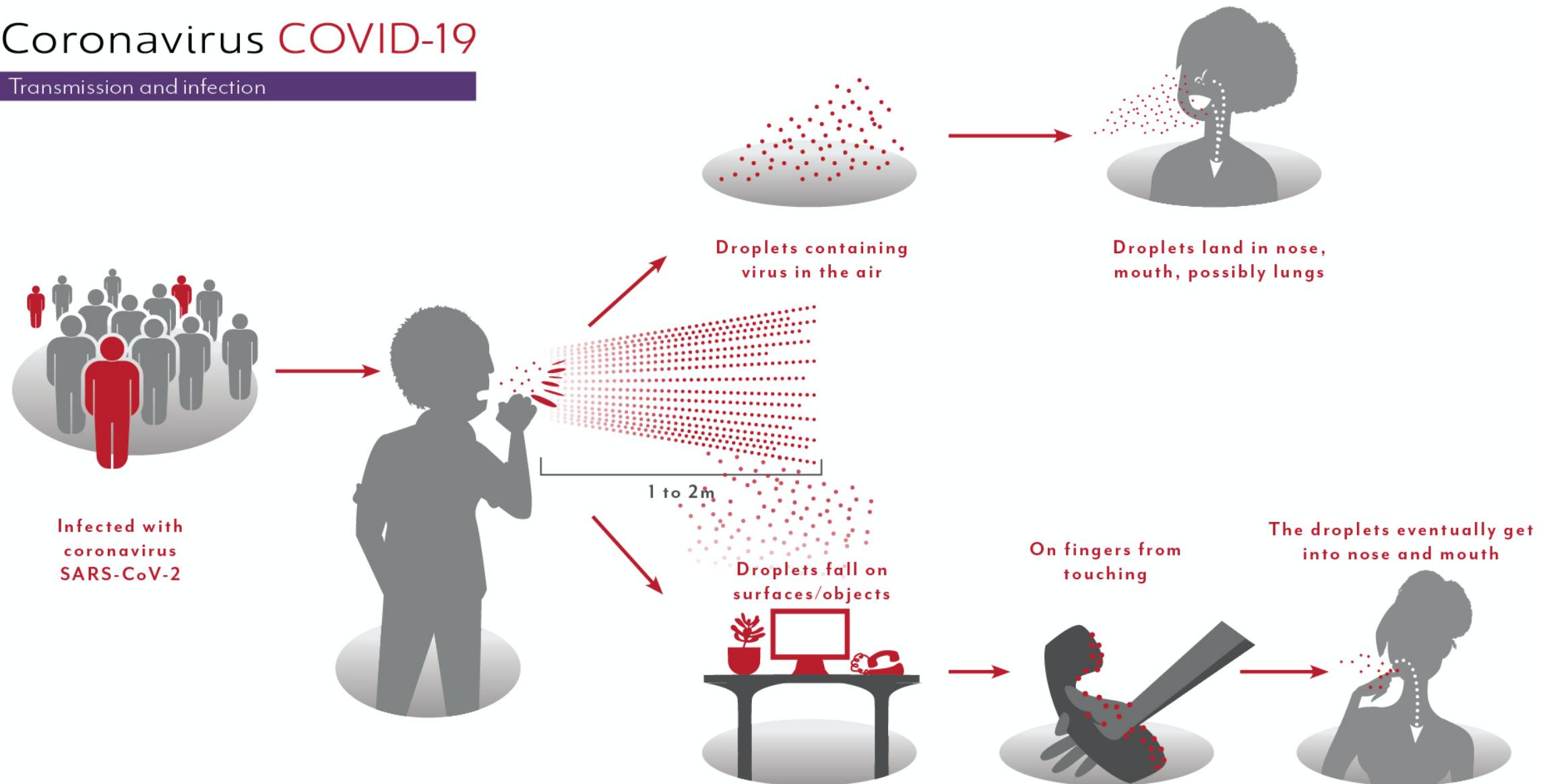
- Appelé 2019-n-COV
- nommé SARS COV-2 par ICTV
  - Analogie avec 70% SARS COV
  - Connus pour causer atteintes respiratoires

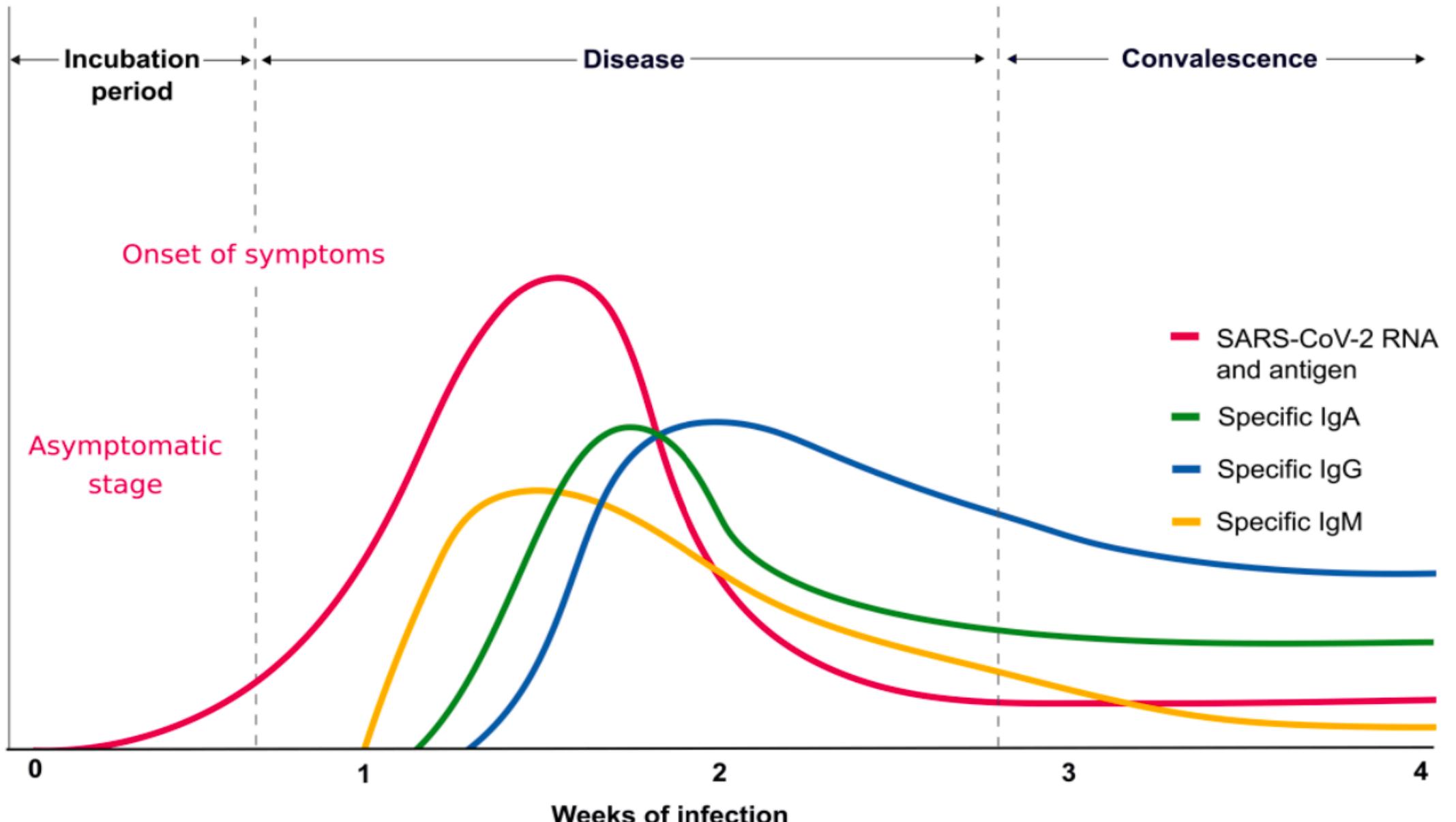


[Yuefen Jin et al, Viruses 2020, 12]

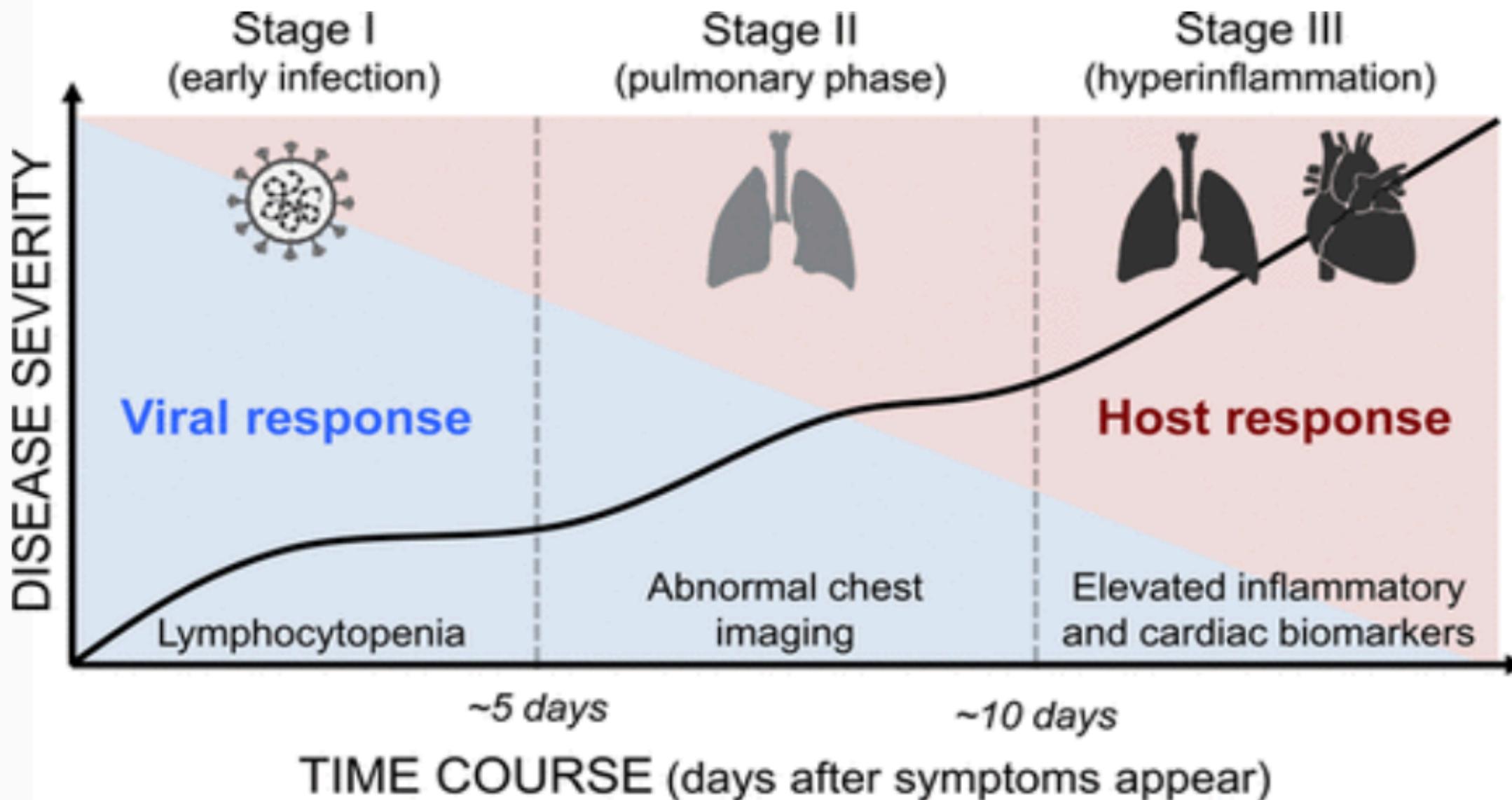
# Coronavirus COVID-19

## Transmission and infection

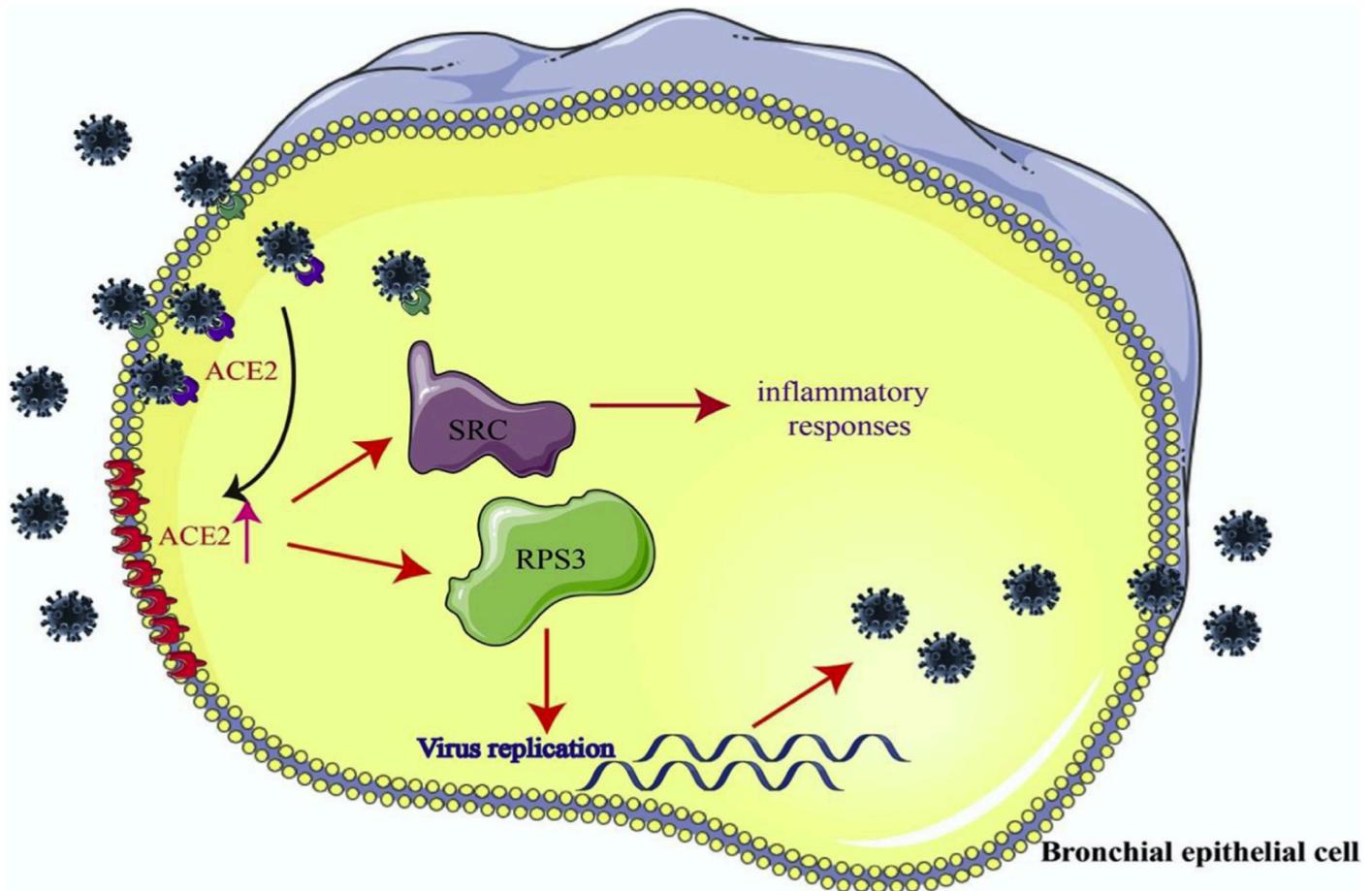




[Ahmet Kursat Azkur et Al, Allergy, Mai 2020]



## PORTE D'ENTRÉE CELLULAIRE SARS-COV-2



**Fig. 4. A schematic model of SARS-CoV-2 infection.** SARS-CoV-2 uses ACE2 as a cellular entry receptor in airway epithelial cells. At the same time, the expression of ACE2 is increased by the infection. Furthermore, the increased expression of ACE2 affected RPS3 and SRC, the two hub genes involved in viral replication and inflammatory responses.

# PORTE D'ENTRÉE CELLULAIRE SARS-COV-2

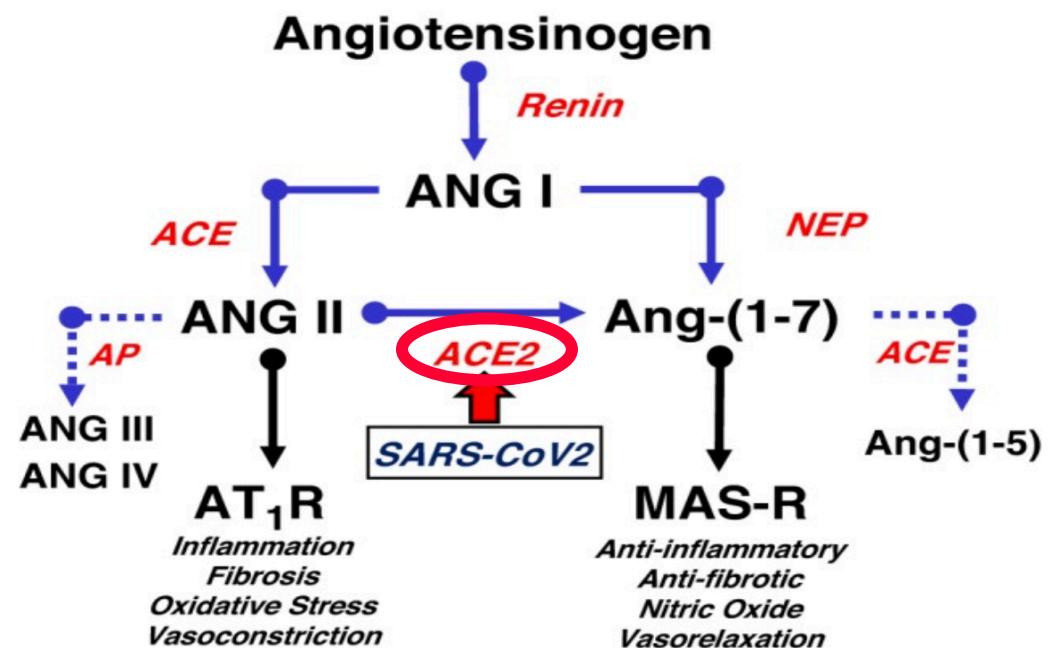
- SARS-COV (2003) identification récepteur ACE 2 liait le virus
- Par analogie lie également SARS COV-2

Am J Physiol Heart Circ Physiol. 2020 May 1; 318(5): H1084–H1090.

Published online 2020 Mar 31. doi: [10.1152/ajpheart.00217.2020](https://doi.org/10.1152/ajpheart.00217.2020)

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Fig. 1.



# RECEPTEUR ACE 2: Clé

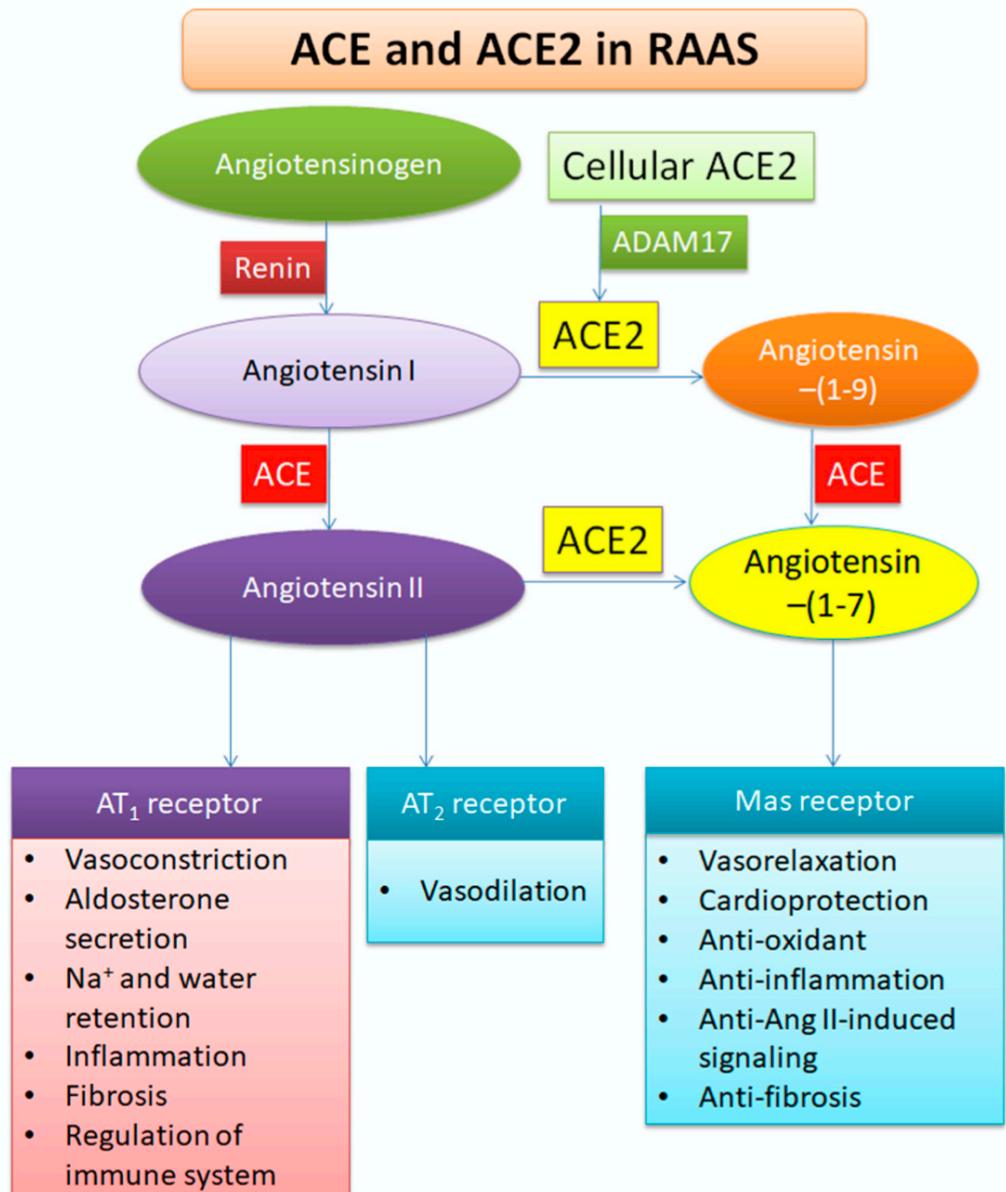
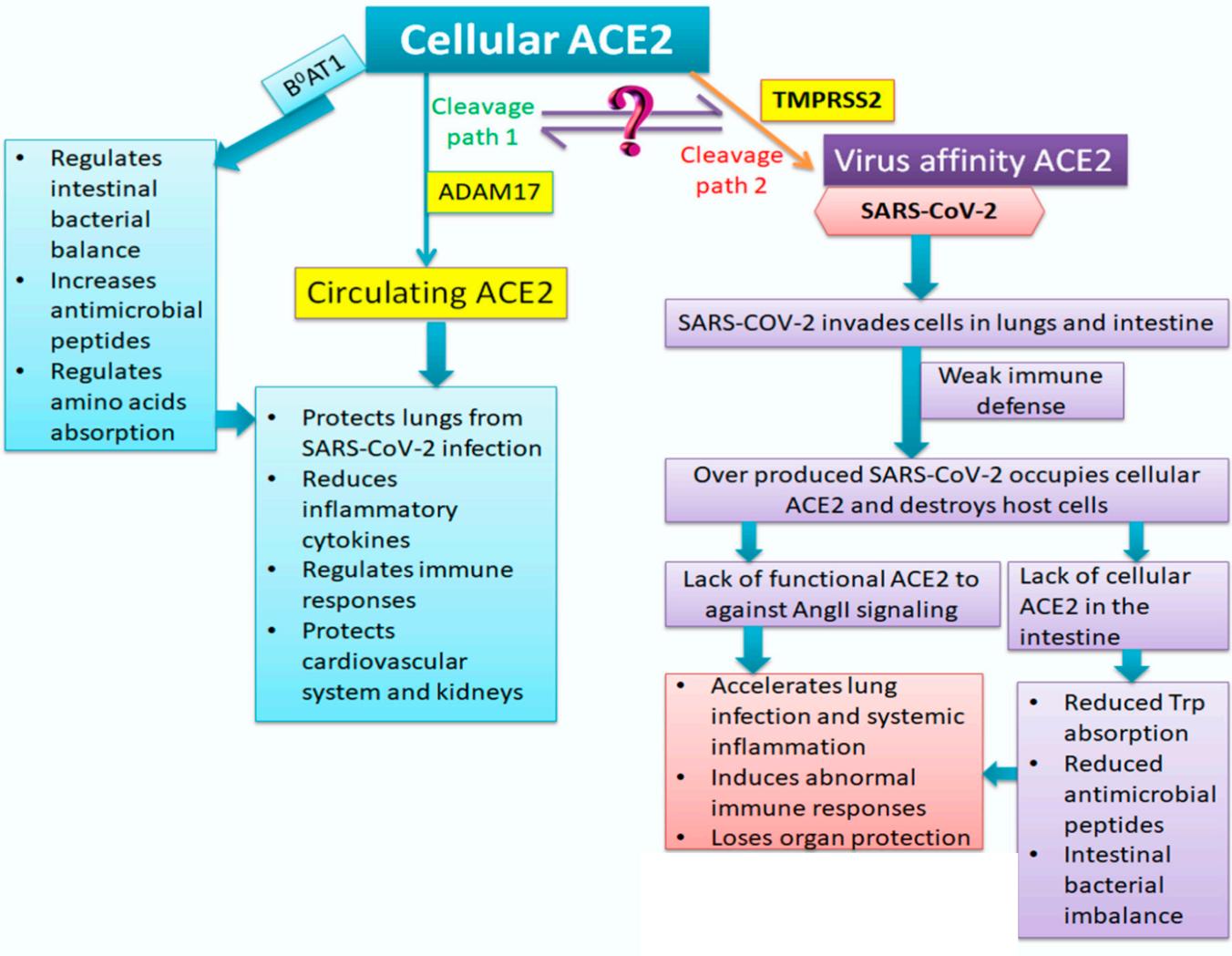
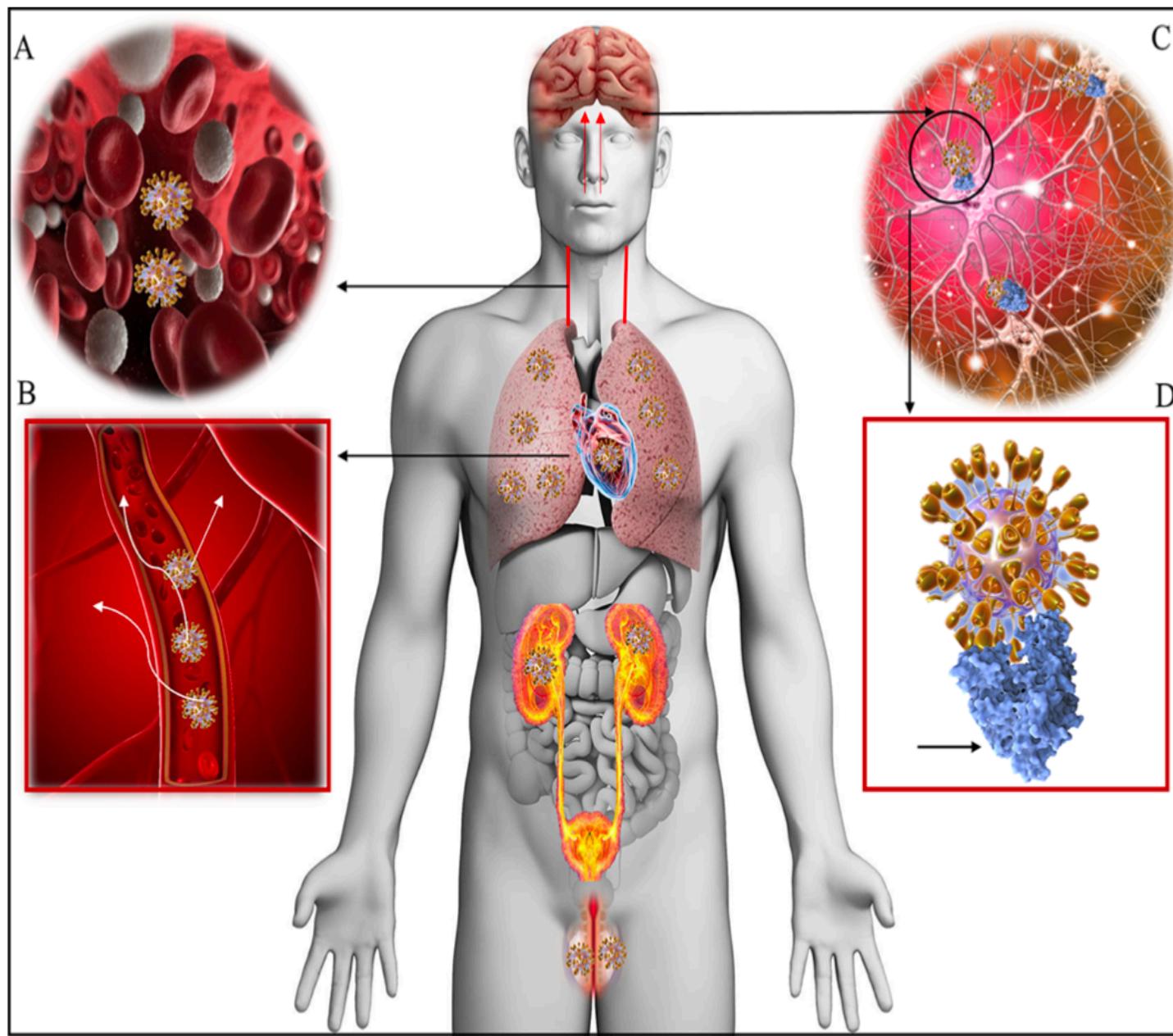


Figure 2. Role of ACE2 in the renin-angiotensin-aldosterone system (RAAS).



- Réceptorielle
- Circulante





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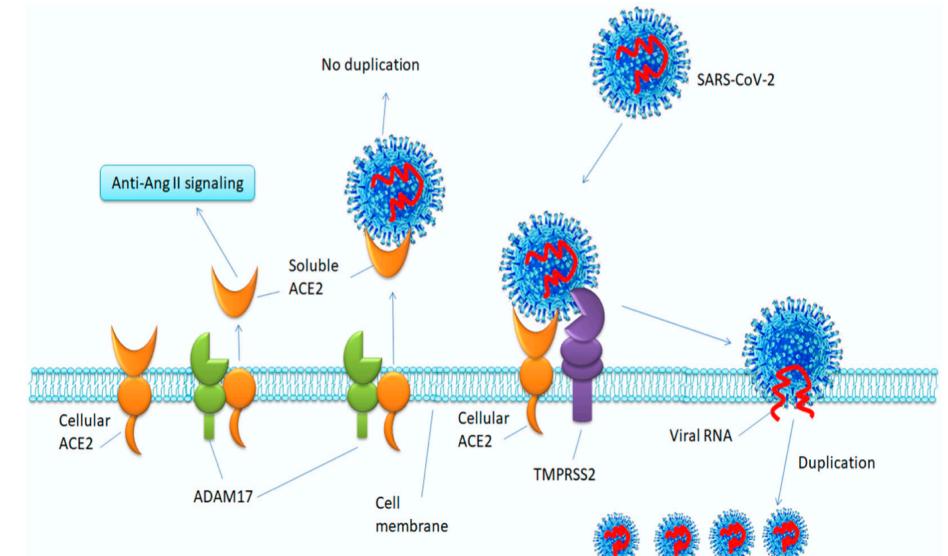
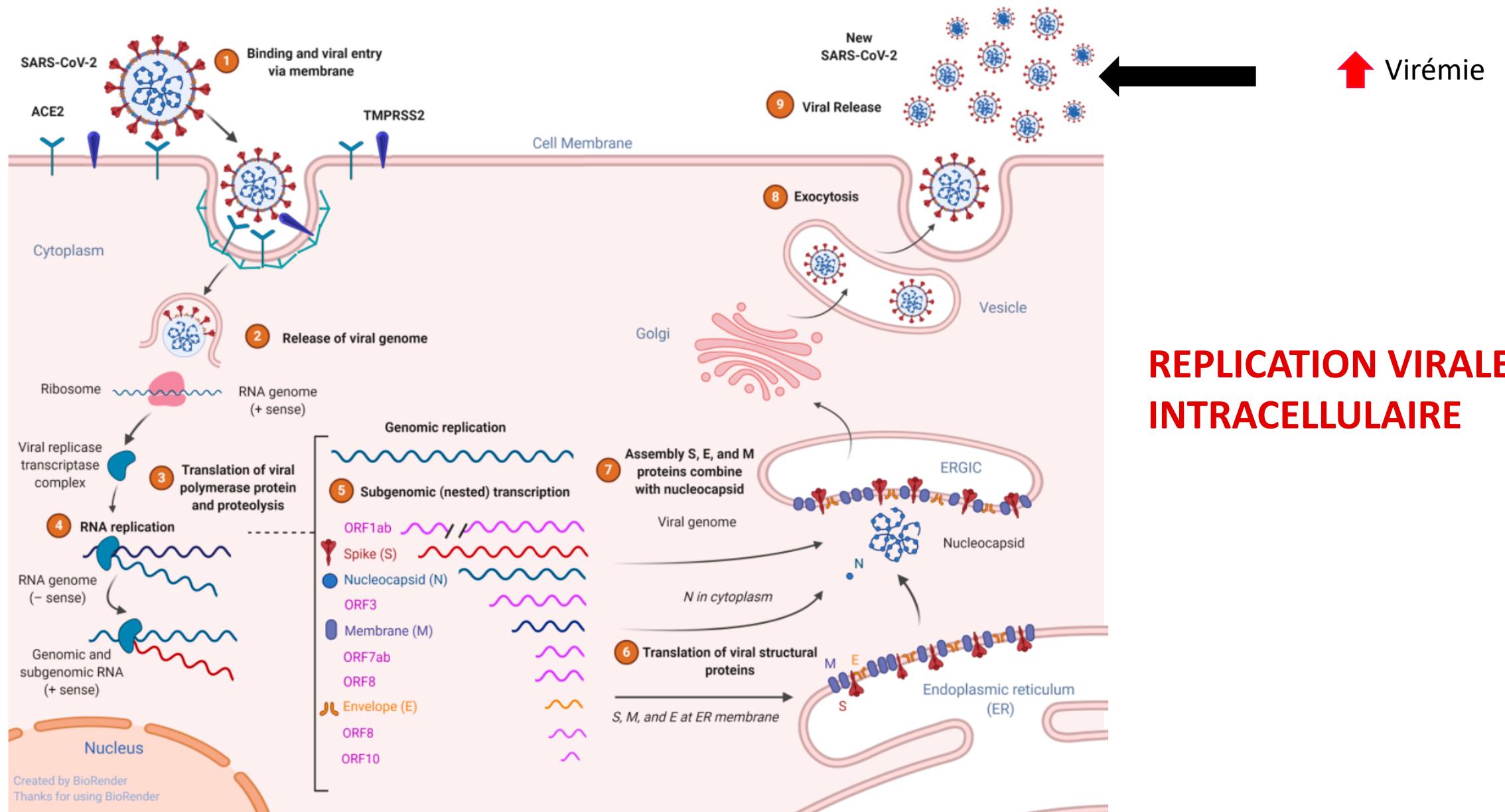


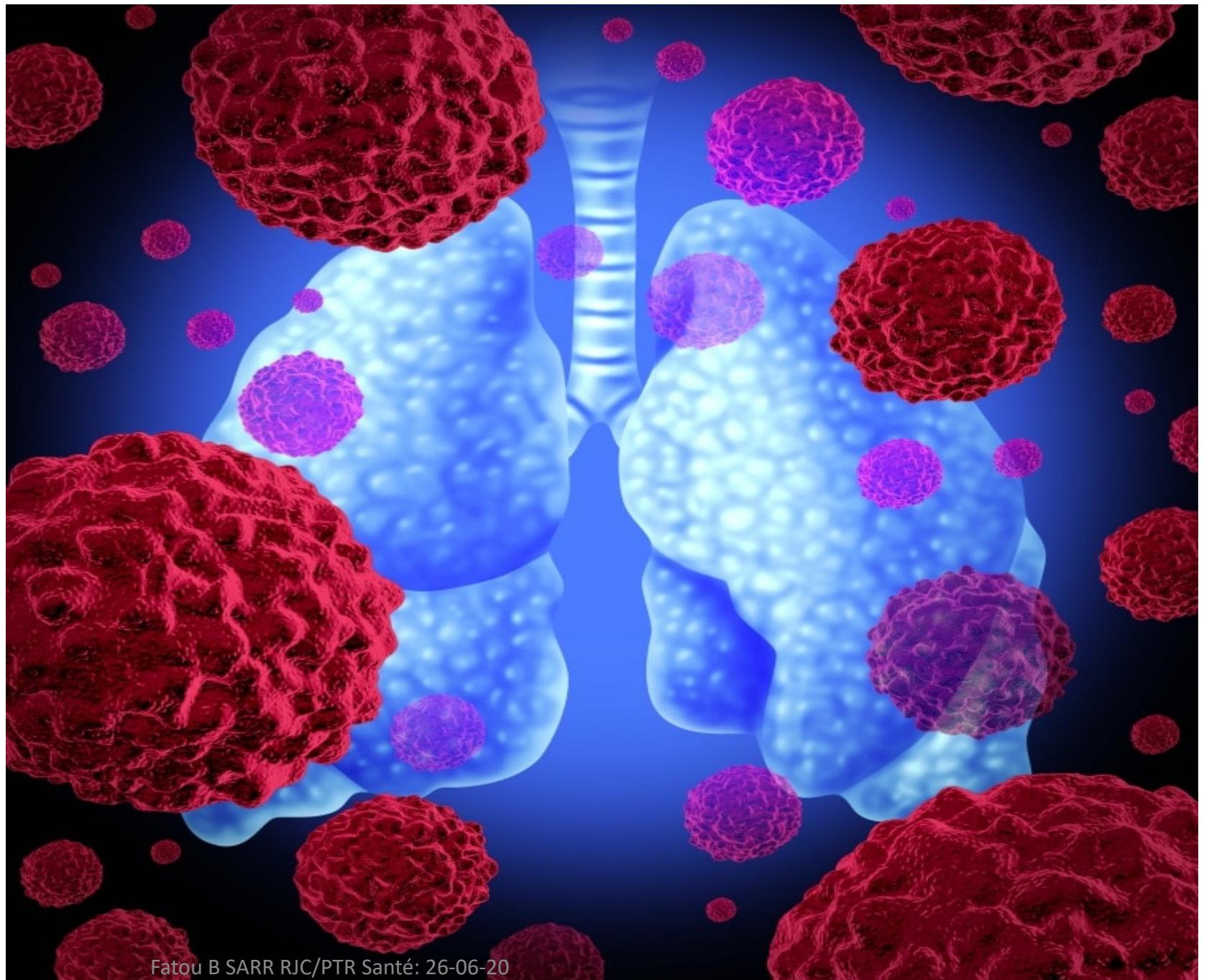
Figure 1. Hypothesis of ACE2 shedding and SARS-CoV-2 entry.

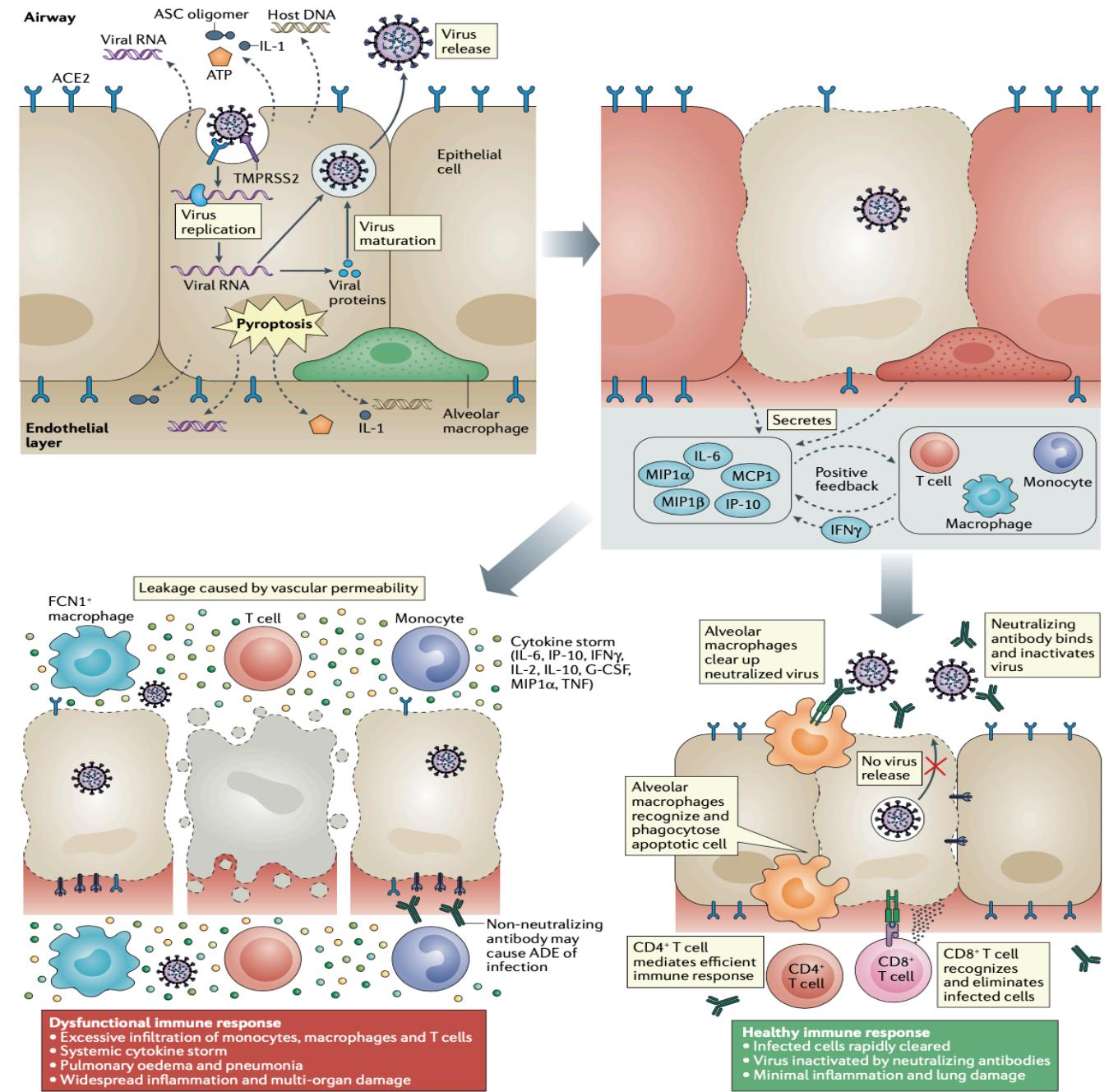
## DISTRIBUTION RECEPTEUR ACE 2

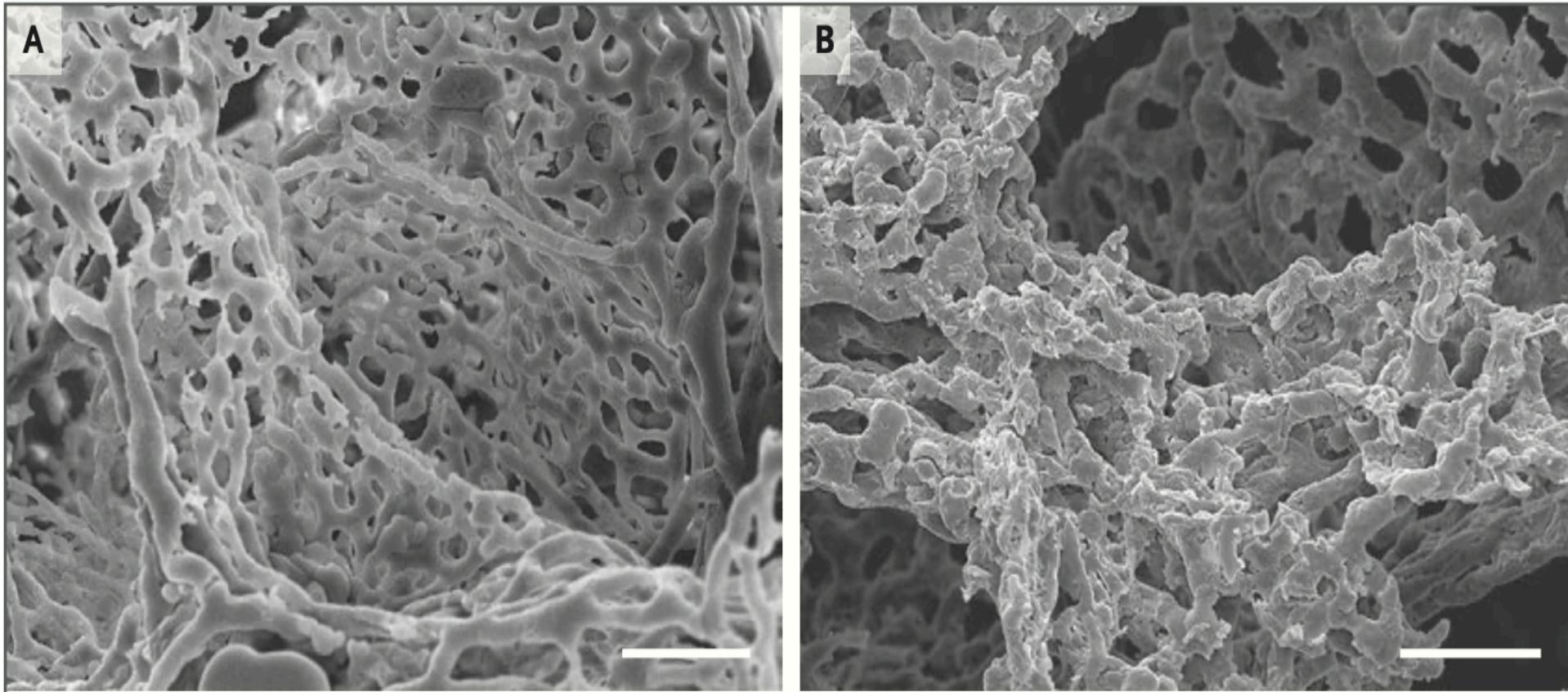


## REPLICATION VIRALE INTRACELLULAIRE

## ATTEINTES RESPIRATOIRES DANS LA COVID -19

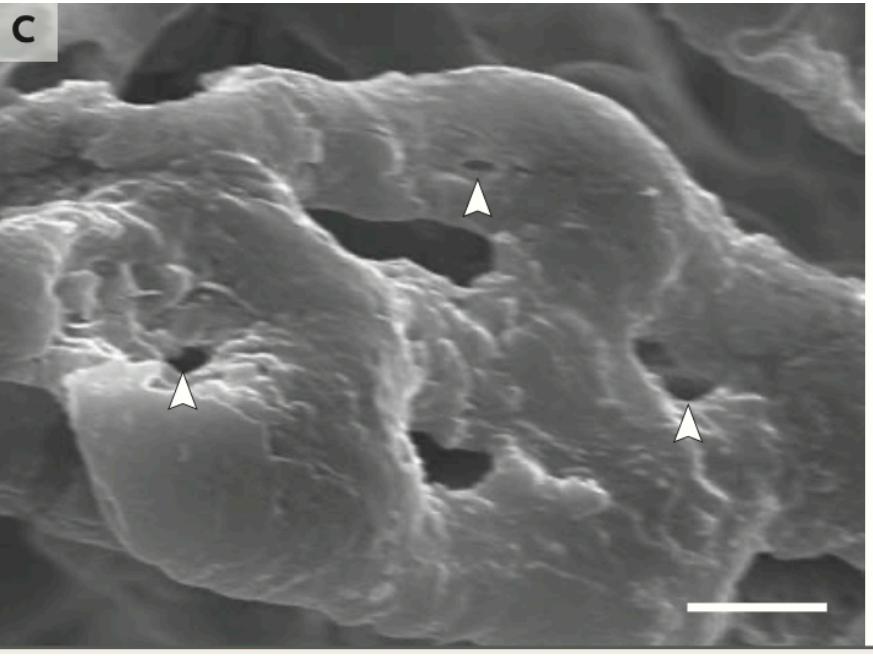




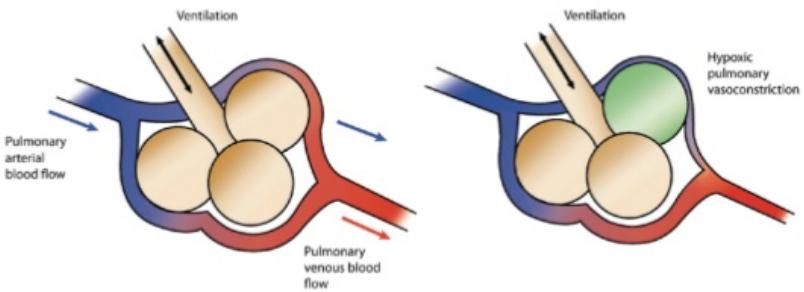


Poumon sain

Poumon COVID +



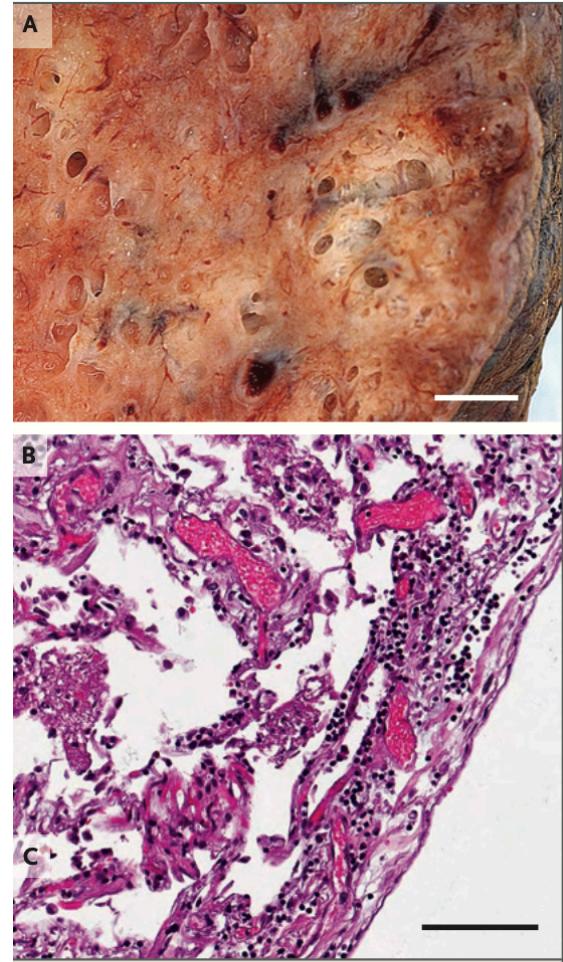
Espace mort = territoire ventilé / non-perfusé  
(Effet shunt = territoire non-ventilé / perfusé)



La vasoconstriction hypoxique évite de faire passer du sang dans un territoire non-ventilé  
=> réduction de l'espace mort

Signes respiratoires  
désaturation

Augmentation volume  
pulmonaire  
Altérations tissulaires

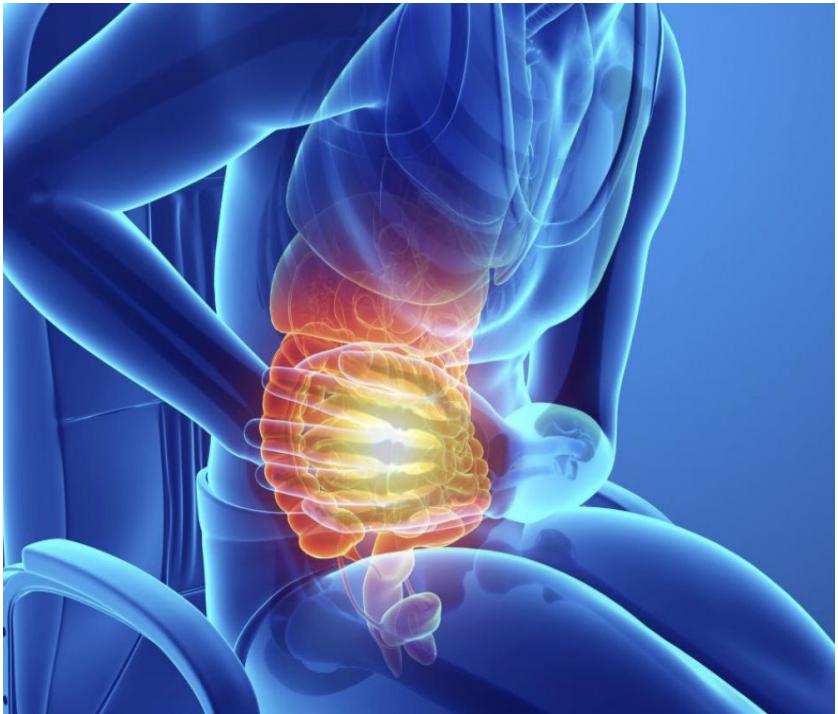


**Figure 1.** Lymphocytic Inflammation in a Lung from a Patient Who Died from Covid-19.

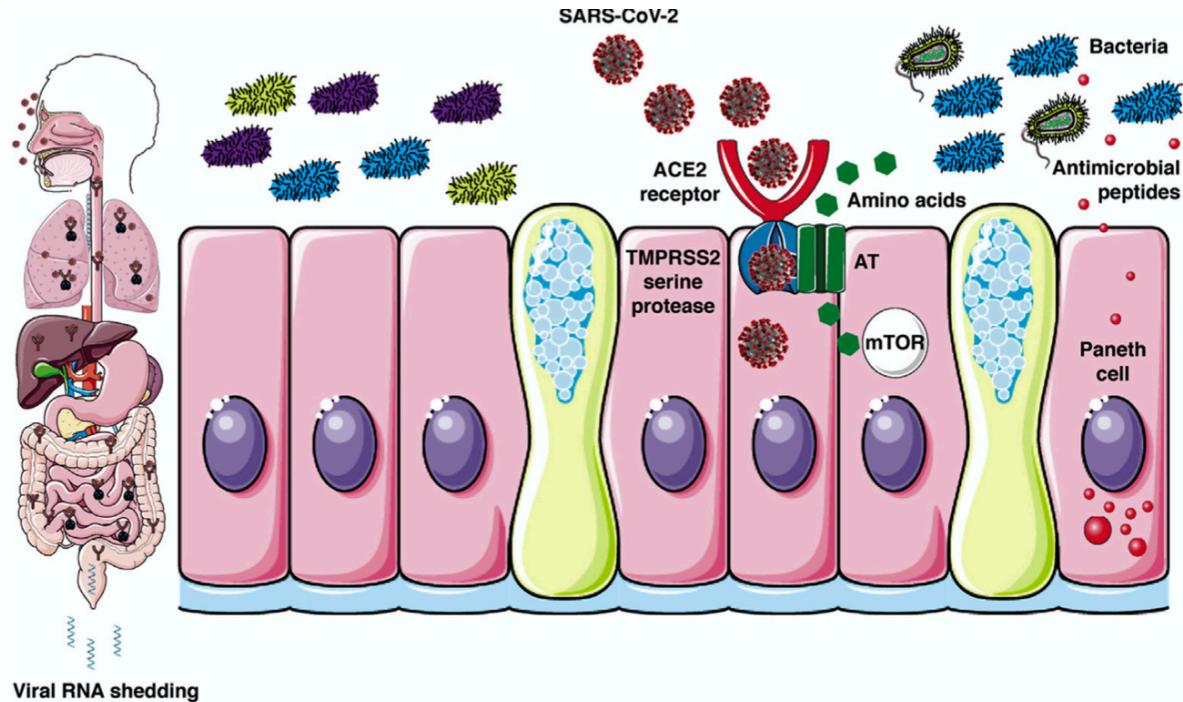
The gross appearance of a lung from a patient who died from coronavirus disease 2019 (Covid-19) is shown in Panel A (the scale bar corresponds to 1 cm). The histopathological examination, shown in Panel B, revealed interstitial and perivascular predominantly lymphocytic pneumonia with multifocal endothelialitis (hematoxylin–eosin staining; the scale bar corresponds to 200  $\mu$ m).

## **ATTEINTES DIGESTIVES DANS LA COVID -19**





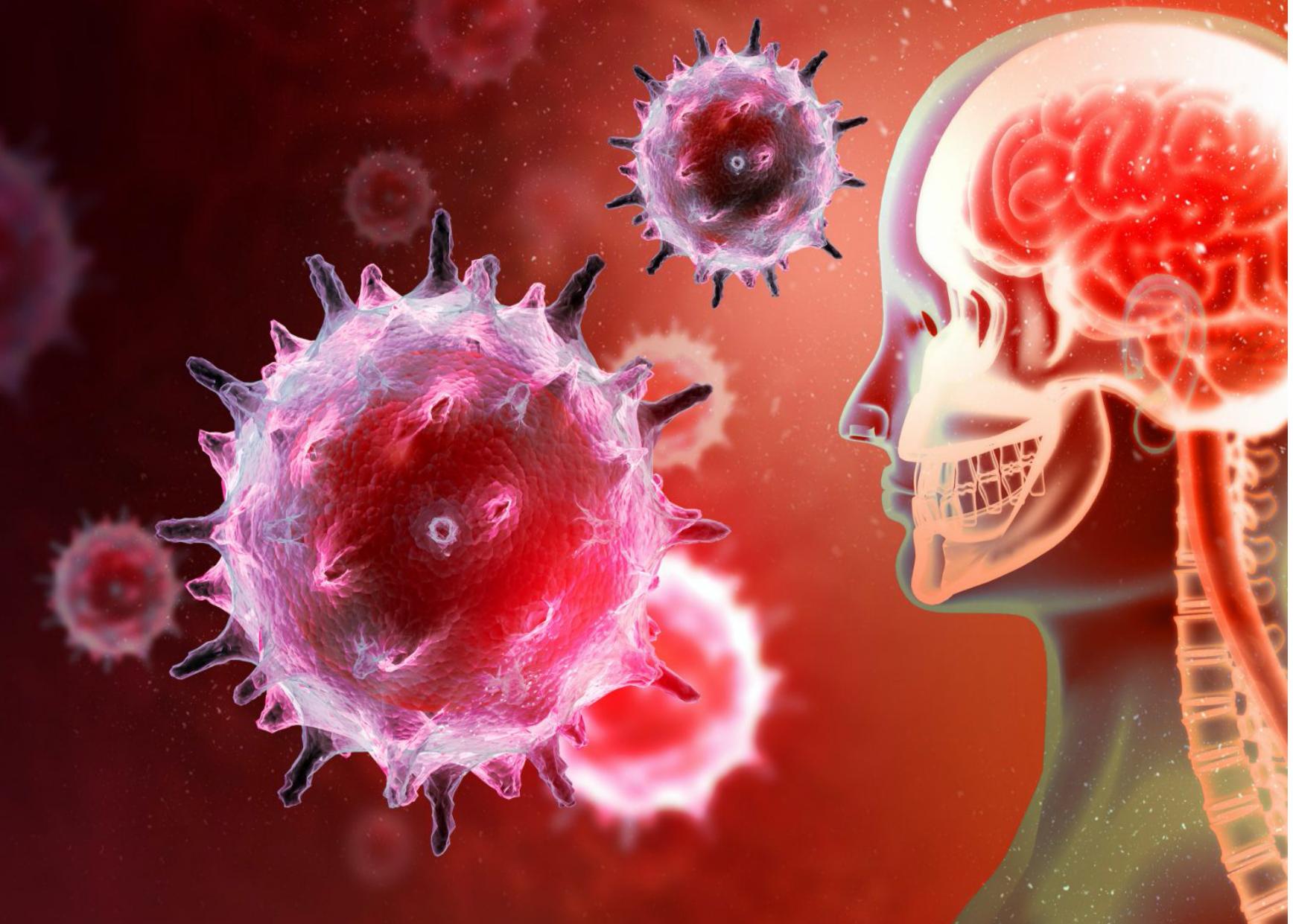
Troubles digestifs  
**Diarrées ++**



**Figure 1.** Proposed model for SARS-CoV-2-associated diarrhea. SARS-CoV uses ACE2 and the serine protease TMPRSS2 for entry in lung AT cells. ACE2 and TMPRSS2 are not only expressed in lung, but also the small intestinal epithelia. ACE2 is expressed in the upper esophagus, liver, and colon. ACE2 is also necessary for the surface expression of amino acid transporters of the small intestine. Amino acids, like tryptophan, regulate the secretion of antimicrobial peptides by Paneth cells via mTOR pathway activation. Antimicrobial peptides impact the composition and diversity of the microbiota. Disturbance of this pathway could drive inflammation (enteritis) and ultimately diarrhea. SARS-CoV-2 rendering courtesy of Centers for

[Fernandino d'Amico et al, Clin Gastr-Hepat Ju 2020]

# **ATTEINTES NEUROLOGIQUES DANS LA COVID -19**





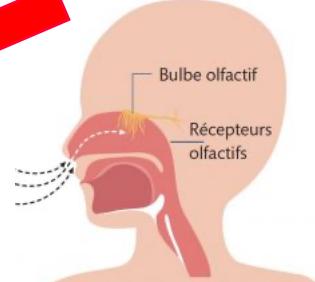
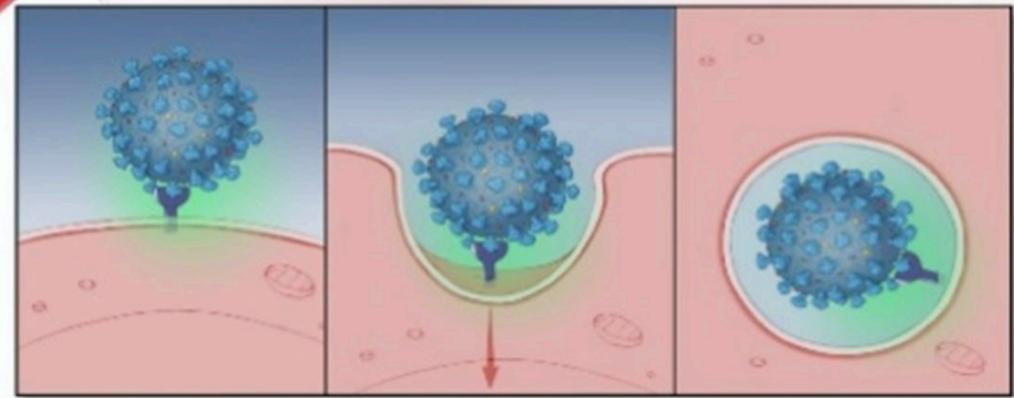
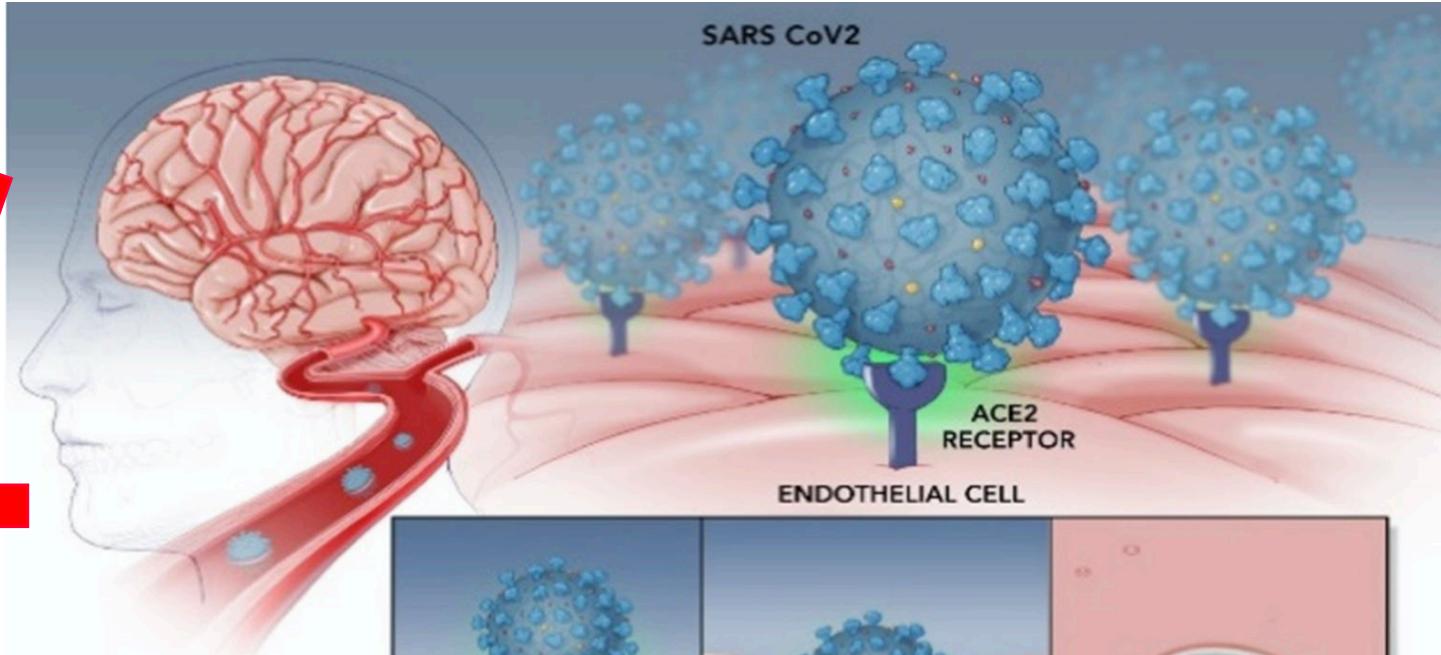
Céphalées



Anosmie



Agueusie



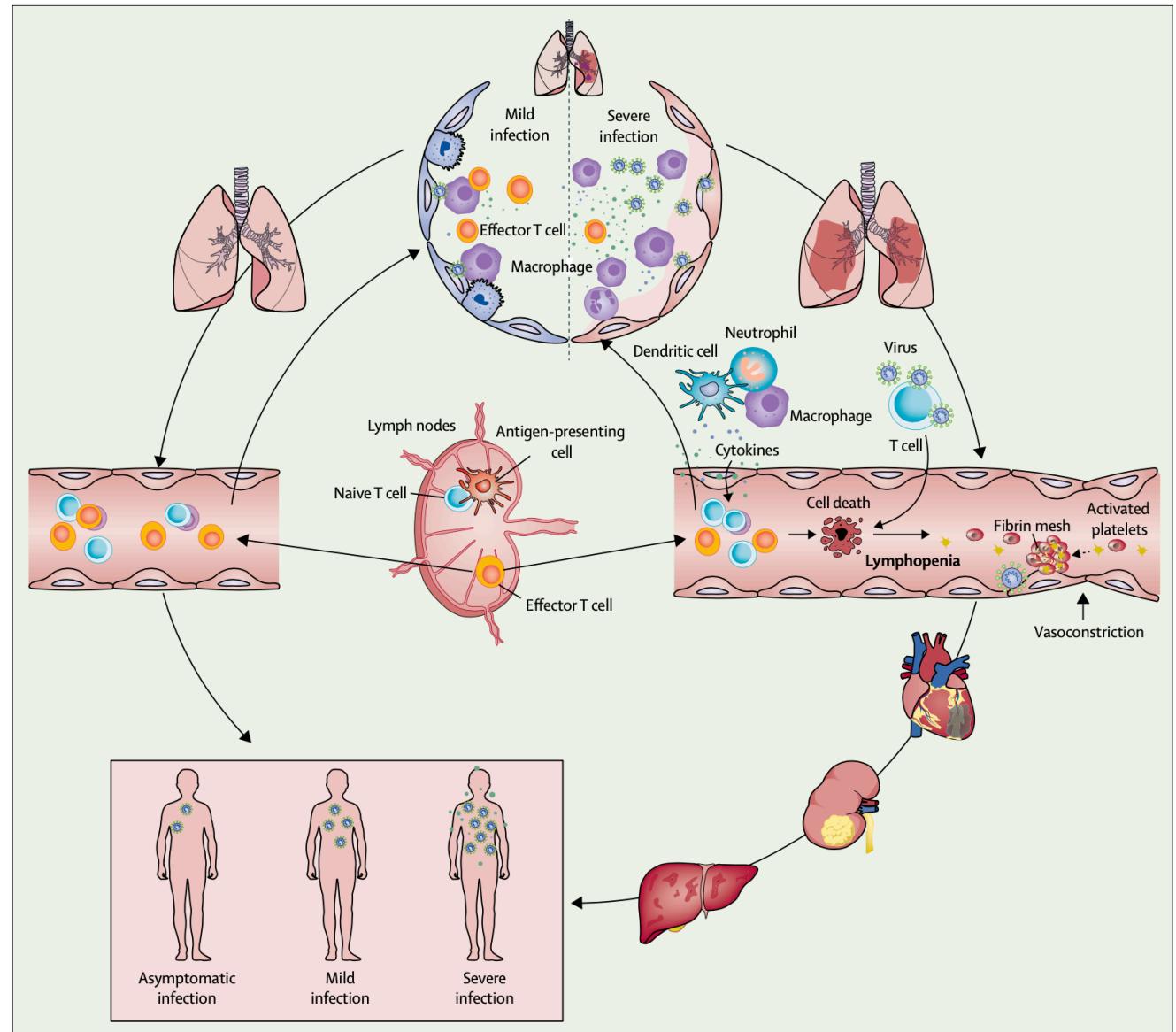
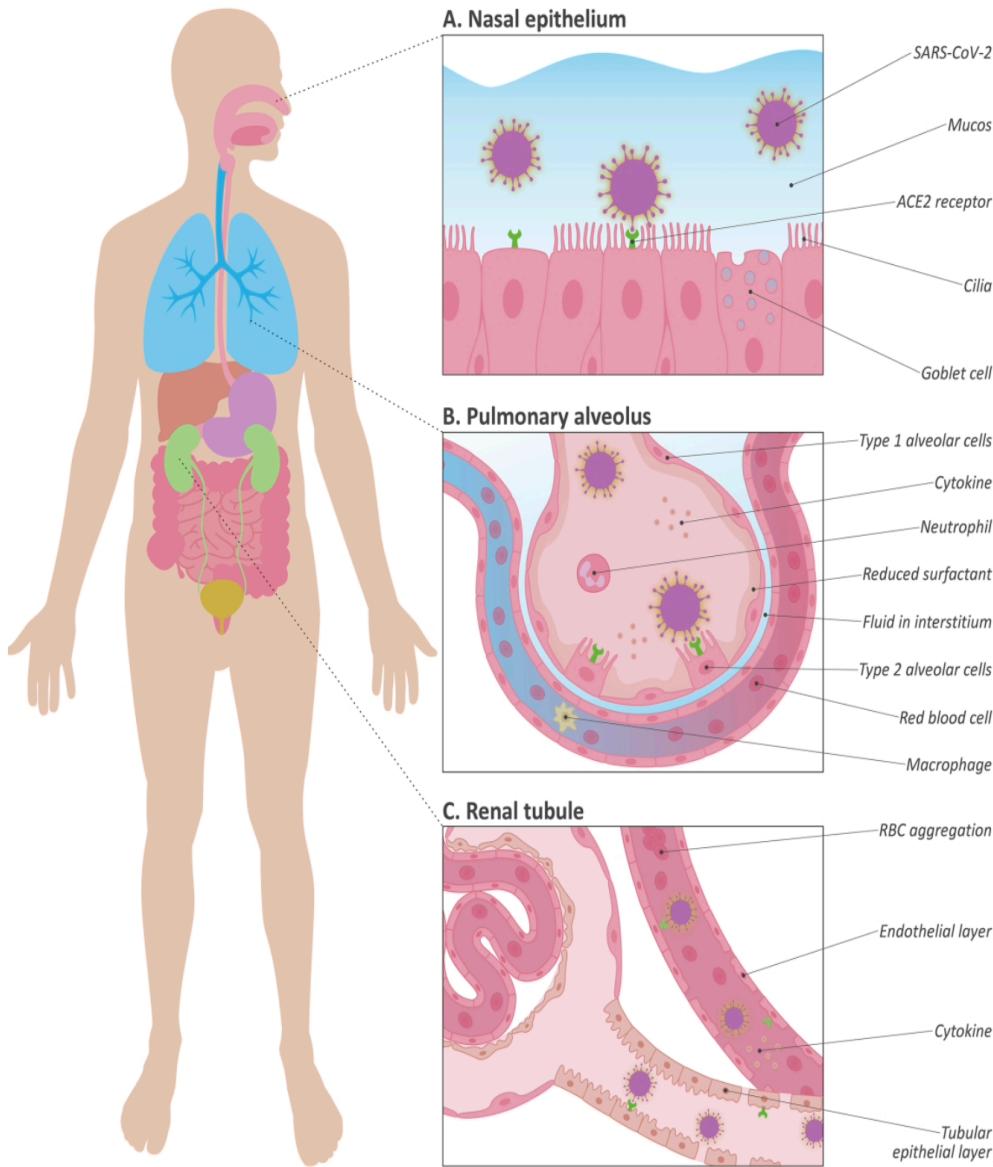
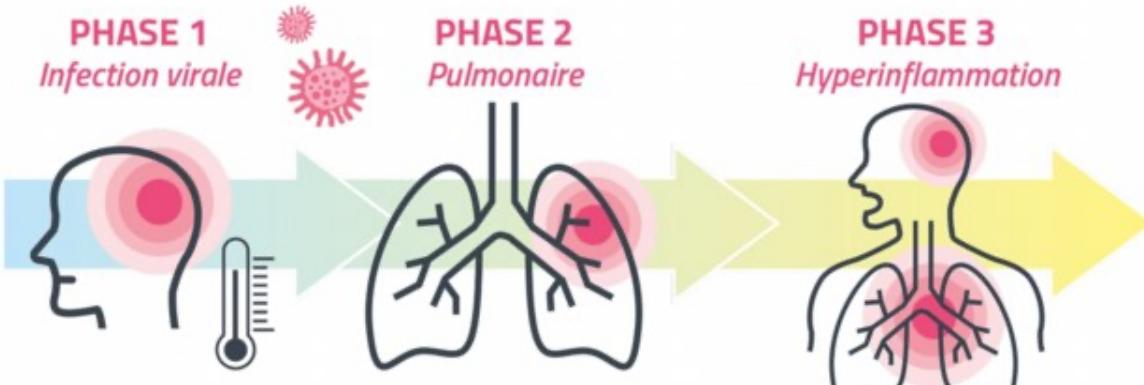


Figure: Occurrence and outcome of severe acute respiratory syndrome coronavirus 2 viral sepsis

[Hui Li et al, hypothesis Lancet, Mai 2020]

## COVID-19, MALADIE EN TROIS PHASES

Chez la majorité des personnes, le Covid-19 se présente comme une infection virale classique : quelques symptômes, suivis d'une guérison. Pour les autres, la maladie peut se prolonger : après l'attaque virale, survient une phase pulmonaire, puis une phase d'hyperinflammation, aussi appelée « orage cytokinique ».



Fièvre (plus de 37,7°C), toux sèche, diarrhée, maux de tête.

Souffle court, hypoxie trop peu d'O<sub>2</sub> dans le sang).

En phase 1, on traite le patient contre le virus, en phase 3, on lutte contre l'hyperinflammation. Lors de la phase 2, les deux problèmes se chevauchent : le virus est encore actif, mais moins fort, tandis que l'inflammation démarre.

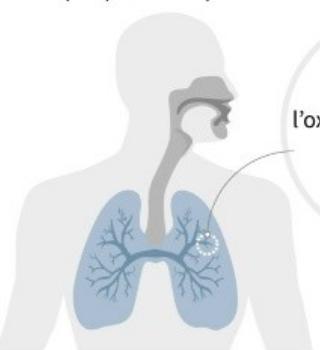
## Quand le système immunitaire s'emballe

Si le mécanisme provoquant les effets les plus graves du Covid-19 est encore à l'étude, certains scientifiques suggèrent qu'une réponse excessive du système immunitaire d'un patient pourrait être la cause de sa mort.

### Choc cytokinique

Une réaction immunitaire trop forte

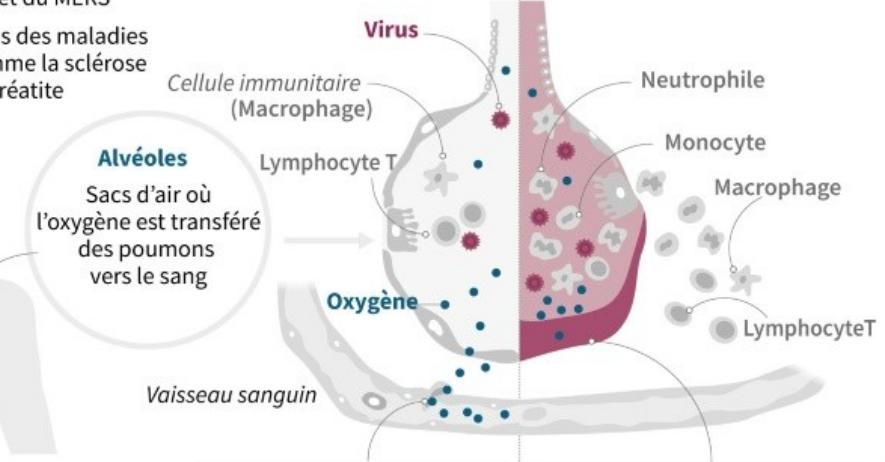
- ▶ Remarqué chez des malades de la grippe, du SARS et du MERS
- ▶ Également visible dans des maladies non contagieuses comme la sclérose en plaques ou la pancréatite



Les molécules de cytokine stimulent le mouvement des cellules vers les inflammations, infections et traumatismes

### Réaction protectrice

Les cellules immunitaires sont présentes sur l'infection en nombre suffisant



Le transfert de l'oxygène peut continuer avec le moins de perturbation possible, les cellules faisant leur travail

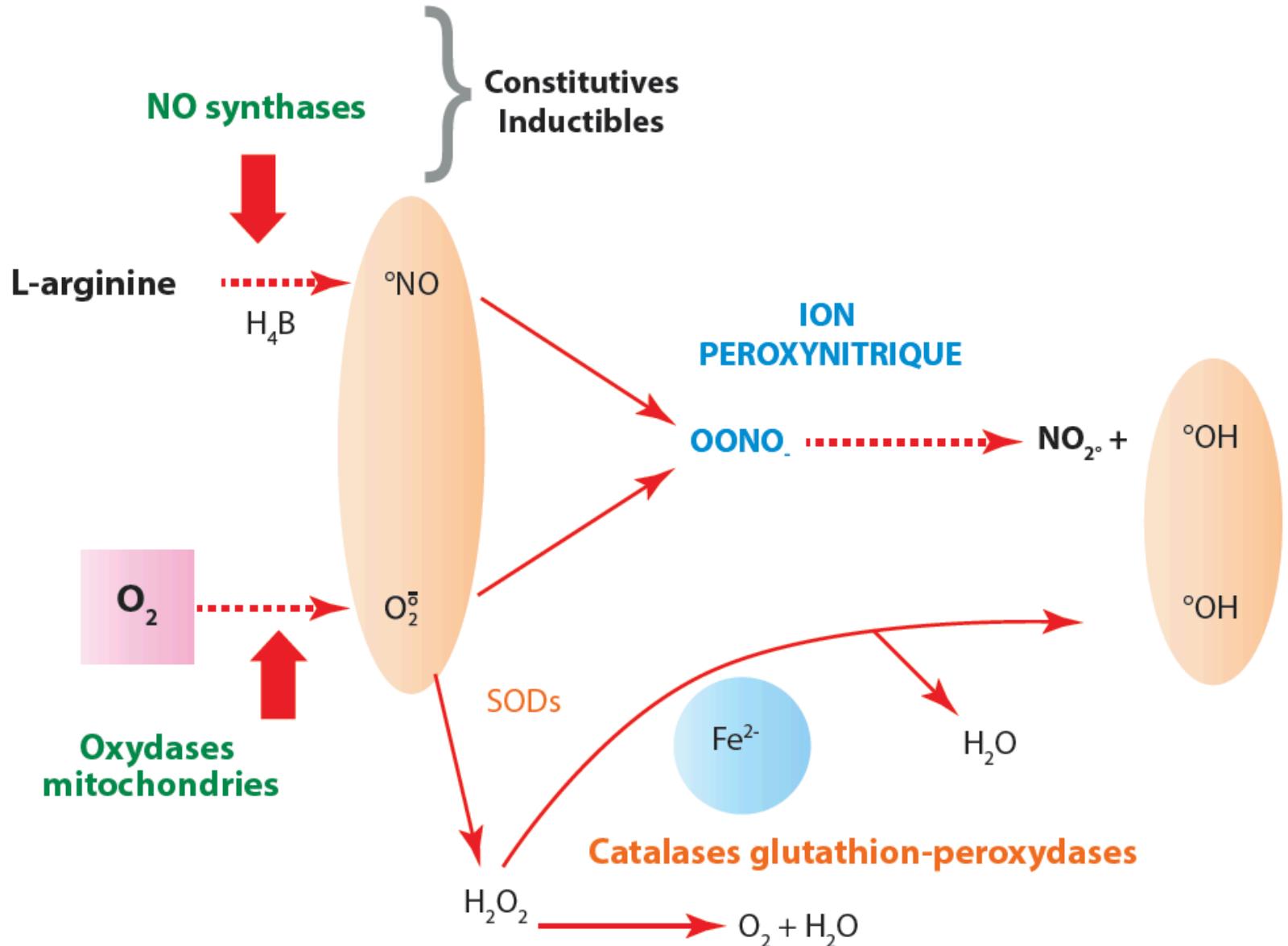
### Réaction excessive

Les cytokines activent trop de cellules immunitaires, menant à une hyperinflammation

Membrane hyaline contenant des débris de cellules mortes, se dépose sur les alvéoles, rendant la respiration difficile

Sources : newscientist.com/thelancet.com/nature.com/www.news-medical.net

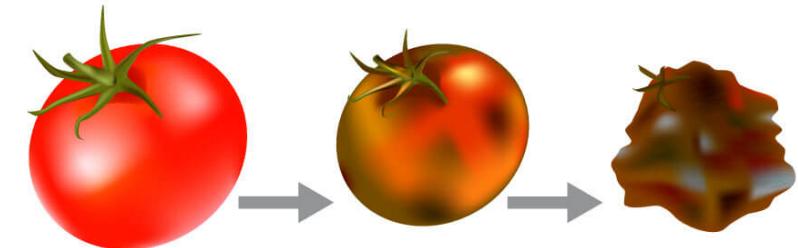
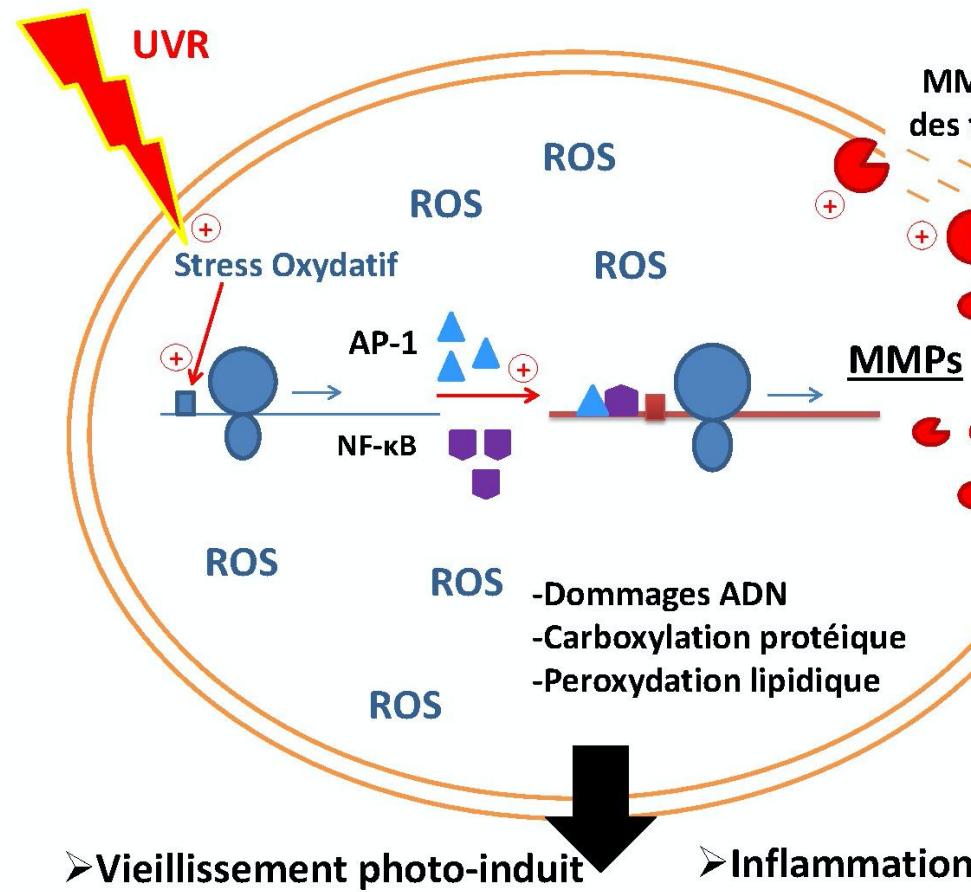
© AFP



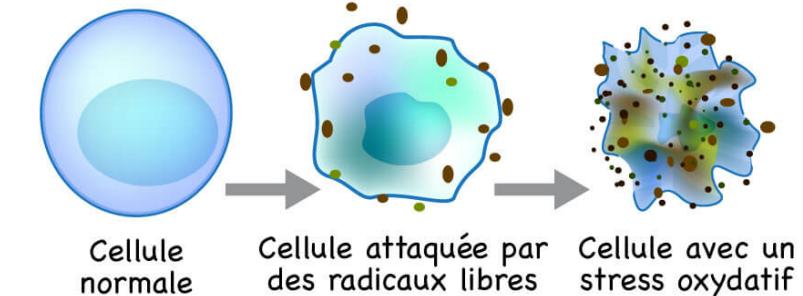
STRESS OXYDATIF

**Le stress oxydatif se produit en raison d'un déséquilibre quotidien et constant dans le corps entre les radicaux libres et les antioxydants**

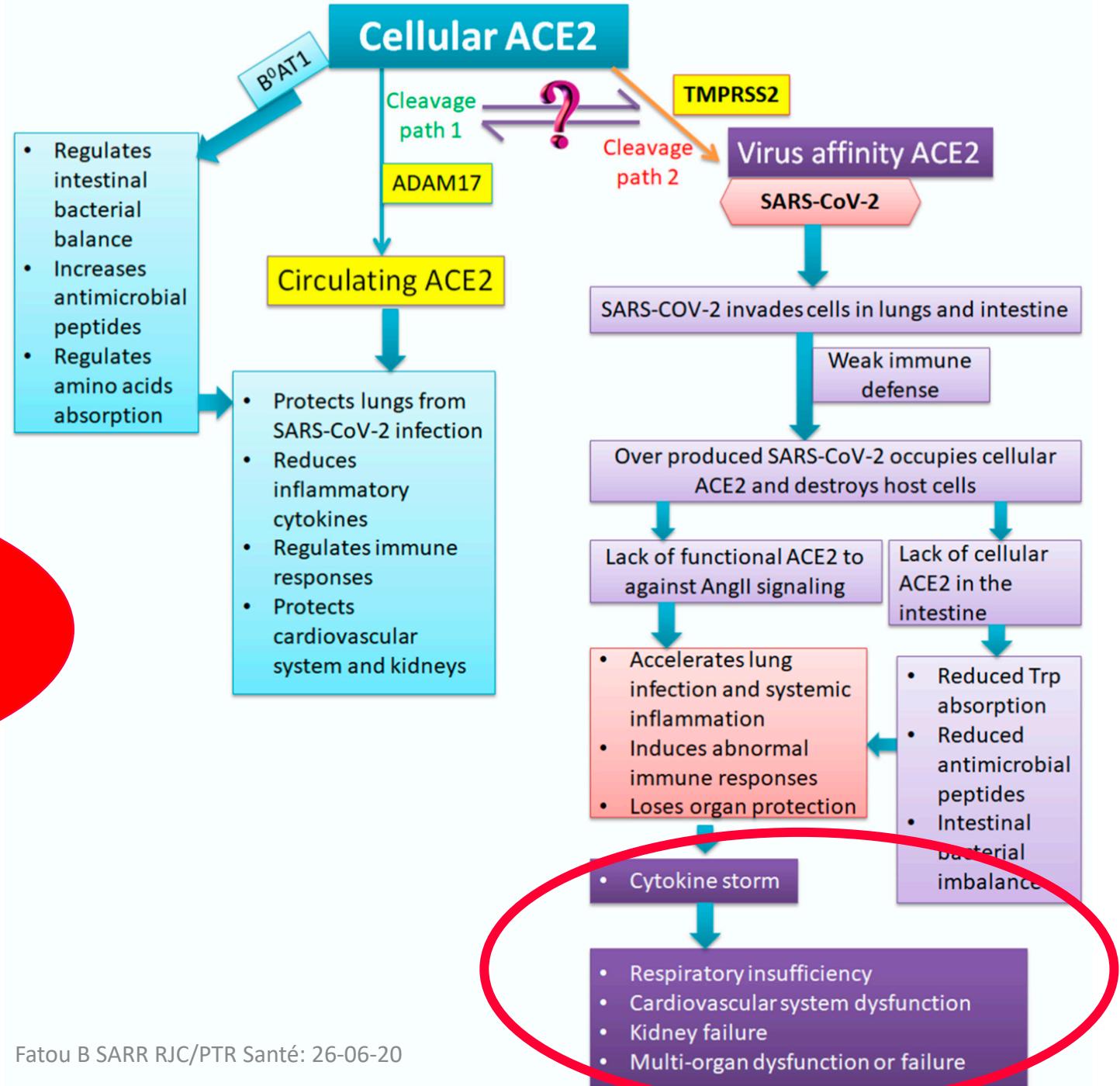




## STRESS OXYDATIF



**CHARGE VIRALE ELEVEE  
TOXICITE VIRALE  
STRESS OXYDANT/INFLAMMATION**



## Infection peu ou modérément symptomatique

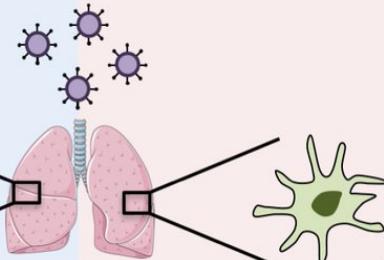
Production et activité efficace des interférons de type I (alpha et bêta)

Eradication du virus



Guérison

## SARS-CoV-2 (Covid-19)



### Inflammation appropriée

Balance adéquate entre les molécules pro-inflammatoires (TNF $\alpha$ , IL-1, IL-6) et anti-inflammatoires (IL-10, IL-1RA)

### Inflammation exagérée

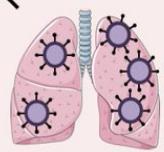
= orage cytokinique  
Excès de molécules pro-inflammatoires (TNF $\alpha$ , IL-6)

Recrutement des cellules inflammatoires dans les tissus

## Infection sévère à très sévère

Production et activité insuffisante des interférons de type I (rôle virus et/ou de facteurs génétiques)

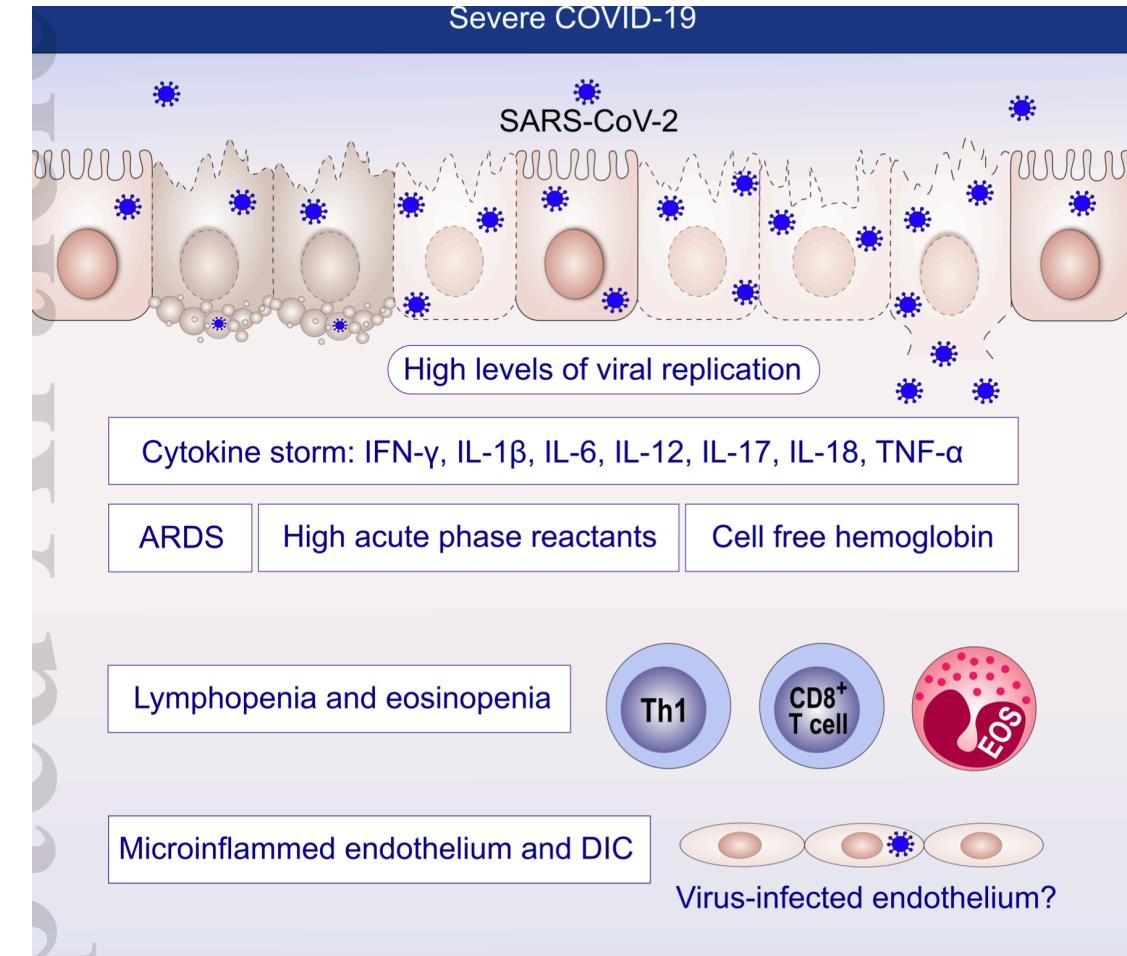
### Persistance du virus



Virus  
Inflammation exagérée  
= orage cytokinique  
Excès de molécules pro-inflammatoires (TNF $\alpha$ , IL-6)  
Boucle d'auto-amplification

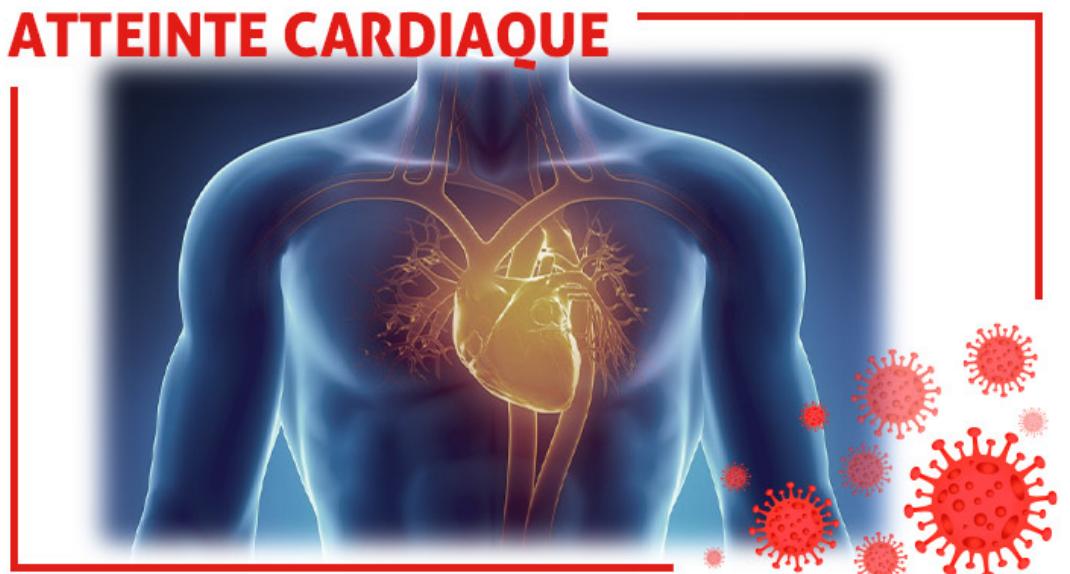
Dommage des tissus  
Détresse respiratoire  
Défaillance des organes

### Maladie faible à modérée

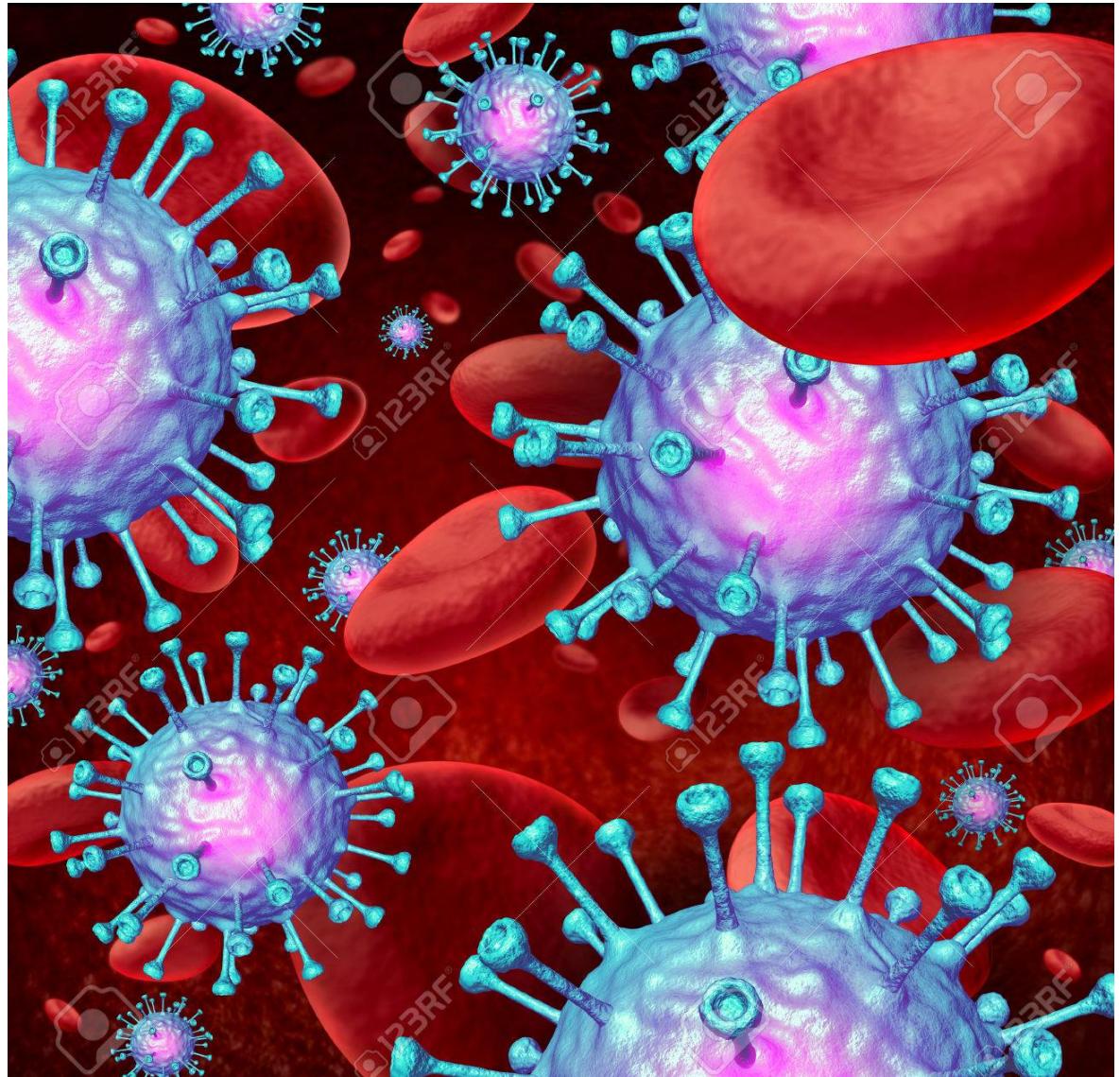


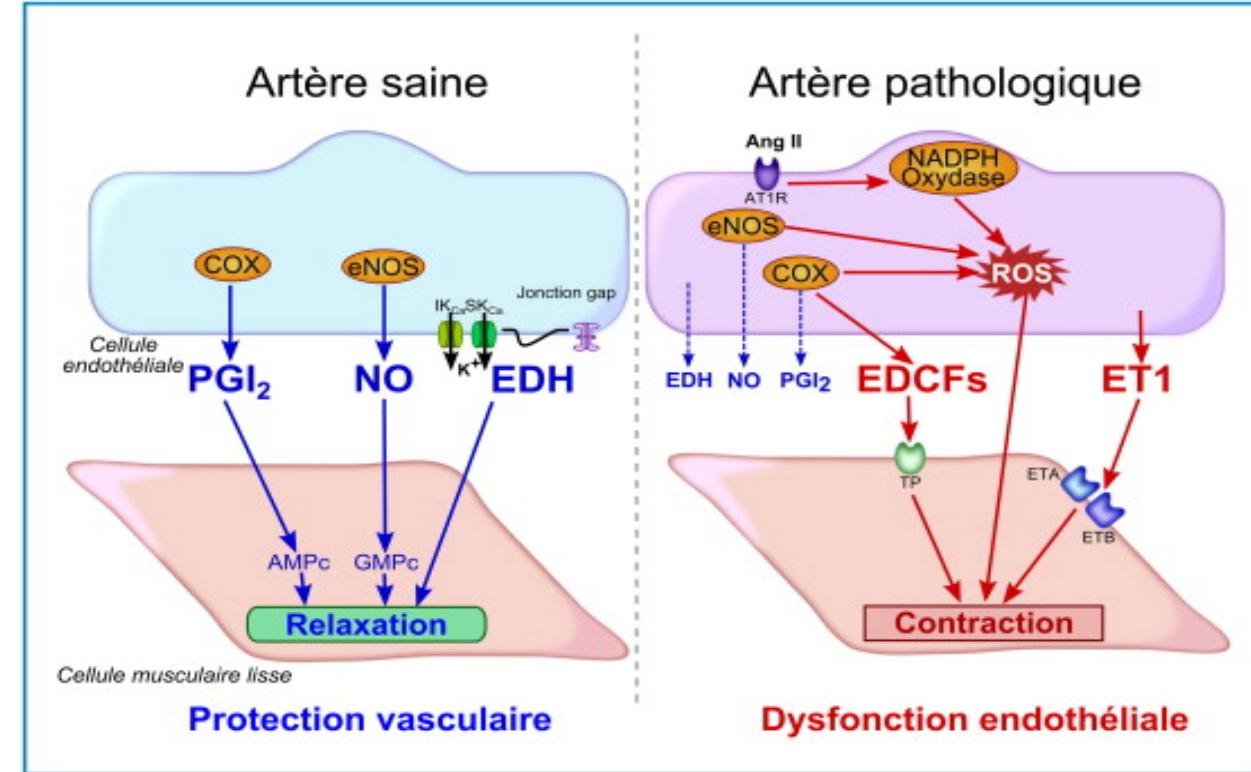
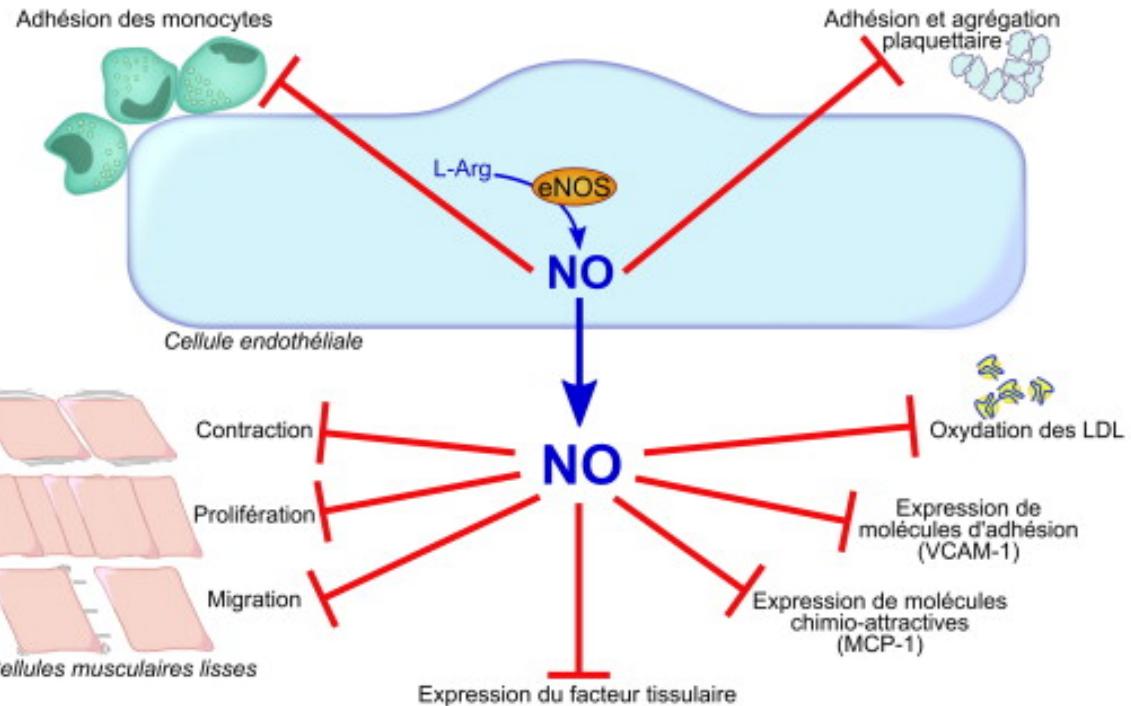
## FORMES SEVERES COVID 19

## ATTEINTE CARDIAQUE



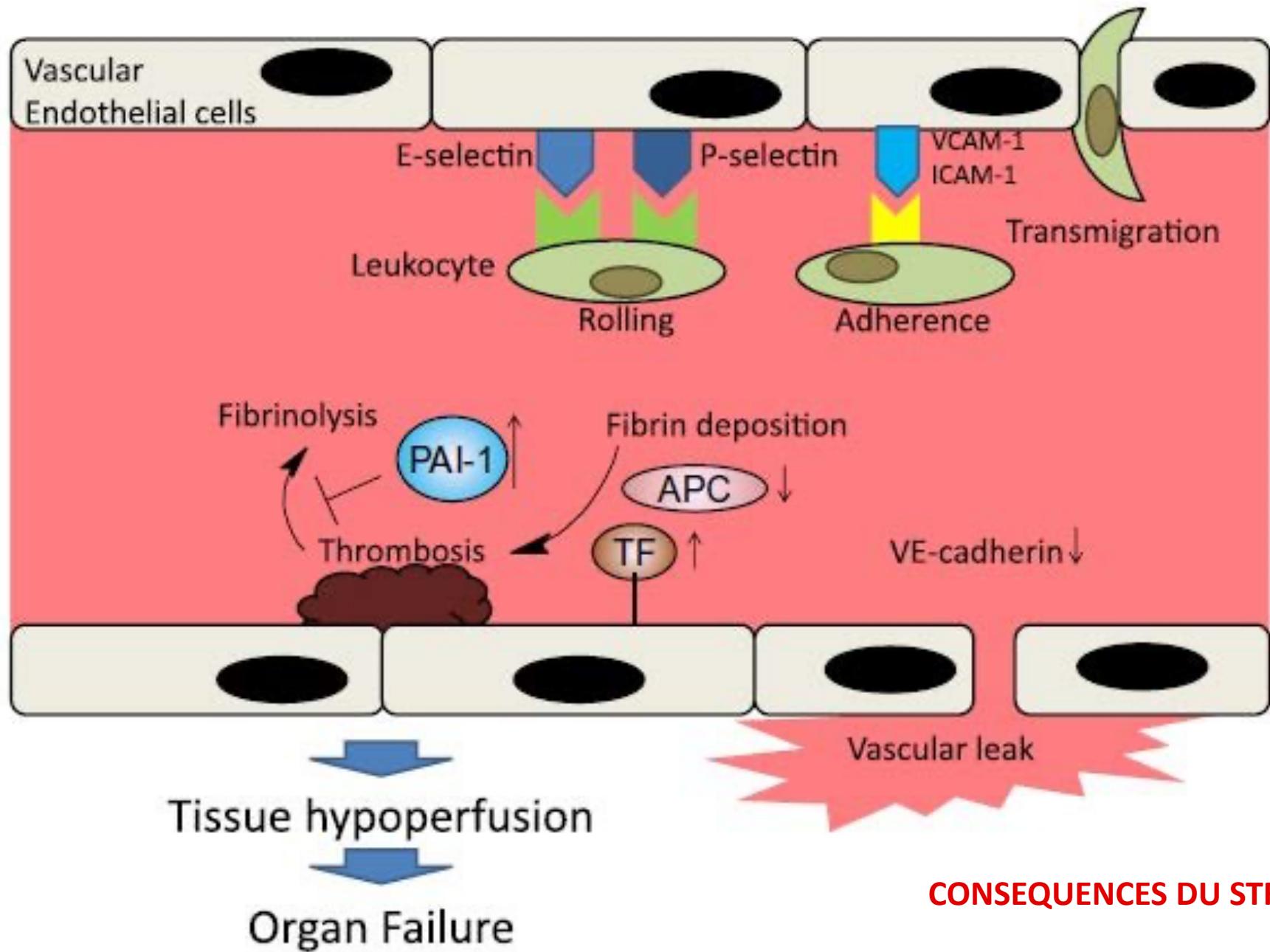
## ATTEINTES CARDIO-VASCULAIRES DE LA COVID-19

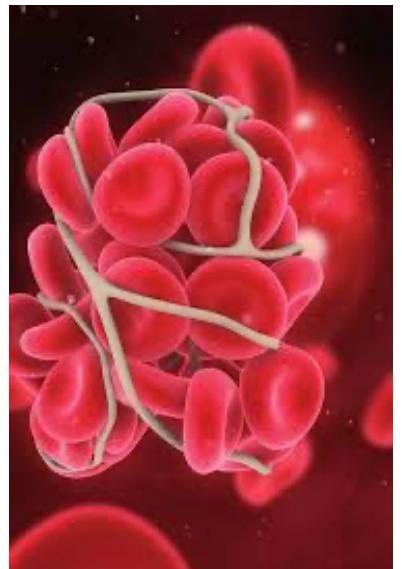
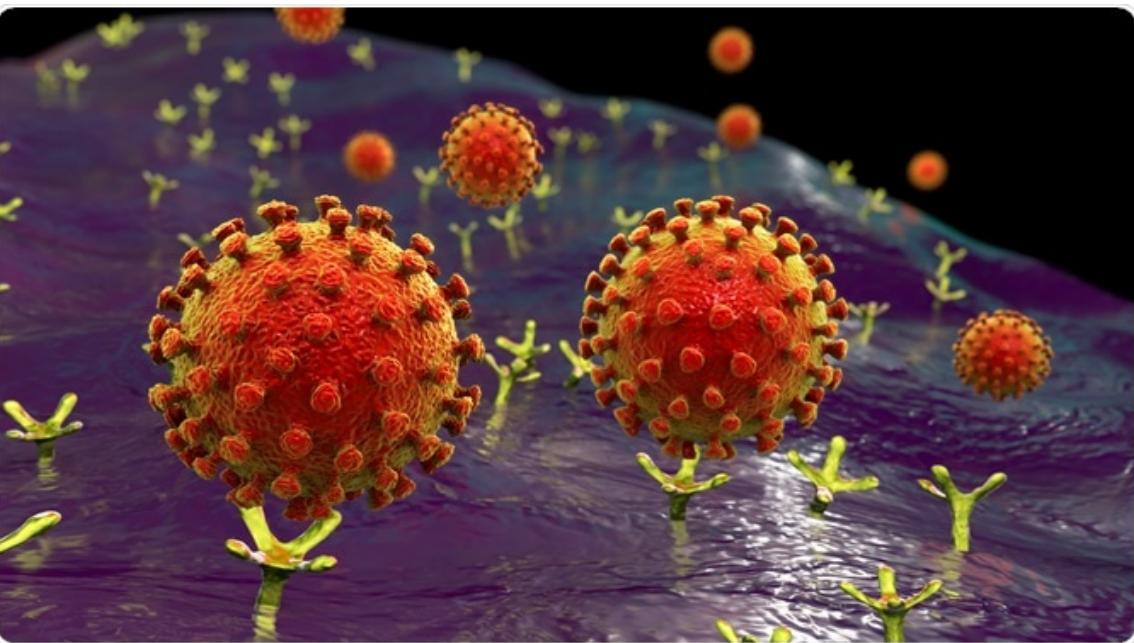
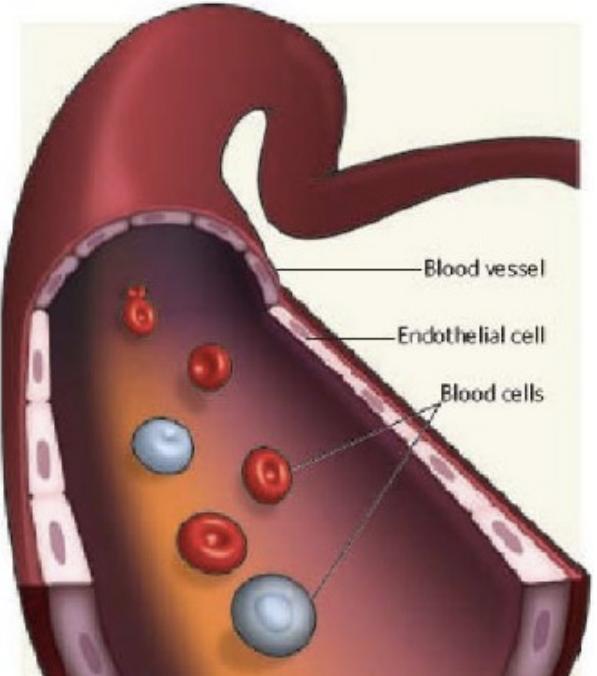




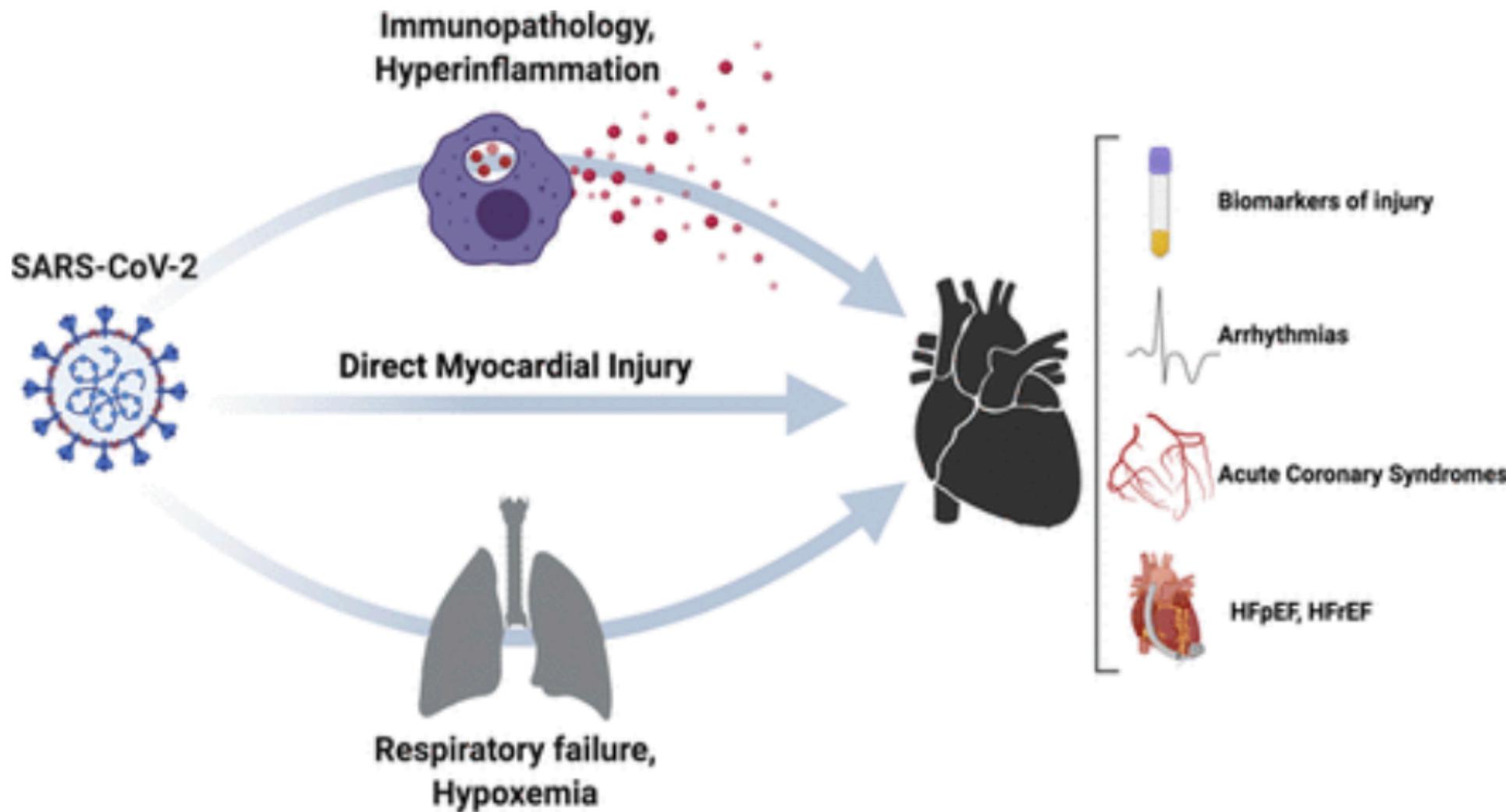
**CONDITIONS PHYSIOLOGIQUES**

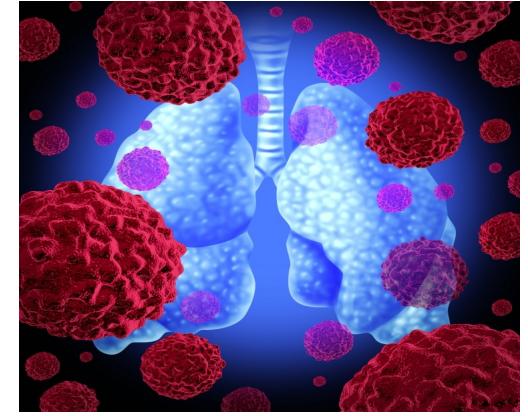
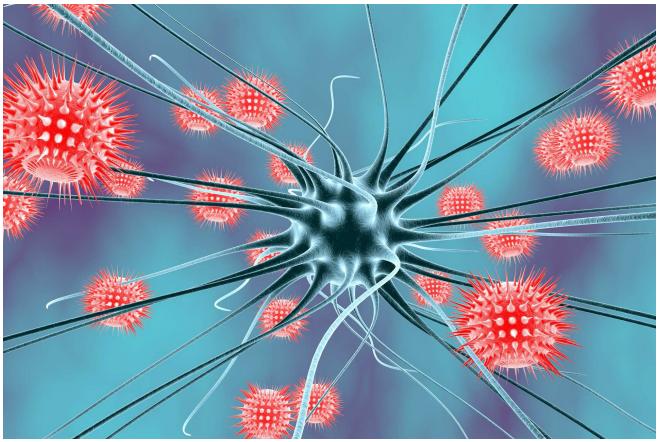
**CONDITIONS PATHOLOGIQUES**



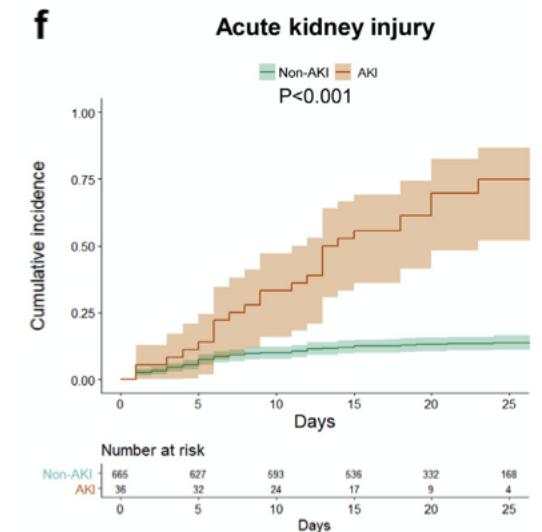
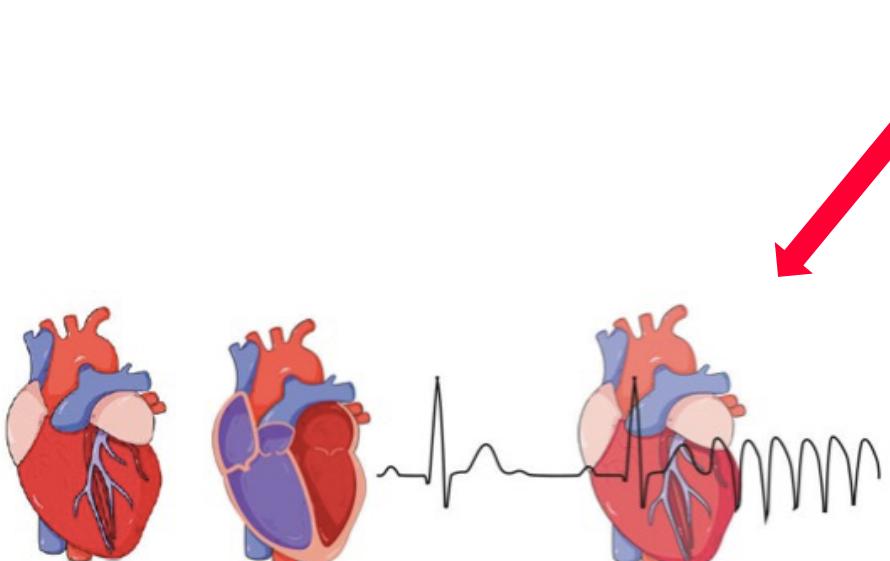


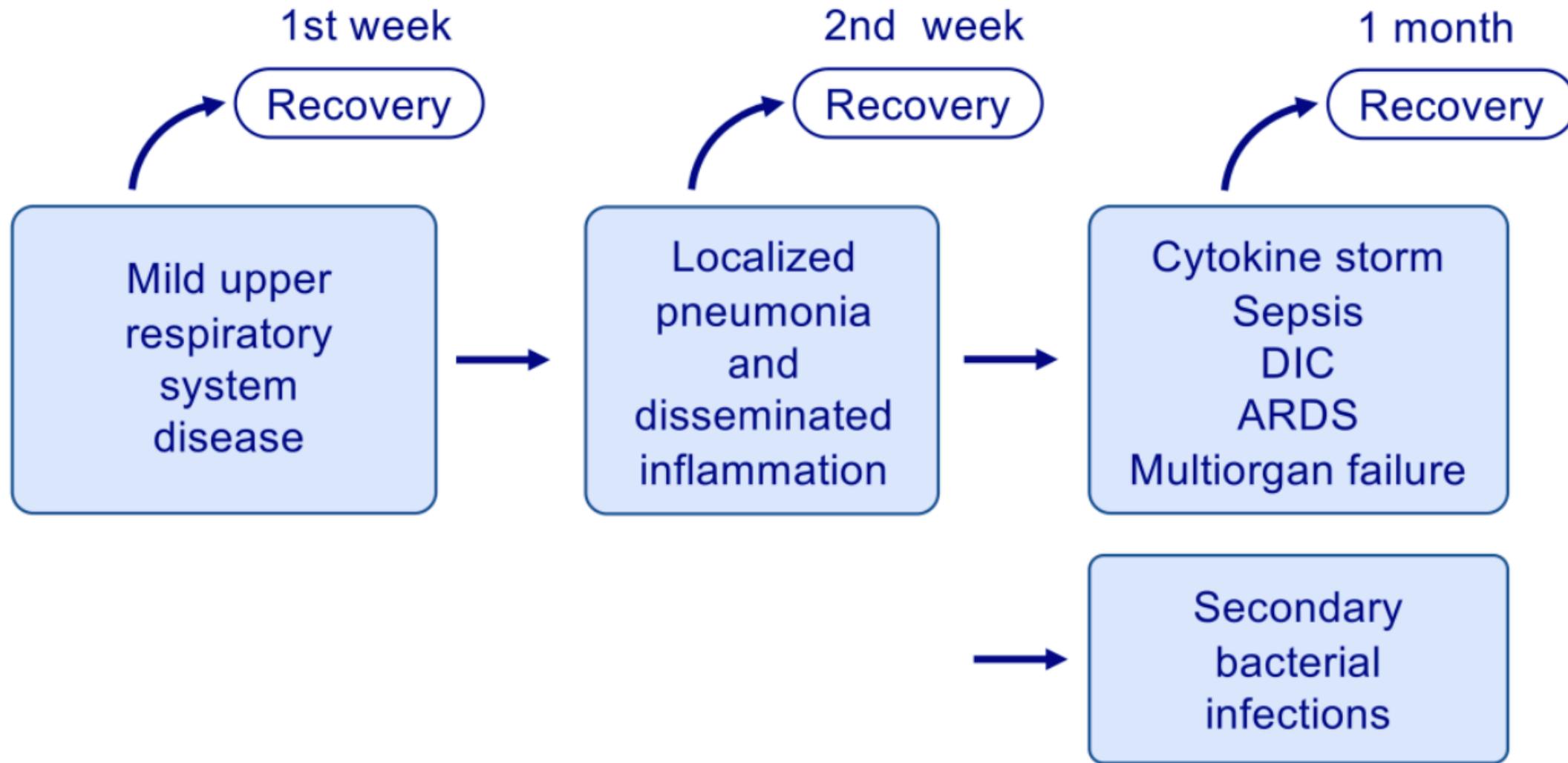
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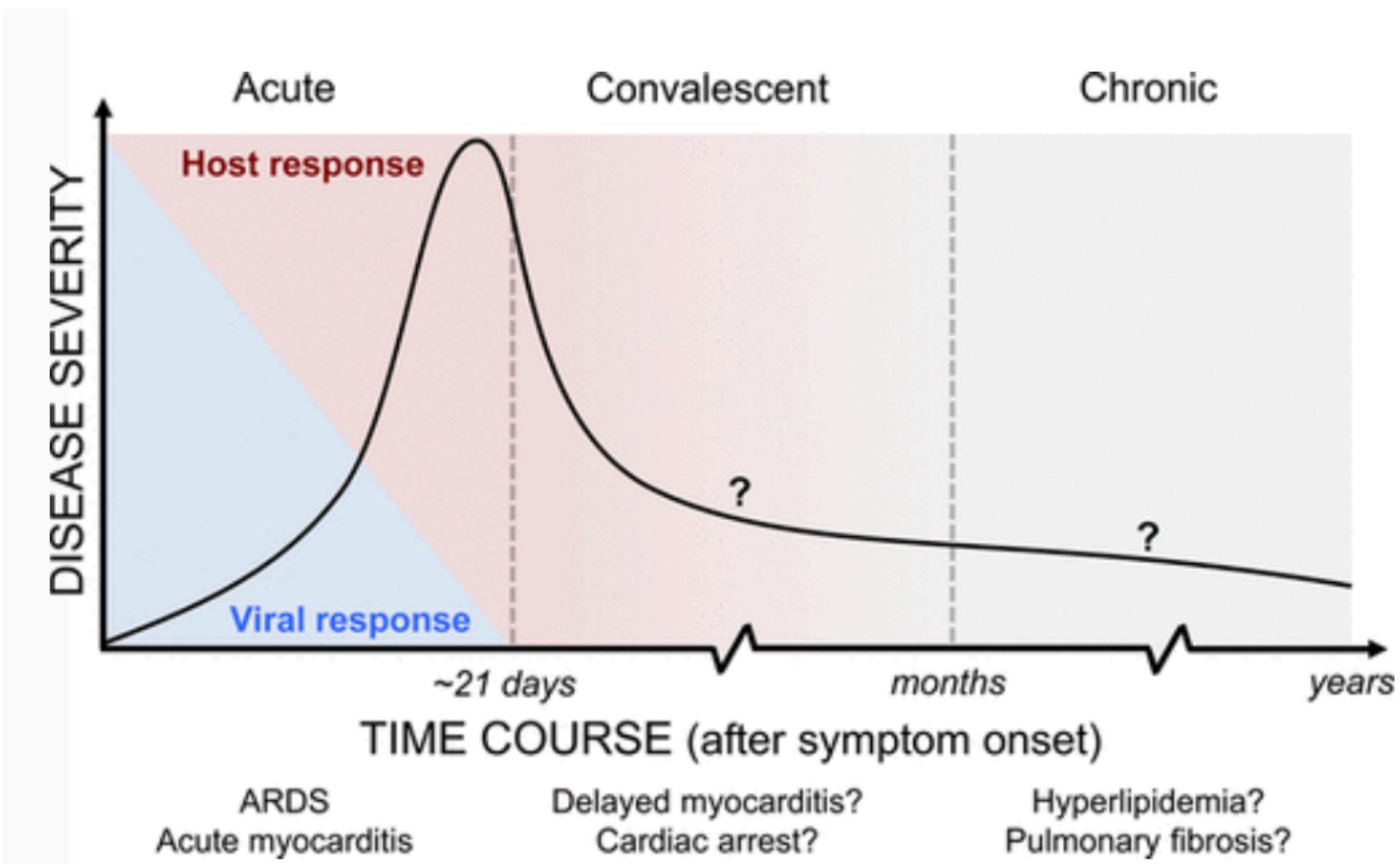




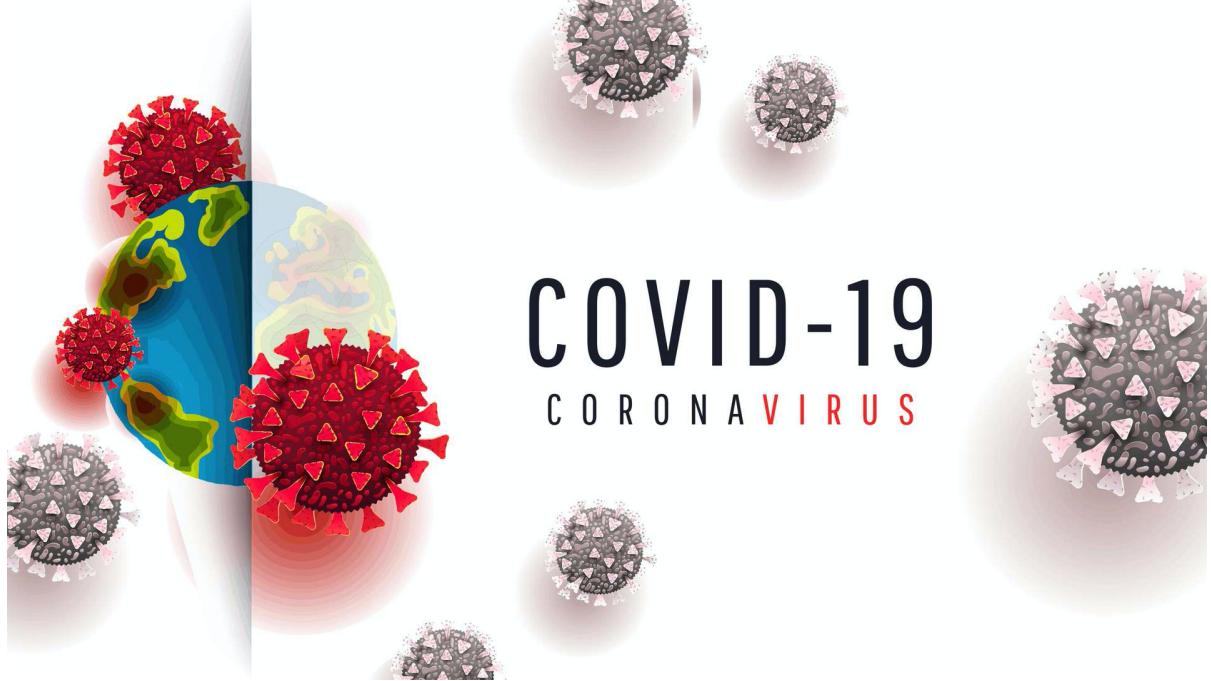
## DEFAILLANCE MULTIVISCERALE





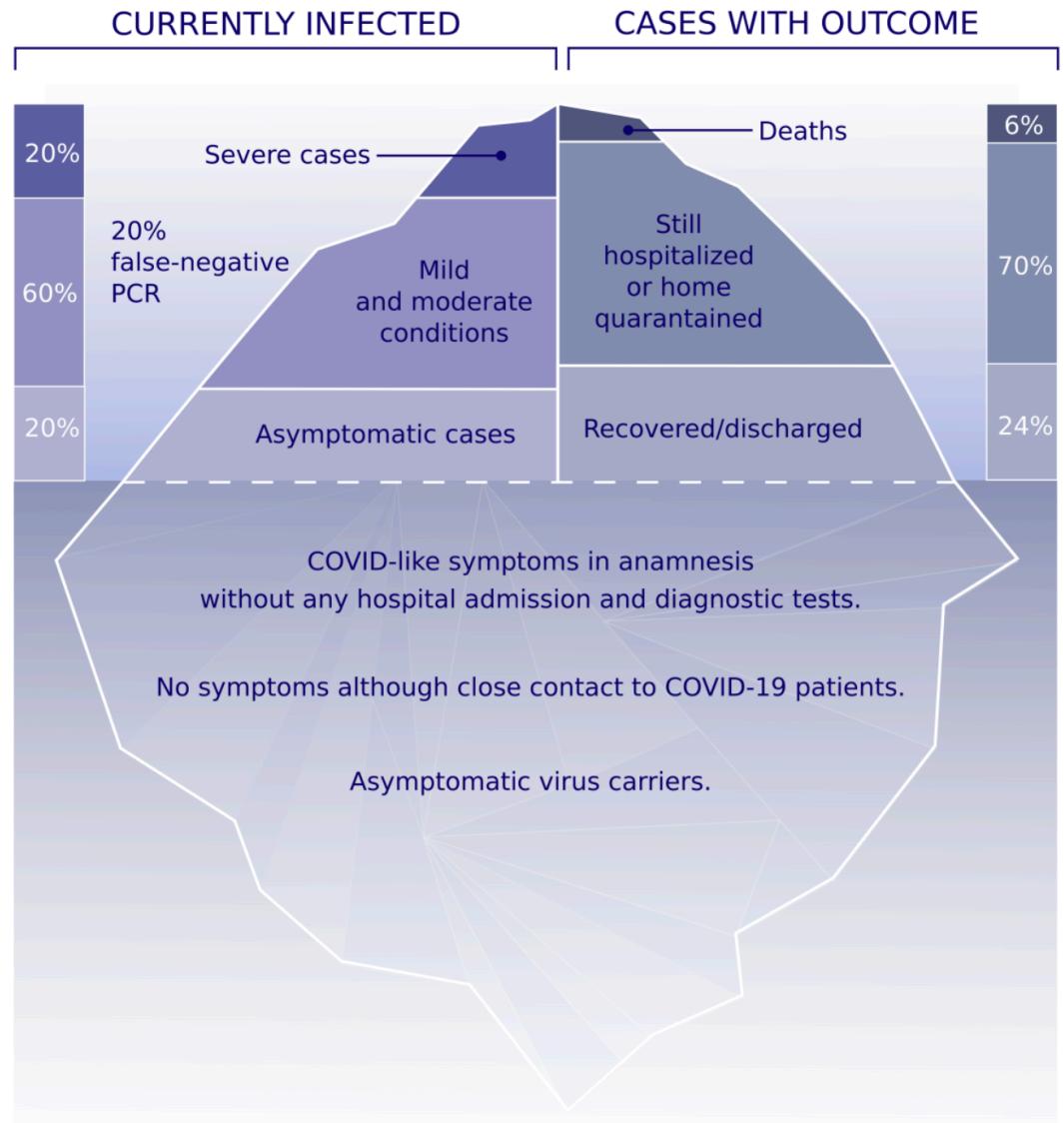


Akbarshakh A, et al, Circulation research 2020



# COVID-19

## CORONAVIRUS



[Ahmet Kursat Azkur et Al, Allergy, Mai 2020]

MERCI DE VOTRE ATTENTION