

Coronavirus SARS-CoV-2

L'avis d'un virologue

Pr Benoît KABAMBA-MUKADI

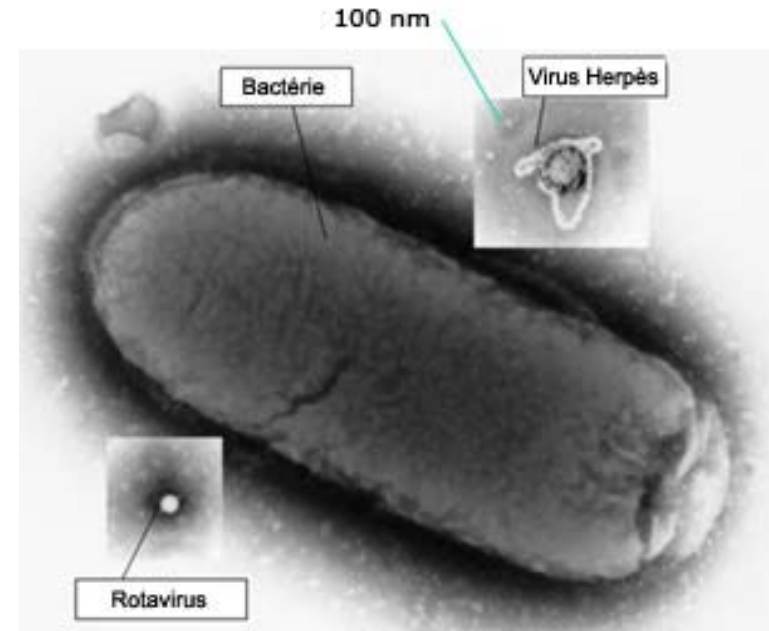
08 octobre 2020



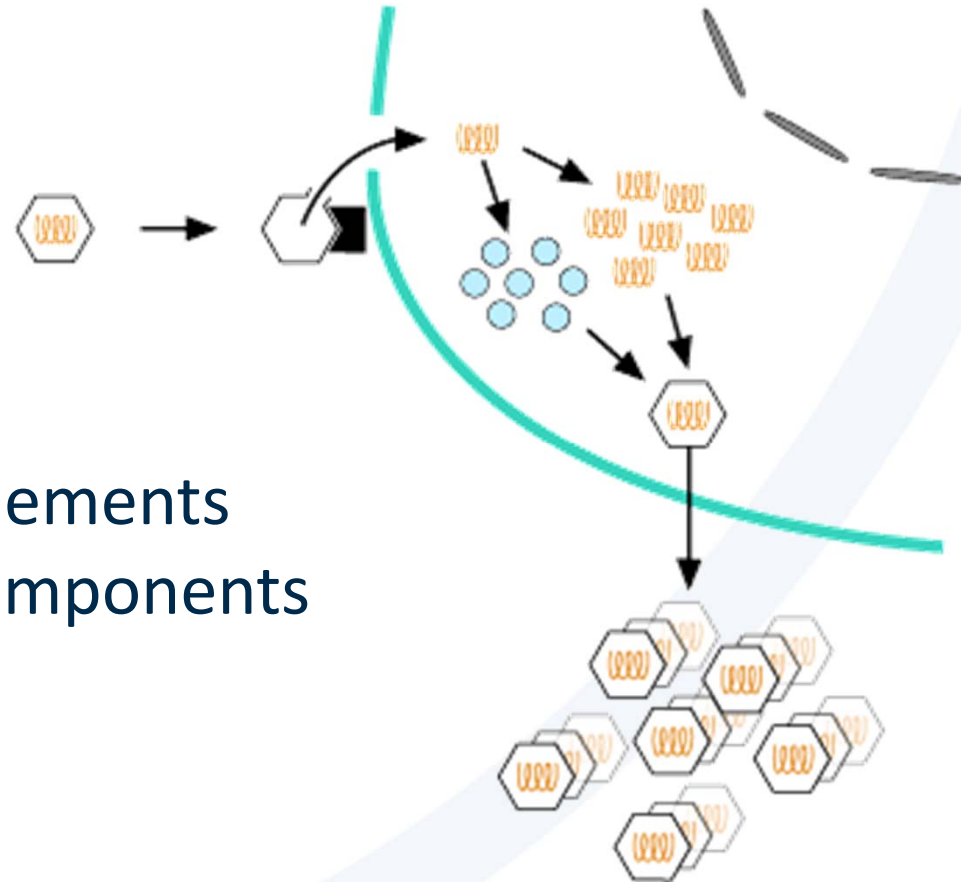
Cliniques universitaires
SAINT-LUC
UCL BRUXELLES

General characteristics of viruses

- Small: ultra-filterable.
- Host and cellular specificity
- Intracellular multiplication.
- Simple structure with few targets.
- Only 1 type of genome: RNA or DNA in the virion
 - Diagnostic and therapeutic implications (Resistance)
- Viral infections do not respond to antibiotic treatment, but to antivirals



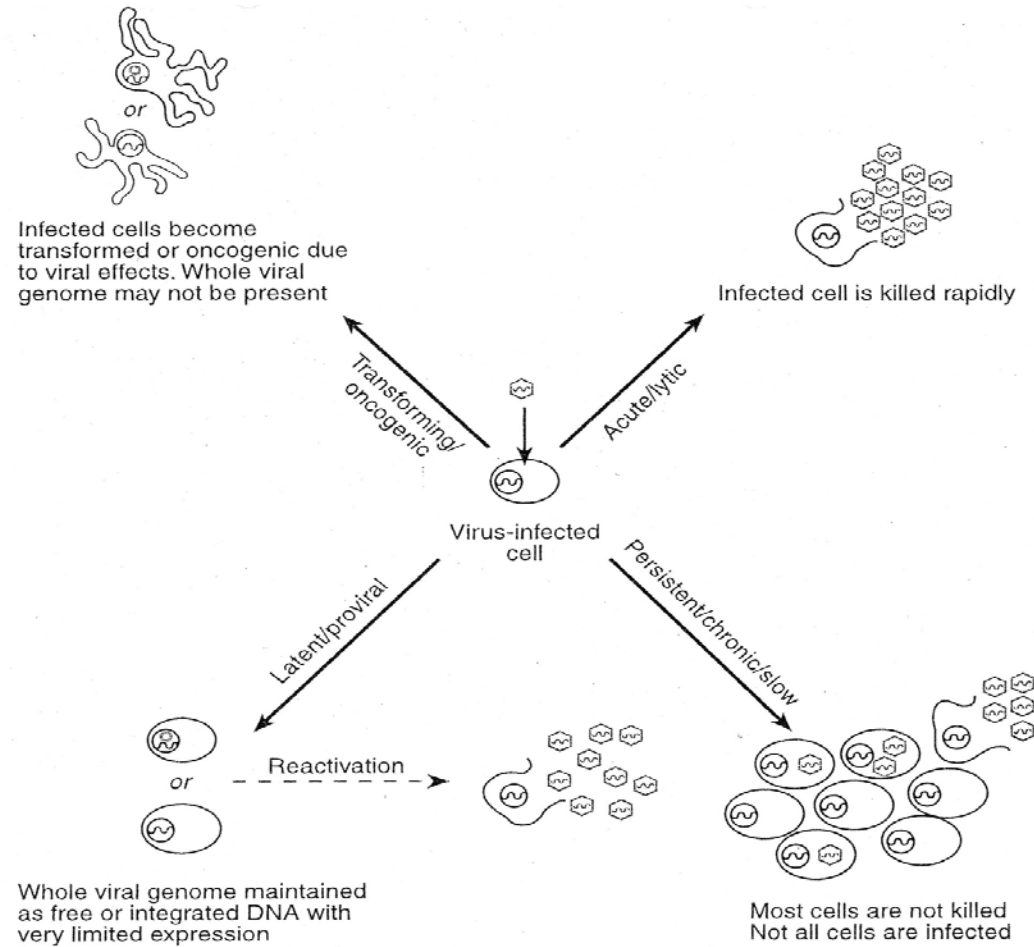
General characteristics of viruses



Viruses are replicative elements assembled from their components



Pathological effects of viruses



Pathological effects of viruses

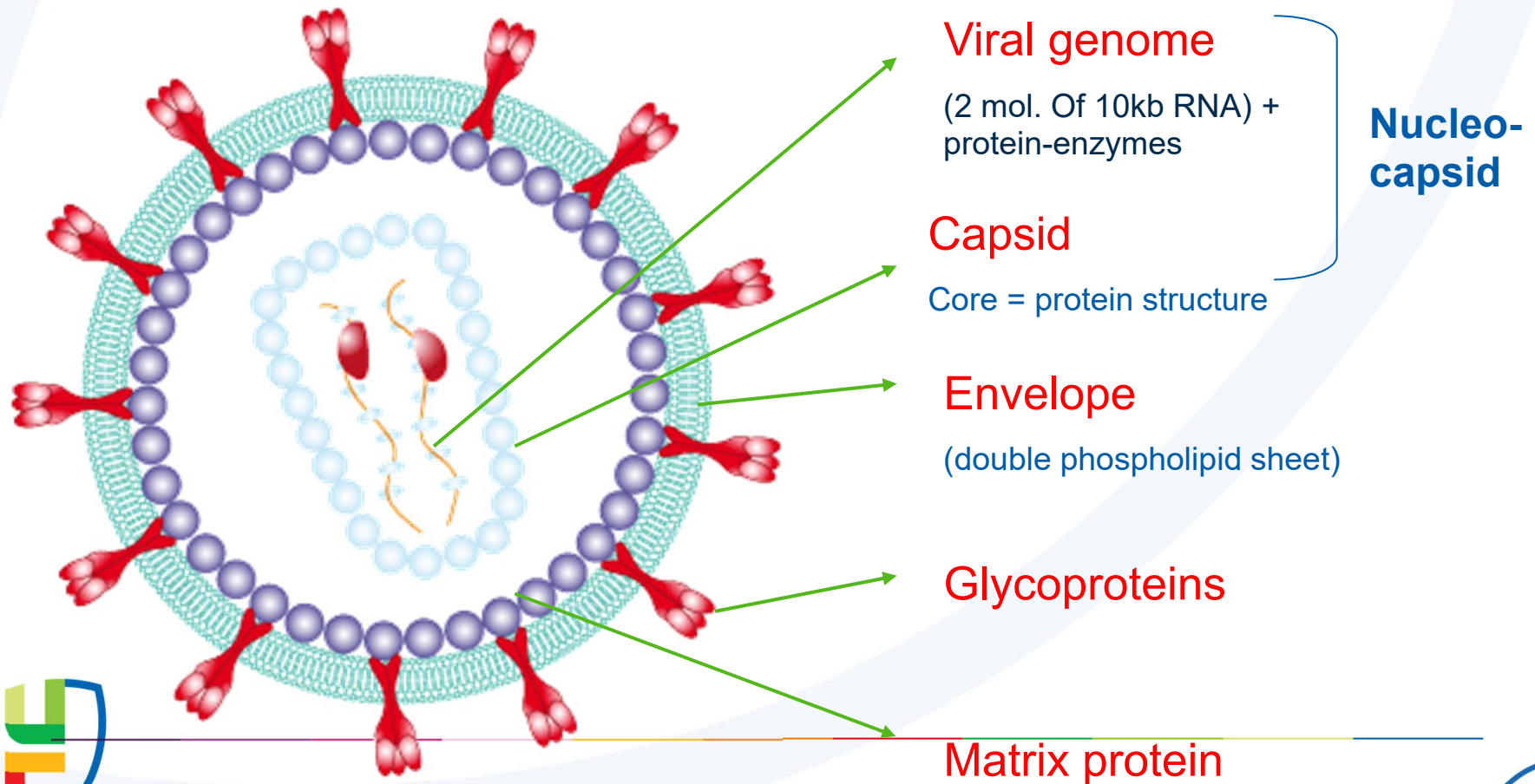
- Different effect by involvement of different organs
 - ✓ Cell alteration by direct viral cytopathic effect (SARS-CoV-2)
 - ✓ Cell transformation (HPV)
 - ✓ Immune reaction (Viral hepatitis)
 - ✓ Action of cytokines (Influenza)



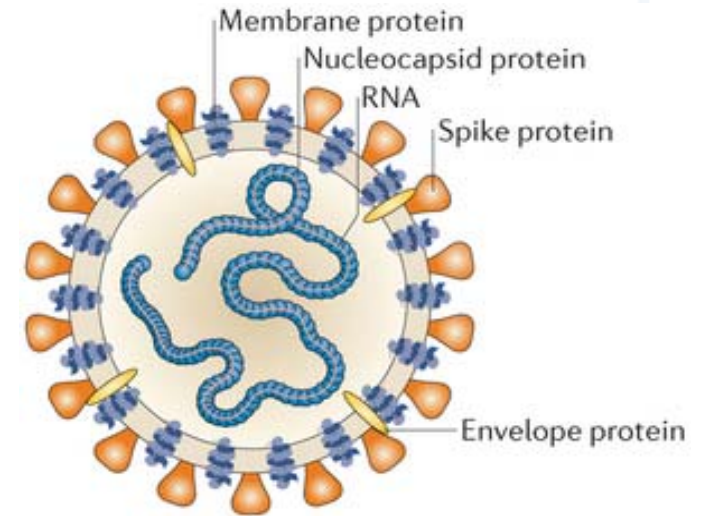
What is a viral particle made of?

Enveloped virus > < Naked virus

Example: retrovirus - AIDS virus +/- 120 nm, genome 10 kb



Coronaviridae

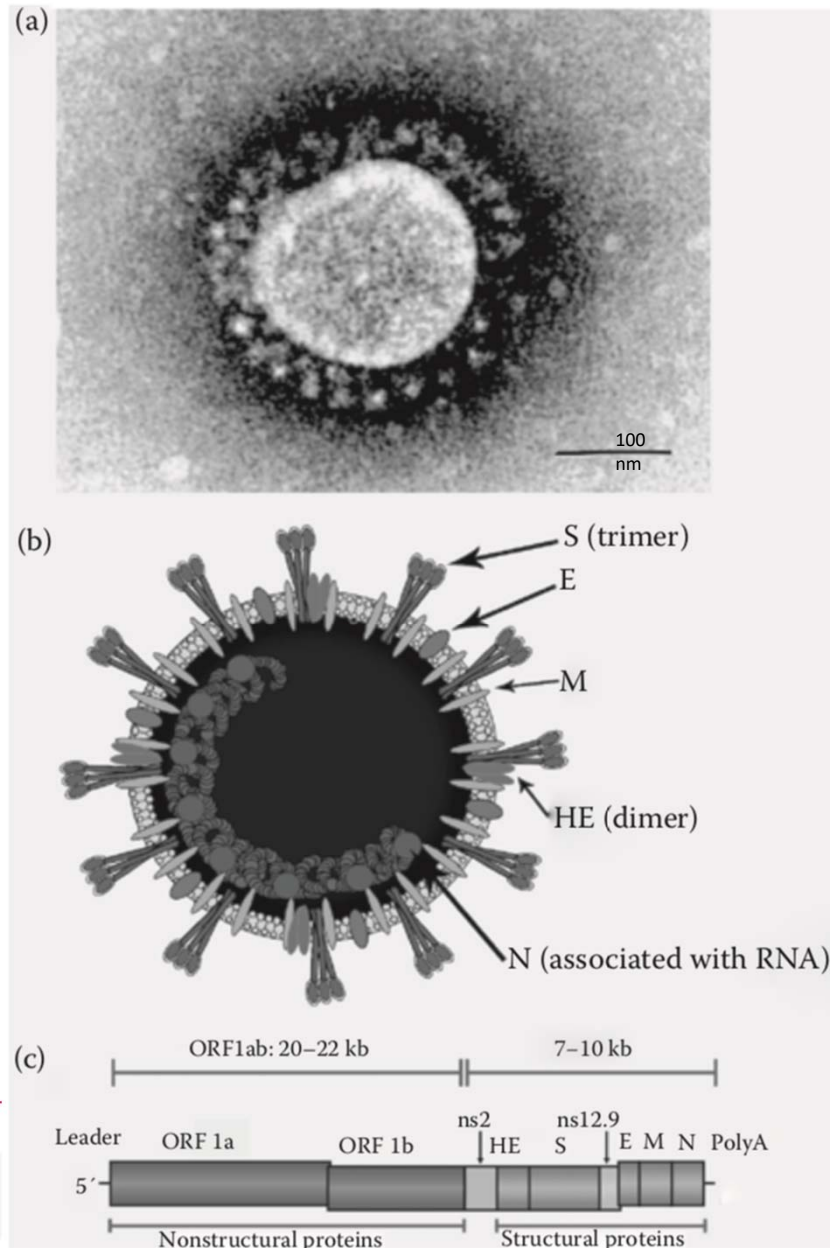


Nature Reviews | Microbiology

- Isolated in the 1930s as agents of
 - Infectious bronchitis in chickens,
 - Transmissible gastroenteritis in pigs,
 - Severe hepatitis and neurological diseases in mice.
- In the 1960s, these viruses, and some human respiratory viruses, were grouped together
 - Most common characteristic revealed by ME
 - The halo of solar corona-shaped spicules
 - Different from orthomyxoviridae and paramyxoviridae.



Coronaviriridae



Electron microscopy (virus)

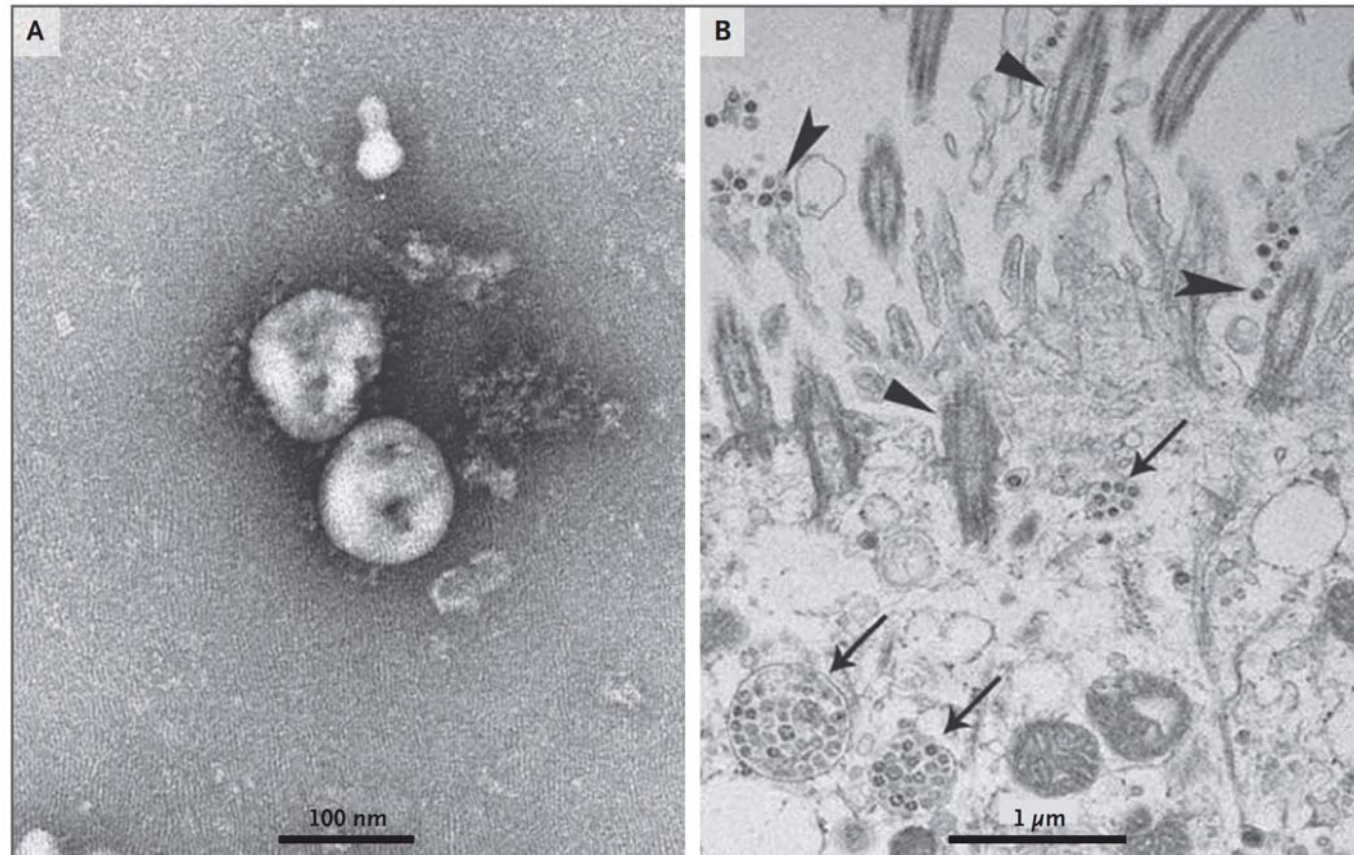


Figure 3. Visualization of 2019-nCoV with Transmission Electron Microscopy.

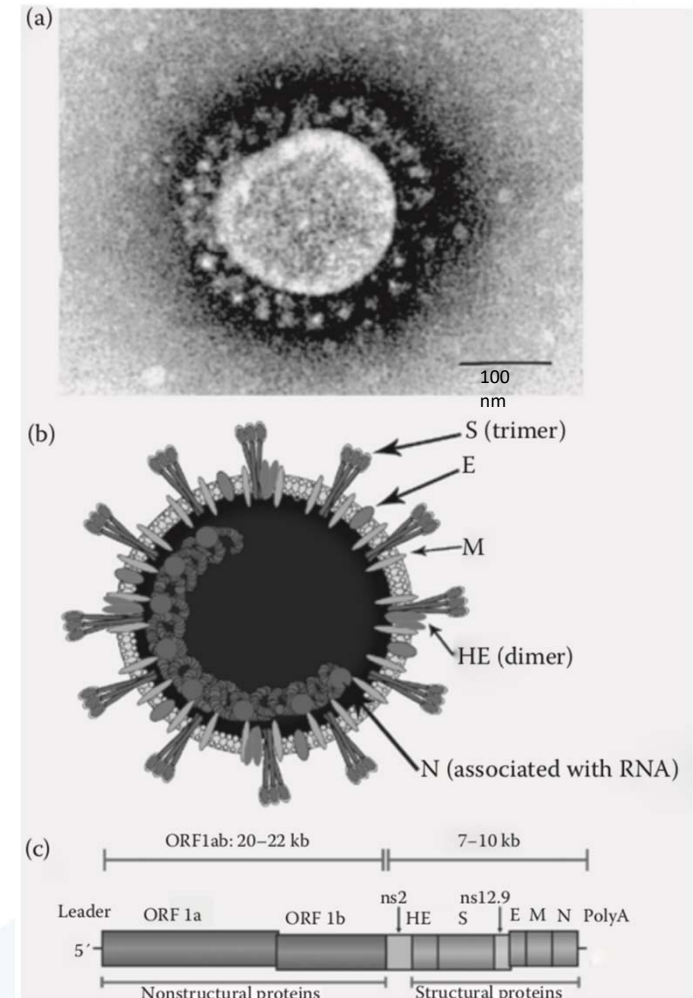
Negative-stained 2019-nCoV particles are shown in Panel A, and 2019-nCoV particles in the human airway epithelial cell ultrathin sections are shown in Panel B. Arrowheads indicate extracellular virus particles, arrows indicate inclusion bodies formed by virus components, and triangles indicate cilia.



Généralités sur les Coronavirus

Structure

- Virus enveloppés
- 80-200 nm
- Nucléocapside tubulaire à symétrie hélicoïdale
 - Protéine N, exception chez virus à ARN+
- Morphologie en couronne des virions en ME
- Génome
 - 26-32 kb
 - ARN simple brin linéaire, non segmenté à polarité positive (groupe IV)
 - ORF1a et 1b codent pour ARN polymérase virale
 - Similarités dans l'organisation et l'expression
 - Plusieurs génogroupes



General information on coronaviruses

Taxonomy

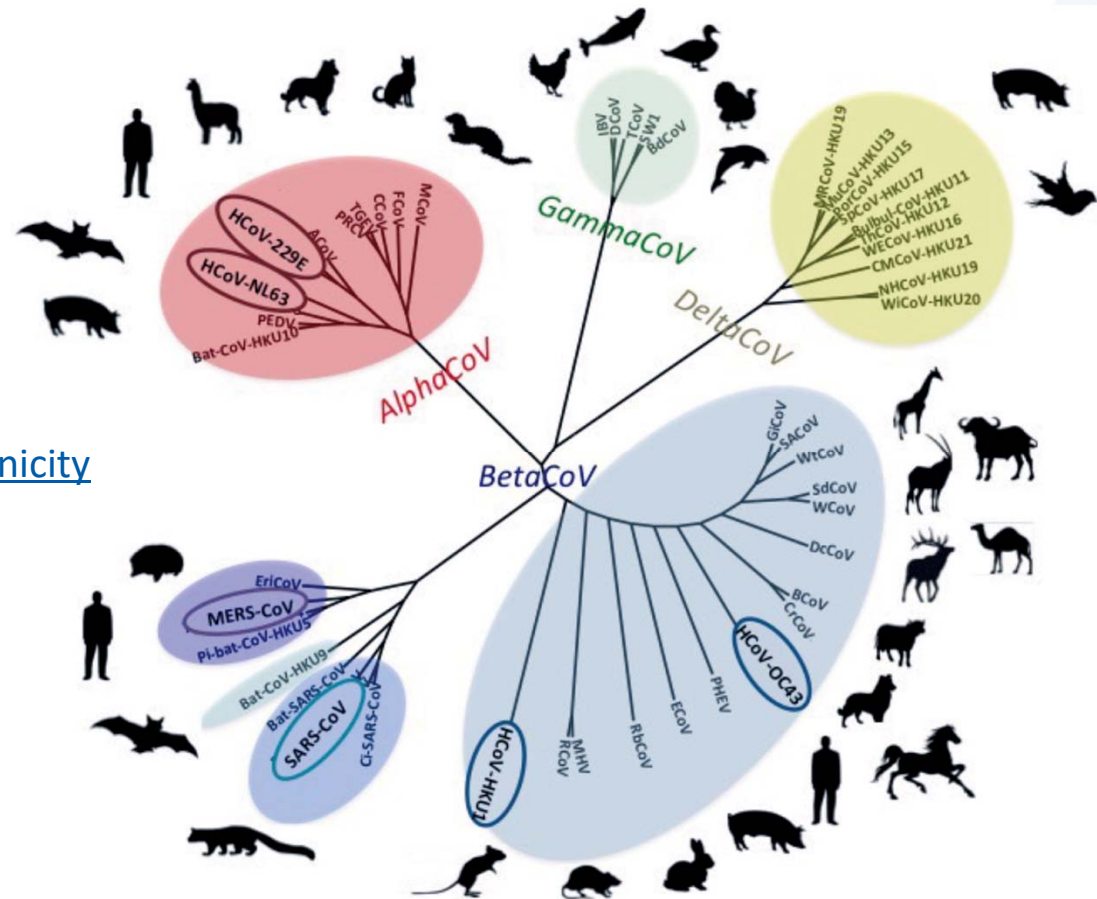
- Order : *Nidovirales*
- Suborder: *Cornidovirineae*
- Family : *Coronaviridae*
- Subfamily : *Orthocoronavirinae*
- Genus: Alpha-, Beta-, Gamma- and Deltacoronavirus

4 human CoVs with low pathogenicity

- HCoV-229E (alpha)
- HCoV-NL63 (alpha)
- HCoV-OC43 (beta)
- HCoV-HKU1 (beta)

3 HCoVs with high pathogenicity

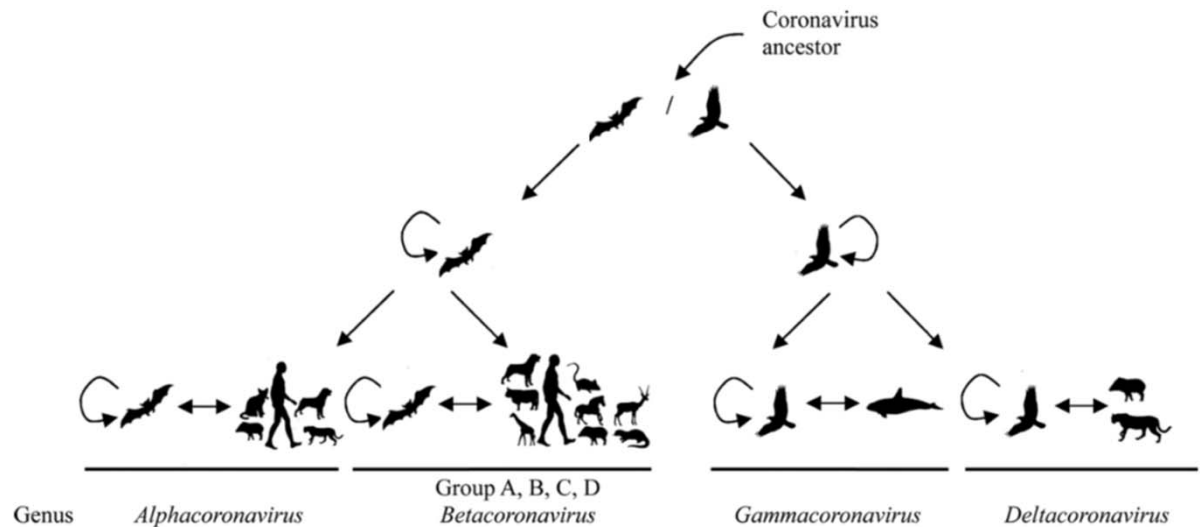
- SARS-CoV (beta; 2003)
- MERS-CoV (beta; 2012)
- SARS-CoV-2 (beta; 2019)



General information on coronaviruses

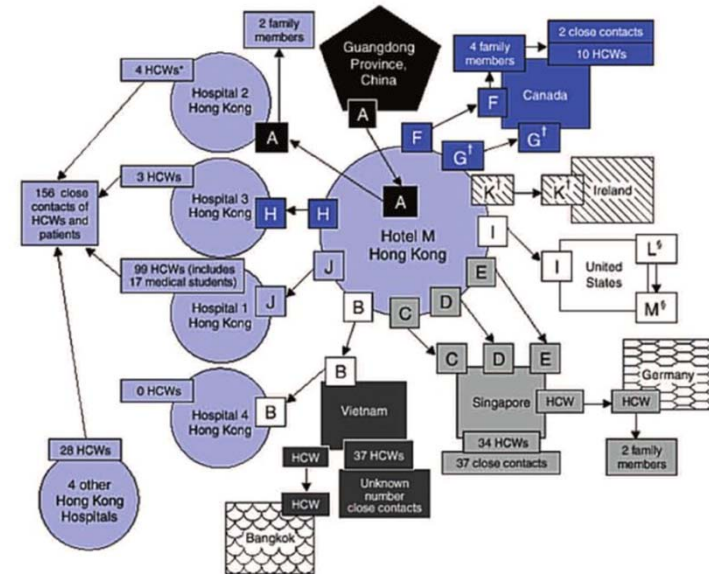
Ecology

- Worldwide distribution
- Viruses present in humans and in many animals
- Specificity of hosts
 - α - et β -CoV \rightarrow mammals
 - γ - et δ - CoV \rightarrow birds (and mammals)
- HCoVs : Major role of **bats**
 - Evolving reservoir
 - Diversity of HCoV correlates with that of bat
- Animal reservoirs
 - Bat
 - Rodents
 - Several intermediate hosts



HCoV - SARS

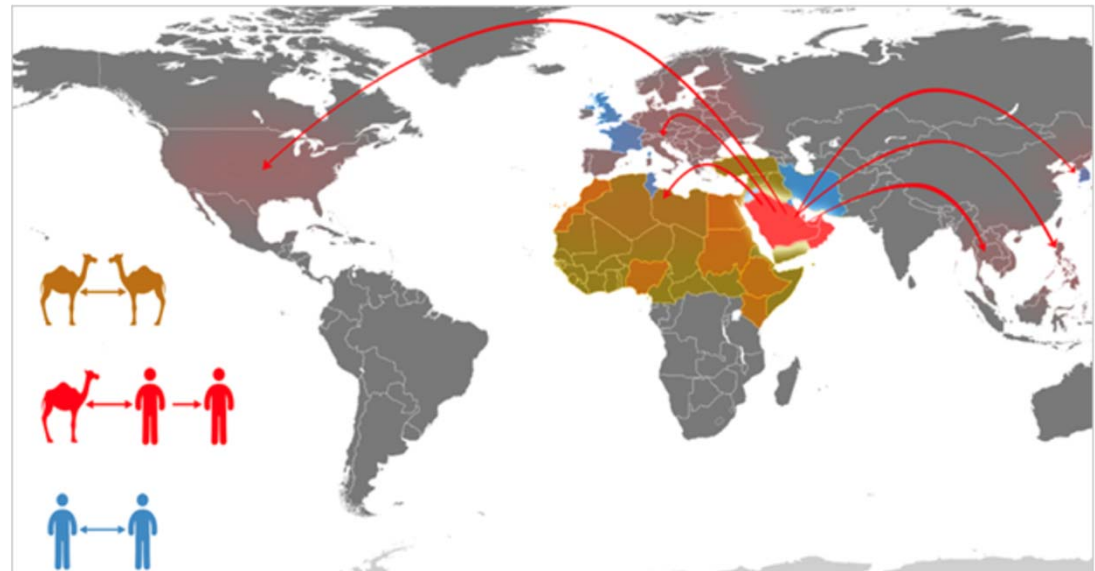
- **November 2002**
 - Guangdong, China
 - Non-epidemiologic atypical pneumonia wave
 - Severe Acute Respiratory Syndrome = SARS
 - Responsible for at least 2 clusters
- **February 2003**
 - Infected doctor spreads infection to Metropole Hotel guests in Hong Kong
- **144 day pandemic**
 - $R_0 = 3$
 - Case fatality rate: 9.6%
 - 8,098 people infected
 - 747 dead
- **Reservoir and source of the epidemic:**
 - Bat, Intermediate host: masked palm civet



HCoV - MERS

2012

- "Middle East respiratory syndrome coronavirus"
- Arabian Peninsula
- 26 countries
- Nosocomial or family clusters from different sources
- $R_0 < 1$
- **Case fatality rate = 34.4%**
- February 12, 2019
 - According to a WHO report
 - Total of 2279 confirmed cases
 - In 27 countries
 - About 806 deaths.



WHO



SARS-CoV-2 – COVID-19

- **Terminology**

- Virus: SARS-CoV-2
- Disease: COVID-19

- Genus β -Coronavirus

- 3rd known zoonotic coronavirus (SARS and MERS)

- Origin?

- Chimeric virus between a coronavirus from bats and a coronavirus of unknown origin (Ji et al.)
- Virus closely related to an isolated bat coronavirus (Benvenuto et al.)
- Virus closely related to SARS but different (Chan et al .; Hui et al.)
- 79.5% sequence homology between SARS and SARS-CoV-2 (Zhou et al .; Wu et al.)
- Significant homology between SARS-CoV-2 and coronavirus isolated from bats (Lu et al.)

- Would come from a bat

- Crossing the species barrier through intermediate hosts to infect humans (Pangolin?)



SARS-CoV-2 – COVID-19



SARS-CoV-2 – COVID-19

DÉCEMBRE 2019

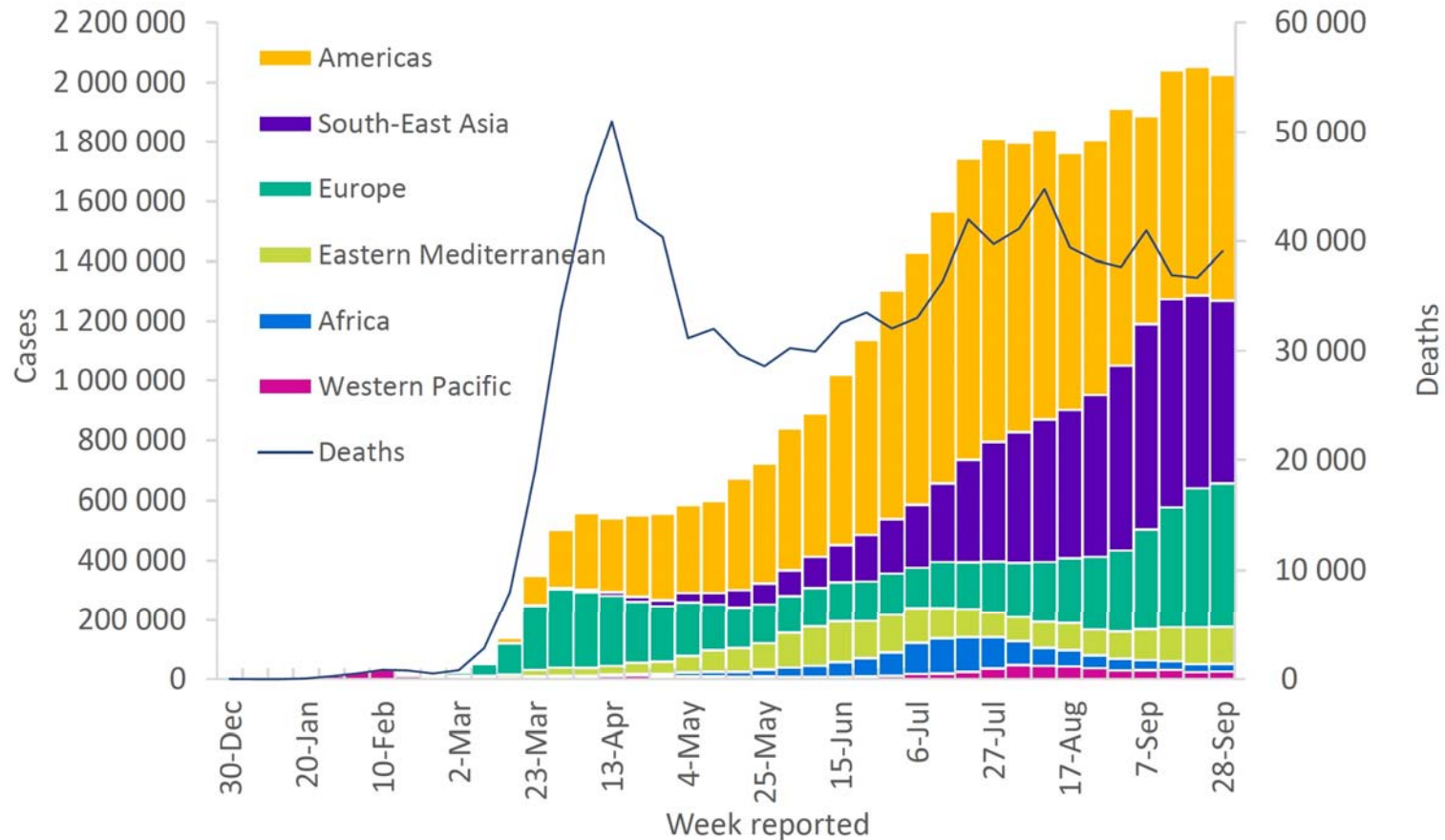
Lundi	Mardi	Mercredi	Jeudi	Vendredi	Samedi	Dimanche
						1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29
30	31					

cases of pneumonia of unknown etiology linked to Huanan Seafood Wholesale Market (Wuhan, Hubei, China)



SARS-CoV-2 : epidemiology (WHO)

Figure 1: Number of COVID-19 cases reported weekly by WHO Region, and global deaths, 30 December 2019 through 04 October 2020**



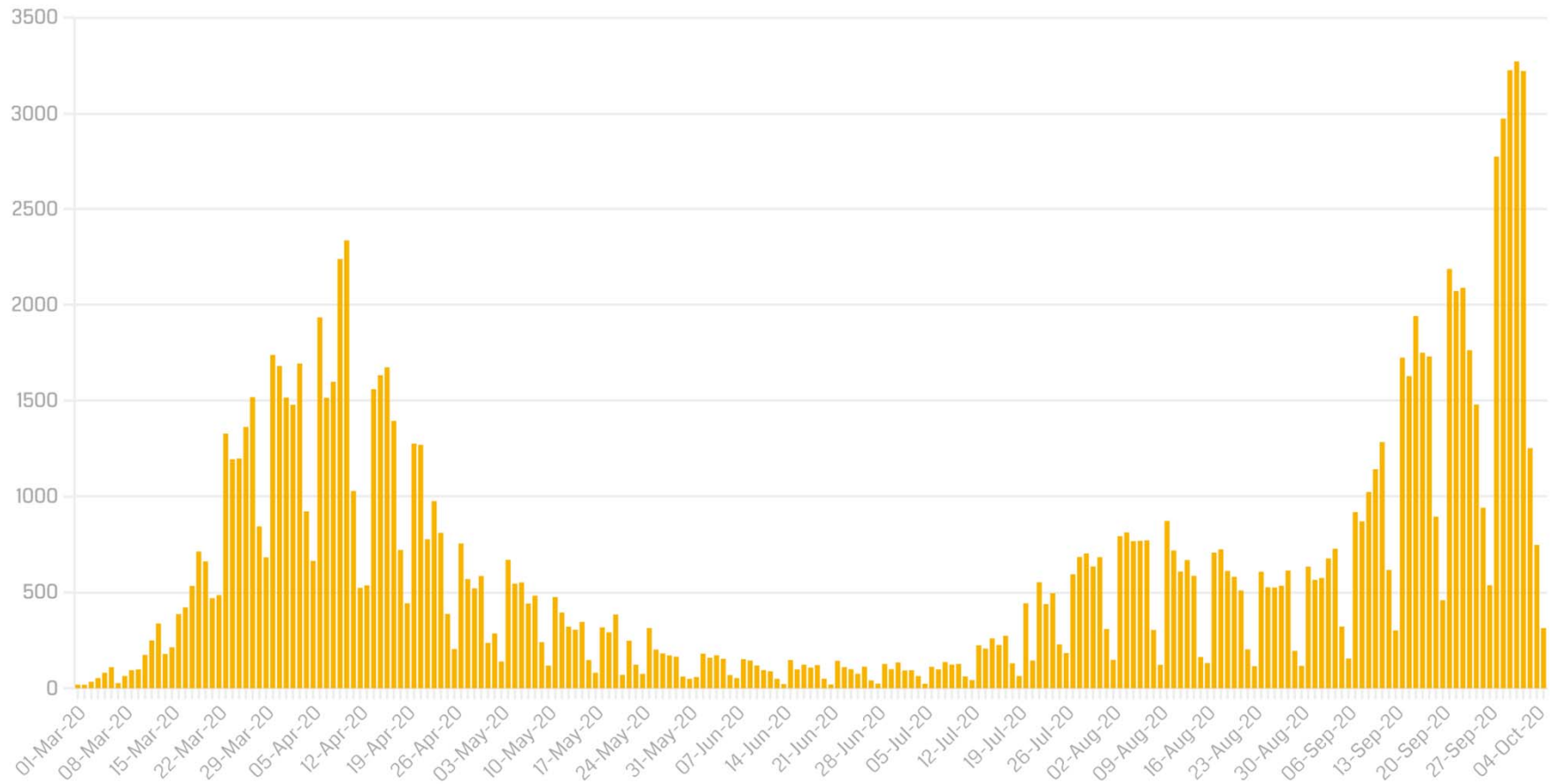
- Cumulative total number over 34.8 million cases.
- Over 1 million deaths



Evolution des cas en Belgique

Depuis le 1er mars

Les données sont considérées comme complètes (consolidées) au bout de 3-5 jours.

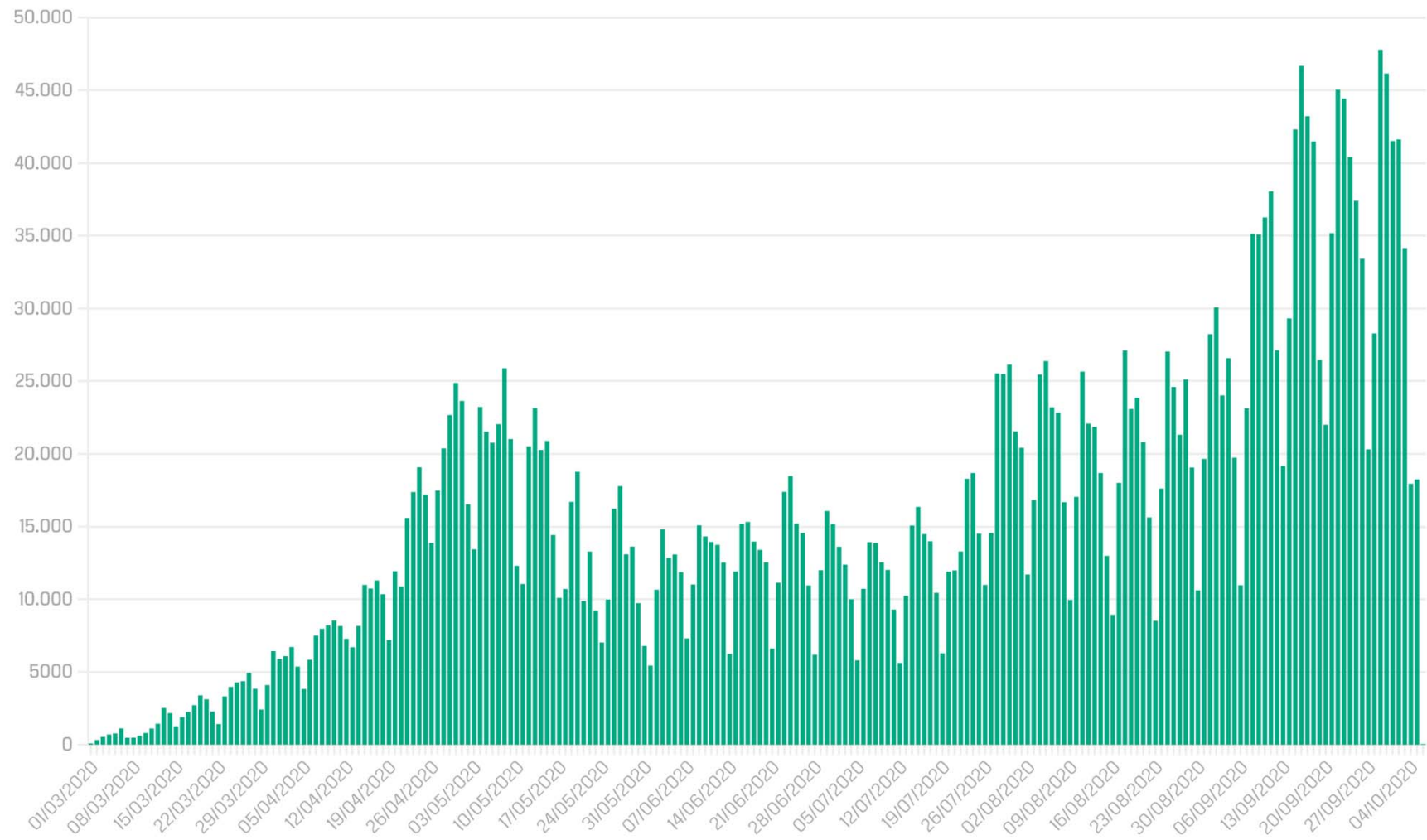


Source: [Sciensano](#)

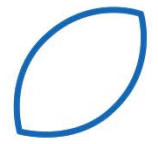
TEMPLATE CREDITS
Line, bar and pie charts by **Flourish team**



Nombre de tests par jour



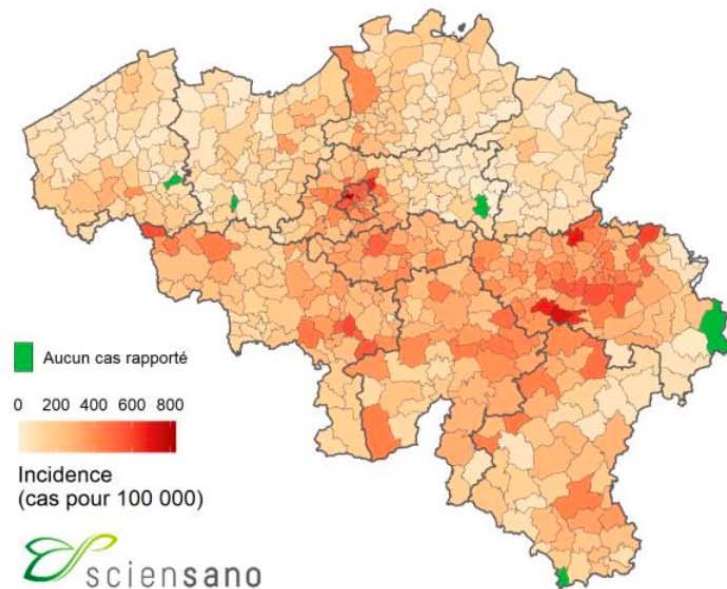
TEMPLATE CREDITS
Line, bar and pie charts by Flourish team



1.4. SITUATION RÉCENTE

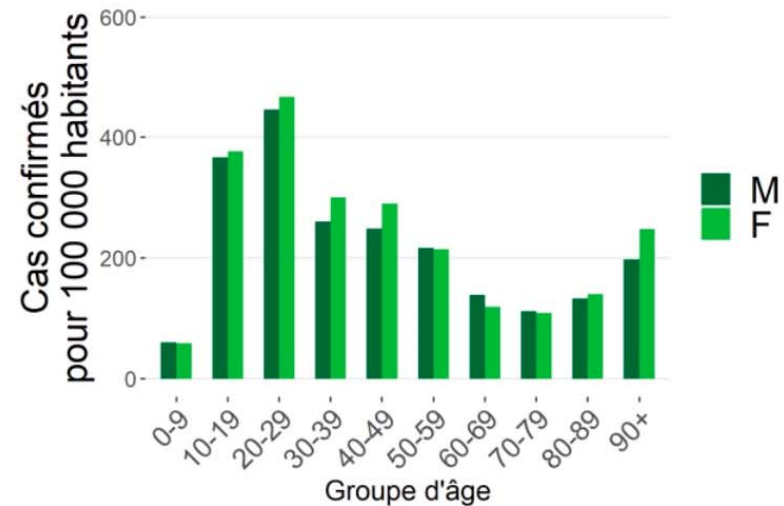
Les chiffres ci-dessous montrent la répartition géographique et la distribution par âge et par sexe pour les 14 derniers jours (données consolidées).

Distribution des cas confirmés par 100 000 habitants entre le 20/9 et le 3/10



Source : Réseau des laboratoires cliniques et plateforme nationale

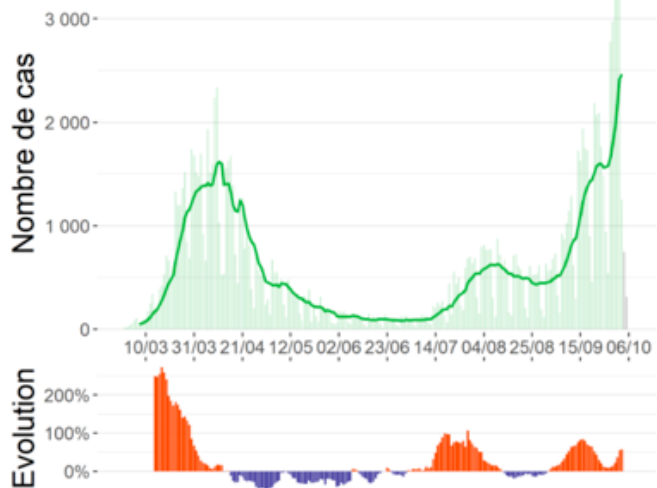
Nombre de cas confirmés par groupe d'âge et sexe par 100 000 habitants entre le 20/9 et le 3/10



Note : L'information sur l'âge et/ou le sexe n'était pas disponible pour 943 cas

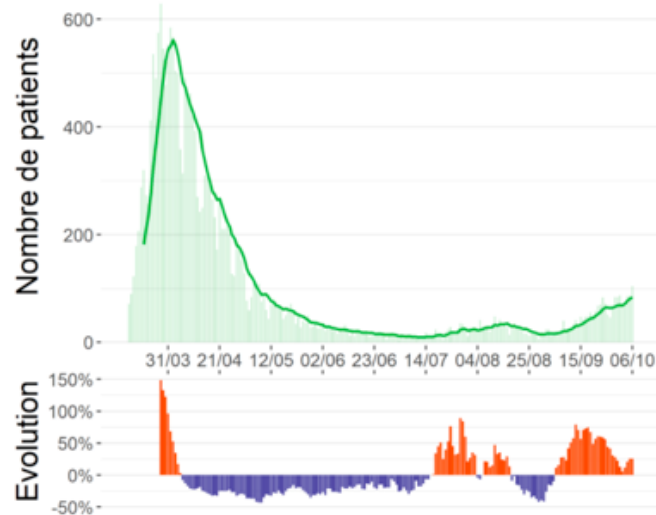


Evolution des nouveaux cas confirmés



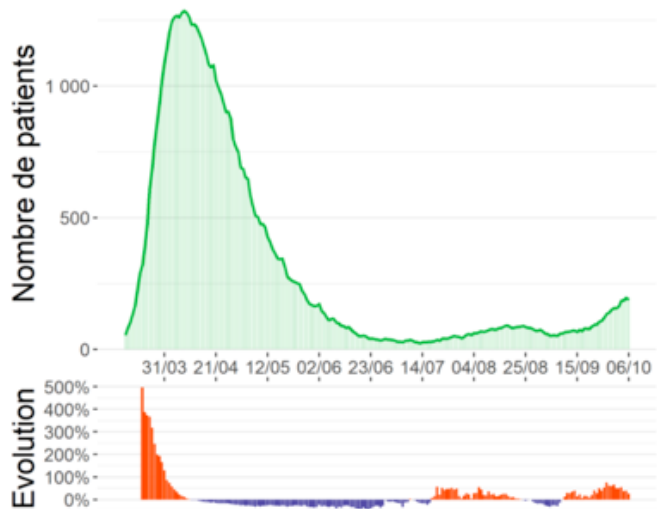
Source : Réseau des laboratoires cliniques et plateforme nationale

Evolution des nouvelles admissions de cas COVID-19 confirmés en laboratoire à l'hôpital



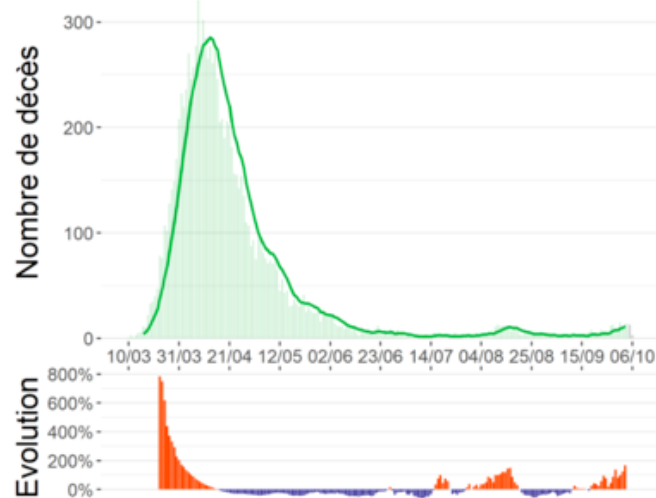
Source : Surveillance des hôpitaux (Sciensano)

Evolution du nombre de patients en USI



Source : Surveillance des hôpitaux (Sciensano)

Evolution du nombre de décès

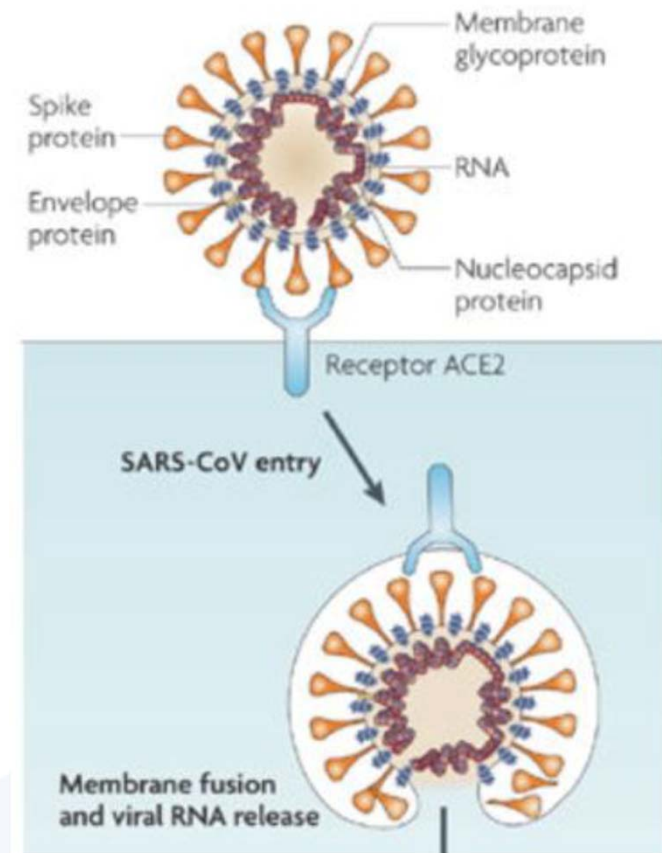


Source : Surveillance mortalité COVID-19 (Sciensano)



SARS-CoV-2 : Mechanisms of infection

- SARS-CoV2 receptor
 - Angiotensin-converting enzyme 2 (ACE2)
 - ACE2 expressed in alveolar epithelial cells type I and II
- ACE2 expression
 - Men > Women
 - Asians > Americans



SARS-CoV-2 : Infection

- Incubation period
 - Mean = 5.2 days (95% CI: 4-7) (Li et al.)
 - Median = 7 days (range: 0-24 days) (Guan et al.)
- Clinical symptoms (<1 week after contagion) = COVID-19
 - Main: fever, cough, and shortness of breath
 - Others: anosmia and dysgeusia, fatigue, myalgia, headache, sore throat, sputum, hemoptysis, viral encephalitis, myocarditis and erythematous rash
 - Uncommon gastrointestinal symptoms (diarrhea, nausea, vomiting)
- Biological signs
 - Leukopenia
 - Lymphopenia
 - Hs-TnI, CRP, ASAT

Chest X-ray, CT-Scan



SARS-CoV-2 : Infection

- **3 stages of COVID-19**
 - Mild infection with symptoms of the upper respiratory tract
 - "Mild" pneumonia
 - Severe pneumonia with ARDS, sepsis and septic shock
- Asymptomatic infections, especially in young people (Chan et al.)
- Risk factors for severe infection
 - The elderly
 - Underlying comorbidities or pathologies

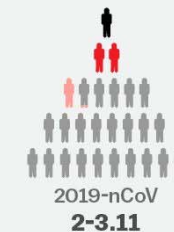


SARS-CoV-2 : routes of transmission

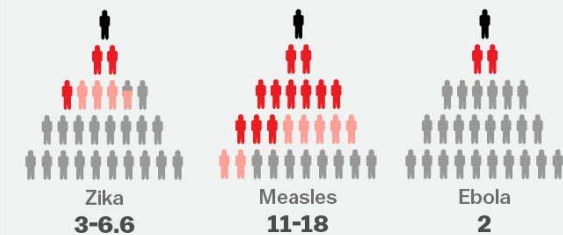
- R0, the basic reproduction number represents the number of secondary infections
 - Estimation varies between research teams
 - 2.47–2.86 (SEIR model, Wu et al.)
 - 2.0–3.3 (IDEA model, Majumder et al.)
- Source of infection
 - Bats are considered to be the natural hosts
 - Pangolins and snakes are thought to be intermediate hosts.

How contagious is a disease?

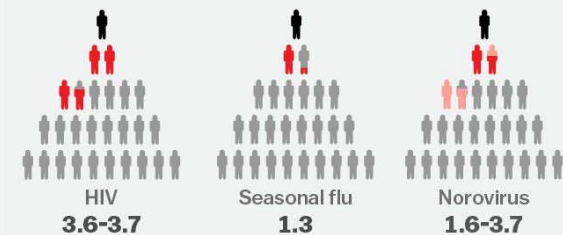
Scientists use "R naught," or R0, to estimate how many other people one sick person is likely to infect



*This estimate is preliminary and likely to change



*An early estimate based on the Colombia outbreak in 2015



*An estimate based on Réunion Island in 2006

SOURCES: Travel Medicine, PLOS One, JAMA Pediatrics, MDPI, NCBI, New England Journal of Medicine, "The Spread and Control of Norovirus Outbreaks Among Hospitals in a Region"

Vox



SARS-CoV-2 : routes of transmission

- Transmission by infectious droplets is the most common routes of human to human transmission of SARS-CoV-2
 - Prolonged close contact is the main risk factor
 - Risk of infection is much higher in household contacts
- Transmission may occur indirectly through infected surfaces
- Aerosol transmission may be another route
- In addition, researchers have detected SARS-CoV-2 in samples of stool, gastrointestinal tract, saliva and urine.



SARS-CoV-2 : routes of transmission

L. Wang, Y. Wang and D. Ye et al. / International Journal of Antimicrobial Agents 55 (2020) 105948

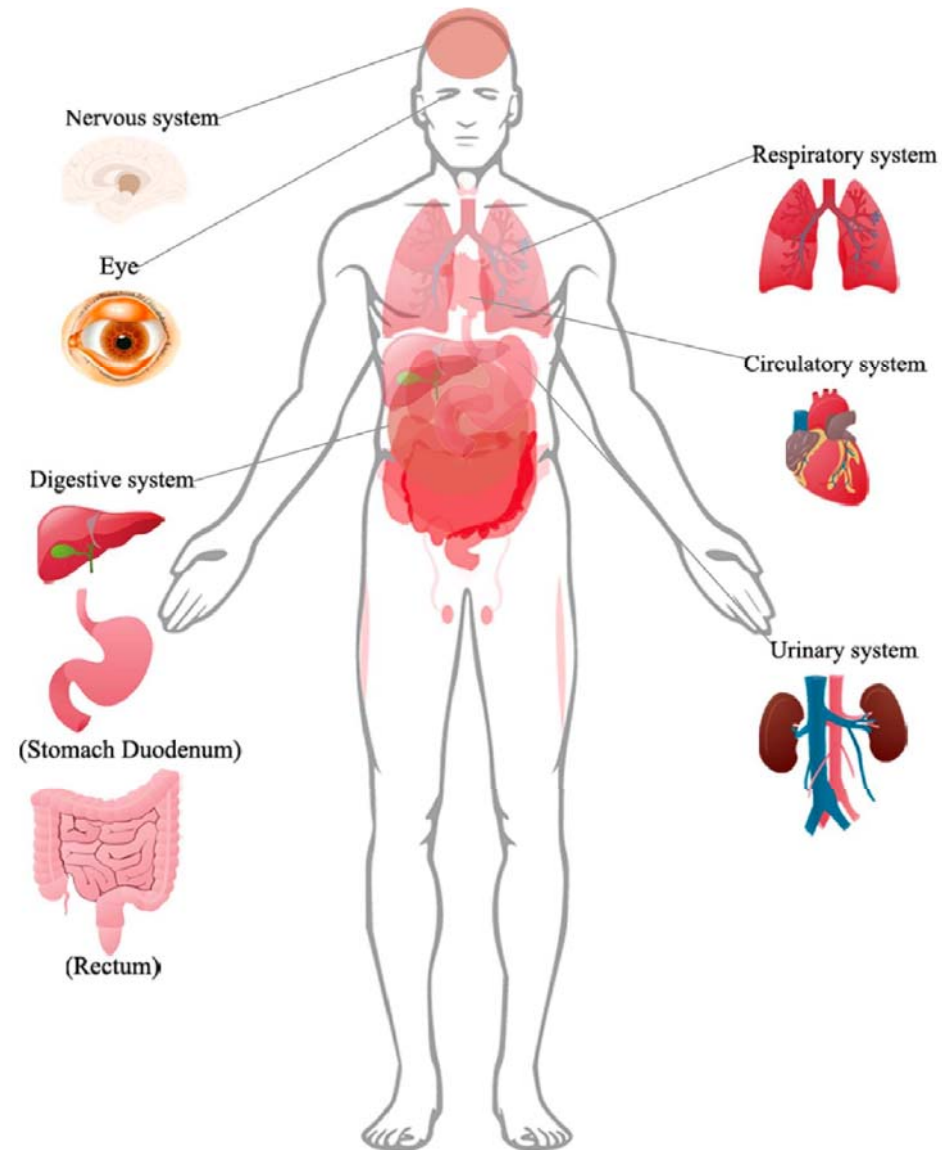


Fig. 2. Organ involvement confirmed by clinical features or biopsy in patients with COVID-19.

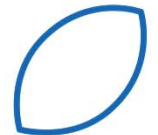
SARS-CoV-2 – COVID-19

- Mortality
 - Case Fatality Rate difficult to estimate: 3.5% -> 1%
 - 1.36% (Guan et al.)
 - 2.84% (Wang et al.)
 - 14% (Wu et al.)
 - 15% (Huang et al.)
 - 33% (Zhu et al.)
- Death
 - Ratio M / F = 3,25 / 1
 - Median age = 75 years
 - Median time between first symptoms and death = 14 days
 - The disease progresses faster in older people



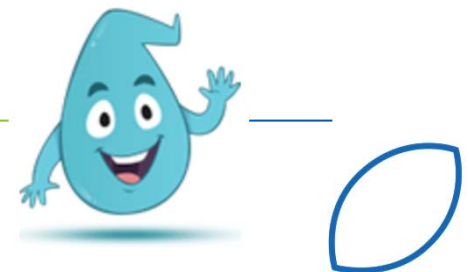
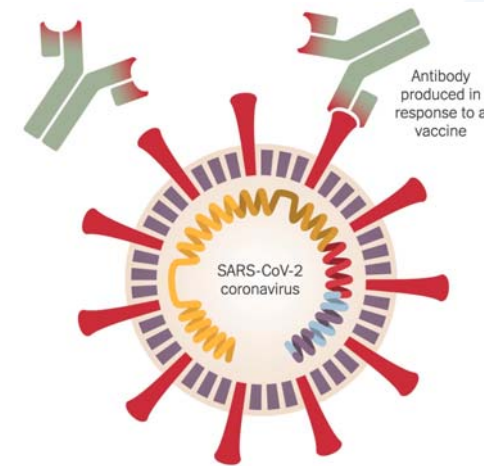
SARS-CoV-2 – COVID-19

Infection control and prevention



SARS-CoV-2: infection control and prevention

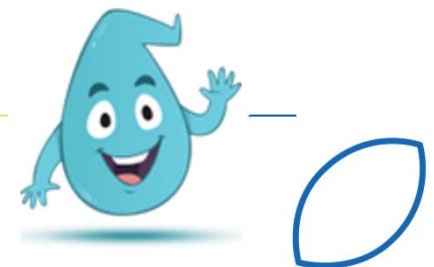
- To date, no specific antiviral treatments or vaccines available
 - Clinical treatment of COVID-19 has been limited to support and palliative care until now
 - Various vaccine technology platforms are being evaluated
 - Nucleic acid (DNA and RNA),
 - Virus-like particle, peptide,
 - Viral vector (replicating and non-replicating),
 - Recombinant protein,
 - Live attenuated virus
 - Inactivated virus approaches
 - On the 4th September,
 - 234 vaccine candidates were identified
 - 39 are currently in clinical testing, of which 8 in phase III trials.



SARS-CoV-2: infection control and prevention

- **In the community**

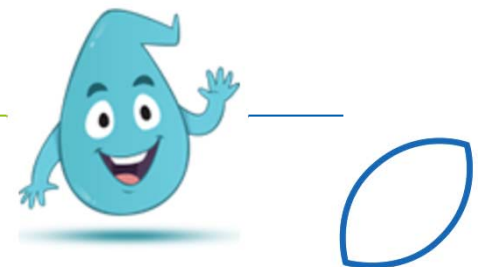
- Handwashing and social distancing measures (>1m) are recommended
- Masks: Droplets are emitted not only when coughing or sneezing, but also when breathing or speaking,
- The filtration capacity of home-made mask is lower but they do offer outward protection, despite imperfect fit or adherence
- N95/FFP2 masks should be used preferentially for aerosol-generating procedures
- Avoid touching your eyes, nose and mouth
- Avoid close contact with individuals showing symptoms of respiratory illnesses
- Stay at home if you have respiratory symptoms



SARS-CoV-2: infection control and prevention

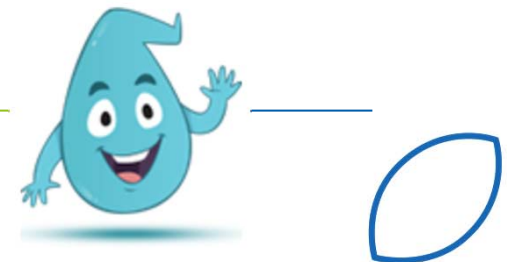
Infection control and prevention

- Home isolation of suspicious patient
 - Watch for symptoms
 - Stay away from loved ones
 - Wear a mask
 - Ventilate living rooms
 - Avoid sharing objects
 - Hand and cough hygiene
 - Cleaning the toilet with bleach (water containing 1% bleach)
 - Measures to be applied at least until symptoms disappear and at least for 7 days



SARS-CoV-2: infection control and prevention

- Management of laboratory samples
 - Contact between the unit and the laboratory
 - Do not use a teletube
 - Double packaging
 - Blood: standard precautions
 - Clinical sample unpackaging
 - Under laminar flow hood
 - Blouse
 - Gloves
 - Mask
 - (Protective glasses)



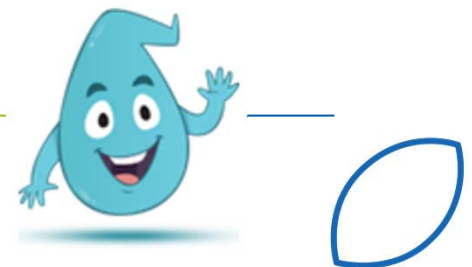
SARS-CoV-2: Infection control and prevention

- Stability of SARS-CoV-2 on surfaces and in the environment
 - Depends on temperature, relative humidity and type of surface
- In the absence of any ventilation (Doremalen N van et al. 2020)
 - SARS-CoV-2 remains viable in aerosols for 3 h, (median 1.1-1.2h)
 - Most stable on plastic and stainless steel up to 72 hours (median 5.6 h /steel and 6.8 h/plastic)
- In the absence of any intervention (eg. no disinfection). (Doremalen N van et al. 2020)
 - No viable virus measured after 4 h on copper and after 24 h on cardboard.
 - On all surfaces and in the air, exponential decay in virus titer over time.
 - SARS-CoV-2 is more stable on smooth surfaces like glass, steel and plastic (several days) than on rough surfaces like paper, wood and cloth (hours) (Chin AWH et al. 2020).



SARS-CoV-2: Infection control and prevention

- Stability of SARS-CoV-2 on surfaces and in the environment
 - Like other coronaviruses, SARS-CoV-2 is very stable at 4° C but sensitive to ultraviolet rays and heat (inactivated within 5' at 70°)
- However, virus sensitive to lipid solvents and conventional disinfectants
 - Hydrogen peroxide (Incidin Oxyfoam S)
 - Chlorine Dioxide (Tristel Fuse Surface)
 - Quaternary ammonium
 - Bleach (1000 ppm or 10,000 ppm)
 - Ether (75%), ethanol, chloroform
 - Soap, which dissolves the lipid bilayer of the virus



SARS-CoV-2 : testing

- National Reference Center (KU UZLeuven)
- Clinical labs
- Federal platforms bis for SARS-CoV-2 testing

- Direct methods
 - Real-Time reverse transcription PCR (RT-qPCR) = reference
 - Antigen detection: rapid test but less sensitive

- Indirect methods
 - Antibody detection, difficulties of result interpretation
 - May help for past infection diagnosis



Mogelijk geval

Een mogelijk geval van COVID-19 is een persoon met

- minstens één van de volgende hoofdsymptomen die acuut ontstaan zijn, zonder andere duidelijke oorzaak : hoest; dyspnoe; thoracale pijn; acute anosmie of dysgeusie;

OF

- minstens twee¹ van de volgende symptomen, zonder andere duidelijke oorzaak, koorts; spierpijn; vermoeidheid; rhinitis; keelpijn; hoofdpijn; anorexie; waterige diarree²; acute verwardheid²; plotse val²;

OF

- verergering van chronische respiratoire symptomen (COPD, astma, chronische hoest...), zonder andere duidelijke oorzaak.

Radiologisch bevestigd geval

Een radiologisch bevestigd geval is een persoon bij wie de PCR voor COVID-19 negatief is, maar bij wie de diagnose van COVID-19 wordt gesteld op basis van een suggestieve klinische presentatie **EN** een compatibele CT thorax.

Bevestigd geval

Een bevestigd geval wordt gedefinieerd als een persoon waar de diagnose van COVID-19 infectie bevestigd werd door een moleculaire test³.



Cas possible

Un cas possible de COVID-19 est une personne avec

- au moins un des symptômes majeurs suivants d'apparition aiguë, sans autre cause évidente: toux; dyspnée; douleur thoracique; anosmie ou dysgueusie;

OU

- au moins deux des symptômes mineurs suivants¹, sans autre cause évidente : fièvre; douleurs musculaires; fatigue; rhinite; maux de gorge; maux de tête; anorexie; diarrhée aqueuse² ; confusion aiguë²; chute soudaine² ;

OU

- une aggravation de symptômes respiratoires chroniques (BPCO, asthme, toux chronique...), sans autre cause évidente.

Définition d'un cas radiologiquement confirmé

Un cas radiologiquement confirmé est une personne dont le test PCR pour SARS-CoV-2 est revenu négatif mais pour lequel le diagnostic de COVID-19 est néanmoins retenu sur la base d'une présentation clinique évocatrice **ET** d'un scanner thoracique compatible.

Cas confirmé

Un cas confirmé est défini comme une personne qui a un diagnostic confirmé par test moléculaire³ de COVID19.



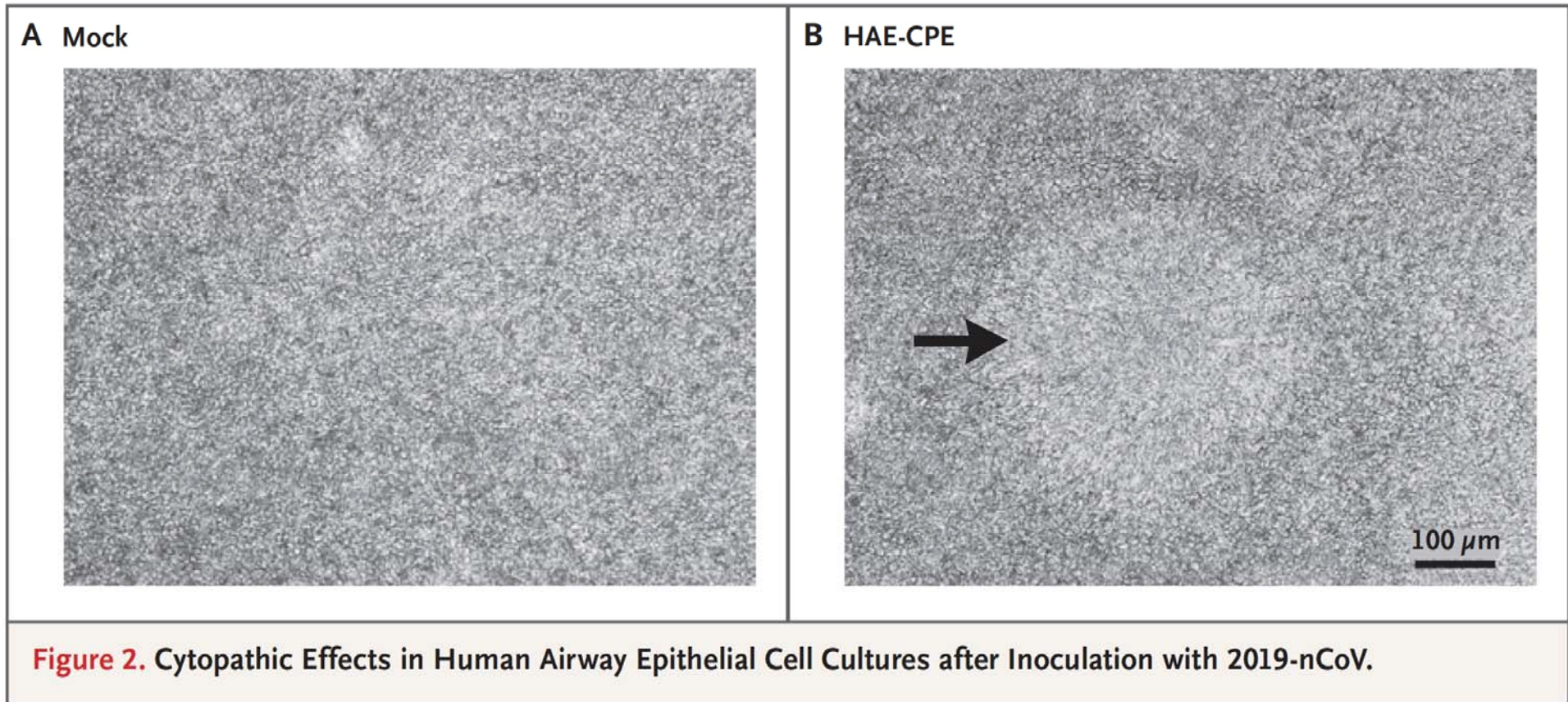
SARS-CoV-2 – COVID-19

Respiratory tract samples

- Upper respiratory tract (nasopharyngeal swab > throat swab) and/or lower respiratory tract
- Flocked swabs in dacron or polyester (not cotton!)
 - In a UTM medium
 - No Ca alginate or swab with wooden handle
- ! In patients suspected of severe COVID-19, a negative upper respiratory tract sample does not exclude the diagnosis (CDC)
- Real-time RT-PCR RT-qPCR with more than 1 target
 - *E, N, RdRp* genes



Cytopathic effects in cell culture



SARS-CoV-2 : Treatments

Symptomatic patients

- Several treatments being evaluated ...
 - Remdesivir = adenosine analogue, viral protein inhibitor
 - Chloroquine: increase in the endosomal pH required for cell-virus fusion and inhibition of MAPK involved in viral replication
 - Lopinavir + ritonavir (effective for SARS)
 - Leronlimab (anti-CCR5)
 - Galidesivir (pol RNA inhibitor)
 - Plasma from healed people
 - Monoclonal antibodies
- Currently, no available vaccine against the SARS-CoV-2
 - Not all vaccine candidates will necessarily result in a marketed vaccine



SARS-CoV-2 - COVID-19

CDC : « There is still more to be learned »



SARS-CoV-2 - COVID-19

There is still more to be learned: Questions not solved

- Intermediate host of this new SARS?
- Other routes of human-to-human transmission?
- Viral pathogenesis? Understand how the virus works,
- Its replication and its interactions with the cell and the host organism, thus identifying biomarkers of infection or even new targets for the development of treatments.
- Immunity? Cellular restriction factors?
- The infectious dose? stability of SARS-CoV-2 on surfaces and in the environment?
- Incubation period?
- Proportion of asymptomatics? Contagiousness?
- Coinfection? Re-infection?
- Treatment ? Vaccine?



SARS-CoV-2 - COVID-19

Fake news (WHO)

- SARS-CoV-2 can be transmitted by mosquito bites
- Children's urine may protect against SARS-CoV-2
- Cold weather and snow can kill the novel coronavirus
- Cocaine may protect against the novel coronavirus
- Novel coronavirus (2019-nCoV) can spread long distances in the air
- Is it safe to receive letter or parcel from China?

- I come back from a "red zone", what should I do?



Overdose d'informations... pouvant créer une épidémie de psychose...

**"2 Corona achetées, une Mort Subite offerte":
l'action qui n'a pas fait rire Delhaize**



"2 Corona achetées, une Mort Subite offerte": l'action qui n'a pas fait rire Delhaize - © Tous droits réservés





Monde

Coronavirus: un chien a été testé positif et placé en quarantaine

AFP

Publié le vendredi 28 février 2020 à 10h07 - Mis à jour



