Temas em discussão

"O perigo da dengue em Portugal"
Carla Sousa

"A vacinação"
Jaime Nina

"A consulta do viajante"
Cláudia Conceição

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H. Egas Moniz
(CHLO)
(*aposentado*)

Presidente
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Ordem dos Médicos

Consultor
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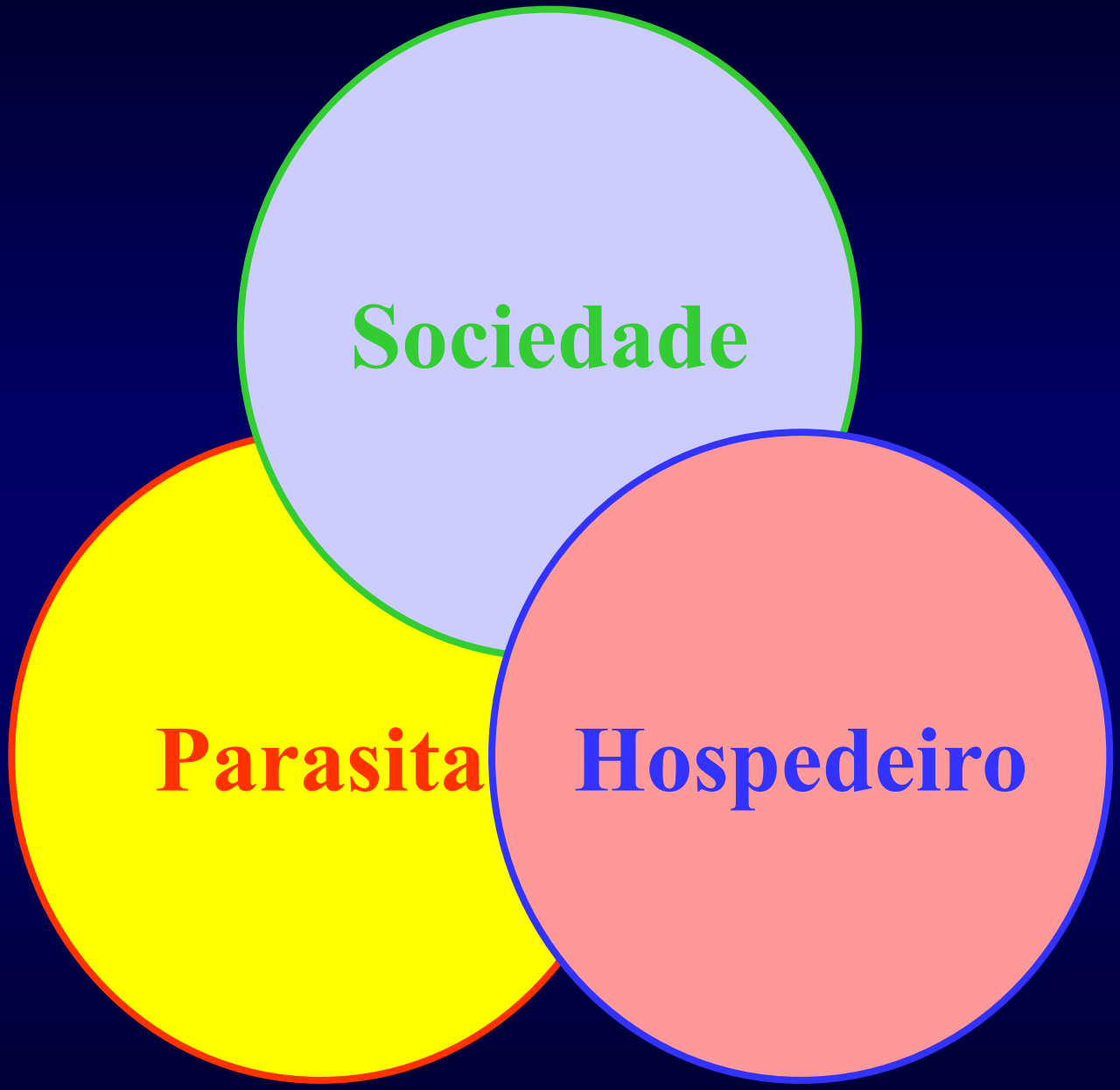
Arboviroses

Dengue

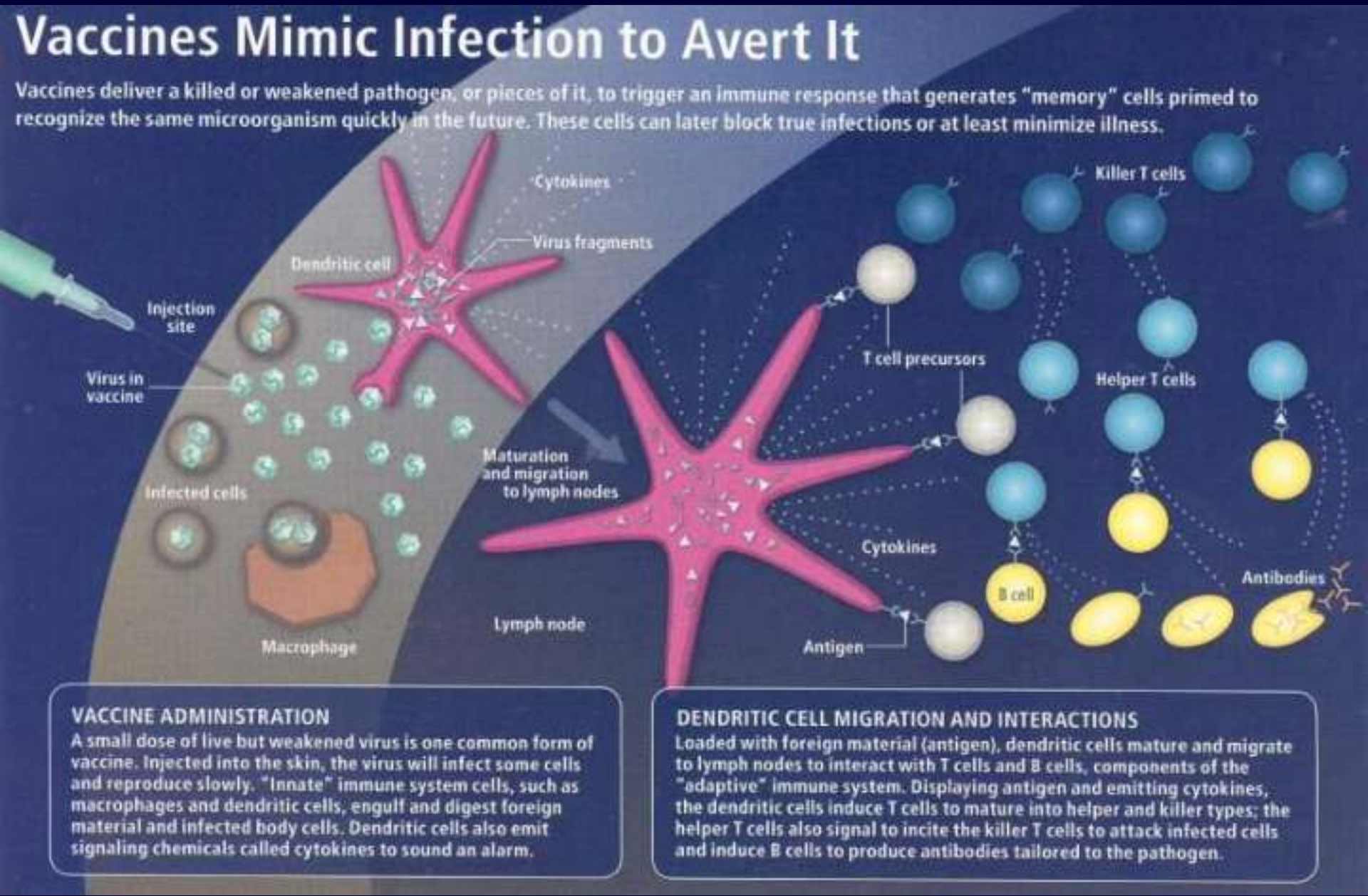
Jaime Nina


Arboviroses
Dengue
A Vacinação
Jaime Nina



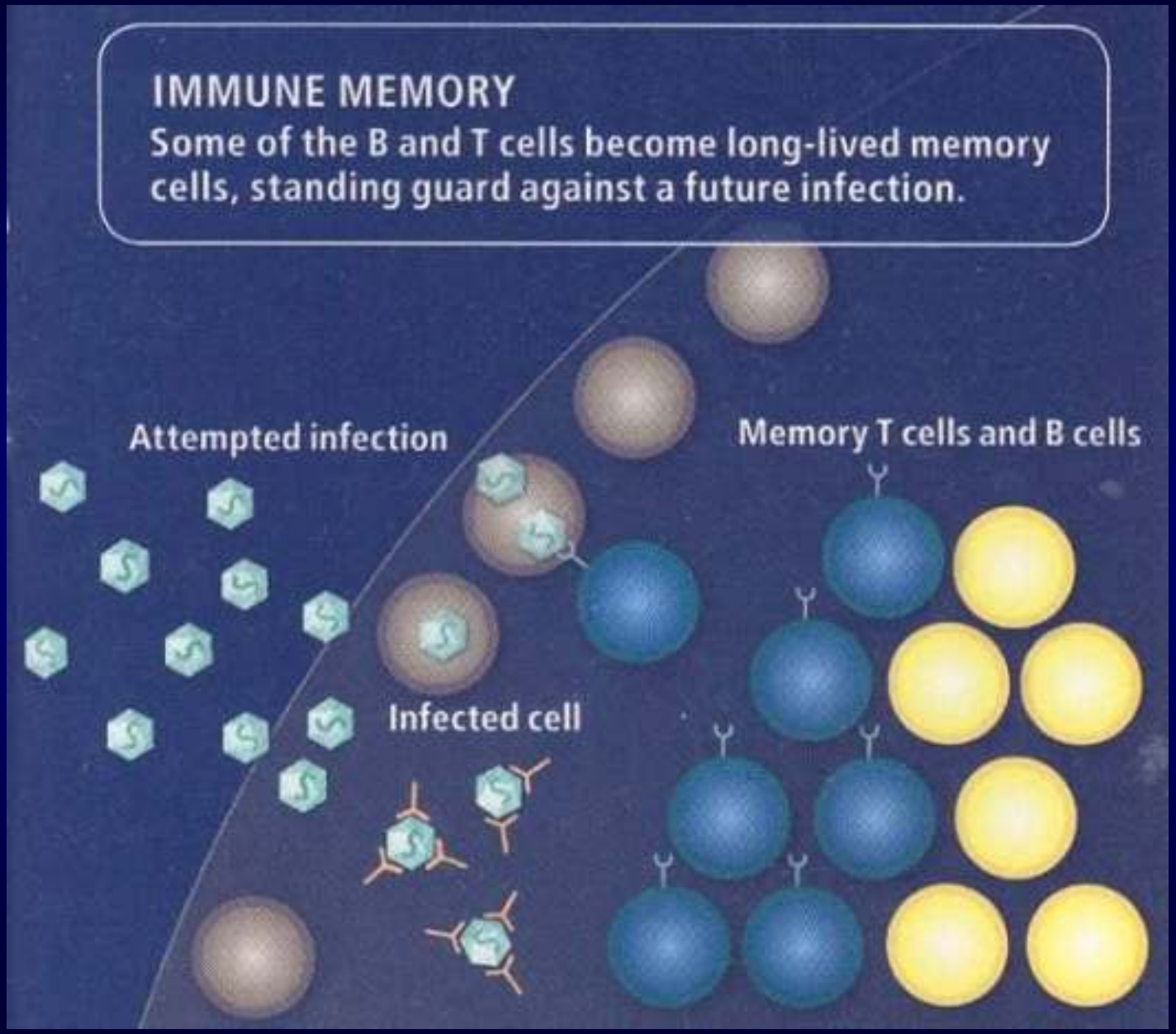
J Nina. 2010.

Vacinas - Básico 1



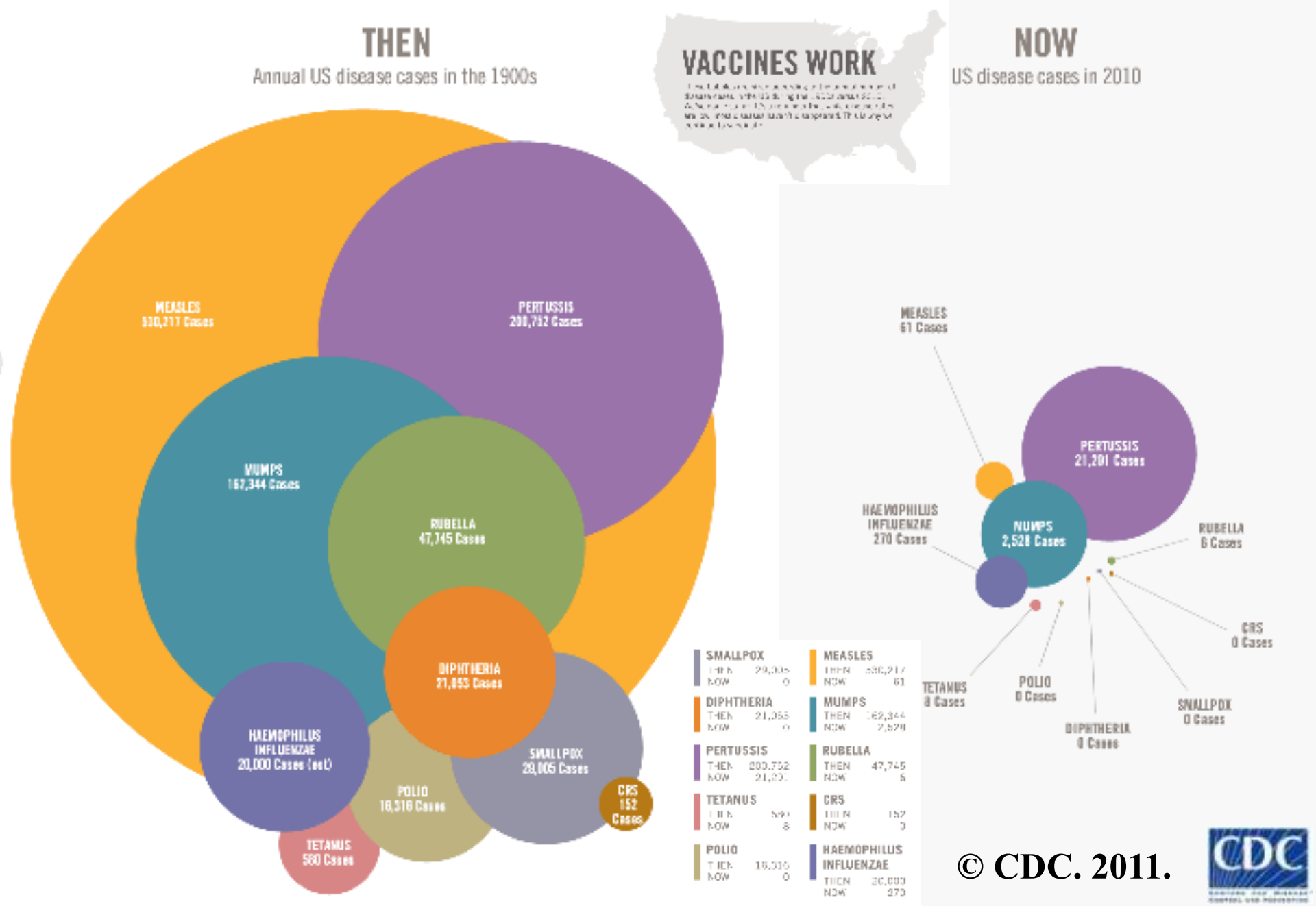
from: N Garçon & M Goldman. 2009. *in* Sci Am 301(4):52-59.

Vacinas - Básico 2

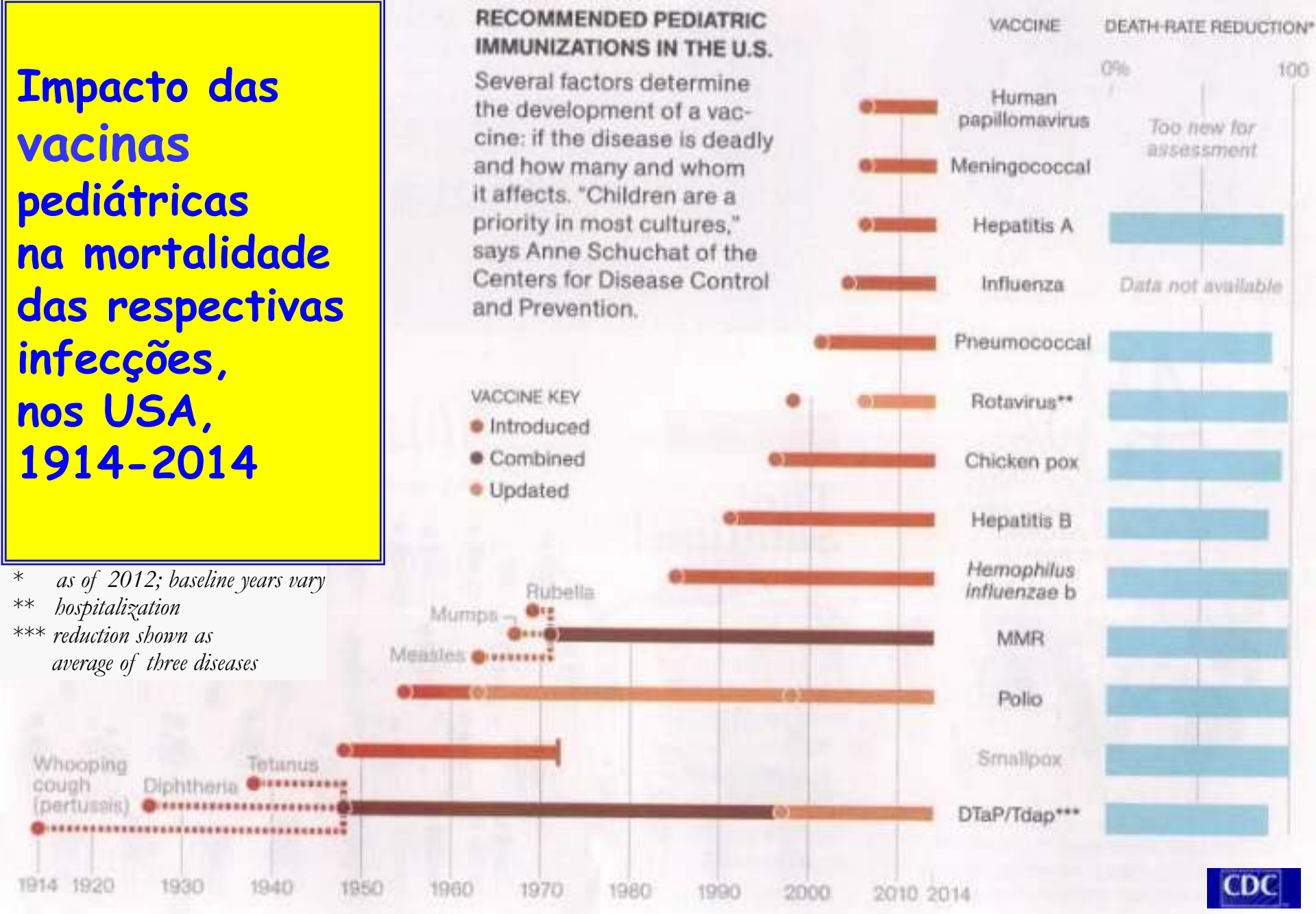


from: N Garçon & M Goldman. 2009. *in* Sci Am 301(4):52-59.

Vaccines work !



Impacto das vacinas pediátricas na mortalidade das respectivas infecções, nos USA, 1914-2014



* *as of 2012; baseline years vary*
** *hospitalization*
*** *reduction shown as average of three diseases*

***source*: CDC**
***graphic*: L Parker / NGM**

Vaccines for Children

Protecting America's children every day

The Vaccines for Children (VFC) program helps ensure that all children have a better chance of getting their recommended vaccines. VFC has helped prevent disease and save lives.

CDC estimates that vaccination of children born between 1994 and 2021 will:

prevent **472 million** illnesses
(29.8 million hospitalizations)

more than the current population of the entire U.S.A.

help avoid **1,052,000** deaths

greater than the population of Seattle, WA

save nearly **$2.2 trillion** in total societal costs
(that includes $479 billion in direct costs)

more than $5,000 for each American

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

www.cdc.gov/vaccines/vfcprogram/

Impacto do PNV (Programa Nacional de Vacinação) em Portugal

Doença	Década 1956-1965 Casos	†	Década 1991-2000 casos	†
Difteria	19 100	1 475	3[1]	1[1]
Polio	2 723	316	0	0
Tétano	3 923	2 625	259	113
Tosse convulsa	14 429	873	204	3
Σ	40 175	5 271	466	117

[1] – *importados*

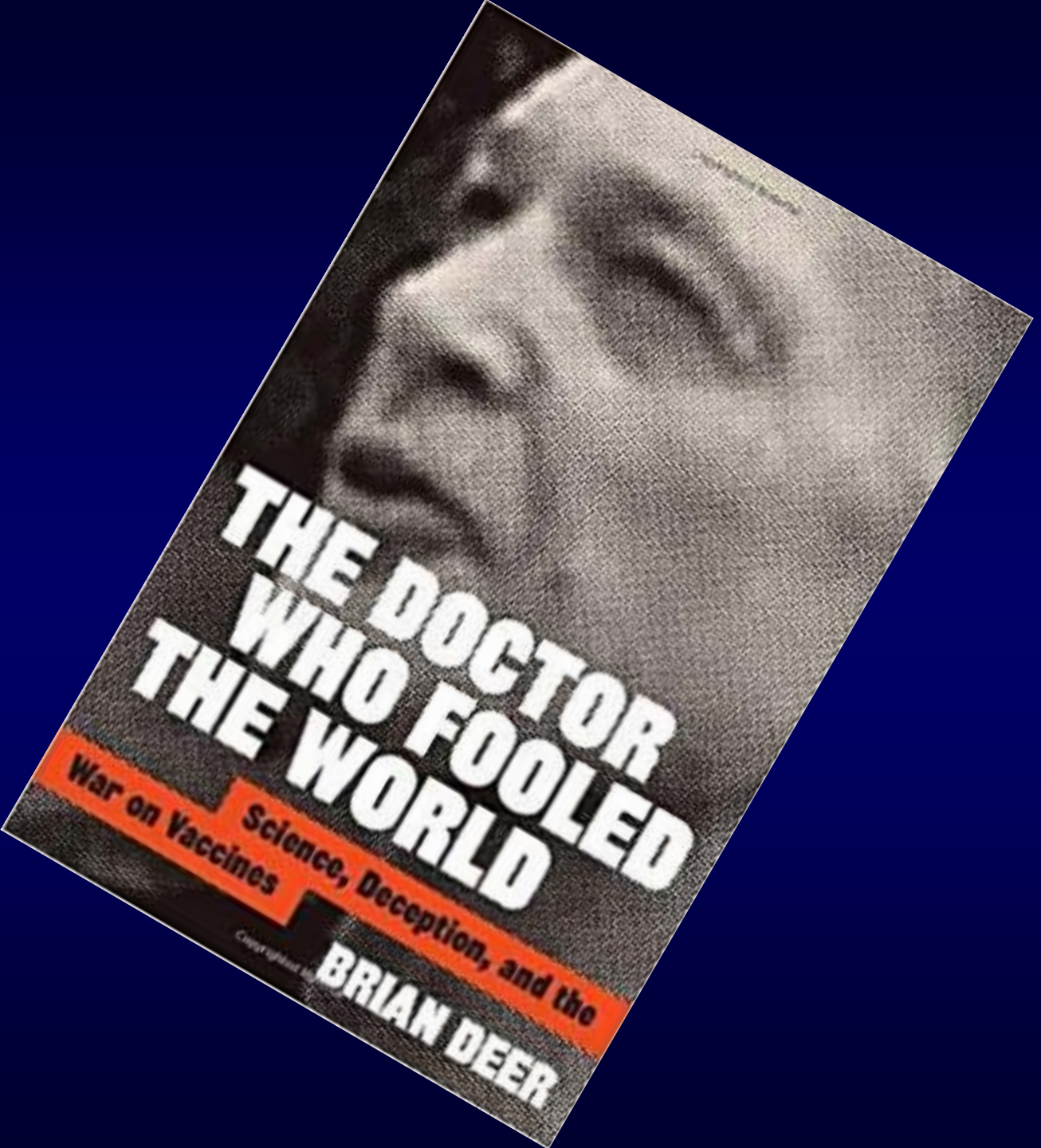
adaptado de - P Valente. 2010. *in* Notíc Méd 11.02.2010.


medo às vacinas ...
Deesillustration.com

Vacinas - boatos & insinuações

One "environmental" factor that has been suggested as contributing to the increase in autism spectrum disorders (ASDs) prevalence is vaccination, particularly vaccines for measles, mumps, and rubella (MMR). This connection has been studied extensively in epidemiological studies around the world. A meta-analysis that integrated the results of 5 cohort studies and 5 case-control studies found no evidence for an association between ASDs and vaccination or any of the components of vaccines suggested to have a role in ASD development.

from: Jeremy Berg. 2017. *in* Science 355(6326):669 - Editorial.

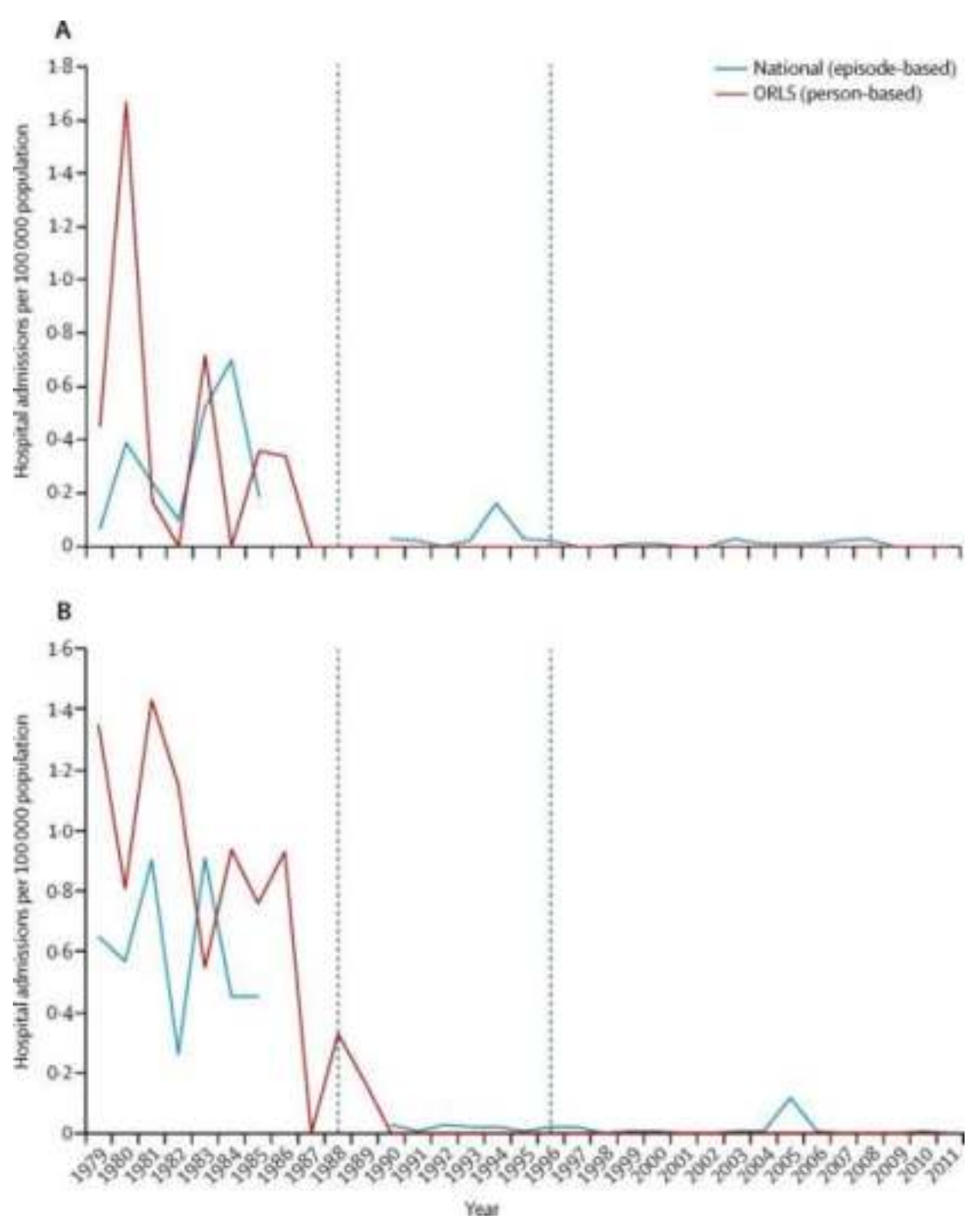


Etiologia do Autismo, vacina do Sarampo, corrupção e *fake-news* científicas

J Nina. 2020.

O médico é um céptico profissional

J Nina. 2024.
***adaptado de* S Novella. 2018**
& ARR Feragen. 2017.



30-year trends in admission rates for encephalitis in children in England and the impact of measles-mumps-rubella vaccination

Hospital admission rates for (A) measles and (B) mumps encephalitis

Rates are for people aged 0–19 years in England. Dashed lines indicate points of introduction of the single-dose (1988) and two-dose (1996) MMR vaccination schedules. MMR=measles-mumps-rubella.

THE LANCET Infectious Diseases

***from*: MA Iro *et al.* 2017. *in* Lancet Inf Dis 17(4):422-430.**


YOU REPRESENT A PARENT'S RIGHT TO CHOOSE, RESIST GOVERNMENT MANDATES AND LIVE FREE!
HOW DOES THAT MAKE YOU FEEL, SON?
SICK.
caglecartoons.com

Voltando às vacinas

JOHNS HOPKINS MEDICINE

Vacinas

Tipos Principais de Vacinas

- **ATTENUATED:** Live but weakened whole virus or bacterium. Minimal reproduction extends immune cells' exposure to antigen without causing disease.

- **INACTIVATED:** Whole but "killed" and unable to reproduce or to cause disease.

- **SUBUNIT:** Fragments of the pathogen, such as genetic material or external proteins, provide antigen for immune cells to recognize.

from: N Garçon & M Goldman. 2009. *in* Sci Am 301(4):52-59.

Vacinas

Tipos Principais de Vacinas

- **ATTENUATED:** Live but weakened whole virus or bacterium. Minimal reproduction extends immune cells' exposure to antigen without causing disease.

FA
Sarampo
Varíola
…

- **INACTIVATED:** Whole but "killed" and unable to reproduce or to cause disease.

TAB
Tosse convulsa
(*clássica*)
…

- **SUBUNIT:** Fragments of the pathogen, such as genetic material or external proteins, provide antigen for immune cells to recognize.

HBV
CoVID-19
(*Pfizer, Moderna*)
…

***from*: N Garçon & M Goldman. 2009. *in* Sci Am 301(4):52-59.**

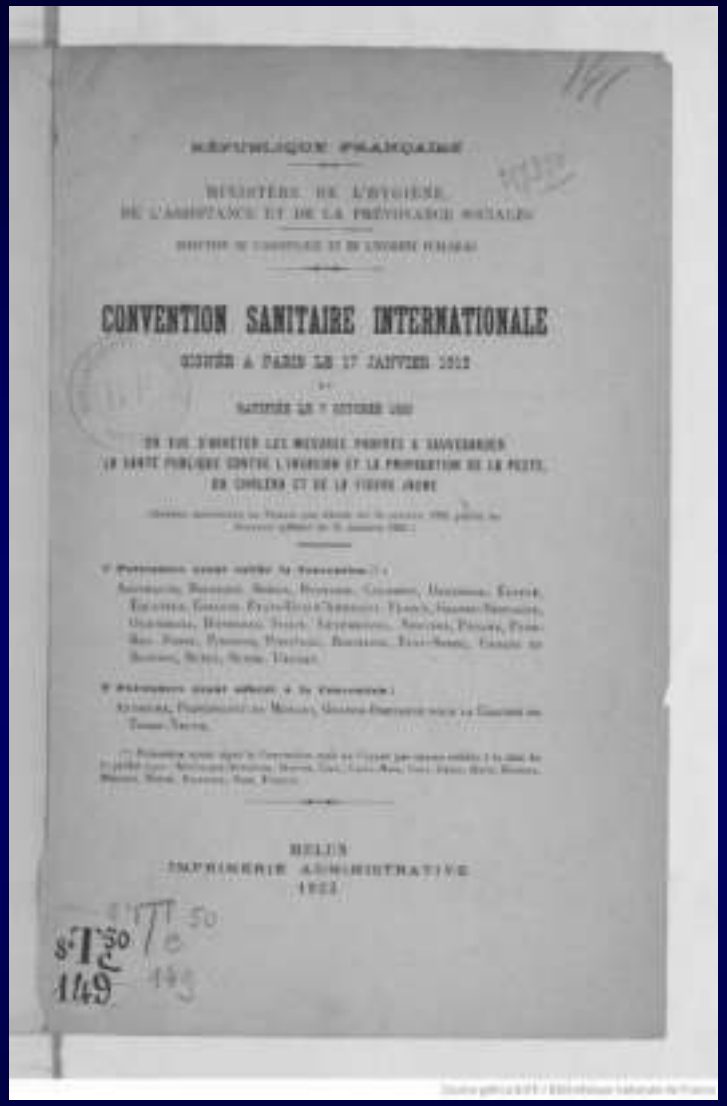
As Vacinas não são "egoístas"

Para além da protecção individual, muitas vacinas oferecem "*herd immunity*", sendo assim importantes armas na protecção da saúde de populações

"A vulnerabilidade às Doenças Infecciosas e Tropicais é universal, dado que as fronteiras geográficas não protegem da invasão dos diversos agentes e vectores"

Medicina Tropical em Portugal: Presente e Futuro
Workshop dos Médicos de Medicina Tropical
Lisboa, Ordem dos Médicos, 23 Abril 2012

Kamal Mansinho
Professor IHMT, Director SDIT



RÉPUBLIQUE FRANÇAISE

MINISTÈRE DE L'HYGIÈNE,
DE L'ASSISTANCE ET DE LA PRÉVOYANCE SOCIALES

CONVENTION SANITAIRE INTERNATIONALE

SIGNÉE A PARIS LE 17 JANVIER 1912

RATIFIÉE LE 7 OCTOBRE 1920

EN VUE D'ARRÊTER LES MESURES PROPRES À SAUVEGARDER
LA SANTÉ PUBLIQUE CONTRE L'INVASION ET LA PROPAGATION DE LA PESTE,
DU CHOLÉRA ET DE LA FIÈVRE JAUNE

PARIS
IMPRIMERIE ADMINISTRATIVE
1921

LN > CSI . 1920

ONU > WHO . 1951

J Nina. 2024.

O caso da varíola

Varíola

Criança indiana com varíola major grave

Exantema da varíola major, num adulto, com distribuição centrífuga das lesões

Smallpox

Epidemic transmission and the Spanish conquest of the Americas.

Vectors trace the diffusion of the "smallpox epidemic" of 1518-1528.

The geographical extents of the Aztec and Inca civilizations at about the time of European contact are indicated for reference.

OXFORD

from: M Smallman-Raynor & AD Cliff. 2012. Oxford, Oxford University Press

Varíola

Vacina:

A vacina da varíola foi a arma que permitiu tornar esta doença na única infecção até hoje erradicada de todo o Mundo

J Nina. 2000, 2010, 2024.

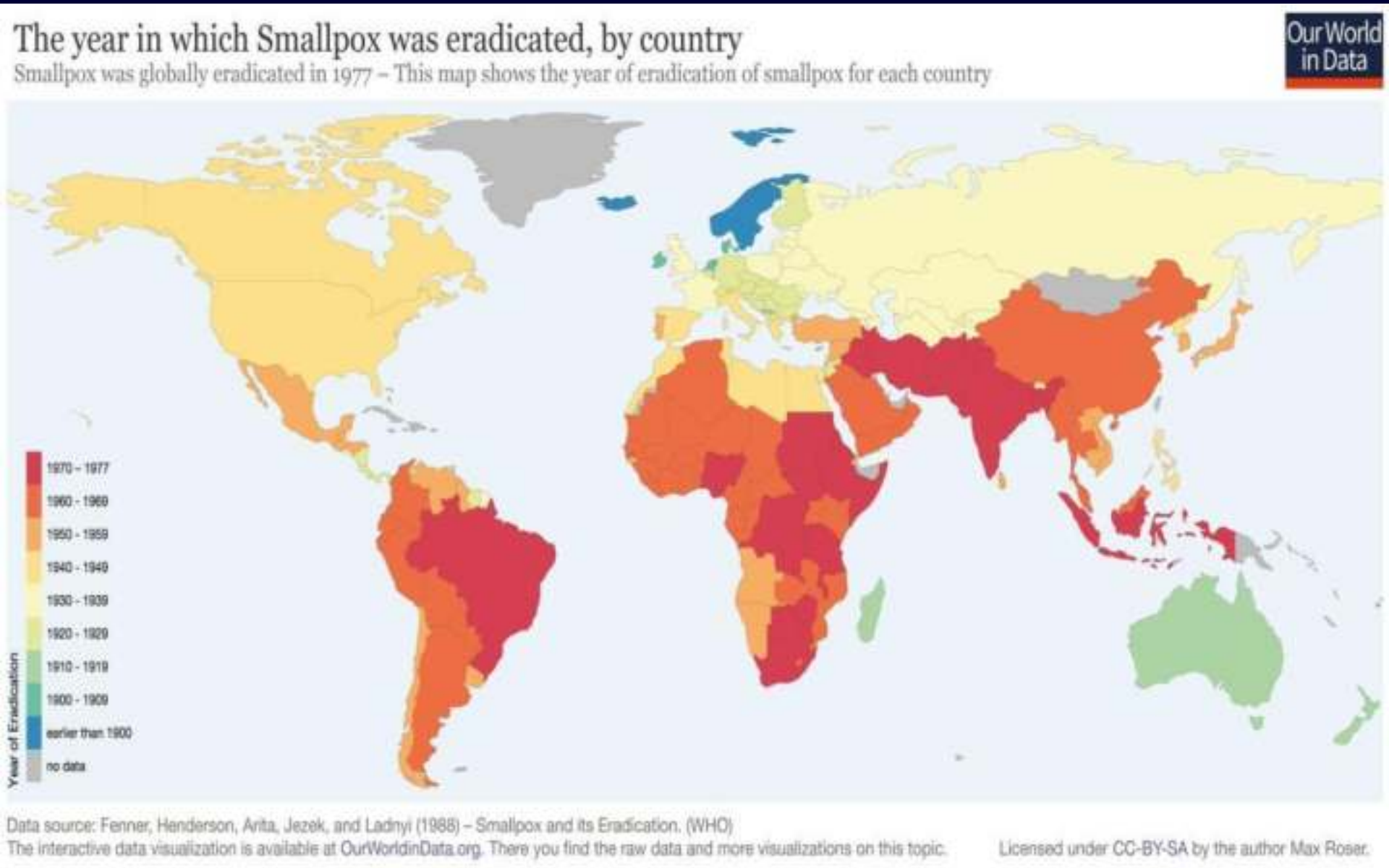
Smallpox vaccination in Britain

Louis Léopold Boilly (1761-1845)

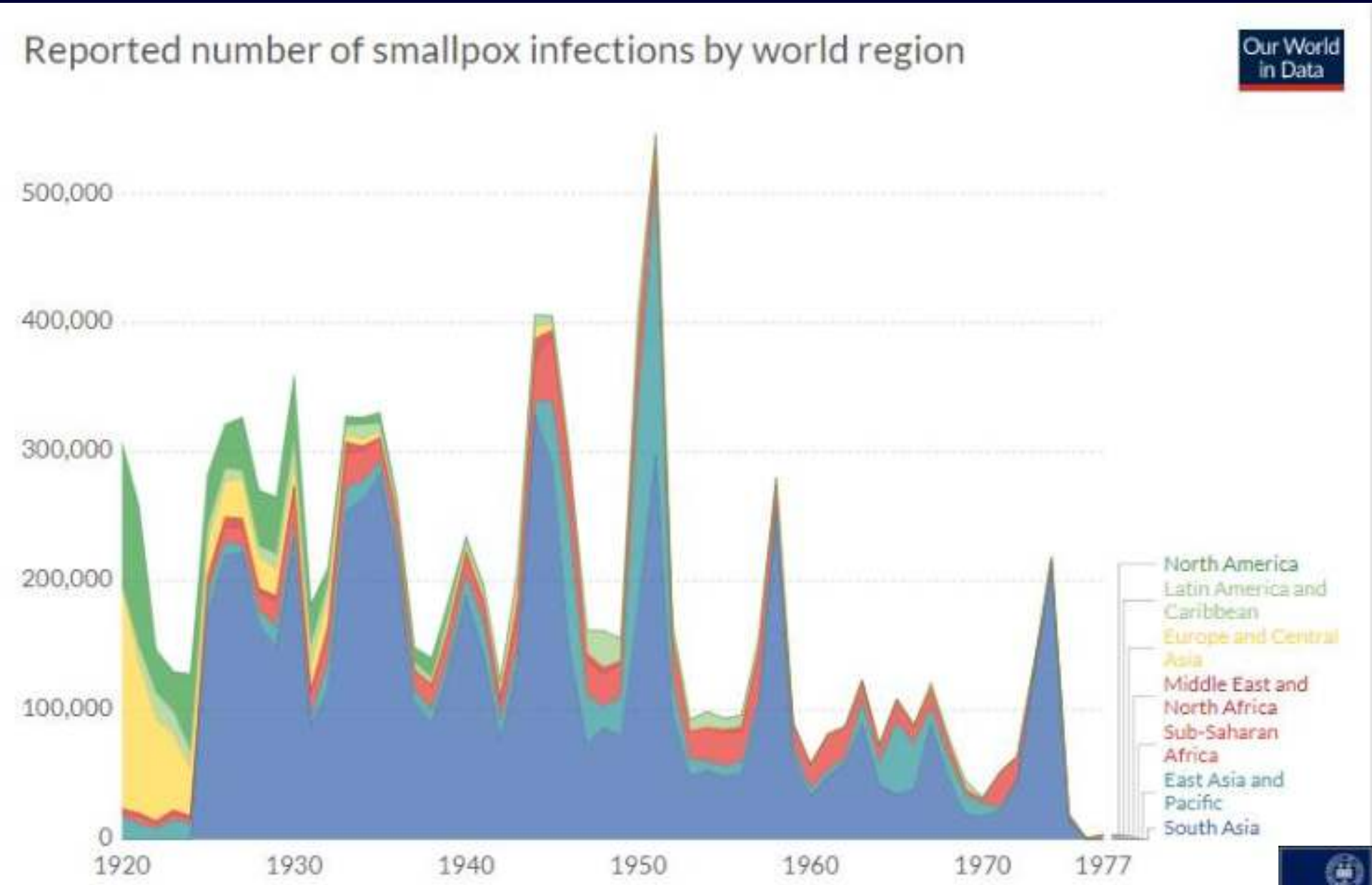
Print (color engraving) published June 12, 1802,
authorship by James Gillray (1756–1815)

In this cartoon, satirist Gillray caricatured a scene at the Smallpox & Inoculation Hospital at St. Pancras, showing cowpox vaccine being administered to frightened young women, and cows emerging from different parts of people's bodies. The cartoon was inspired by the controversy over inoculating against the dreaded disease, smallpox.

Smallpox Eradication progress



Smallpox Eradication progress



from: Sophie Ochmann & Max Roser. 2019.

WE, THE MEMBERS OF THE GLOBAL COMMISSION FOR THE CERTIFICATION OF SMALLPOX ERADICATION, CERTIFY THAT SMALLPOX HAS BEEN ERADICATED FROM THE WORLD

NOUS, MEMBRES DE LA COMMISSION MONDIALE POUR LA CERTIFICATION DE L'ERADICATION DE LA VARIOLE, CERTIFIONS QUE L'ERADICATION DE LA VARIOLE A ETE REALISEE DANS LE MONDE ENTIER

我们，全球扑灭天花证实委员会委员，
证实扑灭天花已经在全世界实现。

NOSOTROS, MIEMBROS DE LA COMISION MUNDIAL PARA LA CERTIFICACION DE LA ERRADICACION DE LA VIRUELA, CERTIFICAMOS QUE LA VIRUELA HA SIDO ERRADICADA EN TODO EL MUNDO

Parchment signet at Geneva on December 9, 1979, by the members of the Global Comission for Certification of Smallpox Eradication

World Health Organization

photo reproduced in Nathan Wolfe. 2011. "The Viral Storm".

Varíola

Relatório Final da Erradicação Mundial da Varíola

OMS
1980

Voltando às vacinas

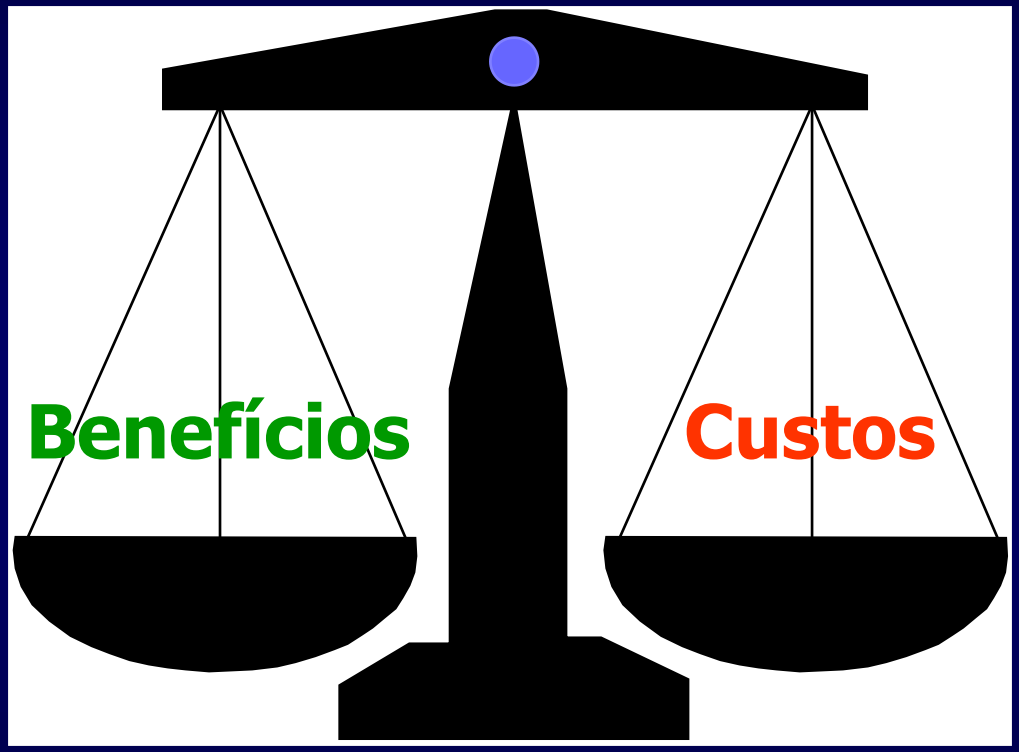
JOHNS HOPKINS MEDICINE

Vacinas

Vacinar: Contra quê?
Com quê?
Quando?
A quem?
Em que sequência?
Como associar?

J Nina. 2010.

Na decisão de vacinar ponderar...



J Nina. 2010.

Vacinas

Ponderar:

Zonas a visitar
Duração da estadia
Objectivo da estadia
Doenças co-existentes
Experiência anterior
Duração da imunidade
Contra-indicações vacina
Efeitos secundários
Reacções locais à vacina
...

Profissão
Idade
Sexo
Gravidez
Aleitamento
Estilo de vida
Alergias
Custo da vacina
Comodidade
...

J Nina. 2010.

Around the world

Kauto County, South Sudan

Vaccine tragedy in South Sudan

Disaster struck in May 2017 during an emergency campaign to stem a surging measles outbreak in troubled South Sudan: Fifteen children were killed and 32 sickened by shots of a contaminated vaccine. The children, who received the shots in remote Kauto county, died of sepsis and toxicity, according to a just-released investigation by the country's ministry of health, along with the World Health Organization and UNICEF. The vaccinators, who were untrained and unqualified to administer the vaccine, incorrectly used the same syringe to reconstitute multiple vials of the vaccine over 4 days, instead of discarding it after a single use, the investigation found. The measles vaccine is safe and effective, but it must be handled carefully: kept cold, reconstituted with the right liquid, and, once mixed, discarded after 6 hours. The tragedy is not the worst to affect the young nation, which has been shattered by war, famine, and now a cholera outbreak. But it is especially distressing because it was avoidable. Still, experts note, far more children will die if they are not protected from the highly contagious measles virus.

J Nina. 2017. *adapted from*: New at a glance. 2017. *in* Science 356(6342):990.

Há riscos, mas com cuidados apropriados podem ser minorados e ultrapassados

mas a vacina do dengue ?

Dengue
Etiologia

Flaviviridae

RNA cadeia simples

Envolvidos por membrana

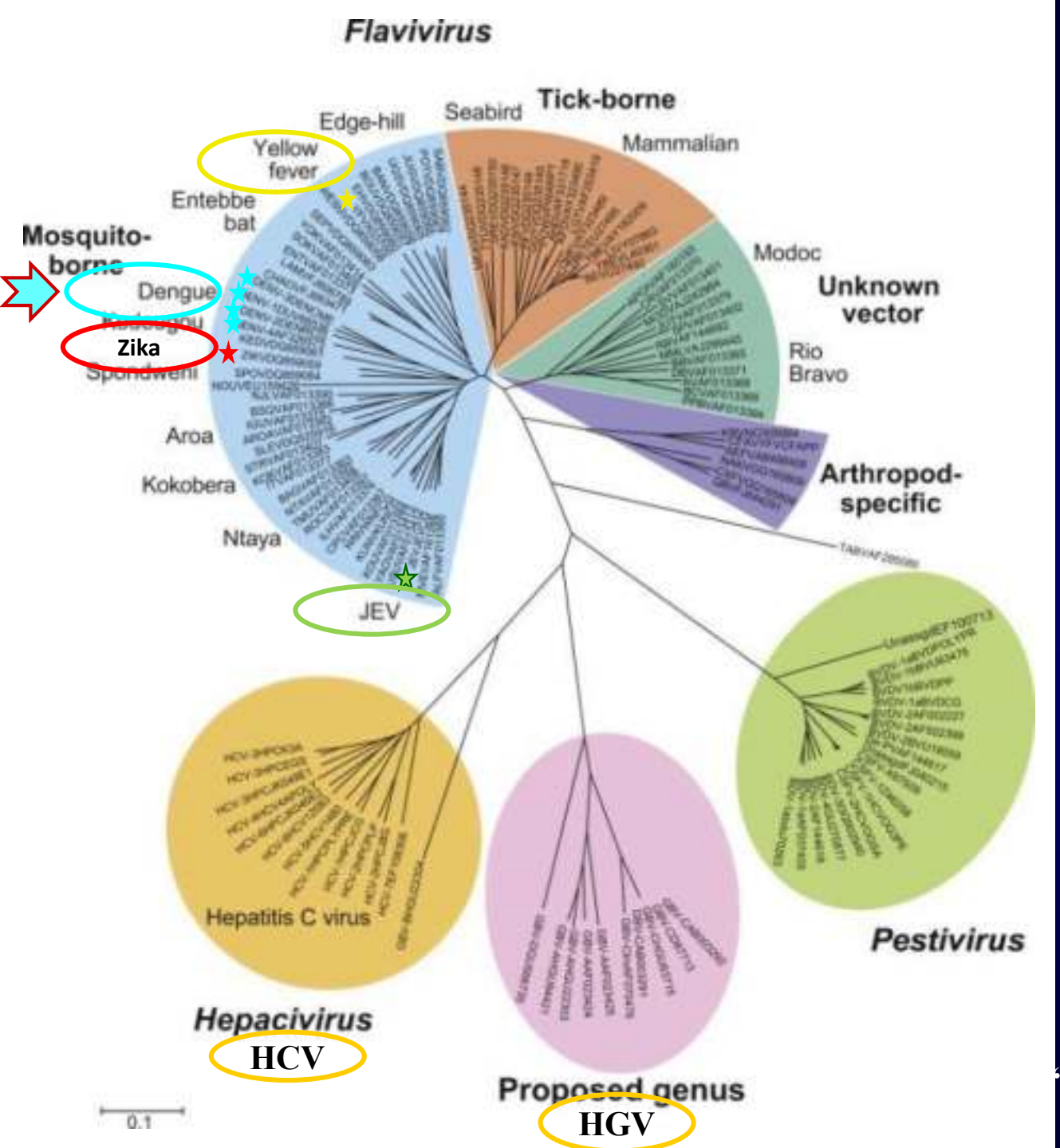
± 30 nm diâmetro

≈ F. Amarela, E Japonesa b, ...

4 serotipos[1]

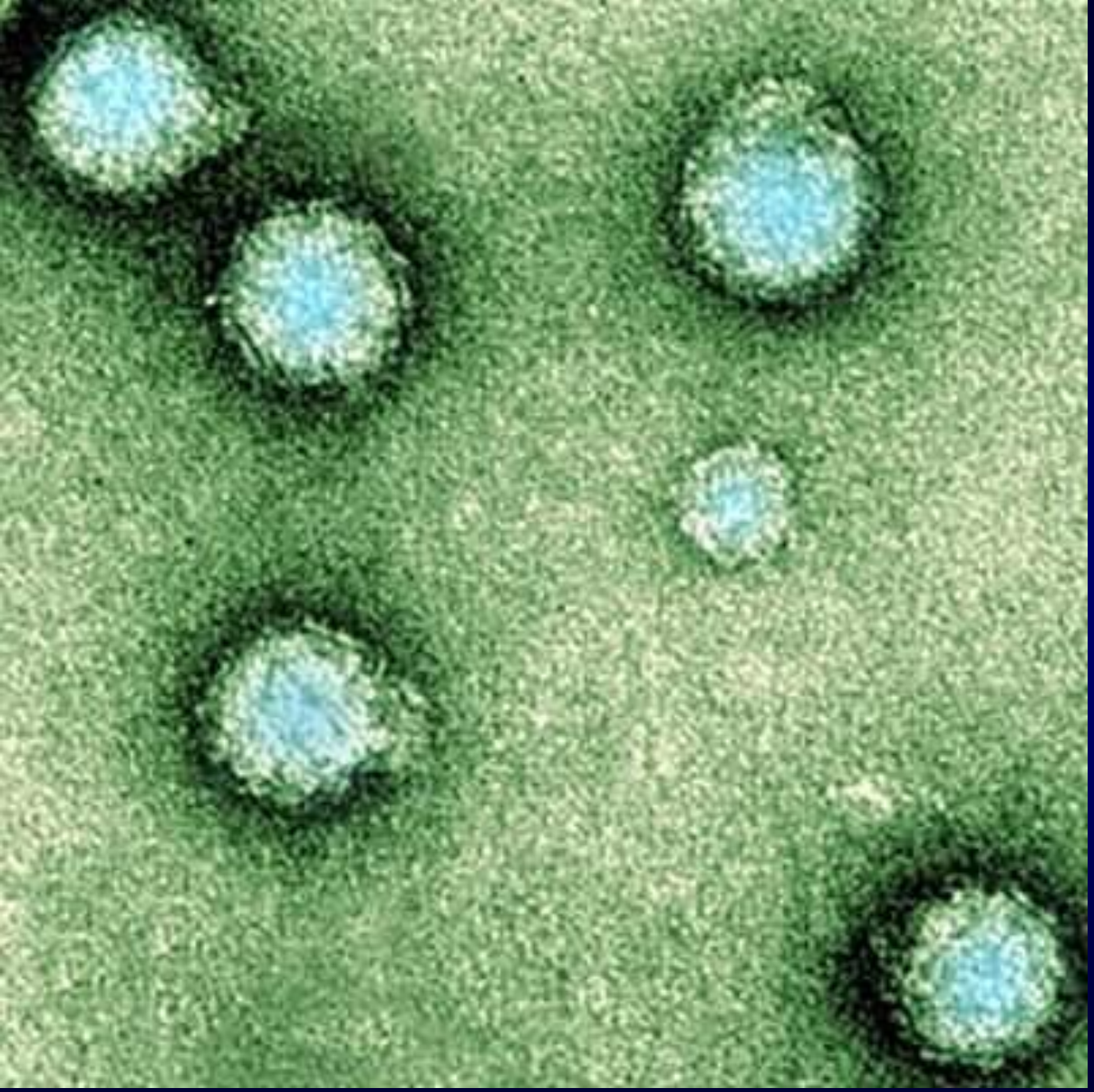
5° serotipo descoberto em 2013[1]

[1] - D Normile. 2013. *in* Science 342(6157):415.



Phylogenetic Tree of *Flavivirus*

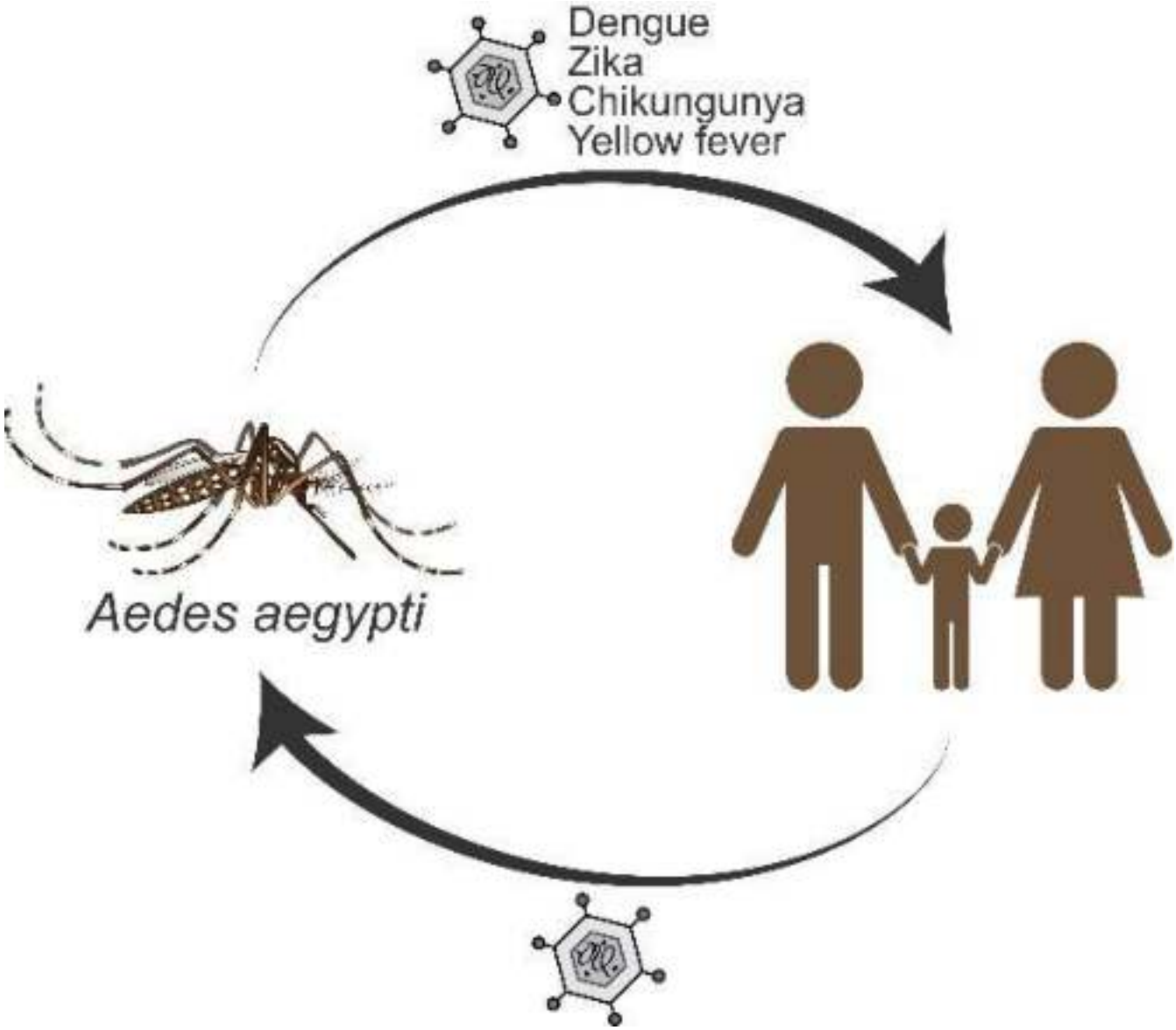
from:
International Committee on Taxonomy of Viruses – 9th Report. 2012.
in AMQ King *et al* (ed.), "Virus Taxonomy", 2sd Ed. 2019. London, Elsevier, pg 1003-1020.



Vírus de dengue, em ME

from: S Brown. 2013. *in* www.EzineMark.com

Dengue cycle



Dengue
Reservatório

Humanos

spp macacos SE Ásia

spp macacos África

spp macacos Américas

J Nina. 2014.

Dengue

Epidemiologia

2.5 - 3.0 x 10^9 pessoas em risco

200 - 600 x 10^6 infecções / ano

58.4 x 10^6 casos sintomáticos / ano

(95 % IC: 24 - 122 x 10^6)

13.6 x 10^3 ✝ / ano (>99% SEA, Índia)

(95 % IC: 4.2 - 34.7 x 10^3)

↑↑↑ - Nº casos x 30 nos últimos 50 anos

↑ ↑ crianças

↑ ↑ época das chuvas

↑ classes carenciadas: ↑ meio rural,

↑ "bairros de lata" • • •

adapted from: Donald S Shepard *et al.* 2016. *in* Lancet Inf Dis 16(8):935–941.
&RF Chen *et al.* 2007. *in* Trans Roy Soc Trop Med Hyg 101:1106-1113.

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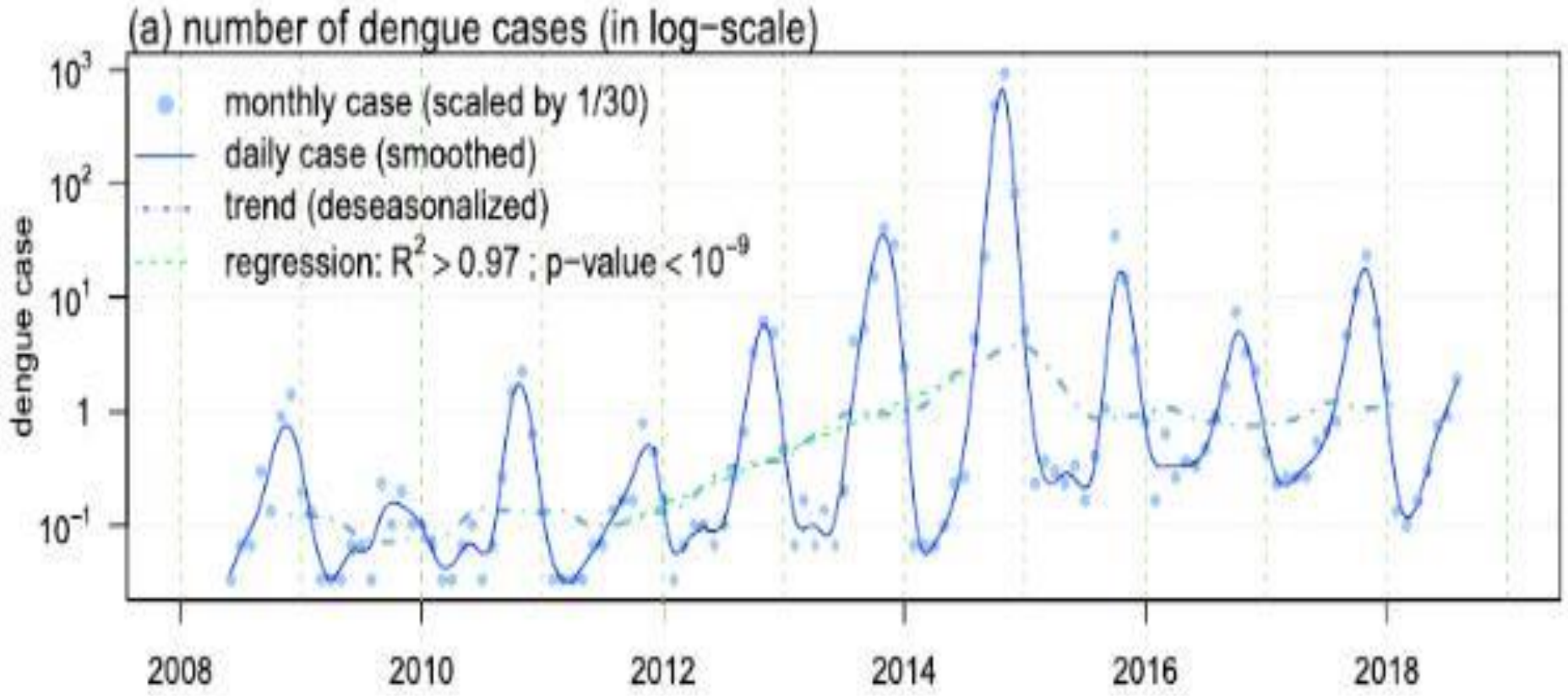
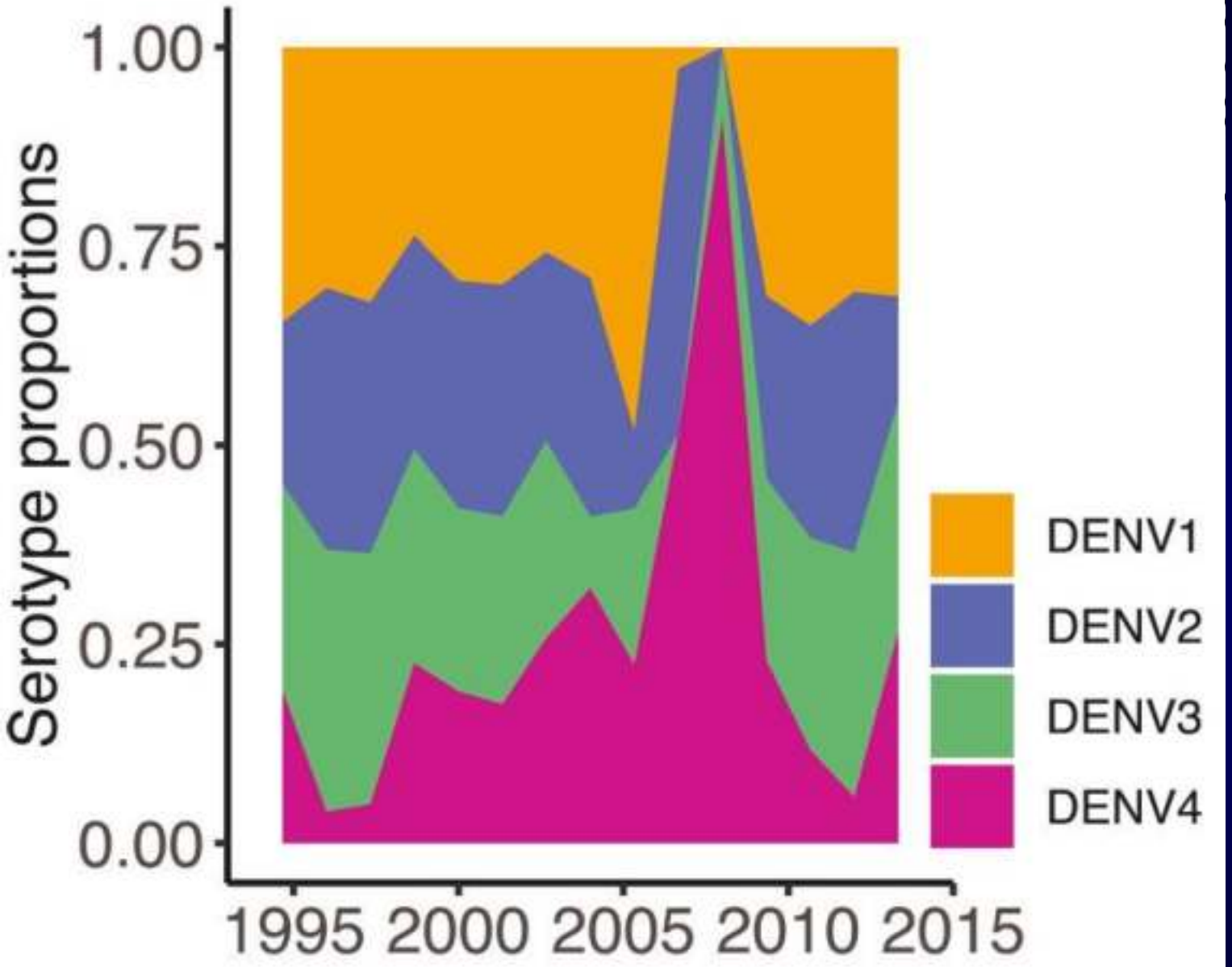
Sazonalidade do Dengue



from: Shi Zhao *et al*. 2020. *in* Trans R Soc Trop Med Hyg 114(1):62-71.

Dengue

Proportion by serotype of 1944 clinical DENV strains isolated between 1994 and 2014, at Bangkok

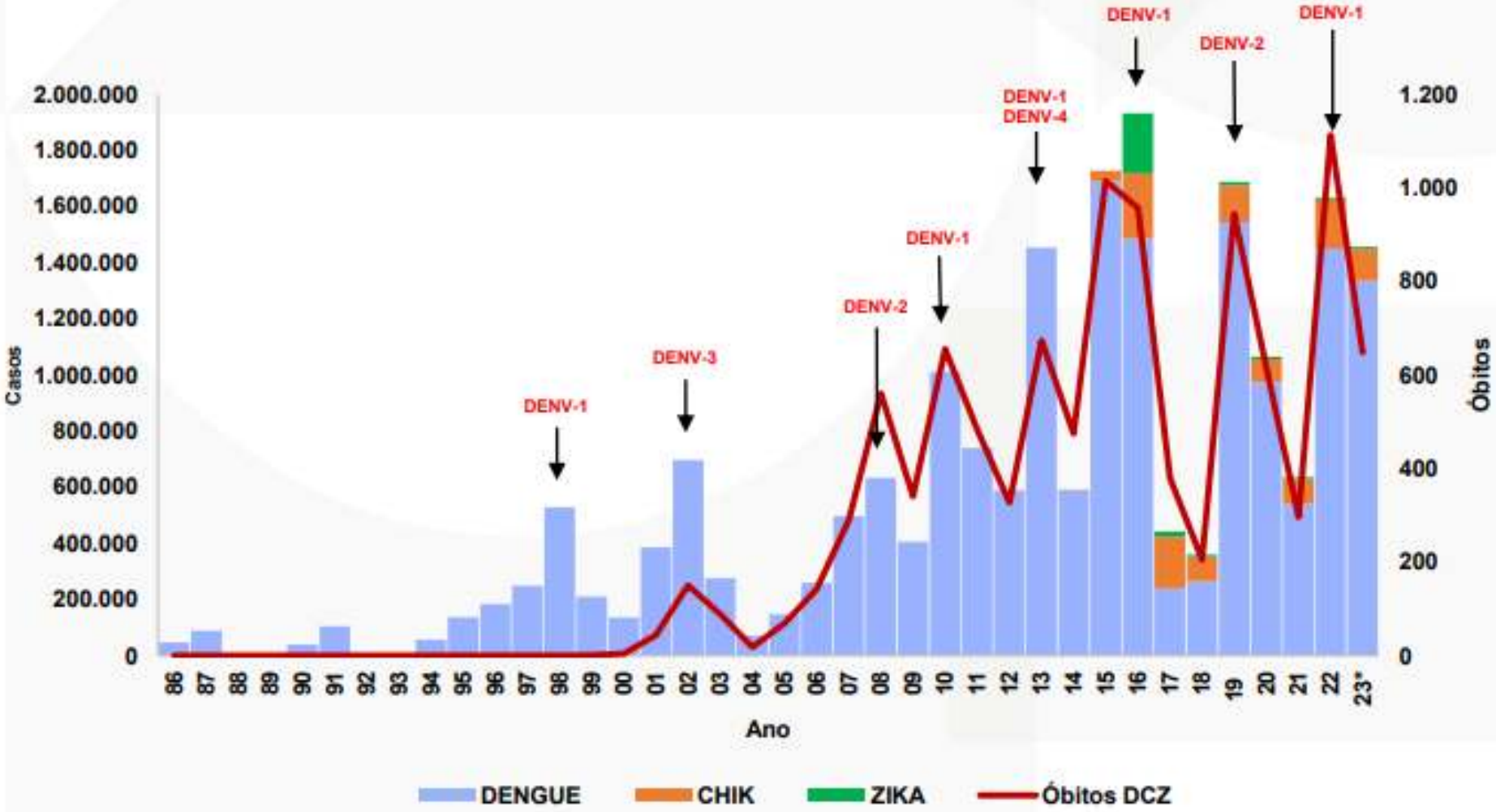


from: LC Katzelnick *et al*. 2021. *in* Science 374(6570):999-1004.

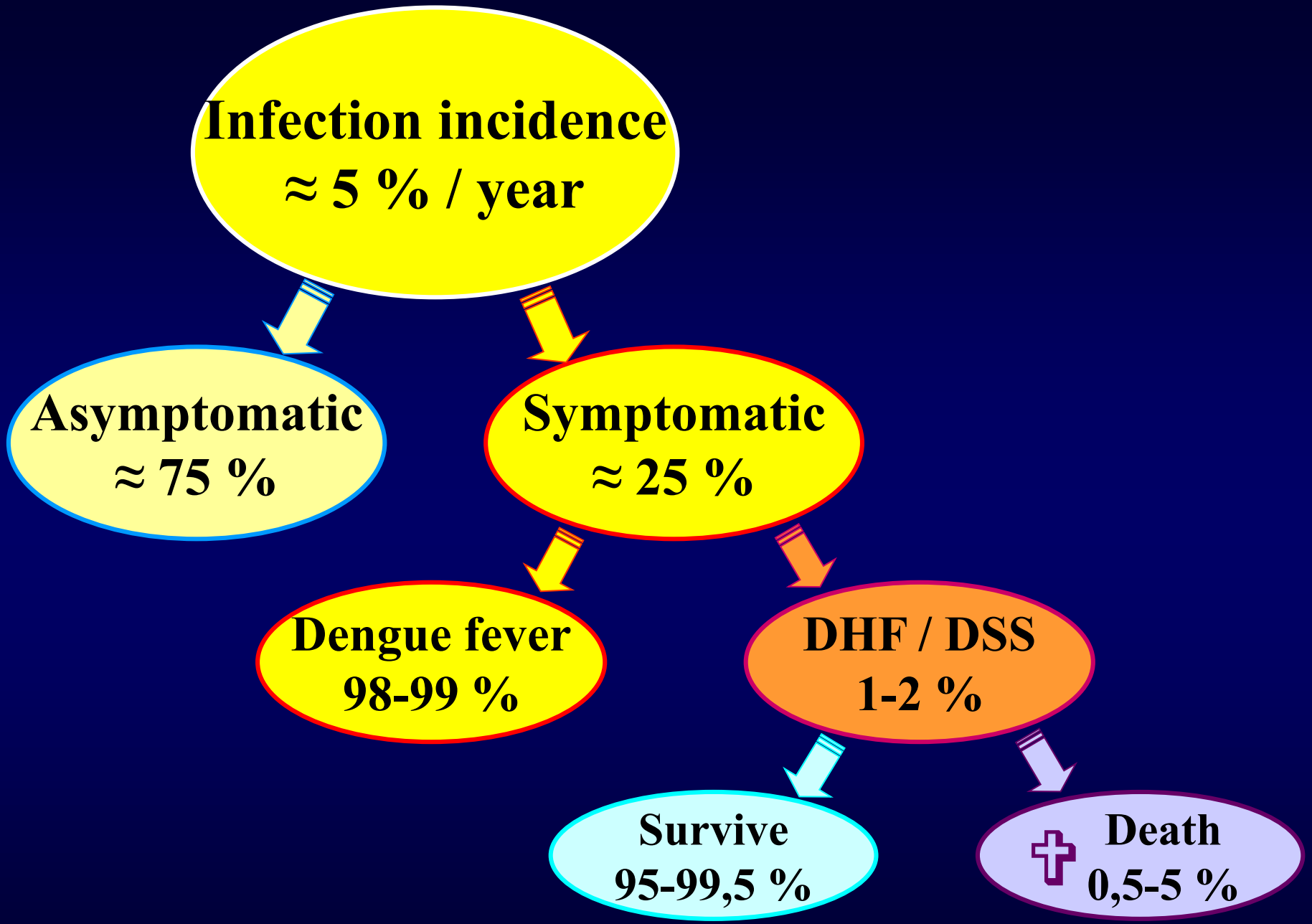
Situação Epidemiológica

GOV.BR/SAUDE
minsaude

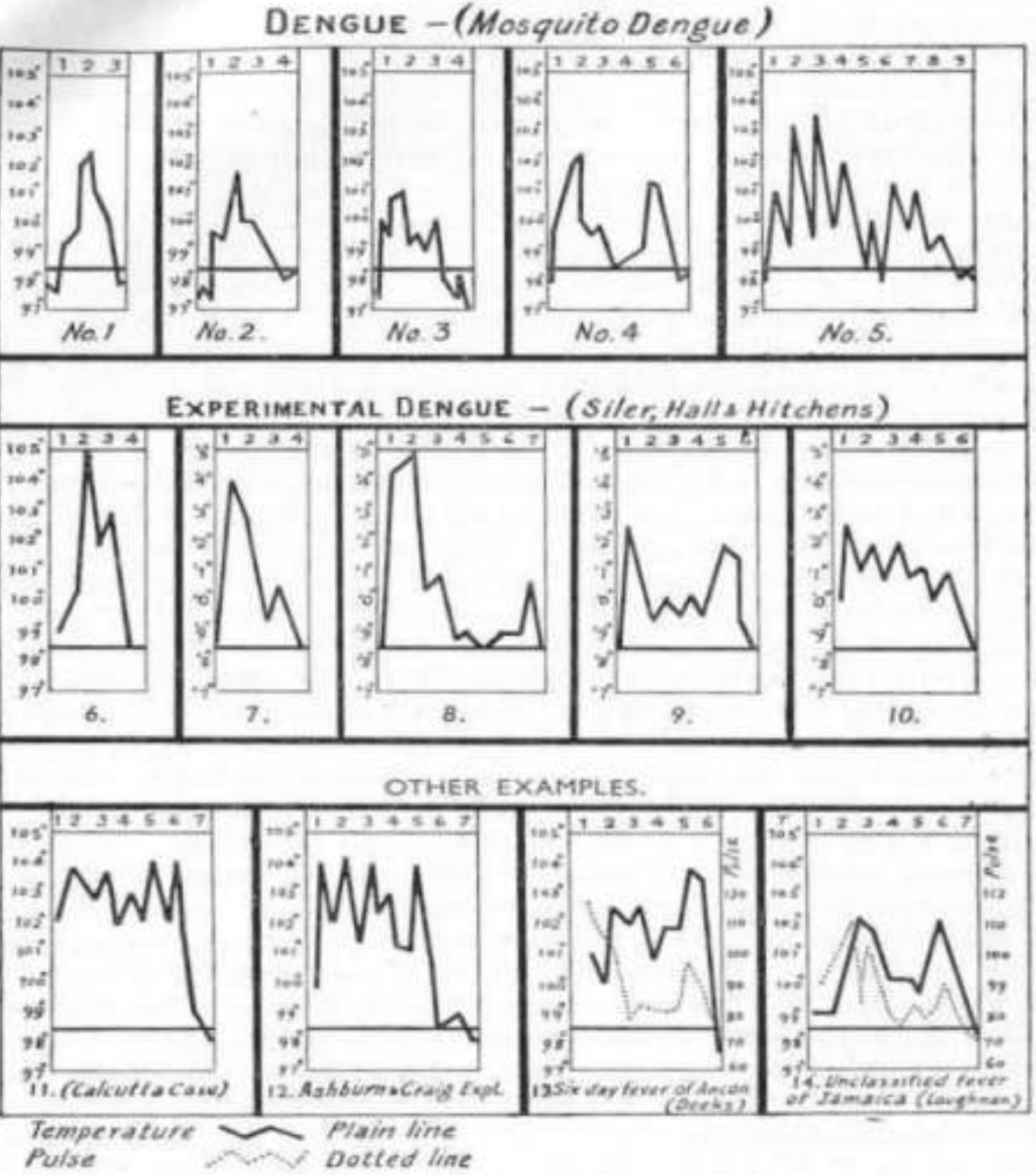
CASOS E ÓBITOS POR DENGUE, CHIKUNGUNYA E ZIKA NO BRAZIL (1986 a 2023)



BRASIL
gov.br



adapted from Margolis (2010); & *Vaccine* 2002; 3043–3046.



Temperature charts of mosquito dengue.

Dengue:
gráficos febre (linha)
e pulso (tracejado)

***in* L Rogers &**
JWD Megaw. 1939.

Dengue rash

Diffuse macular recovery rash in an adult patient with dengue. The rash may appear between 3 and 6 days after fever onset. Note the 'islands of white' of normal skin surrounded by erythematous rash

Typical skin rash in an infant with dengue

from: NK Jones & S Yacoub. 2024. *in* J Farrar *et al* (eds.). 2024. *in* "Mason´s Tropical Diseases", Amsterdam, Elsevier, 1898 24th ed. 2024.

ELSEVIER

Dengue patient from Dhaka

from: www.SOS-arsenic.net

Dengue hemorrágico

Peters & Gilles. 1991.

Severe (haemorrhagic) Dengue

Haematoma in a patient with severe dengue:
combination of increased vascular fragility, platelet dysfunction/thrombocytopenia, and coagulation disorders is believed to explain its haemorrhagic manifestations

Minor bleeding, particularly around injection sites, is a very common feature in dengue

from: NK Jones & S Yacoub. 2024.
in J Farrar *et al* (eds.). 2024.
in "Mason´s Tropical Diseases",
Amsterdam, Elsevier, 1898 24th ed. 2024.

Criança com dengue hemorrágico

from: J Genesio. 2012. *in* www.naturalunsenseenhazardsblog.com

A severe dengue outbreak stretches to the limit the health services response capacity in Dhaka, Bangladesh

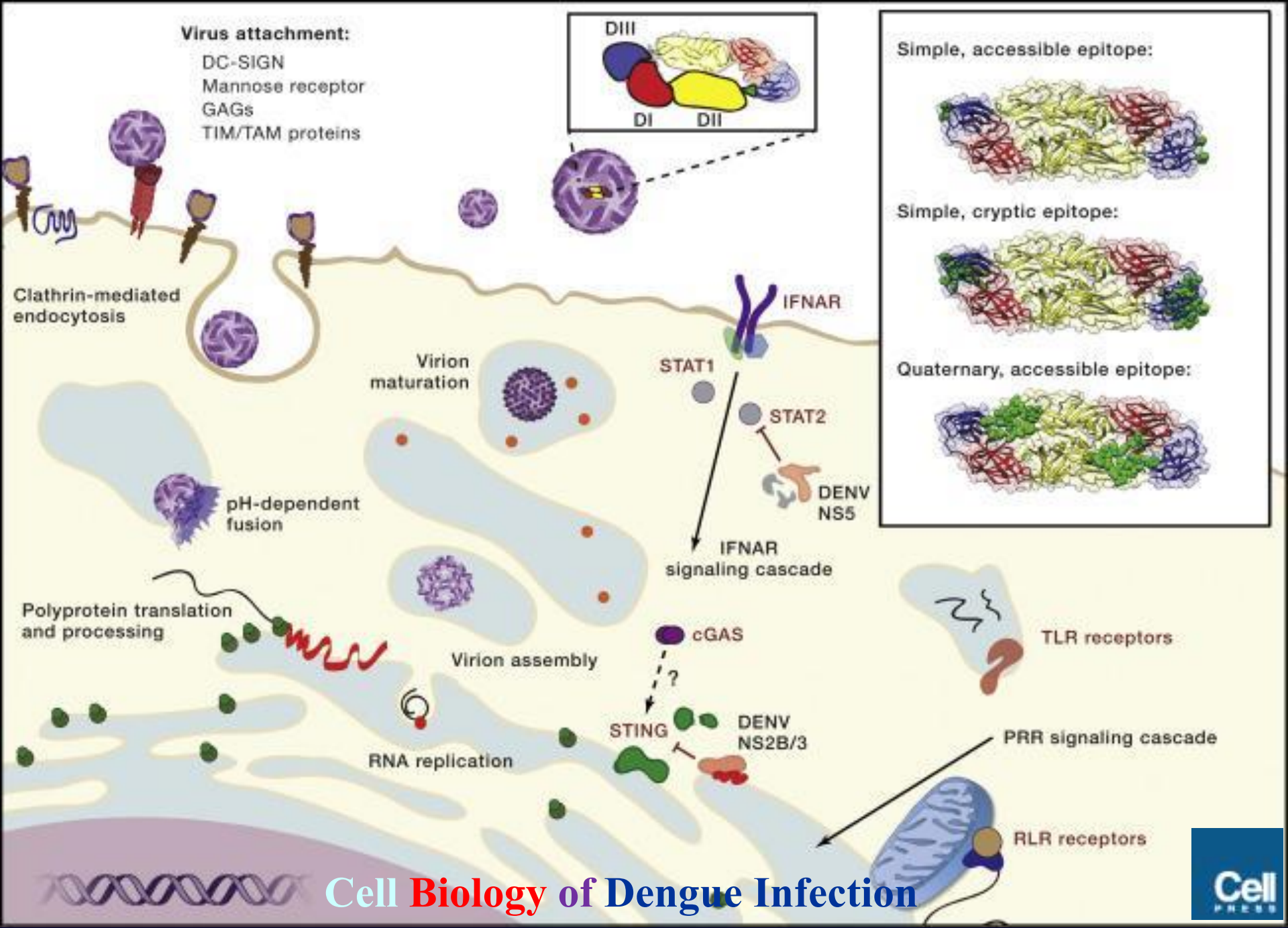
from: V Chandrashekhar. 2023. *at* November 30. YaleEnvironment360

Dengue

Clínica Gravidez

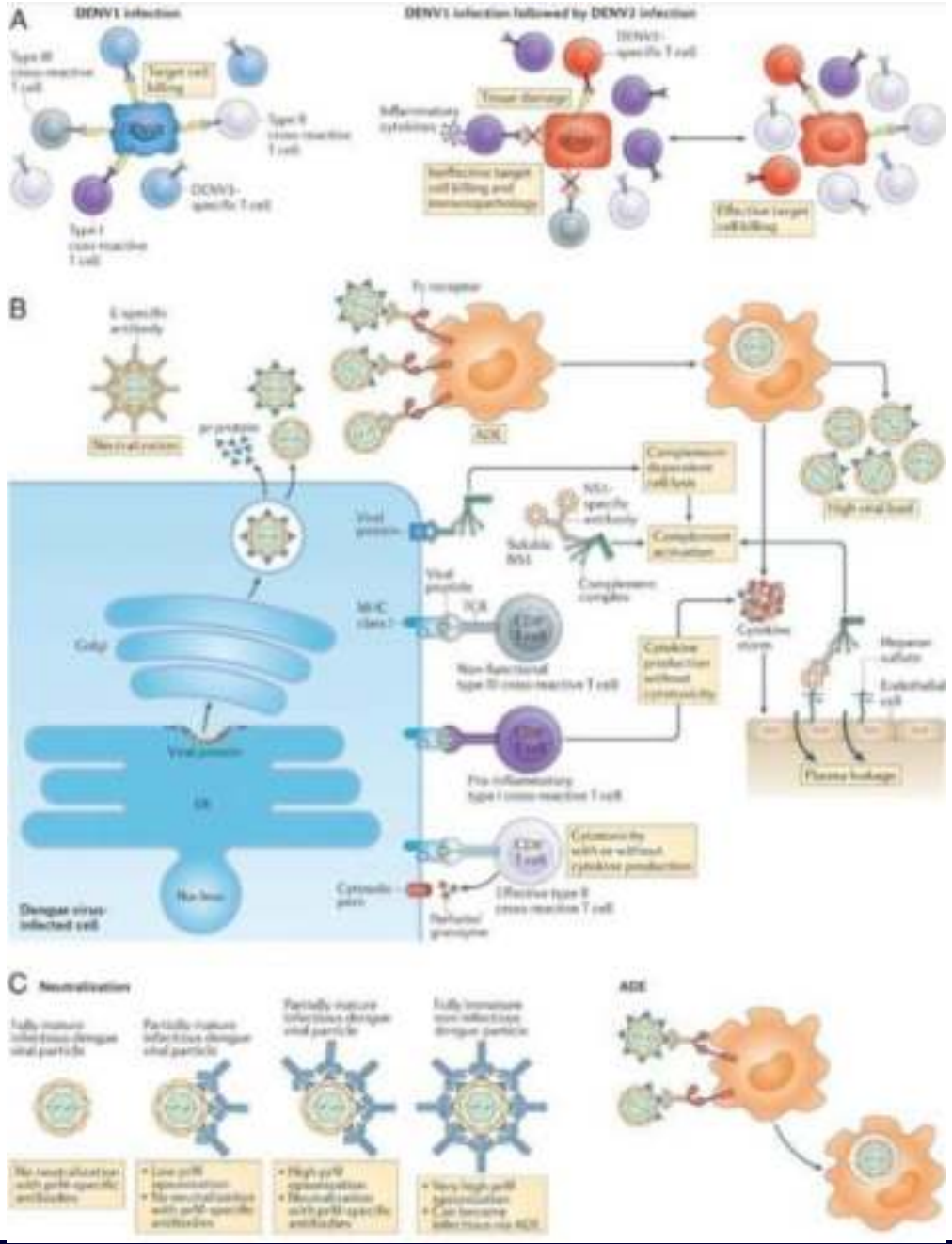
- ↑ risco morte fetal
  - mOR dengue sintomático 1,9 (CI – 1,6 - 2,2)
  - mOR dengue severo 4,9 (CI – 2,3 – 10,2)
- ↑ parto pré-termo
  - mOR 1,26 (CI – 1,06 -1,49)
- Não associado ↓ peso à nascença
- Não associado a malformações
- Dengue ≠ Zika

J Nina. 2018. *adaptado de* RL Goldenberg & EM McClure. 2017. *in* Lancet Inf Dis 17(9):886-887, E Paixão *et al*. 2017. *in* Lancet Inf Dis 17(9):957-964, P Brasil & O Lupi. 2017. *in* Lancet Inf Dis 17(9):885-886 & LB Nascimento *et al*. 2017. *in* Lancet Inf Dis *in* http//dx.doi.org/10.1016/S1473-3099(17)30169-X.



Cell Biology of Dengue Infection

from: MS Diamond & TC Pierson. 2015. *in* Cell 162(3):488-492.



Adaptive immune responses to dengue virus infection

adapted from:
G Screaton, J Mongkolsapaya, S Yacoub, S. *et al.*
"New insights into the immunopathology and control of dengue virus infection".
in Nat Rev Immunol 15:745-759.

from: NK Jones & S Yacoub. 2024. *in* J Farrar *et al* (eds.). 2024. *in* "Mason´s Tropical Diseases", Amsterdam, Elsevier, 1898 24th ed. 2024.

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Dengue

Fisiopatologia

A importante diferença entre Anticorpos Neutralizantes e Anticorpos Facilitadores

A complicar a "construção" de uma vacina contra a dengue está o facto que o vírus ocorre em quatro serotipos (mais um 5º raro e só no SEA) e a imunidade contra um dos serotipos não garante imunidade duradoura contra qualquer dos outros três, daí a necessidade de uma vacina tetravalente.

Pior, ser infectado com – e desenvolver imunidade para – um serotipo pode ser o factor desencadeador que leva o doente a sofrer uma forma mais grave da doença, se subsequentemente infectado com um serotipo diferente, um fenómeno conhecido como facilitação anticorpo-dependente.

Mas infecções com um 3º e/ou um 4º serotipo diferente, se acontecerem, em regra provocam doença ligeira.

***from*: Editorial. 2018. *in* Lancet Inf Dis 18(2):123.**

THE LANCET Infectious Diseases

Dengue

Fisiopatologia

A importante diferença entre Anticorpos Neutralizantes e Anticorpos Facilitadores

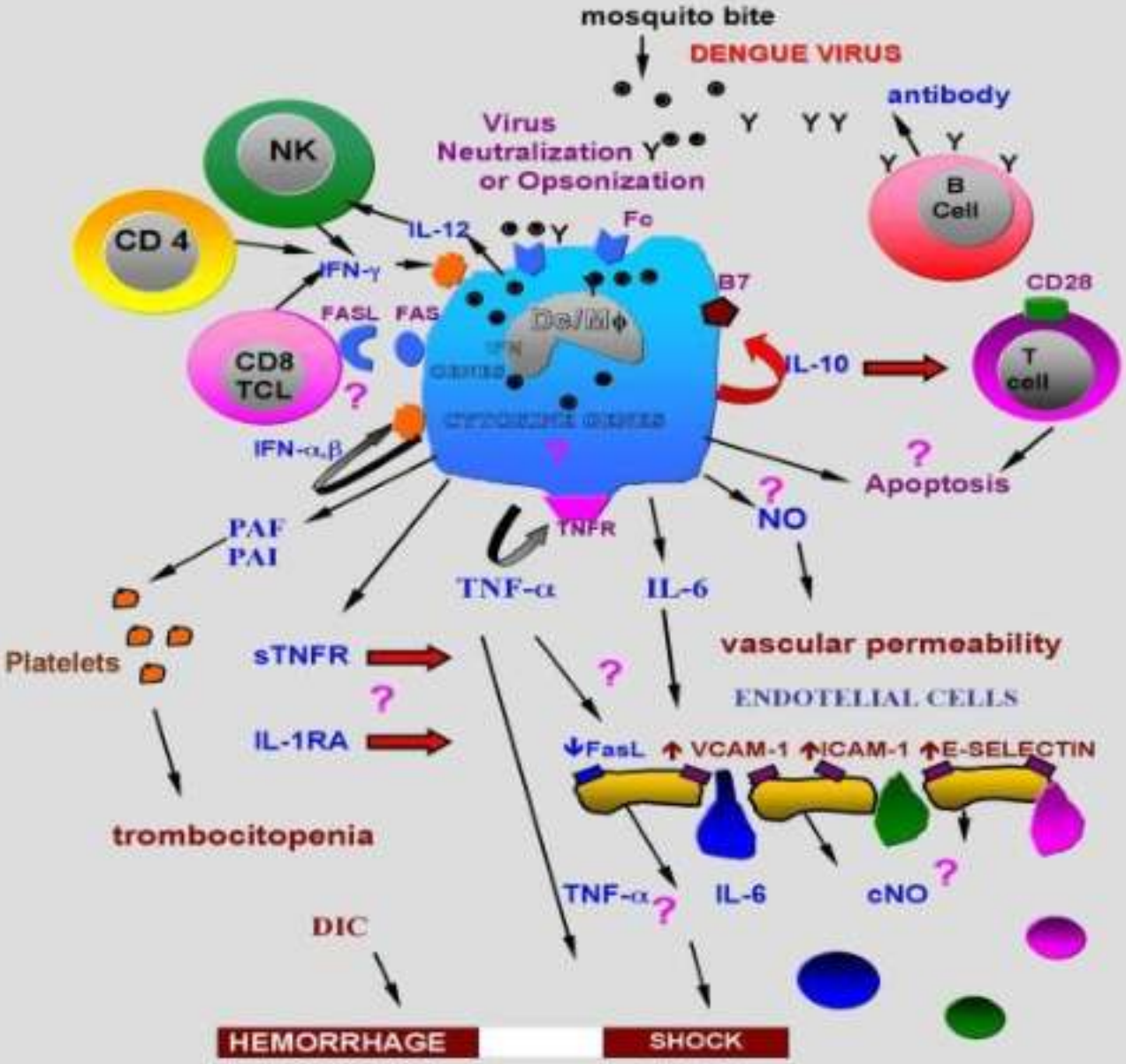
A fisiopatologia do dengue devido ao processo patogénico mediado por anticorpos pode ser ainda mais complicado, visto haver quatro vírus de dengue diferentes, e que cada um pode afectar de forma diferente infecções de dengue subsequentes. Por exemplo, infecções com dengue virus 1 seguido de dengue virus 2, ou dengue virus 1 e depois dengue virus 3, resultam em doença clínica mais grave que infecções em outras sequencias.

from: S Mahalingam *et al*. 2017. *in* Lancet Inf Dis 17(7):686-688
& MG Guzman *et al*. 2013. *in* Arch Virol 158(7):1445-1459.

THE LANCET Infectious Diseases

J Nina. 2018, 2024.

Fisiopatologia e Imunopatologia do dengue



Dengue
Vacina

-Vacina anos 70s:

Exemplo falhanço

(*cross-reacting enhancing Acs*)[1]

com ↑ Mortalidade nos vacinados !!!

[1] – SB Halstead & EJ O'Rourke. 1977. J Exp Med 146:201.
& W Dejnirattisai *et al*. 2010. Science 328(5079):745-748.

Dengue
Vacina

-Vacina anos 70s: Exemplo falhanço (*cross-reacting enhancing Acs*)[1] com ↑ Mortalidade nos vacinados !!!

-Condicionantes vacina:
1. Tetravalente
2. Indução AC neutralizantes ↑ (sem Ac heterotípicos †)
3. Segura

[1] – SB Halstead & EJ O'Rourke. 1977. J Exp Med 146:201. & W Dejnirattisai *et al*. 2010. Science 328(5079):745-748.

Dengue Vacinas

Up-and-coming dengue vaccines

Manufacturers for the two dengue vaccines following Sanofi Pasteur's are collecting more data to evaluate safety; results are expected by the end of 2018.

VACCINE	MANUFACTURER	VACCINE TYPE	MECHANISM	STATUS
Dengvaxia	Sanofi Pasteur	Live attenuated	Yellow fever vaccine backbone with key genes from four dengue viruses	In use
DENVax	Takeda	Live attenuated	Dengue serotype 2 backbone with key genes from other three dengue viruses	Initial results late 2018
TV003/ TV005	National Institute of Allergy and Infectious Diseases and Butantan Institute	Live attenuated	Wild-type strains with genetic mutations	Initial results late 2018

***table*: *adapted from*: L Schwartz *et al*. 2015. in Vaccine 33:3293.**

***from*: D Normile. 2017. *in* Science 358(6370):1514-1515.**

Science AAAS


Dengvaxia™
Powder and solvent for suspension for injection
Polvo y disolvente para suspensión inyectable
Dengue tetravalent vaccine (live, attenuated)
Vacuna tetravalente contra el dengue (de virus vivos atenuados)
Powder (1 dose) in vial + 0.5 mL of solvent in a pre-filled syringe with 2 separate needles - Pack size of 1
Manufactured by:
Sanofi Pasteur SA
Lyon, France
Imported by:
Sanofi Pasteur, Inc.
Makati City, Philippines
Caution: Foods, Drugs, Devices & Cosmetics Act prohibits dispensing without prescription.
Subcutaneous (SC) use after reconstitution
Subcutánea (SC) después de la reconstitución
SANOFI PASTEUR

Dengvaxia

- **Segurança +++**
- **Elevada protecção contra infecção, doença, hospitalização, complicações, e morte – em pessoas já parcialmente imunes**
- **Parece aumentar estes riscos em seronegativos, nomeadamente em crianças dos 2 aos 5 anos**
- **Assim, só é recomendada para, cumulativamente:**
  - **Zonas hiperendémicas**
  - **Crianças > 9 anos**

from: Tikki Pang. 2016. *in* Lancet Inf Dis 16(8):880-882
& M Aguiar *et al*. 2016. *in* Lancet Inf Dis 16(8):882-883.

THE LANCET Infectious Diseases

Licenciada (*até finais de 2016*):

Filipinas

México
Brasil
El Salvador
Costa Rica

Licenciamento em análise (*finais de 2016*):

Tailândia
Indonésia
Malásia
Singapura
…

from: Tikki Pang. 2016. *in* Lancet Inf Dis 16(8):880-882.

THE LANCET Infectious Diseases

Dengvaxia

mas …

- ↑ casos graves e internamentos em crianças que tinham tido dengue antes de serem vacinadas, nas Filipinas
- Suspeitas semelhantes noutros países – em pessoas já parcialmente imunes
- a WHO revê as indicações, tornando-as muito mais restritas (*ver* WER 2018, 7/09 - No 93(36):457–476 & WER 2024, 3/05 - No 99(18):203-224, *at* http://www.who.int/wer)

J Nina. 2024. *adaptado de* WHO. 2018.

World Health Organization

Licenciada (*até finais de 2016*) ou não:

Filipinas → anulação do licenciamento 2021

México
Brasil
El Salvador
Costa Rica

Licenciamento em reanálise:

Tailândia
Indonésia
Malásia
Singapura
…

Reanálise de licenciamento em inúmeros outros estados

J Nina. 2024. *adapted from*: Tikki Pang. 2016. *in* Lancet Inf Dis 16(8):880-882.

THE LANCET Infectious Diseases

Takeda's QDENGA®

- **Vacina Dengue Tetravalente, viva, atenuada, baseada no serotipo 2 mas modificado para exprimir Ags dos 4 serotipos**
- **Aprovada na EU, 14-12-2022, e no Brasil, 10-04-2023**
- **Estudos da empresa com evidência de eficácia > 80 % e boa segurança, nomeadamente ≠ Dengvaxia**
- **A empresa retirou candidatura a aprovação pela FDA**

J Nina. 2023. ***adaptado de***

European Medicines Agency emea

ANVISA

Takeda's QDENGA®

WHO recommendations for endemic areas, May 2024:

1. **Countries should consider introducing TAK-003 vaccine into their routine immunization programmes for age 6-16 years but only in settings with dengue transmission intensity (WHO suggests a 60% seroprevalence threshold). Within the age range of 6-16 years, WHO recommends the introduction about 1-2 years prior to the mean age of peak incidence. Until the efficacy-risk profile in seronegative persons for DENV3 and DENV4 has been more precisely assessed, WHO does not recommend the programmatic use of this vaccine in low to moderate dengue transmission settings.**
2. **Administration considerations:**

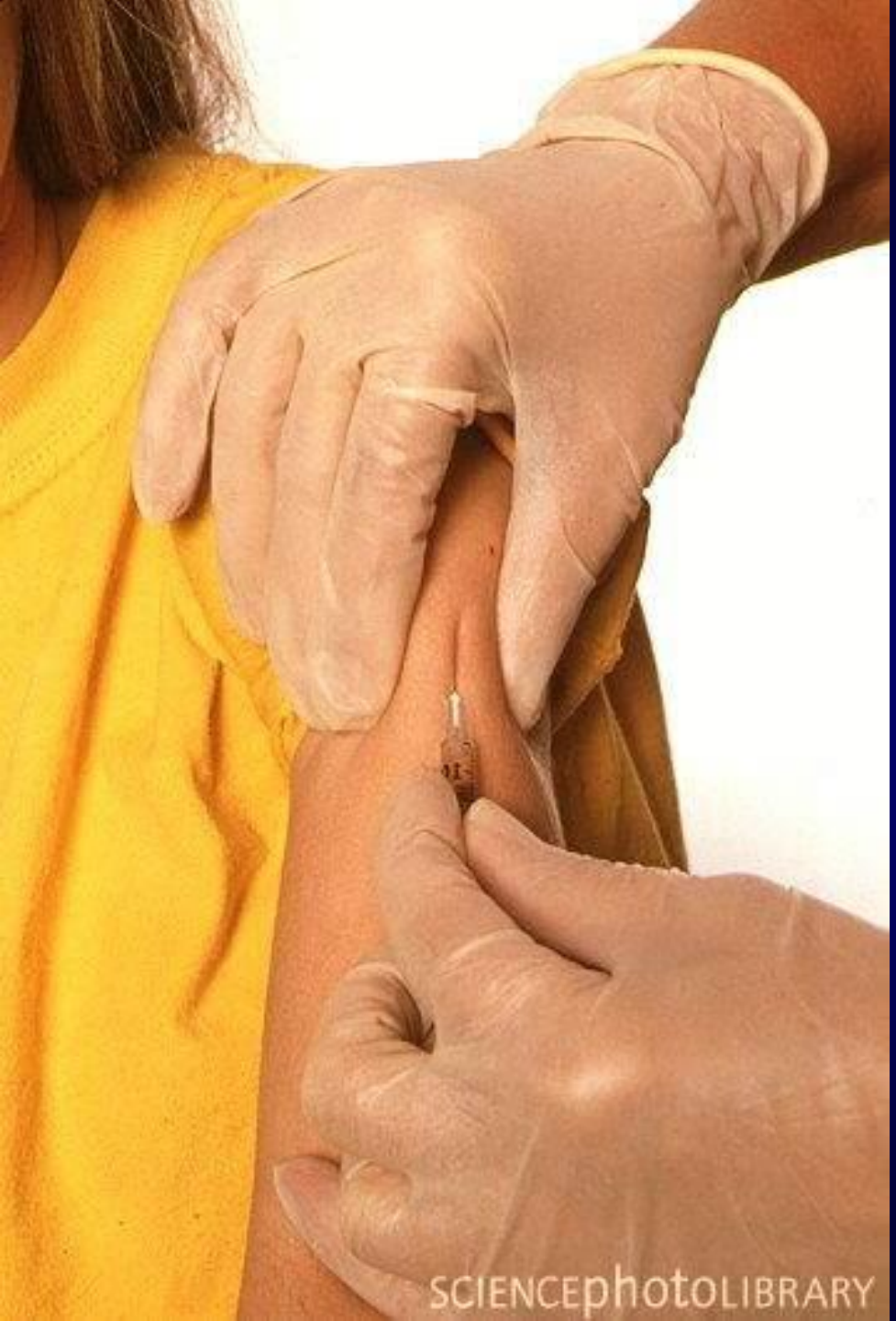
2.1. 2-doses s/c to be spaced at a minimum interval of 3 months.

2.2. No maximum interval; 2nd dose should be administered at the next opportunity.

2.3. TAK-003 is not recommended for pregnant women, and pregnancy should be avoid pregnancy for at least 1 month after vaccination.

Dengue vaccine (TAK-003) GRADE tables for consideration by the Strategic Advisory Group of Experts (SAGE) on Immunization September 2023 & WER 2024 No 99(18):203-224.

World Health Organization



SC injection technique

Vacinas

Lembrar:

Timing

is everything

J Nina. 2012.

Takeda's QDENGA®

WHO recommendations for endemic areas, September 2023:

2. Administration considerations:

2.4. TAK-003 is contraindicated in persons with congenital or acquired immune deficiency, including immunosuppressive therapies within 4 weeks prior to vaccination.

2.5. TAK-003 contraindicated in persons with symptomatic HIV or with asymptomatic HIV and laboratory or other evidence of impaired immune function.

2.6. No current recommendation has been made for a booster dose due to lack of data, but dengue-naïve persons are likely to require a booster.

2.7. Co-administration of TAK-003 with yellow fever and hepatitis A vaccines is supported by data. Countries could consider coadministration with other inactivated, sub-unit or messenger RNA vaccines, except for live vaccines (pending more data).

Dengue vaccine (TAK-003) GRADE tables for consideration by the Strategic Advisory Group of Experts (SAGE) on Immunization September 2023 & WER 2024 No 99(18):203-224.

World Health Organization

Takeda's QDENGA®

1. Studies to assess efficacy of TAK-003 against VCD caused by any serotype in adolescents and adults 18 years and older have not yet been conducted. Only immunogenicity results are available. Efficacy is inferred based on a comparison of neutralizing antibody levels elicited in adults and among children in whom efficacy data are available.

2. Evidence supports a moderate level of confidence that the true effect lies close to the estimate of the effect on the health outcome.

3. There is no observed safety signal (non-dengue severe adverse events) associated with TAK-003 among immunocompetent trial participants 4-16 years of age. TAK-003 is not associated with a statistically significant increased risk of severe dengue or DHF among immunocompetent children ages 4-16 who were seronegative at baseline. A risk of excess cases of severe dengue or DHF cannot be ruled out with the available data. Evidence supports a very low level of confidence that the true effect lies close to the estimate of the effect on the health outcome.

Dengue vaccine (TAK-003) GRADE tables for consideration by the Strategic Advisory Group of Experts (SAGE) on Immunization September 2023 & WER 2024 No 99(18):203-224.

World Health Organization

WHO considerations for travellers

Takeda's QDENGA®

WHO considerations for travellers

- Travellers from dengue non-endemic countries with previous travel-related dengue (any serotype) may benefit from TAK-003 vaccination to prevent a secondary dengue during future dengue risk travel.
- Dengue-naïve travellers have less potential benefit from vaccination than previously infected travellers and as well an unclear but likely increased risk of dengue complications with a future dengue exposure during travel.
- Frequent travellers, long-term travellers, migrants and long-term expatriates have a higher likelihood of having had a dengue infection in the past (and may therefore be seropositive) compared with first-time or short-term travellers.
- Travellers need to understand that TAK-003 has not, yet, been showed to confer protection against DENV3 and DENV4 if they are dengue-naïve; and that there is a theoretical risk of severe dengue if seronegative individuals are exposed to DENV3 and DENV4, a risk which currently cannot be ruled out with the available data.

Dengue vaccine (TAK-003) GRADE tables for consideration by the Strategic Advisory Group of Experts (SAGE) on Immunization September 2023 & WER 2024 No 99(18):203-224.

World Health Organization

Takeda's QDENGA®

WHO considerations for travellers

- Protection starts 14 days after the first dose and a VE of 81% has been demonstrated between the 1st and 2nd dose, hence the 1st dose can be given up to 14 days prior to travel to a dengue-endemic country. To ensure the durability of the protection, a 2nd dose is needed after a minimum interval of 3 months. Based on current data on efficacy and safety only travellers between 6 and 60 years of age should consider vaccination.
- New vaccines tend to be costly in non-endemic rich countries and dengue risk is very variable between regions of most endemic countries. Mapping of estimated risk levels for specific sub-national itineraries, such as is now done for yellow fever and malaria, may be necessary, even if approximate and difficult.

Dengue vaccine (TAK-003) GRADE tables for consideration by the Strategic Advisory Group of Experts (SAGE) on Immunization September 2023 & WER 2024 No 99(18):203-224.

World Health Organization

Takeda's QDENGA®

WHO considerations for travellers

- National guidelines in non-endemic countries where TAK-003 is commercially available are likely to remain permissive rather than prescriptive pending more data.
- For travellers from 17–60 years of age the strongest indication would be for long-stay or frequent travel to the highest risk destinations in a dengue experienced traveller. Dengue-naïve travellers to such high-risk areas would benefit from specific information if available on the likelihood of DENV-3 or -4 at the destination.

- Several other live attenuated dengue vaccine candidates remain in the pipeline with the further goal of a balanced infectivity profile for all four vaccine components. The option of waiting for one of them should also be considered.

Dengue vaccine (TAK-003) GRADE tables for consideration by the Strategic Advisory Group of Experts (SAGE) on Immunization September 2023 & WER 2024 No 99(18):203-224.

World Health Organization

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record

Relevé épidémiologique hebdomadaire

Contents

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WHO position paper on dengue vaccines – May 2024

Introduction

Note de synthèse: position de l'OMS sur les vaccins contre la dengue – mai 2024

Introduction

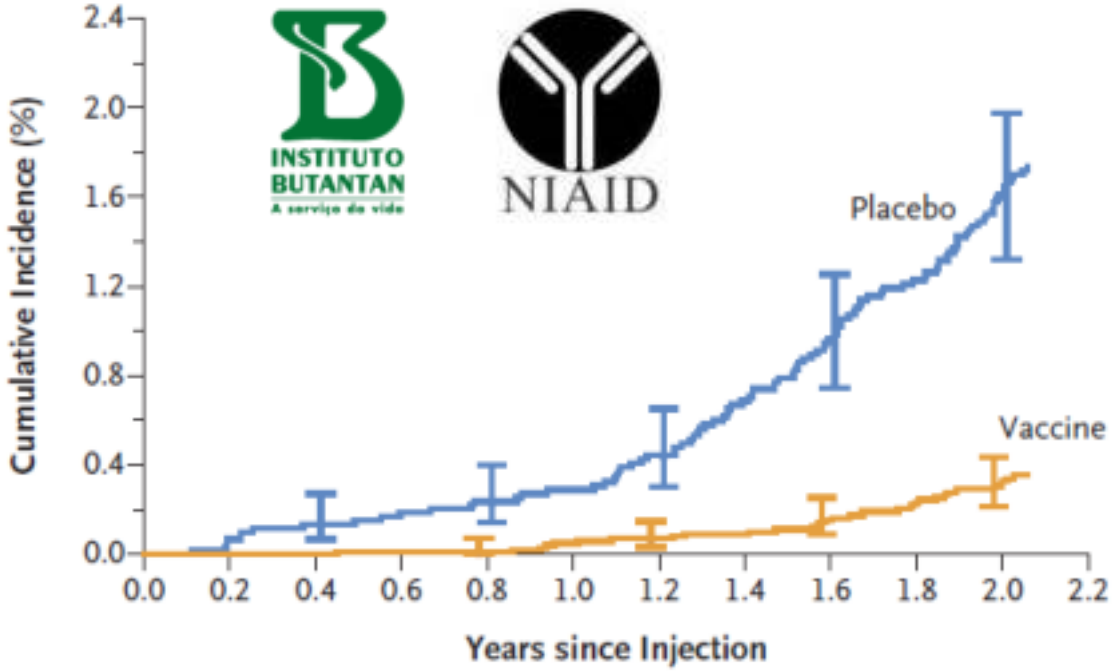
O Ministério da Saúde informou que 521 municípios brasileiros foram seleccionados para iniciar a vacinação contra a dengue via Sistema Único de Saúde (SUS) a partir de Fevereiro.

publicado em 25/01/2024 - 10:41
por Paula Laboissière - Repórter da Agência Brasil - Brasília

EBC | EMPRESA BRASIL DE COMUNICAÇÃO

3rd Dengue vaccine

Live, Attenuated, Tetravalent NIAID / Butantan - Dengue Vaccine showed impressive results at 2 years interim analysis, in Children and Adults with a single dose, and good safety profile



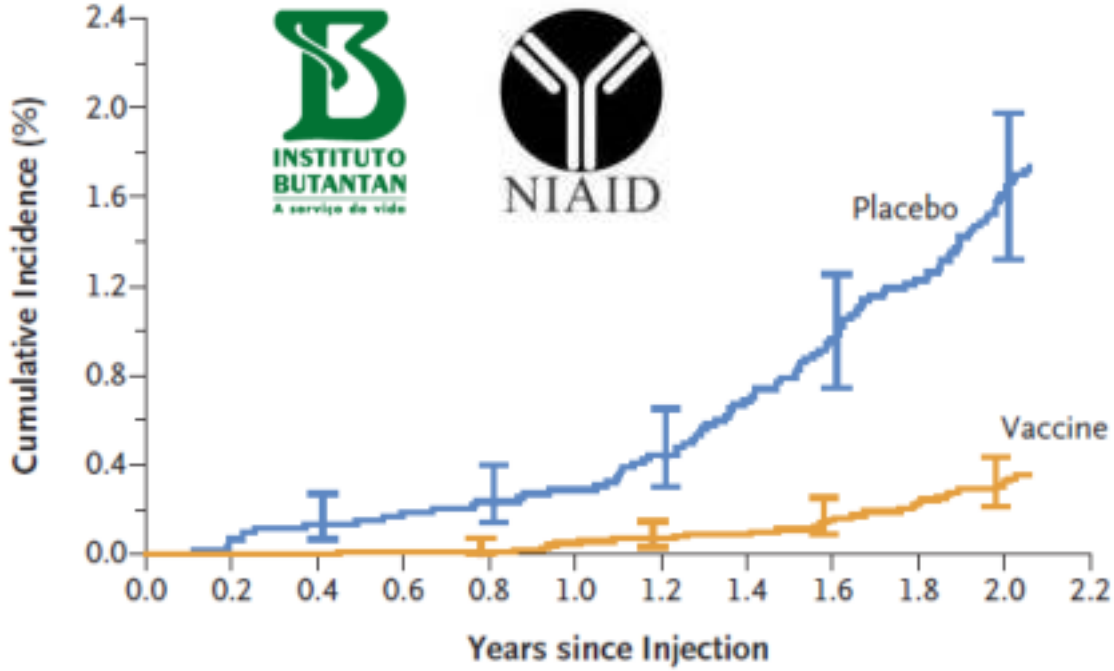
No. at Risk						
Placebo	5,946	5,865	5,811	5,741	5,668	5,571
Vaccine	10,213	10,014	9,925	9,840	9,750	9,628

Figure 2. Cumulative Incidence of Virologically Confirmed Dengue through 2-Year Follow-Up.

Shown is the incidence of symptomatic, virologically confirmed dengue occurring more than 28 days after injection through the end of the 2-year follow-up period. Analysis excludes results that did not follow standard operating procedures for the reverse-transcriptase–polymerase-chain-reaction-assay. I bars indicate 95% confidence intervals.

J Nina. 2024. *adapted from*:
SB Thalstead. 2024. *in* N Engl J Med 390(5):464-465.
& EG Kallás *et al*. 2024. *in* N Engl J Med 390(5):397-408.

The New England Journal of Medicine



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3rd Dengue vaccine

Live, Attenuated, Tetravalent NIAID / Butantan - Dengue Vaccine showed impressive results at 2 years interim analysis, in Children and Adults with a single dose, and good safety profile

But:

- 3 years study remain
- No cases of DENV-3 and DENV-4, yet
- Effect on mortality?
- Immunity previous Zika infection?

J Nina. 2024. *adapted from*:
SB Thalstead. 2024. *in* N Engl J Med 390(5):464-465.
& EG Kallás *et al*. 2024. *in* N Engl J Med 390(5):397-408.

The New England Journal of Medicine

3 vacinas para a dengue

- **Dengvaxia® - Sanofi Pasteur**

- **Qdenga® - Takeda**

- **??? - Butantan**

J Nina. 2024.

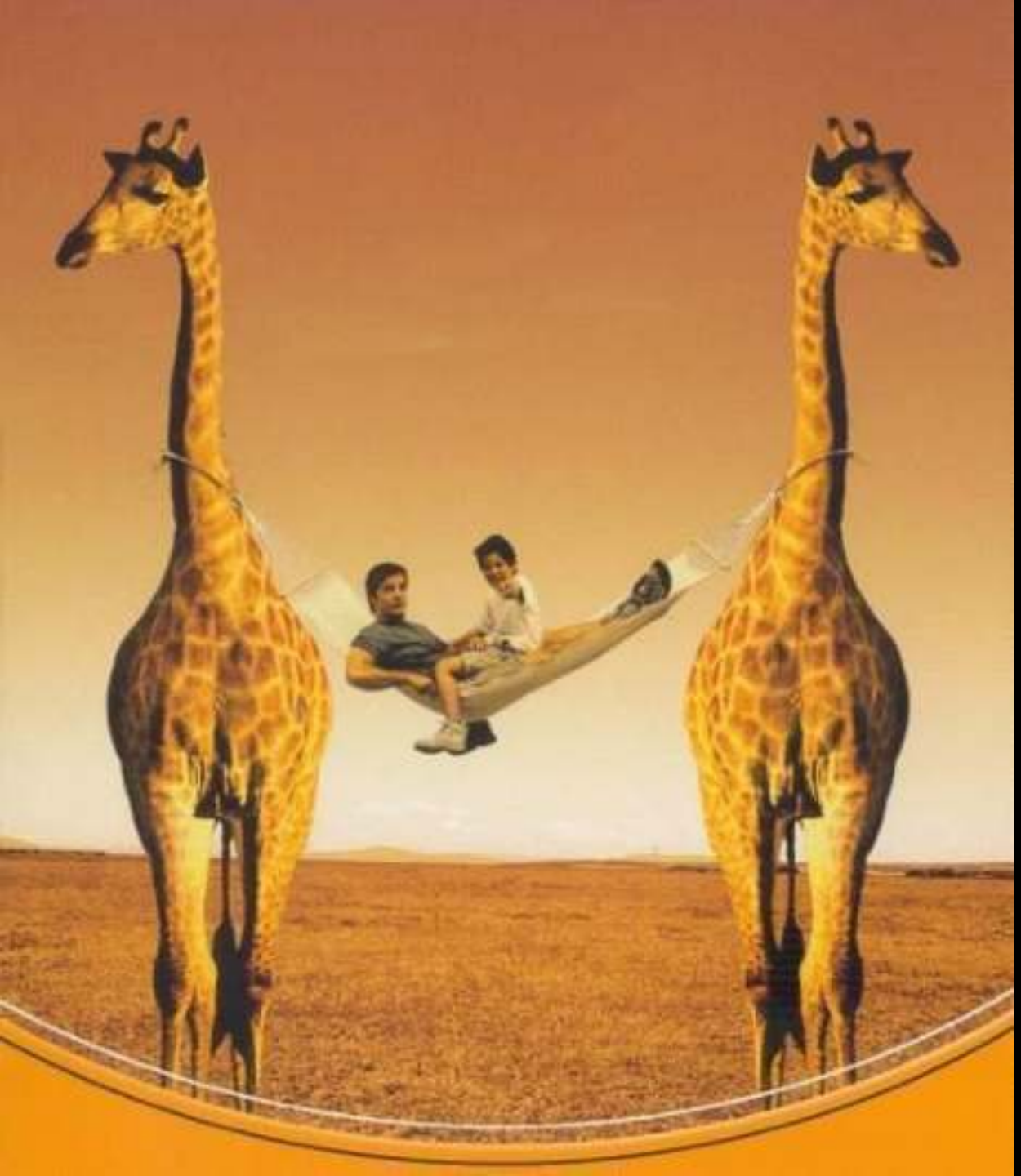
O médico é um céptico profissional

J Nina. 2024.
***adaptado de* S Novella. 2018**
& ARR Feragen. 2017.


RANGER DIARIES.COM
WILDLIFE PHOTOGRAPHY

A vida é boa…

Thomas D Mangelsen / Comedy Wildlife Photo Awards 2019



A vida é boa…

from: evanson.org.uk