

Herpes, Vírus Respiratórios , Sarampo e Caxumba

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Vírus Dermotrópicos

Máculo - papulares



Vírus do Sarampo

Vírus da Rubéola

Parvovírus B19

Mácula



Pápula



Vesícula

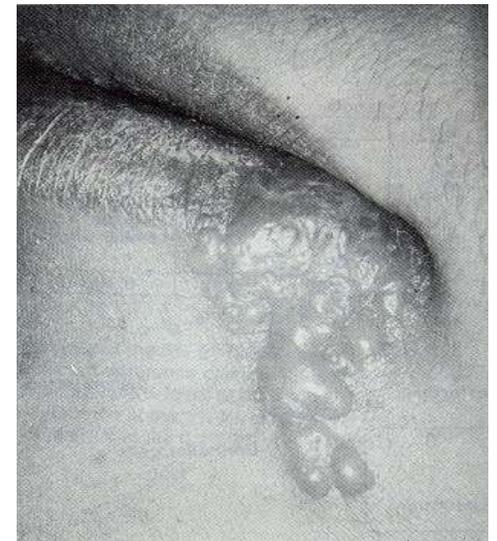


Pústula



Crosta

Vesículo - pustulares



Herpesvírus

Vírus da varíola



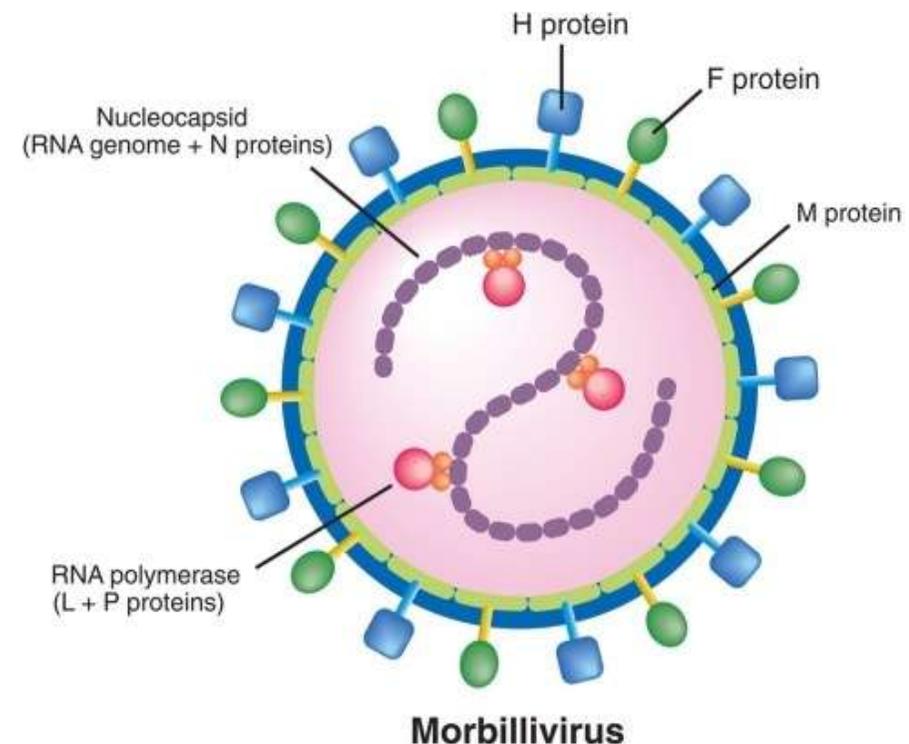


Virus Máculo-Papulares

VÍRUS DO SARAMPO

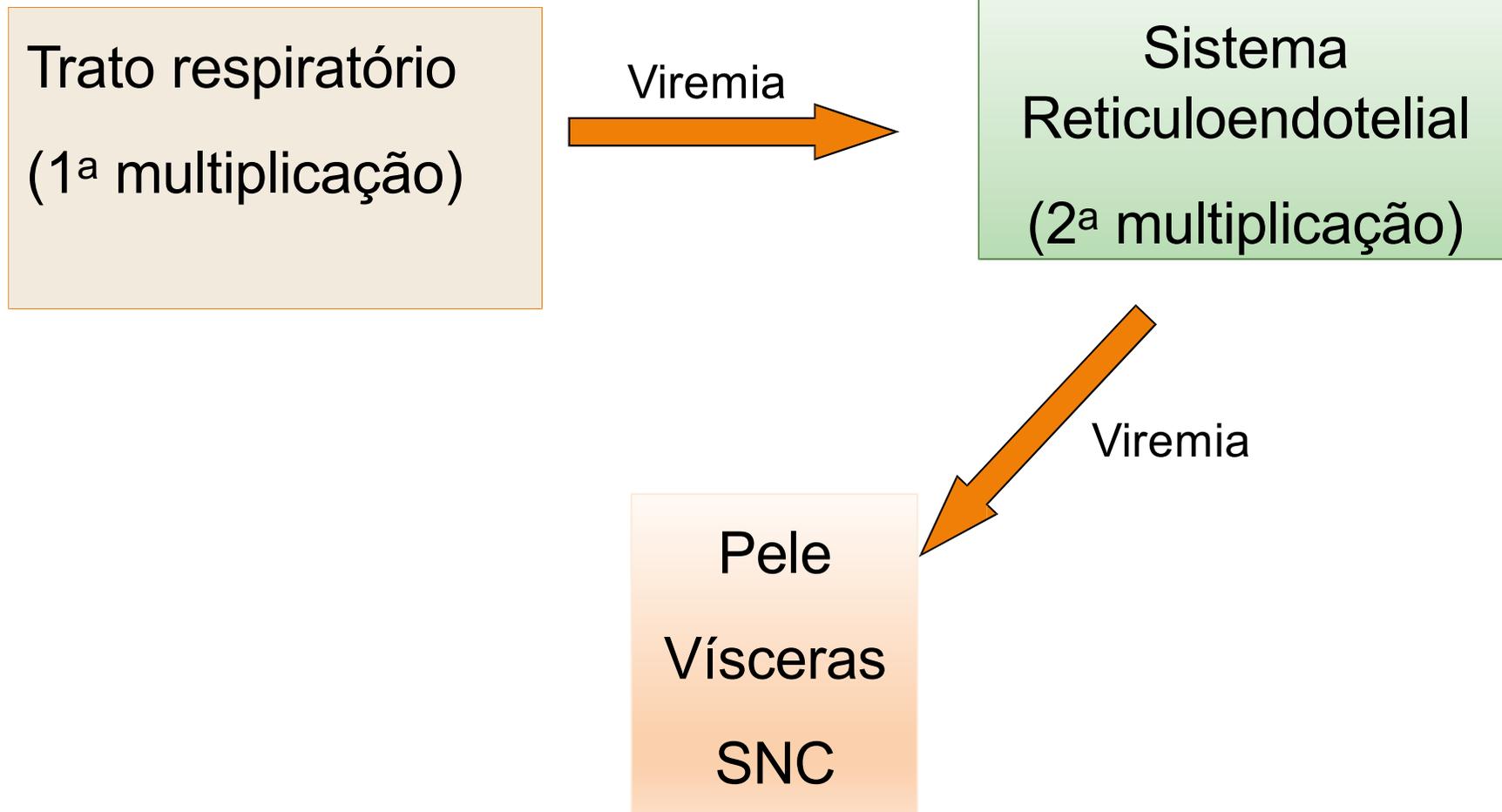
Características gerais

- ✓ Família *Paramyxoviridae*
- ✓ Genoma RNA fita simples de polaridade negativa
- ✓ Capsídeo de estrutura helicoidal
- ✓ Envoltório com espículas hemaglutinantes (H) e para fusão (F)
- ✓ Só 1 tipo antigênico
- ✓ Complexo replicativo (RNA+L+P+N)



Patogenia

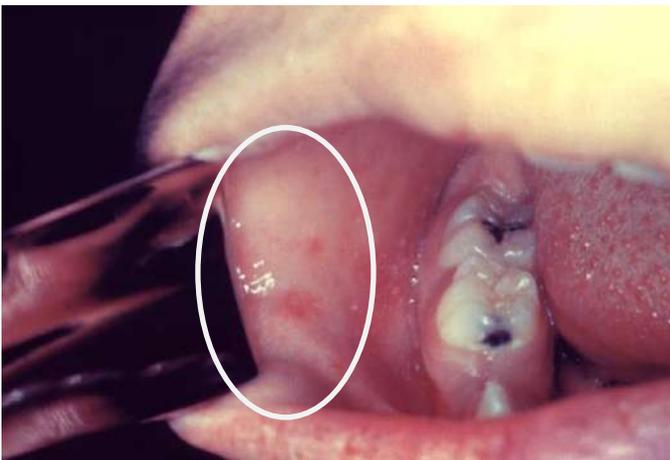
VÍRUS DO SARAMPO



Manifestações clínicas

Exantema (pele)

Enantema (mucosa)



Manchas de
Koplik

Complicações

- Quadros respiratórios graves
- Otite
- Encefalite
- Panencefalite esclerosante subaguda (SSPE)



Histórico

- MATON (1815)
- GREGG (1941)

Características Gerais

Família *Togaviridae*

Genoma RNA fita simples

Morfologia esférica

Duplo envelope

Só 1 tipo antigênico

Manifestação clínica



Exantema

Febre baixa

Dores nas articulações

VÍRUS DA RUBÉOLA

Complicações

Catarata

Microcefalia

Deformações ósseas

Retardo Mental

Defeitos
cardiovasculares



Anomalias dentais

Lábio e céu da boca fendidos

Irrupção dental retardada

Hiper e hipotireoidismo

Tratamento de Sarampo e Rubéola:

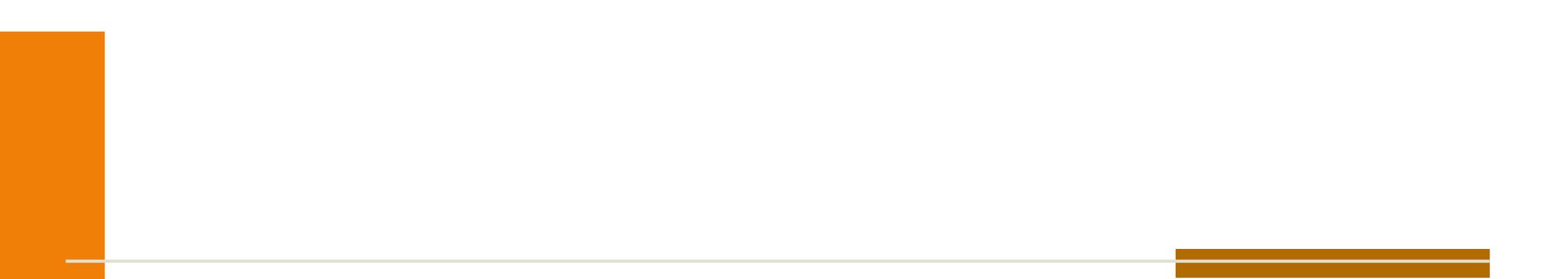
Sintomático : analgésicos e antitérmicos

Antibiótico só para infecção secundária bacteriana

Prevenção ou profilaxia:

Vacina MMR (measles, mumps & rubella)

Evitar contato pessoa-pessoa



Virus vesículo-pustulares

Vírus Vesículo-Pustulares:

Herpesvírus



Herpein = rastejar

1950 – Burnet e Buddingh

latência após primo-infecção

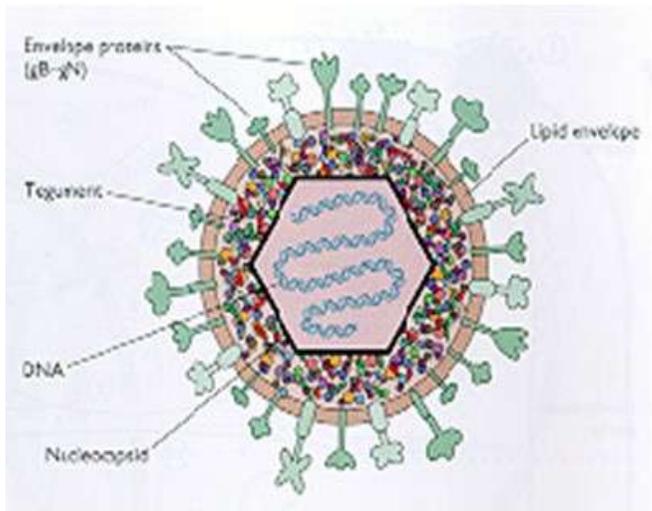
Herpesvírus patogênicos humanos

Herpesviridae

Sub-família	Vírus	Quadro clínico
<i>Alphaherpesvirinae</i>	Herpes simples tipo 1 (HHV-1)	herpes labial
	Herpes simples tipo 2 (HHV-2)	herpes genital
	Vírus da Varicela-Zóster (HHV-3)	catapora/ herpes-zóster
<i>Betaherpesvirinae</i>	Vírus de Epstein-Barr (HHV-4)	linfomas, leucoplasia pilosa
	Vírus da Citomegalia (HHV-5)	citomegalia
<i>Gammaherpesvirinae</i>	Herpesvírus tipo 6 (HHV-6)	exantema súbito
	Herpesvírus tipo 7 (HHV-7)	nenhum
	Herpesvírus tipo 8 (HHV-8)	sarcoma de Kaposi

Características gerais

Herpesvírus



Tamanho varia de 180 a 200 nm.

Genoma DNA dupla fita de 150 a 180 kb
(70 a 200 proteínas)

Capsídeo com capsômeros hexaméricos

Tegumento

Envoltório lipoprotéico, trilaminar, com espículas

Sensíveis a ácidos (pH 6,8), solventes
lipídicos, radiação UV desinfetantes
diversos.

Tipos de multiplicação viral

Herpesvírus

Produtiva

**Não
Produtiva**

Latente

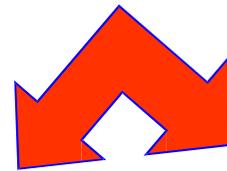
Vírus do herpes simples tipo 1 (HHV-1 ou labial)
Vírus do herpes simples tipo 2 (HHV-2 ou genital)

Oncogênica

Vírus de Epstein-Barr (EBV ou HHV-4)
Vírus do Sarcoma de Kaposi (HHV-8)

Vias de transmissão

Contato



Saliva
secreções genitais
exsudatos das lesões
cutâneas

herpes simples tipo 1
herpes simples tipo 2

Saliva
Urina

HHV-5
HHV-6

Produtos sangüíneos

Transplantes de
órgãos e tecidos

HHV-4
HHV-5
HHV-6

Vias de transmissão

Inalação



vírus da
varicela – zoster
ou
vírus da catapora
(HHV-3)

Vertical ou Perinatal



CMV ou HHV-5 (40% dos casos)
Herpes simplex tipo 2

Patogenia

Pele ou Mucosa
(1ª multiplicação)

Viremia

Orgãos Alvo

Pele

Visceras

SNC

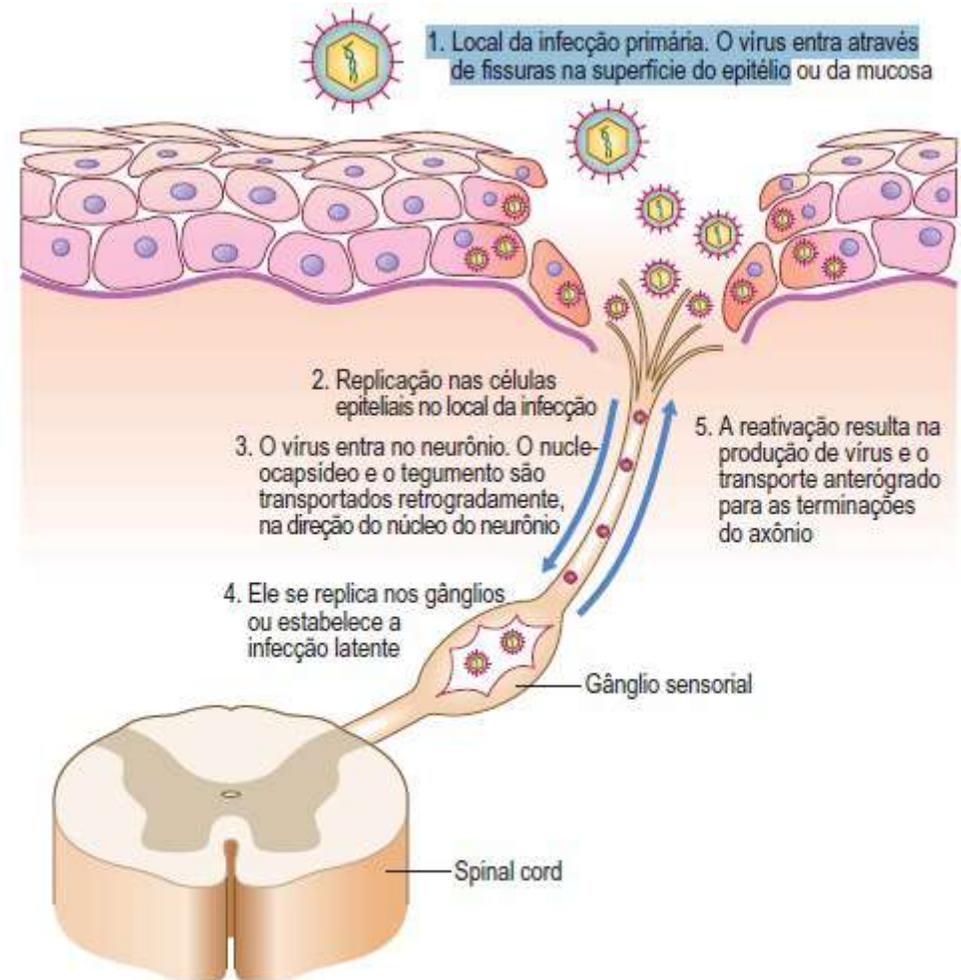
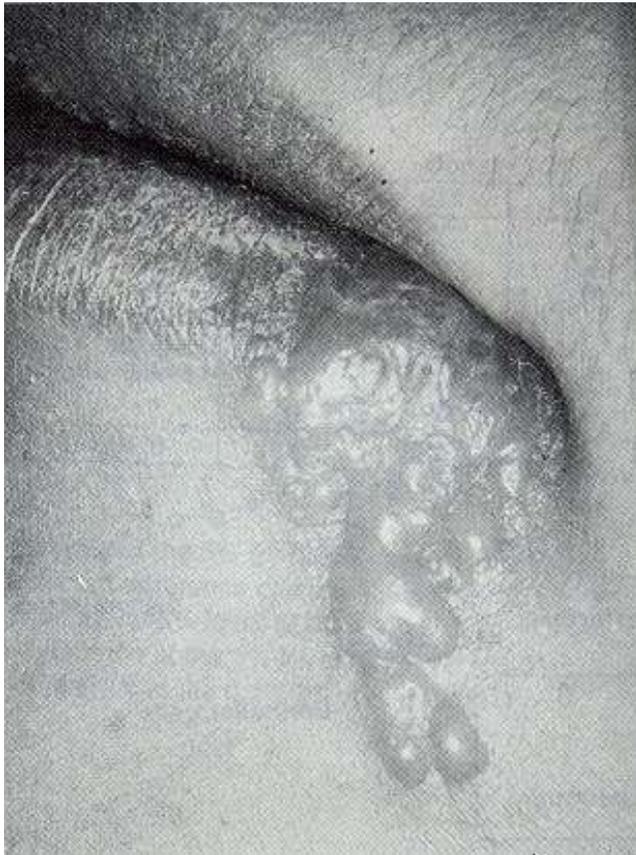


Fig. 2 Infecção primária, latência e reativação do HSV.

Patogenia



Mácula



Pápula



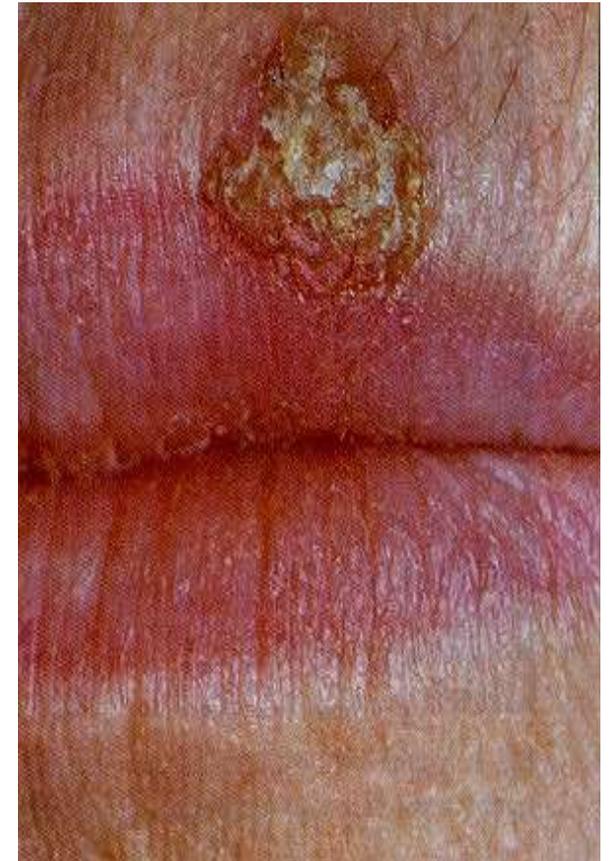
Vesícula



Pústula



Crosta



Manifestações clínicas

Herpes labial (Herpes simplex tipo 1 ou HHV-1)

Gengivoestomatite herpética

Eczema herpético

Ceratoconjuntivite

Encefalite



Herpes genital (Herpes simplex tipo 2 ou HHV-2)

Vulvovaginite

Meningoencefalite

Manifestações clínicas

Varicela – zóster ou catapora

HHV-3



Zóster (Infecção recorrente)



EBV ou HHV-4

Manifestações clínicas



Mononucleose infecciosa

Leucoplasia pilosa

Linfoma de Burkitt ou
Linfoma de células B

CMV ou HHV-5

Doença da inclusão
citomegálica ou citomegalia

Seqüelas no feto:

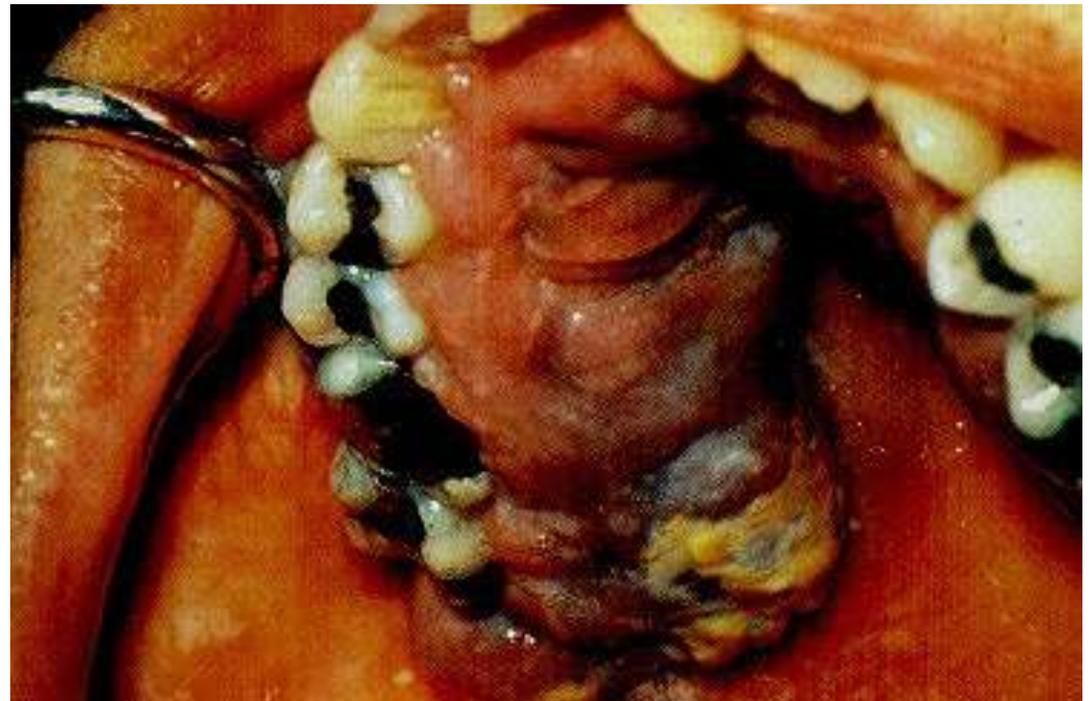
hepatoesplenomegalia (icterícia)
ao óbito



Exantema súbito
(HHV-6)



Sarcoma de Kaposi
(HHV-8)



Sintomático

Drogas anti-virais:

Acyclovir

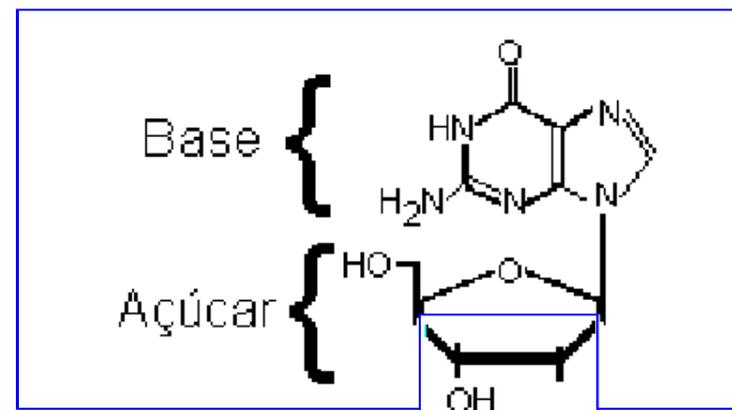
Ganciclovir

5-iodo-2-deoxiuridina



Inibidores da DNA polimerase viral

Análogos da Deoxiguanosina



Profilaxia

HHV-1 e HHV-2

Evitar contato com saliva e fluído de lesões

Uso de preservativos

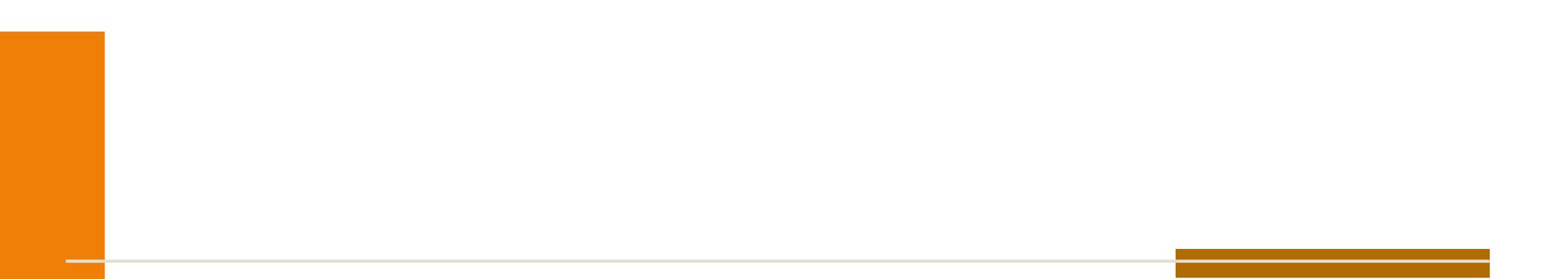
HHV-3

Evitar inalação

Vacina Oka (atenuada)

Administração de imunoglobulina (imunodeficientes, transplantados, pré-quimio e radioterapia)

Demais tipos: algumas vacinas em fase experimental, mas sem eficiência



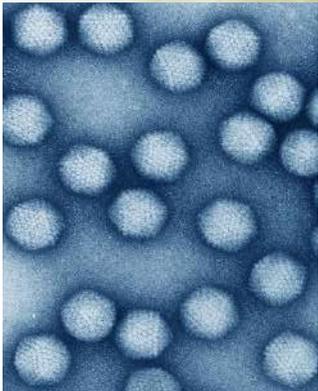
Fim da primeira parte!!!

Vírus associados a quadros respiratórios



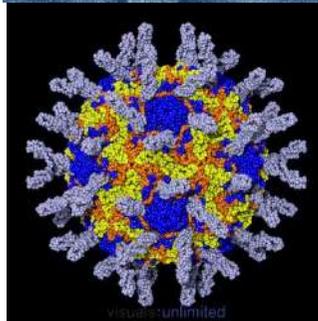
Vírus da Parainfluenza

5 sorotipos: 1, 2, 3, 4a, 4b



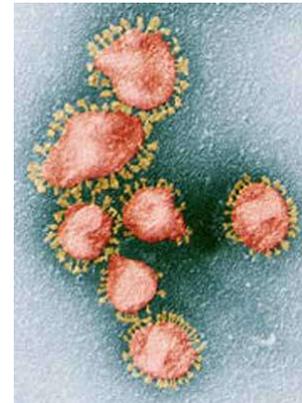
Adenovírus

52 tipos distribuídos em 6 subgêneros (A-F)



Rinovírus

114 tipos conhecidos até o momento

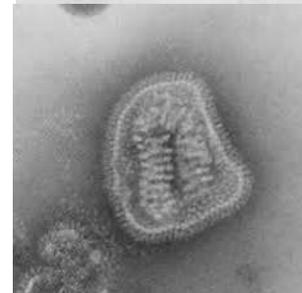


Coronavírus

2 sorogrupos: OC43 e 229E



Vírus Respiratório Sincicial (RSV)



Vírus da Influenza

Tipos A, B, C

Outros Vírus Respiratórios

Vírus	Grupo de pacientes	Prevalência	Sinais Clínicos	Referência
Metapneumovírus Humano	Crianças e idosos	3-25%	Bronquiolite, pneumonia, broncoespasmo, rinorréia, tosse, dor de garganta	van den Hoogen et al (2001)
Influenza Aviária	Todas as idades	Esporádica	Pneumonia síndrome gripal	Bridges et al (1997)
Síndrome respiratória aguda grave (SARS)	Todas idades	Esporádica	Pneumonia	Ksiazek et al (2003)
Coronavírus NL63 e HKU1	Crianças e idosos	1-10%	Bronquiolite, pneumonia, rinorréia, febre, tosse e sibilância	van der Hoek et al (2004), Woo et al (2005)
Bocavírus Humano	Crianças	1-11%	Bronquiolite, pneumonia, OMA, broncoespasmo	Allander et al (2005)
Polyomavírus KI e WU	Crianças	1-7%	Bronquiolite, pneumonia, tosse	Allander et al (2007), Gaynor et al (2007)

Diversidade de quadros respiratórios

Pneumonite

Bronqueolite

Laringotraqueobronquite
ou
crupe

Infecção respiratória aguda
(incluindo resfriado comum)

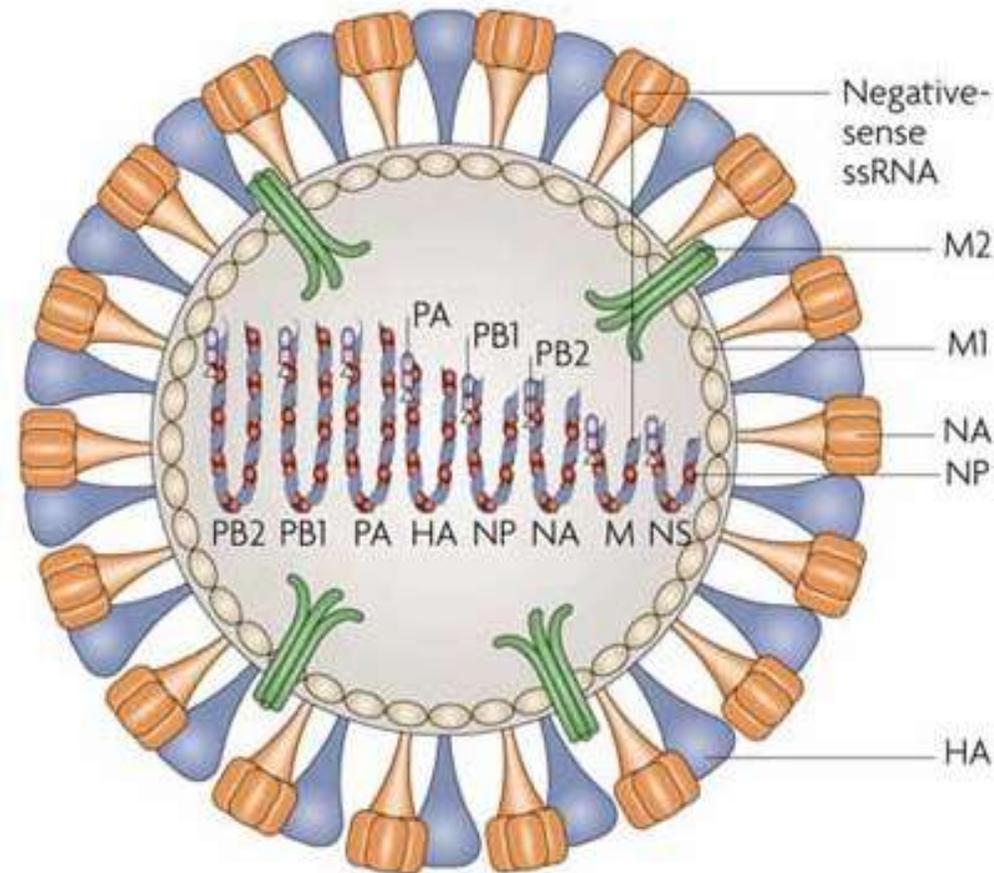
Comparison of Flu and the Common Cold

Symptom	Influenza	Common Cold
Symptom onset	Sudden	Gradual
Fever	Common, 100° to 104° F	Uncommon or low grade
Myalgia	Common, severe	Uncommon
Arthralgia	Common, severe	Uncommon
Anorexia	Common	Uncommon
Headache	Common, severe	Mild
Cough	Common, severe	Mild to moderate
Malaise	Common, severe	Mild
Fatigue, weakness	Common, lasts 2 to 3 weeks	Mild, short duration
Nasal congestion	Occasional	Common
Sneezing	Occasional	Common
Sore throat	Occasional	Common

Gripe ou Influenza



Estrutura viral



Genoma

RNA fita simples fragmentado;

Antígeno S

associado ao nucleocapsídeo
(tipos A, B, C);

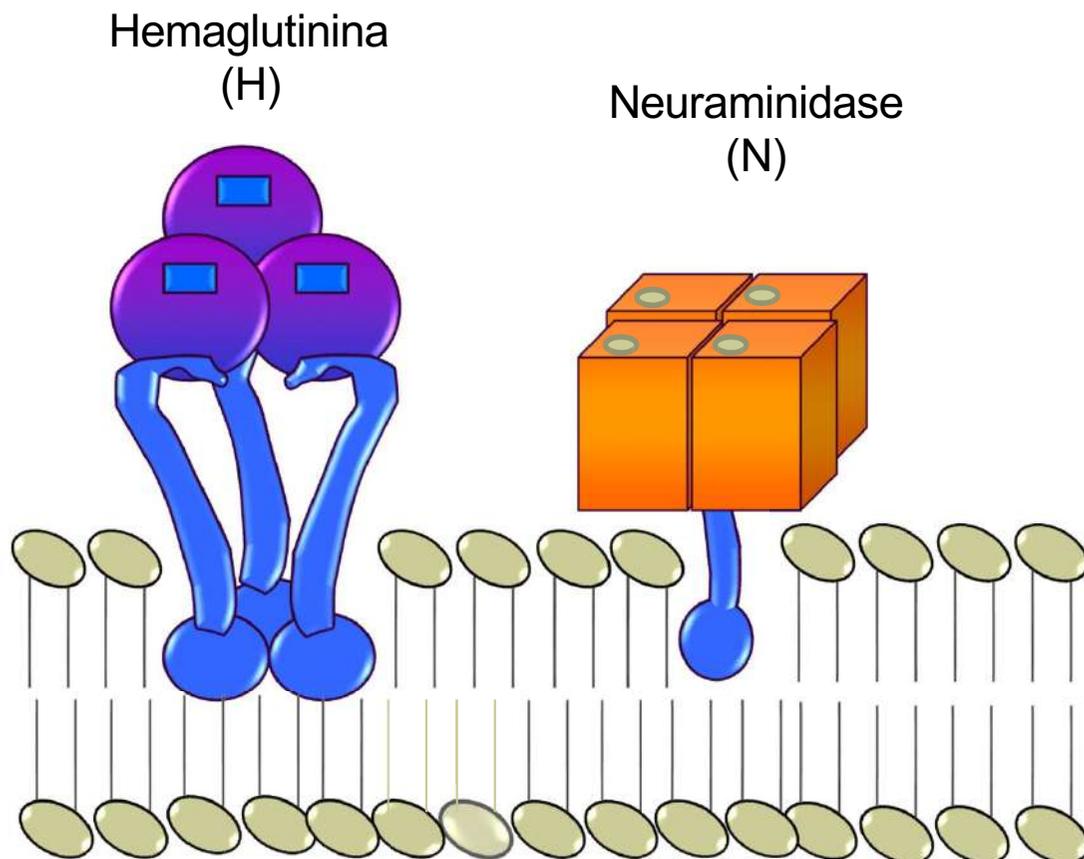
Presença de envoltório viral com dois tipos de espículas:

Hemaglutinina (H)

Neuraminidase (N)

Vírus da Influenza

Estrutura das espículas



15 variantes H e 9 N

Humanos

H1, H2 e H3

N1 e N2

Aves, eqüinos, suínos

Fórmula antigênica

A/São Paulo/32/2009 (H1N1)

Variações antigênicas

SHIFT

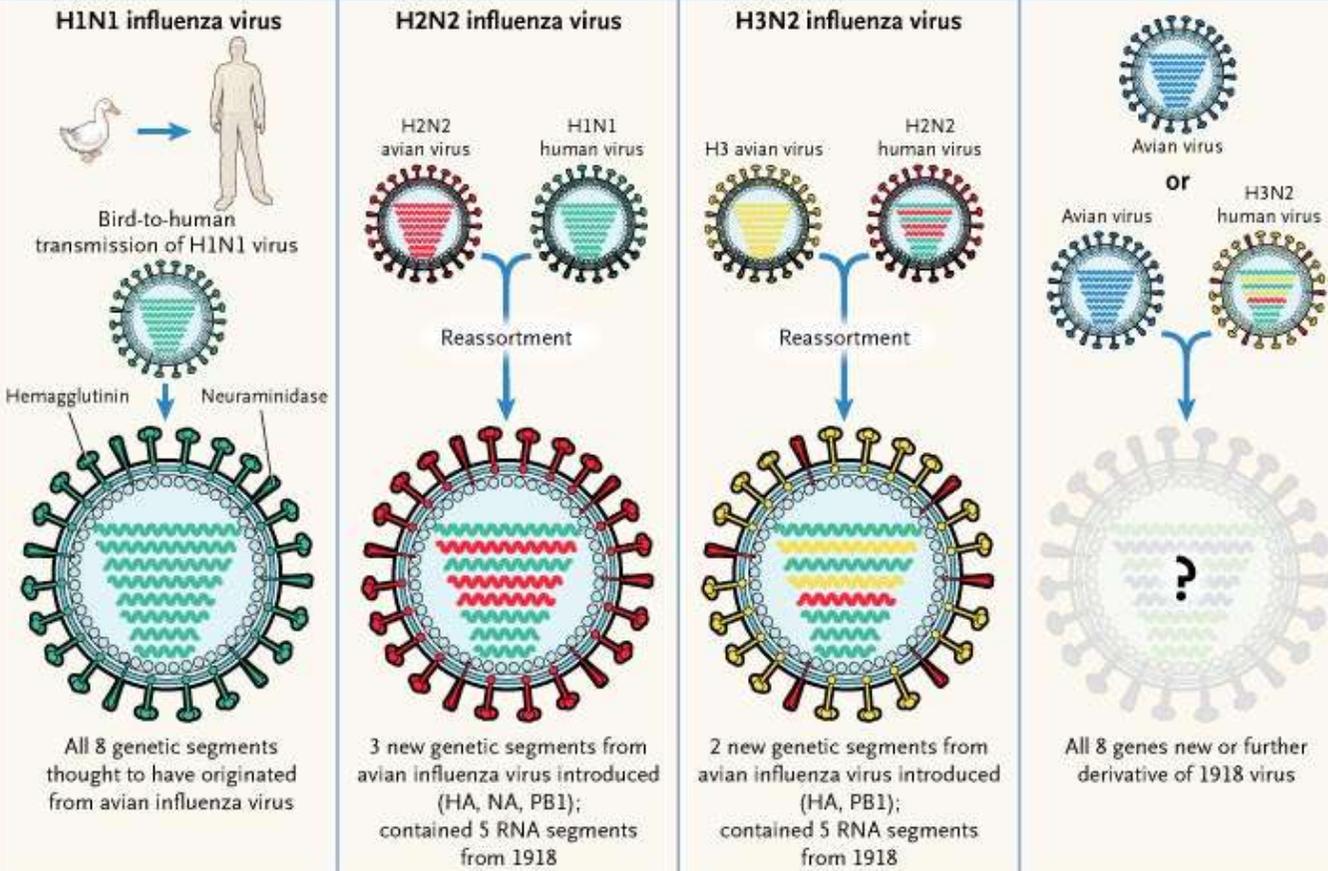
- Variação antigênica abrupta
- Ocorre nas hemaglutininas e neuraminidases
- Vírus novo não guarda relação antigênica com o original
- Epidemiologicamente - PANDEMIAS
- Só tipo A

DRIFT

- Variação antigênica leve
- Ocorre nas hemaglutininas e neuraminidases
- Vírus novo ainda guarda relação antigênica com o original
- Epidemiologicamente - EPIDEMIAS
- Tanto tipo A como B

1918 "Spanish influenza" → 1957 "Asian influenza" → 1968 "Hong Kong influenza" → Next pandemic influenza

Vírus da Influenza

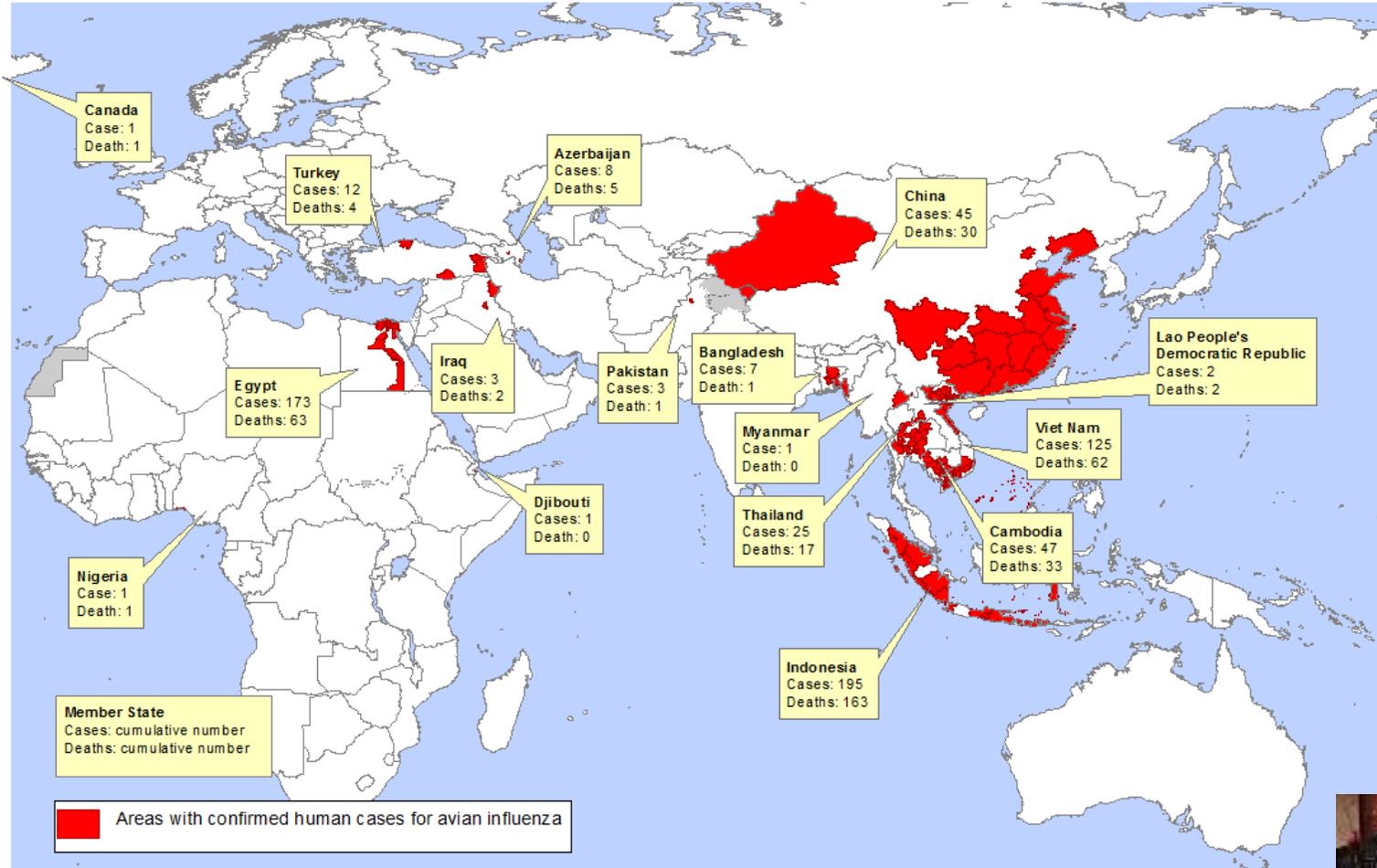


SHIFTS

1918	H1N1	"Gripe espanhola"	20-40 milhões de óbitos
1957	H2N2	"Flu Asiática"	1-2 milhões de óbitos
1968	H3N2	"Flu Hong Kong"	700.000 óbitos
1977	H1N1	Re-emergente	não pandêmico
2009	H1N1	Suína	letalidade 0,5%

Influenza Aviária (H5N1)

Areas with confirmed human cases for avian influenza A(H5N1) reported to WHO, 2003-2013*



Total de casos
(2003 – 2015)

846 (53% letalidade)

Novos
variantes

- H5N2
- H5N3
- H5N6
- H5N8

*All dates refer to onset of illness
Data as of 24 January 2014
Source: WHO/GIP

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Do not and dashed lines on maps represent approximate border lines for which there may not be full agreement.
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Fonte:

http://gamapserver.who.int/mapLibrary/Files/Maps/2003_2013_AvianInfluenza_Global_Map_24Jan14.png

Outros tipos circulantes

H9N2
H9N7



Vírus da Influenza

Transmissão

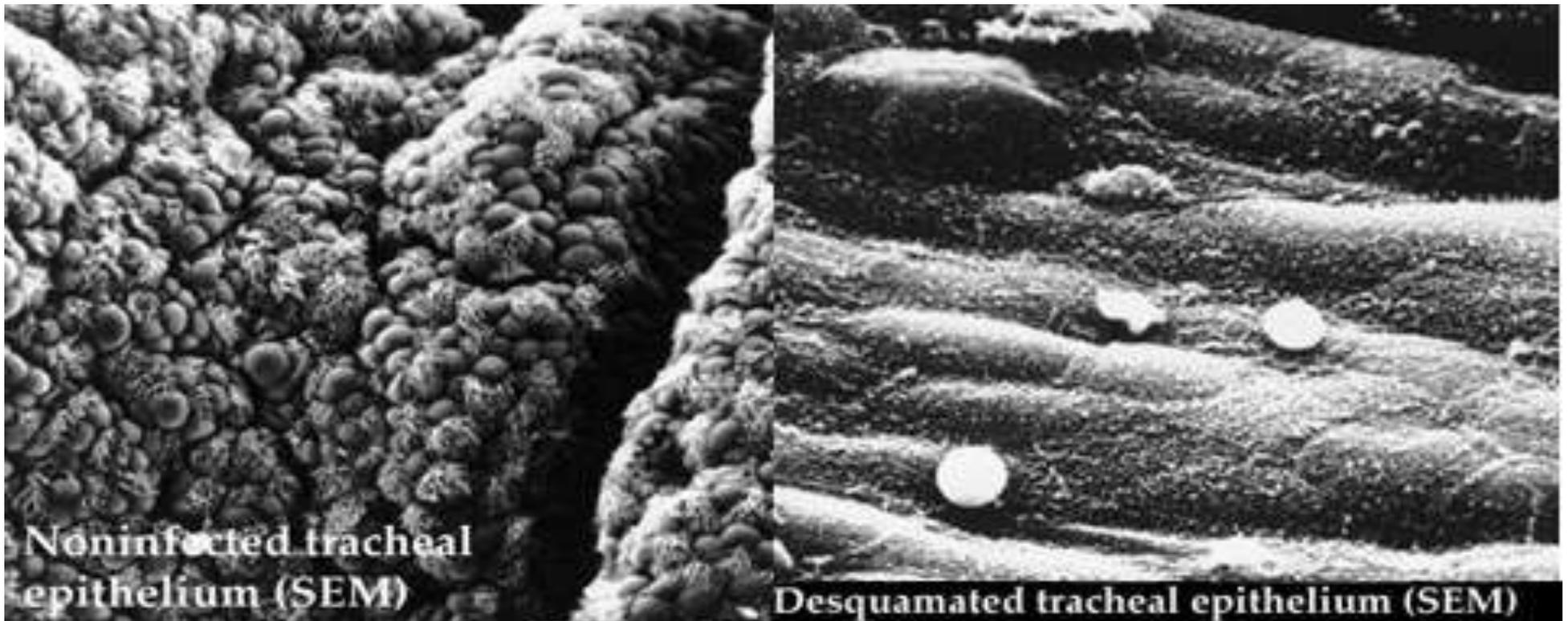


<http://www.youtube.com/watch?v=Rpj0emEGShQ>

Sintomas

Patogênia e

Manifestações clínicas



Tratamento

Sintomático

Drogas anti-virais

Bloqueadores da etapa de desnudamento viral

Amantidina
Rimantidina
Ribavirina

Drogas inibidoras de neuraminidase

Zanamivir
Oseltamivir (Tamiflu)



www.youtube.com/watch?v=kSLRmj0APZw

Profilaxia

- Vacinas
 - subunidades dos vírus tipos A e B
 - trivalentes contendo A/H3N2, A/H1N1 e B (variante Yamagata)

2016

Quadrivalente

A/H1N1

A/H3N2

B/Phuket/3073/2013 (variante Yamagata)

B/Brisbane/60/2008 (variante Victória)

Profilaxia

- Vacinas
 - subunidades dos vírus tipos A e B
 - trivalentes contendo A/H3N2, A/H1N1 e B (variante Yamagata)

2016

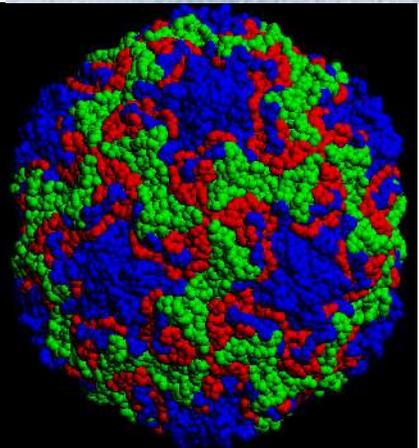
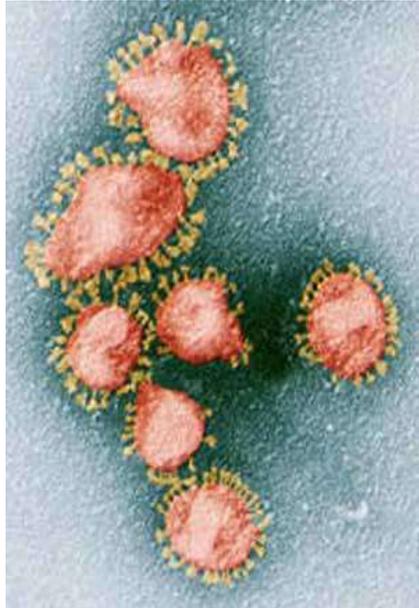
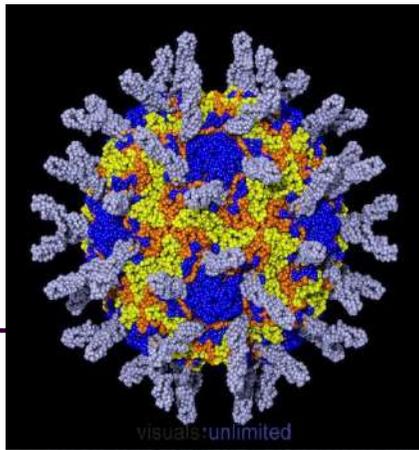
Quadrivalente

A/H1N1

A/H3N2

B/Phuket/3073/2013 (variante Yamagata)

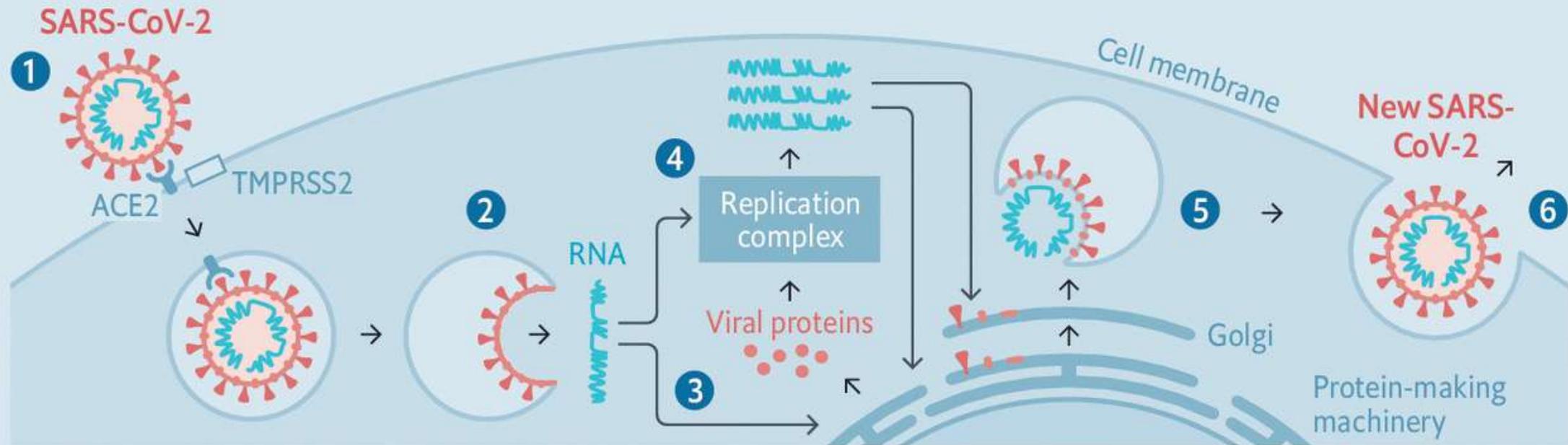
B/Brisbane/60/2008 (variante Victória)



SARS-CoV-2 COVID-19

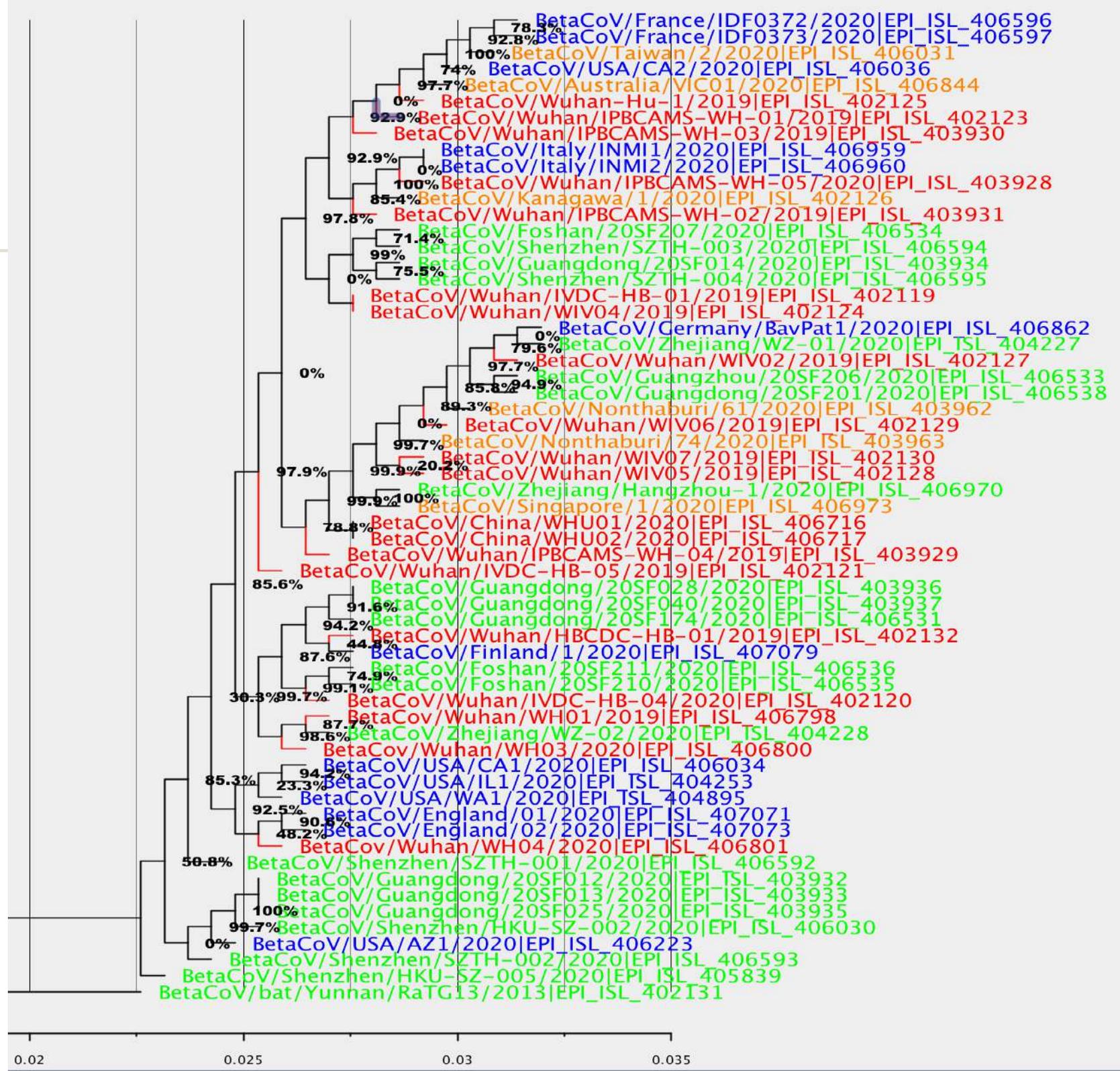
Hijack

How SARS-CoV-2 replicates itself in the cells of those infected



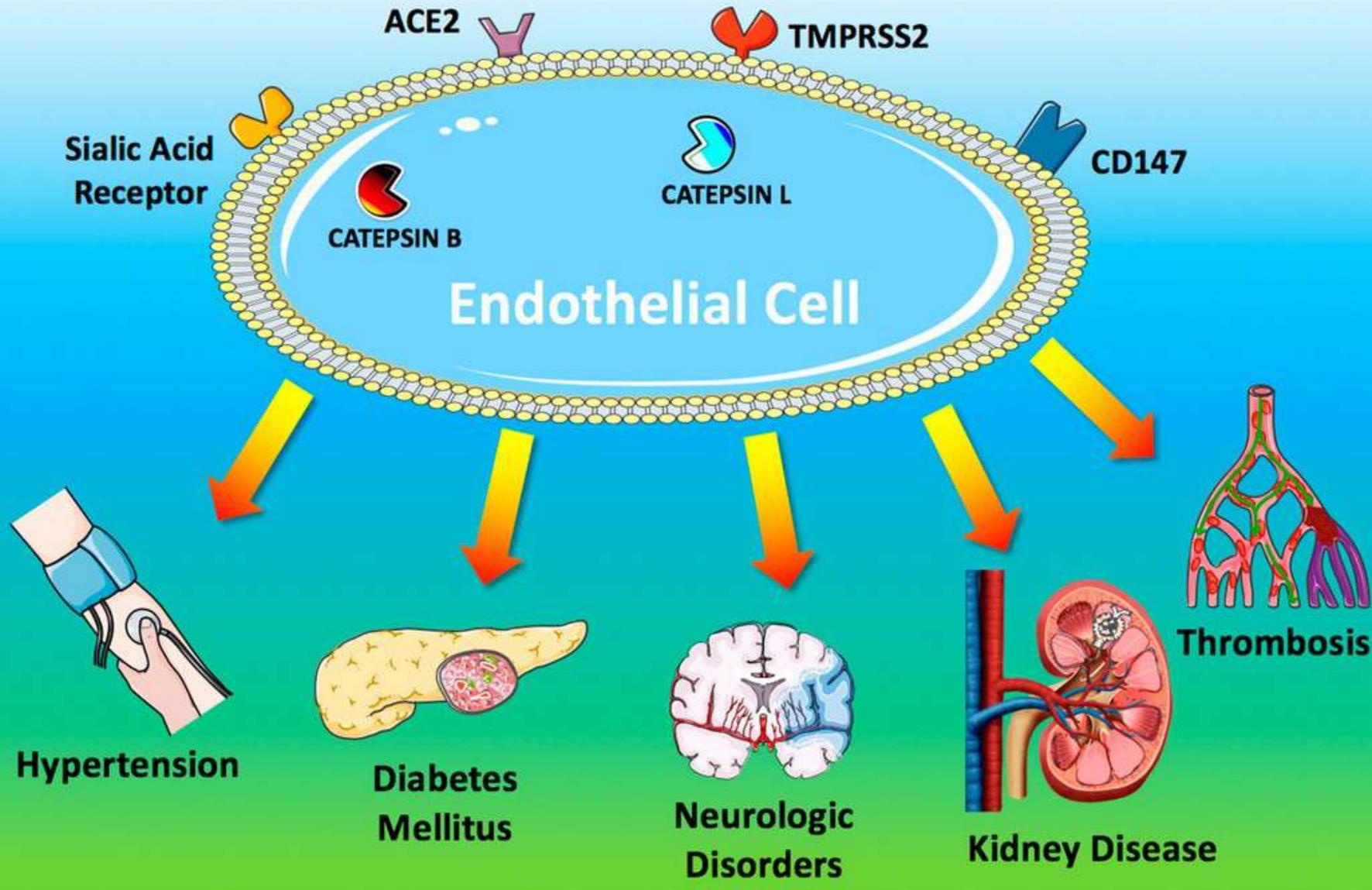
1 Spike protein on the virion binds to ACE2, a cell-surface protein. TMPRSS2, an enzyme, helps the virion enter **2** The virion releases its RNA **3** Some RNA is translated into proteins by the cell's machinery **4** Some of these proteins form a replication complex to make more RNA **5** Proteins and RNA are assembled into a new virion in the Golgi and **6** released

Sources: Song et al., *Viruses*, 2019; Jiang et al., *Emerging Microbes and Infections*, 2012; *The Economist*

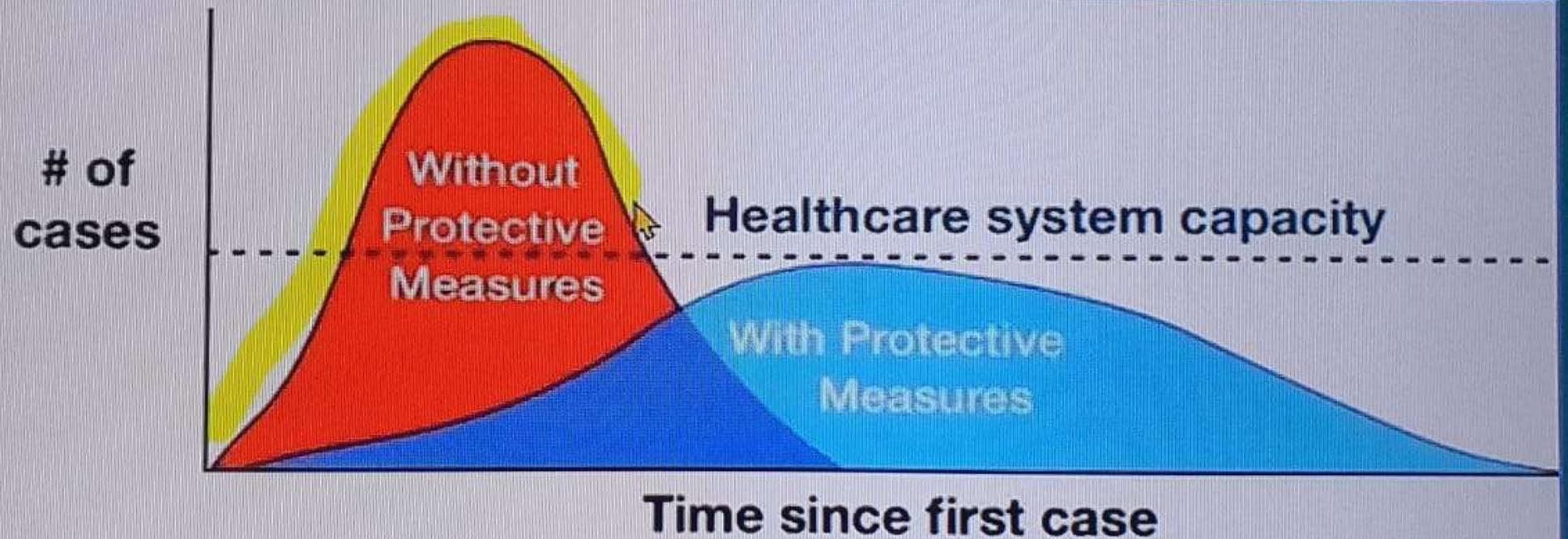


SARS-CoV-2 2019/20
Surto na China

SARS-CoV-2



Why Protective Measures (NPIs) Matter

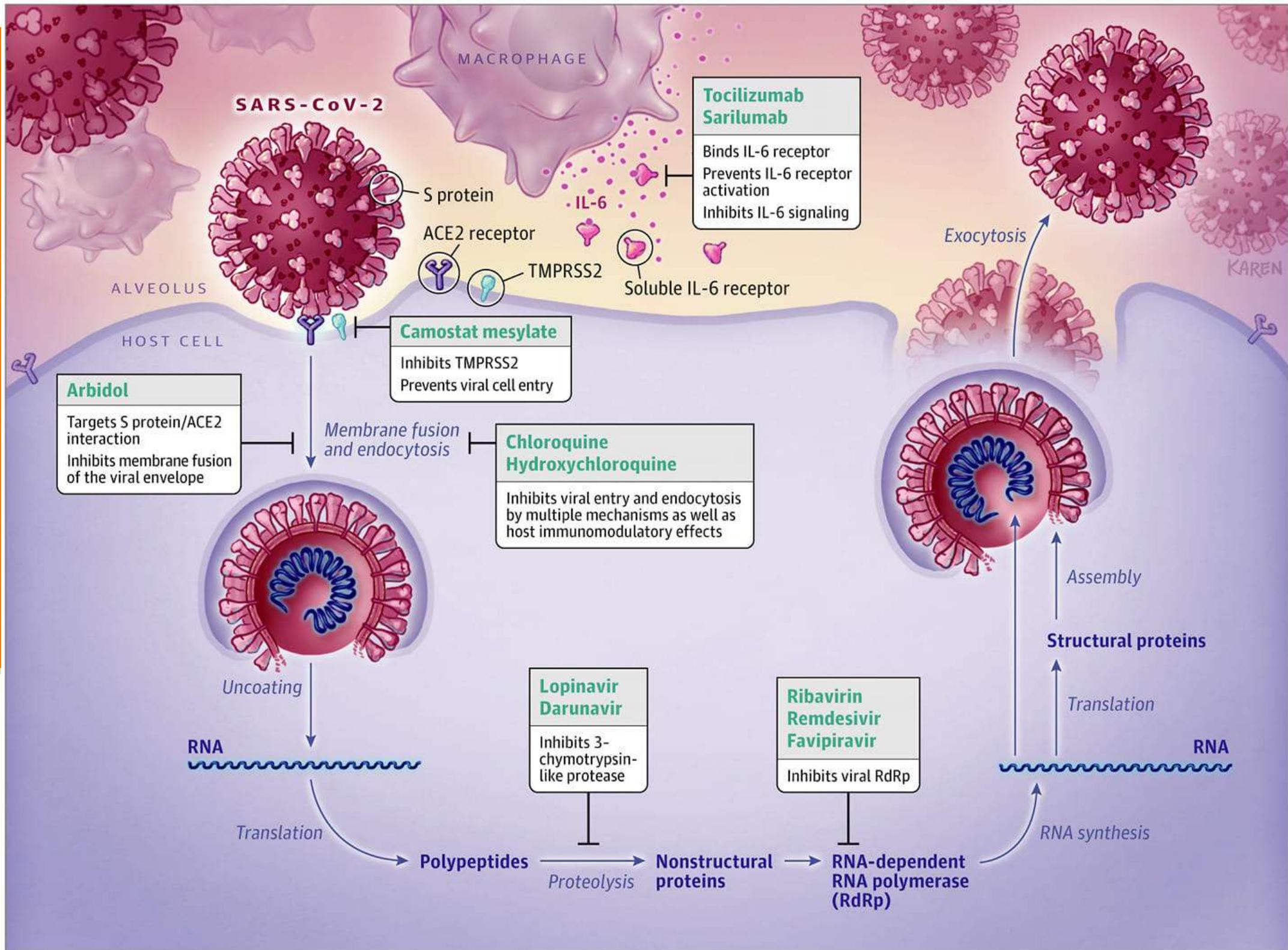


Adapted from CDC / The Economist

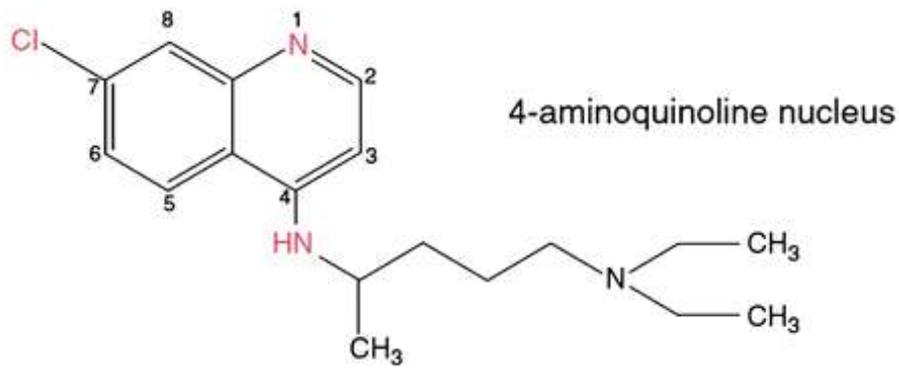
Covid-19 for states/countries with 101 to 300 confirmed cases as at 3/9/2020, 4:03:10 PM (AU Time)

Source: Novel Coronavirus (COVID-19) Cases, provided by JHU CSSE. Time variation are due to slow release of WHO stats and +1 day on US time. Analysis: @StandfieldKen
 Note: World Health Organization (WHO) official numbers typically understate the JHU CSSE dashboard numbers for the same time period.

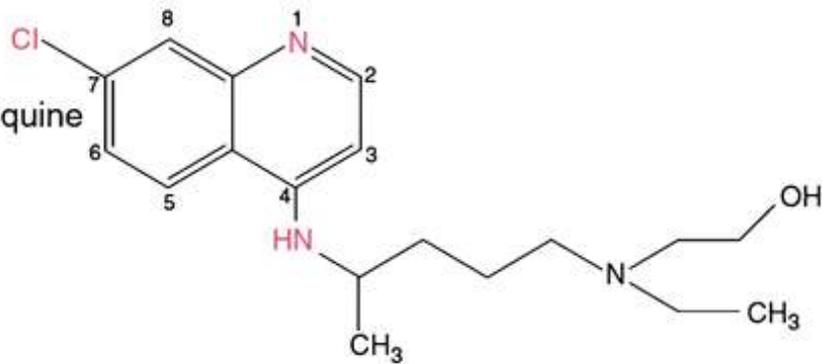




Chloroquine



Hydroxychloroquine



Quinacrine



Aminoquinilonas

number

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RECEPTOR-MEDIATED ENDOCYTOSIS AND THE CELLULAR UPTAKE OF TRANSPORT PROTEINS, HORMONES, ENZYMES, VIRUSES, AND TOXINS

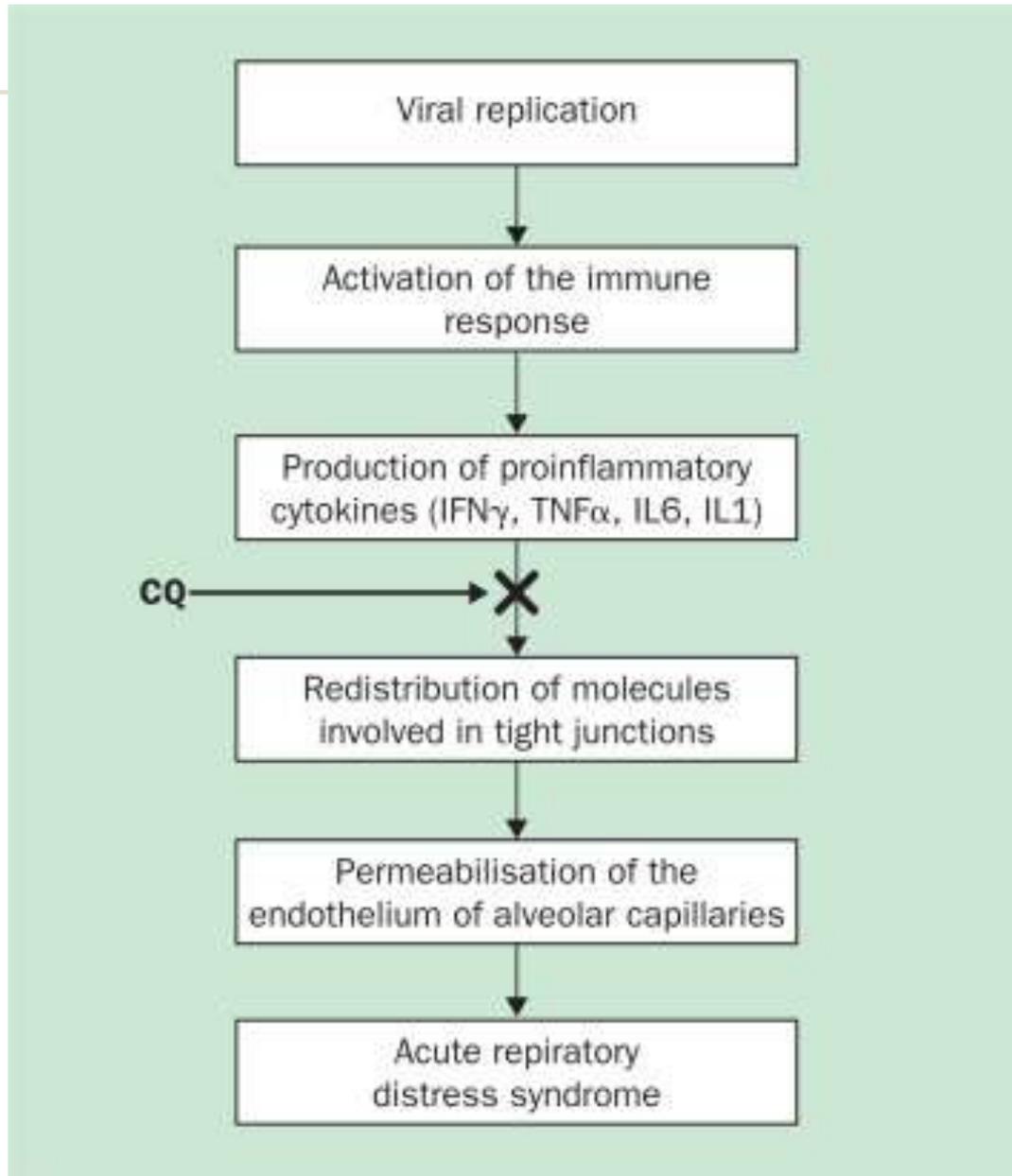
CHAPTER 25

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of sugar residues. The terminal sugar in many of the chains is sialic acid (*N*-acetylneuraminic acid). When the sialic acid is removed from these proteins, an underlying galactose residue is exposed. Liver cells contain a receptor that recognizes this galactose but only when it is exposed. In their native form, plasma glycoproteins (such as alpha₁ antitrypsin and ceruloplasmin) do not bind to this receptor and circulate for long periods in plasma. However, once the terminal sialic acid is removed and the galactose is exposed, the proteins bind to the liver receptor. Within minutes they are removed from the circulation and degraded in lysosomes. This receptor system is believed to play a role in the removal of circulating glycoproteins from plasma.

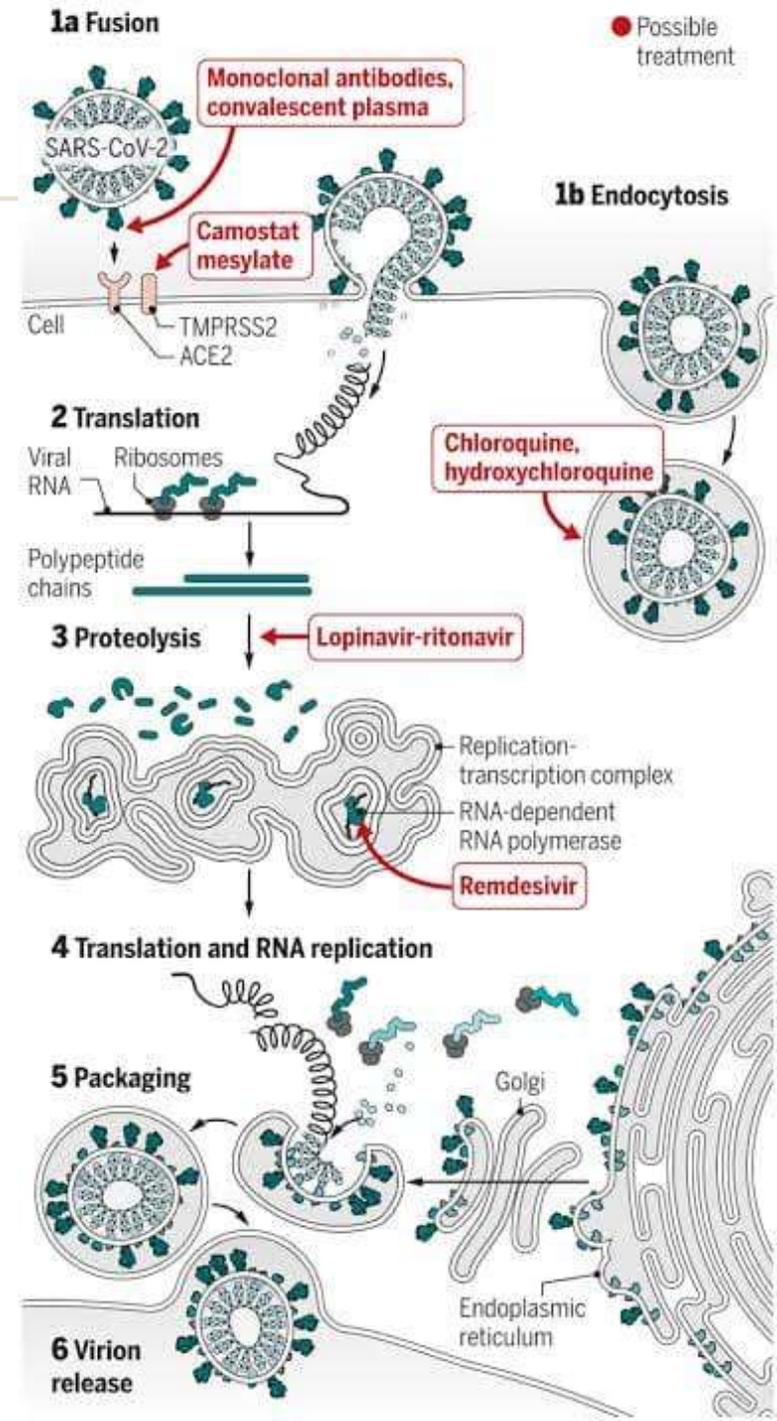
Viruses Certain viruses that are surrounded by a lipid envelope bind to the plasma membrane of target cells by attaching to specific proteins on the cell surface. These viruses are then internalized by receptor-mediated endocytosis and delivered to lysosomes. At acid pH the membrane surrounding the virus fuses with the membrane of the lysosome, allowing the nucleic acid of the virus to cross the lysosomal membrane and enter the cytoplasm where the virus replicates. Infection of tissue culture cells by these viruses (such as Semliki Forest virus, vesicular stomatitis virus, and certain strains of influenza virus) can be prevented by chloroquine, an agent that blocks the function of lysosomes. Chloroquine is a weak base that diffuses into lysosomes and becomes protonated, raising the pH and the ionic strength of the lysosome. When the pH rises, the lysosomal enzymes fail to function. Viruses that require acid pH to fuse with cell membranes can no longer do so in the presence of chloroquine, and the cells are protected from infection. Amantadine, which is used clinically in the prevention and symptomatic treatment of infections caused by influenza A virus, prevents viral infection in vitro by a mechanism simi-

Tratamento Antiviral

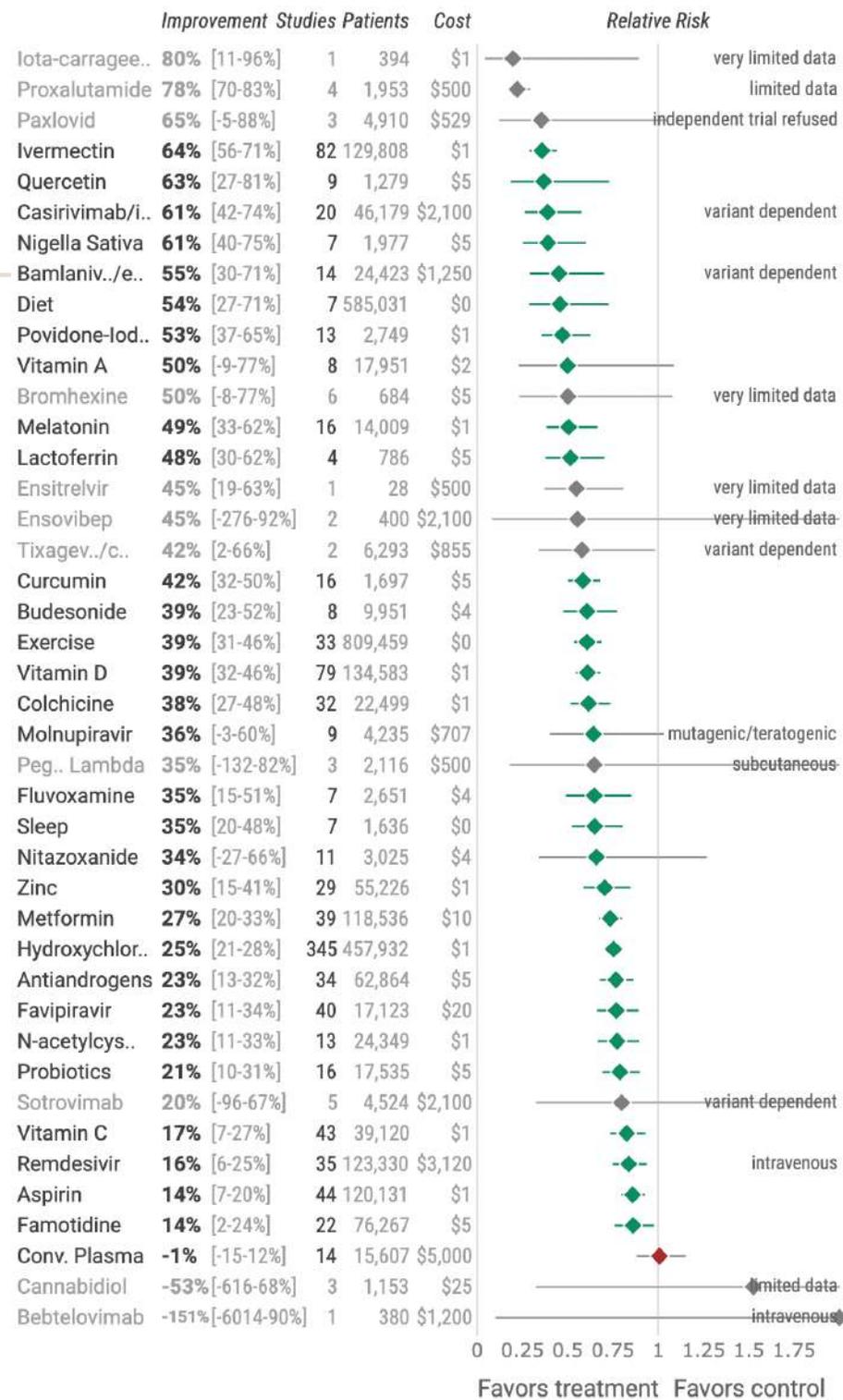


Lines of attack

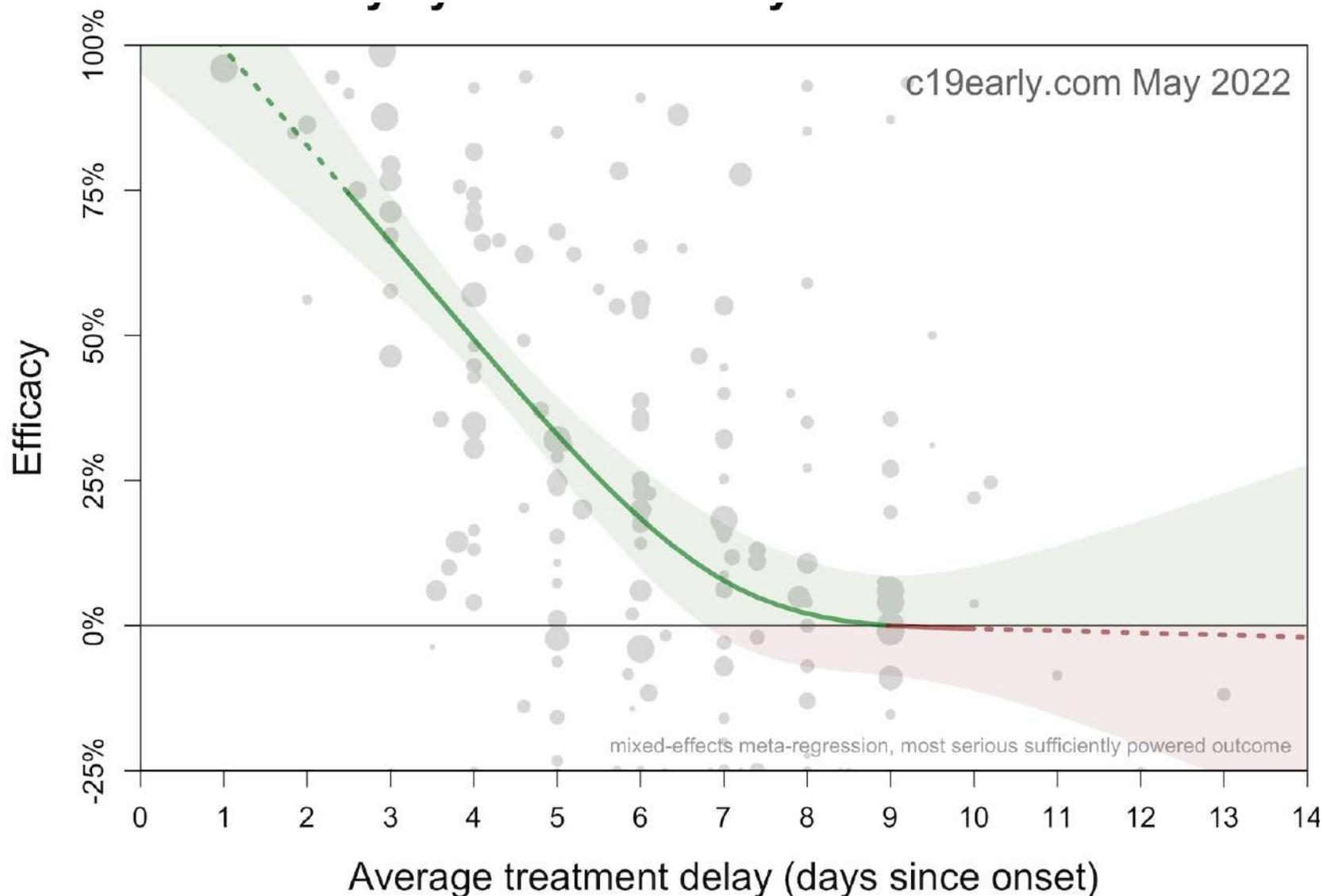
Experimental treatment strategies attempt to interfere with different steps (numbered) in the coronavirus replication cycle.



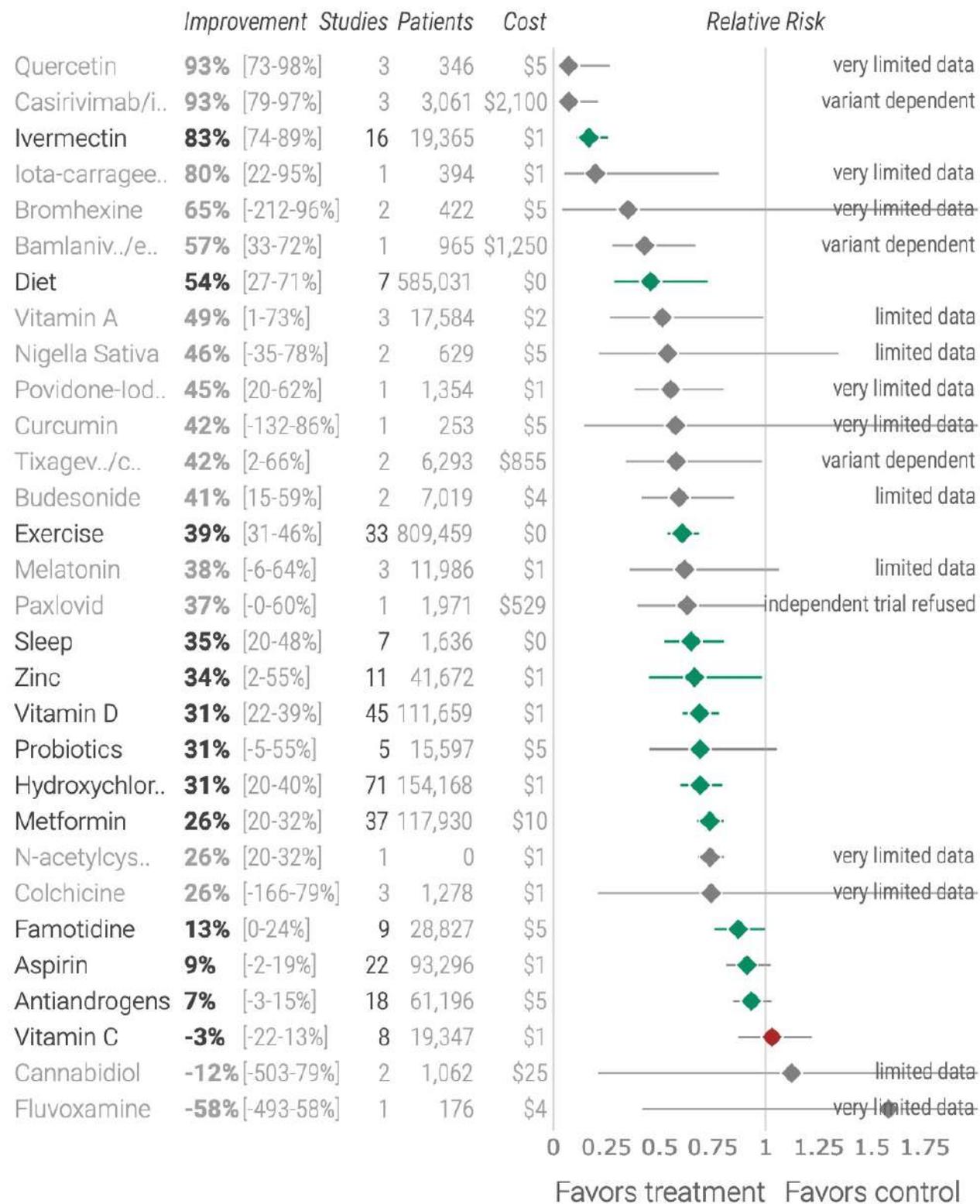
Todos os estudos (efeitos conjuntos, todas as etapas) c19early.com 23 de maio de 2022



Análise de 42 tratamentos precoces COVID, aprovações em 72 países, banco de dados de 834 tratamentos.



Profilaxia



-
- Muito obrigado pela atenção!
 - Quaisquer perguntas contatar o Paolo: *pzanotto@usp.br*