Curriculum Vitae

Name : Djoni Djunaedi
Place / Date of Birth : Mojokerto, January 7, 1945

	Education	Periods
1.	M.D., General, Faculty of Medicine Airlangga University, Surabaya	1971
2.	SP1, Internist, Faculty of Medicine Padjajaran University, B&ung	1983
3.	SP2, Consultant in Tropics & Infectious Diseases (KPTI), Jakarta	1996
4.	Ph.D., Airlangga University, Surabaya	2004
5.	Professor, Full, Faculty of Medicine Muhammadiyah University, Malang	2007 – current

	Position	Periods
1.	Researcher of Tropical Infectious Disease, PETRI Malang	2005 – current
2.	Professor of Internal Medicine, Faculty of Medicine Muhammadiyah University, Malang	2007 – current
3.	Assessor – NIRA 0812743026001747	2008 – current
4.	Lecturer of Postgraduate Studies (SP2) in Tropical & Infectious Disease, Faculty of Medicine Brawijaya University, Malang	2009 – current
5.	Fellow of the Indonesian Society of Internal Medicine (FINASIM)	2009 – current
6.	Director of the Muhammadiyah University Hospital, Malang	2014 - current

All about Vaccination

Djoni Djunaedi
FK UMM Malang

Presented in HOGSI
Update Plasma Konvalesen dan vaksin COVID19
Zoominar sesi 70

FOKUS

NEGERI SARANG PENYAKIT

APA yang salah di negeri ini? Beragam penyakit kerap bermunculan. Parahnya, hampir sebagian besar penyakit yang pernah mewabah di negeri ini berulang-ulang terjadi dengan jumlah penderita yang terus meningkat dari masa ke masa. Berikut beberapa jenis penyakit yang sempat menghebohkan kehidupan masyarakat.

DEMAM BERDARAH

Penyakit demam berdarah dengue (DBD) pertama kali ditemukan di Manila, Filipina, pada tahun 1953. Di Indonesia, wabah penyakit yang ditularkan lewat gigitan nyamuk *Aedes Aegypti* ini pertama kali dilaporkan terjadi di Surabaya dan Jakarta p... meninggal du... kasus yang m... meninggal. Peny... siklus lima tahur... pada tahun 199... penderita seban... mengakibatkan ... Wabah di tahun 2004 kali ini diperkirakan merupakan siklus lima tahunan DBD. Data Departemen Kesehatan (Depkes) menyebutkan, pada tahun 1999 terjadi 21.134 kasus, tahu... 33.443 kasus, tahun 2001 terja... 40.377 kas... kasus denga... orang. Sampai 24 Februari 2004 korban tewas di Indonesia telah mencapai 247 orang dengan jumlah penderita sebanyak 12.294 orang.

MUNTABER

Wabah penyakit muntah berak (muntaber) yang ...akteri melanda Indonesia pada tahun 1976 dan mengakibatkasn sekitar 360 orang meninggal dunia. Ini terjadi di Jawa Barat dan Kalimantan Selatan. Sebelumnya, 136 orang meninggal karena terserang muntaber di Pontianak dan Palembang. Pada tahun 1975 sebanyak 120 orang tewas terkena

KUSTA

...penjajahan Belanda, kusta sudah menjadi penyakit rakyat. Pengasingan tanpa paksa bagi penderita kusta sudah dimulai pada tahun 1665 dengan didirikannya tempat penampungan (leproseri) di Kepulauan Seribu. Tahun 1940 di Indonesia, tercatat sebanyak 1.955 orang menderita kusta. Selama kurun

...lan tahun 1948 yang melanda ...wesi dan

CACAR

...car termasuk golongan penyakit menular. Cacar mewabah di Indonesia pada

kasus. Penderita cacar terak... ditemukan di Kabupaten Ta... Januari 1972. Selanjutnya I... dinyatakan bebas cacar oleh ... tanggal 25 April 1974.

DEMAM CHIKUNGUNYA

...li dilaporkan di Tanzania pada tahun 1952, kemudian ...ar ke dunia. Penyakit yang gejalanya ...engan penyakit demam berdarah ini ...an oleh nyamuk *Aedes Aegepty*, yang ...abkan penderitanya mengalami

Jember, Cirebon, Lombok Tengah dan Bantul pada tahun 2003. Jum... chikungunya yang terjadi sepanja... 2001-2003 mencapai 3.918 kasus kematian.

ANTHRAX

...penyakit menular ... disebabkan oleh bakteri dan dapa... ...aupun manusia (zoonosi... sejenis b... anthrax ... 99 di Karesidenan Jepara, Jateng, yang menyerang sebanyak 311 sapi, 207 di antaranya mati. Menurut laporan

TUBERKULOSIS (TBC)

TBC adalah penyakit menular menahun yang menyerang paru-paru, disebabkan oleh kuman

PENYAKIT PES (SAMPAR)

Penyakit pes mulai berjangkit di Indonesia pada

HIV/AIDS

AIDS atau *acquired immune deficiency syndrome* adalah kumpulan gejala penurunan kekebalan tubuh manusia terhadap penyakit. Penyebab sindrom ini adalah HIV atau *human immunodeficiency virus*. Kasus AIDS pertama kali ditemukan di Amerika Serikat tahun 1981. Sindrom ini kemudian menyebar ke hampir seluruh dunia dan menimbulkan pandemi. AIDS pertama mengetuk pintu Indonesia di Bali pada bulan April 1987. Saat itu ditemukan dua penderita dan empat orang yang seropositif HIV. Seorang wisatawan asing meninggal di Pulau Dewata itu. Kurva pengidap AIDS/HIV ini kemudian pada tahun-tahun berikutnya menujukkan perkembangan. Tahun 1991 ditemukan 9 kasus AIDS dan 9 HIV positif. Tahun 1993 ditemukan 49 kasus AIDS dan 144 kasus HIV positif (seluruhnya berjumlah 193 orang) di 12 provinsi. Pada tahun 2000 dilaporkan sudah mencapai 1.559 kasus dan kembali bertambah menjadi 2.575 kasus pada tahun 2001, 635 orang di antaranya positif AIDS. Jumlah kumulatif pengidap HIV/AIDS sepanjang tahun 1987-2003 sebanyak 4.091 kasus, dengan perincian sebanyak 2.720 adalah kasus HIV dan 1.371 adalah pengidap AIDS.

...1986 yang menempatkan penyakit ini pada urutan keempat. Hasil survei Depkes 2001 memperlihatkan, di Indonesia setiap tahunnya

RABIES

...nyakit anjing gila infeksi akut pada susunan s... disebabkan oleh virus rabies

...1998 terjadi 14.885 kasus ya... 84 orang. Korban terbesar te... NTT, sebanyak 166 kasus dan mengakibatkan belasan orang meninggal. Tahun 1999 terjadi 12.186 kasus, 144 di antaranya meninggal dunia. Tahun 2000 terjadi 12.581 kasus yang mengakibatkan 120 orang meninggal dengan penderita rabies terbesar di NTT. Pada tahun 2003 rabies melanda Maluku dan sekitarnya yang mengakibatkan 1.050 orang terkena gigitan anjing dan 20 orang meninggal dunia.

MALARIA

...ata Depkes 2001, di Indonesia setiap tahunnya terdapat sekitar 15 juta

19,7 per... dan 10,2...

CAMP...

...yang dit... selaput ... tubuh. I... hidung, ... yang te... merupak... yang di... menewa... Data D... 42 kasu... kasus. ... Banjarn... dilapork... menimb...

DIARE

Sampai ... kematia... pendudu... diare. P... diare de... Selama ... pernah ... yang pe... pada ta... Sulawe... menjadi ... itu Depk... ember... ...asus d... ...997 te... orang d... terdapa... orang m... terjadi 5... mening...

ISPA

... infeksi ... merupa... pada se... urutan ... pember...

Introduction

- The word “vaccine” originates from the Latin Variolae vaccinae (cowpox)
- Edward Jenner demonstrated in 1798 prevent smallpox in humans.
- Today the term ‘vaccine’ applies to all biological preparations
- Enhance immunity against disease & either prevent (prophylactic vaccines)
- In some cases, treat disease (therapeutic vaccines).
- Vaccines are administered in liquid form, either by injection, by oral, or by intranasal routes.

Baxby D (January 1999).
http://phrma-docs.phrma.org/files/dmfile/Vaccines_ReportLong_2017.pdf

Characteristics of vaccines

- Effective protection againts the pathogen
- Must occur without significant danger of actually causing the disease
- The protection that is provided must be long lasting
- The vaccine must induce the immune responses (e.g CTLs)
- Neutralizing antibodies must be stimulated in order to minimize reinfection
- The vaccine must be economically feasible to produce
- The vaccine must be suitable for storage, transport, and use.

Doan T et al, (2013)

Examples of Vaccines by Type

Type of vaccine	Examples
Live-attenuated	Measles, Mumps, Rubella, Varicella zoster
Inactivated	Hepatitis A, Influenza, Pneumococcal polysaccharide
	Sinovac
Recombinant sub-unit	Hepatitis B
Toxoid	Tetanus, Diphtheria
Conjugate polysaccharide-protein	Pneumococcal, meningococcal, *Haemophlius influenzea* type b (Hib)

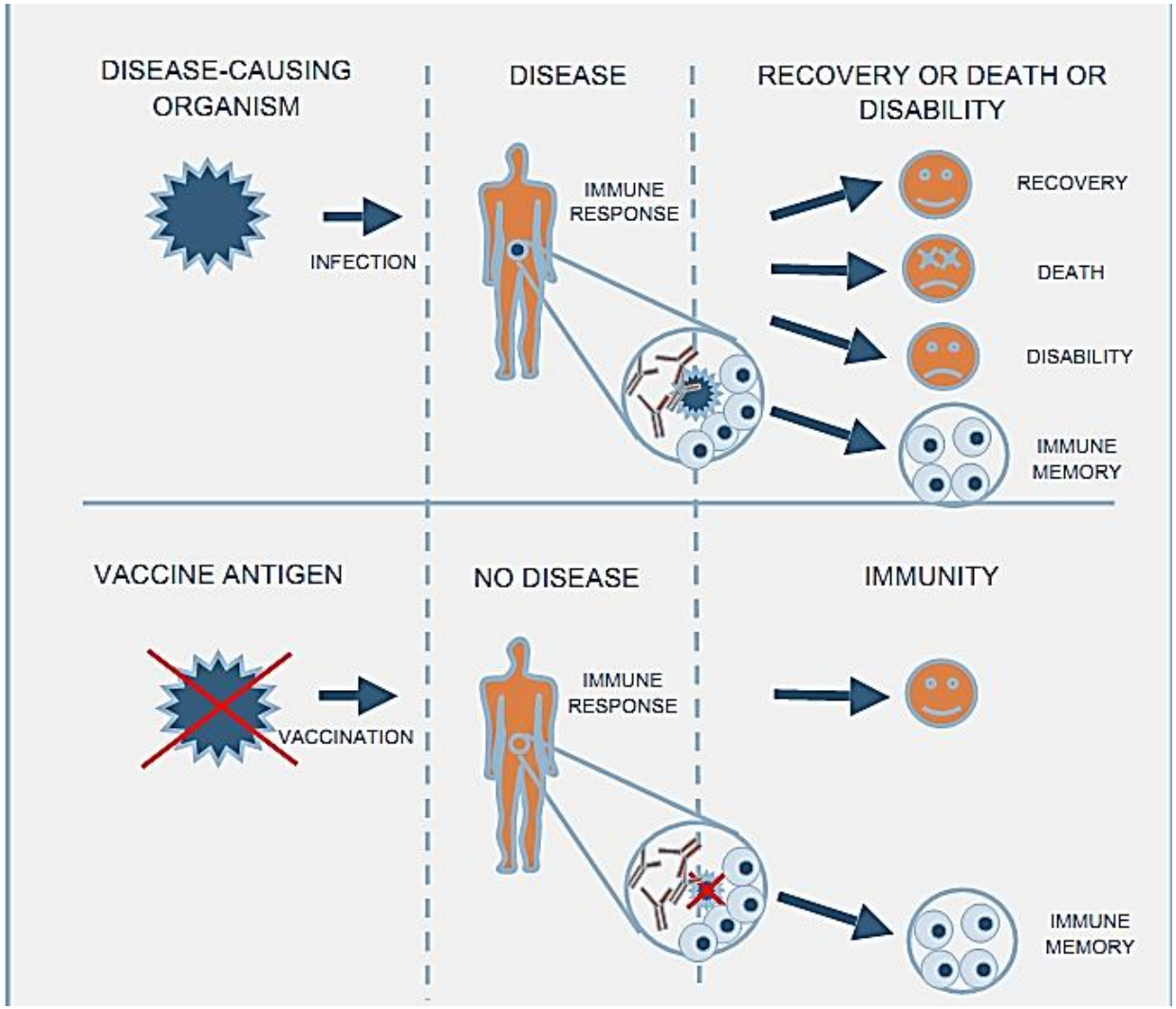
http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf
U.S. NIH, National Institute of Allergy & Infectious Diseases (NIAID). Vaccine Types. https://www.niaid.nih.gov/research/vaccine-types.
http://phrma-docs.phrma.org/files/dmfile/Vaccines_ReportLong_2017.pdf

Vaccines composition

- Vaccines are composed → entire disease-causing microorganism or its components.
- From living organisms that have been weakened, under sub-optimal conditions (attenuation)
- Or from genetic modification→ effect of reducing their ability to cause disease
- From whole organisms →inactivated by chemical, thermal or other means
- From components of the disease-causing organism→ specific proteins & polysaccharides, or nucleic acids
- From inactivated toxins (toxin-producing bacteria)
- From the linkage (conjugation) of polysaccharides to proteins (this increases the effectiveness of polysaccharide vaccines in young children)

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

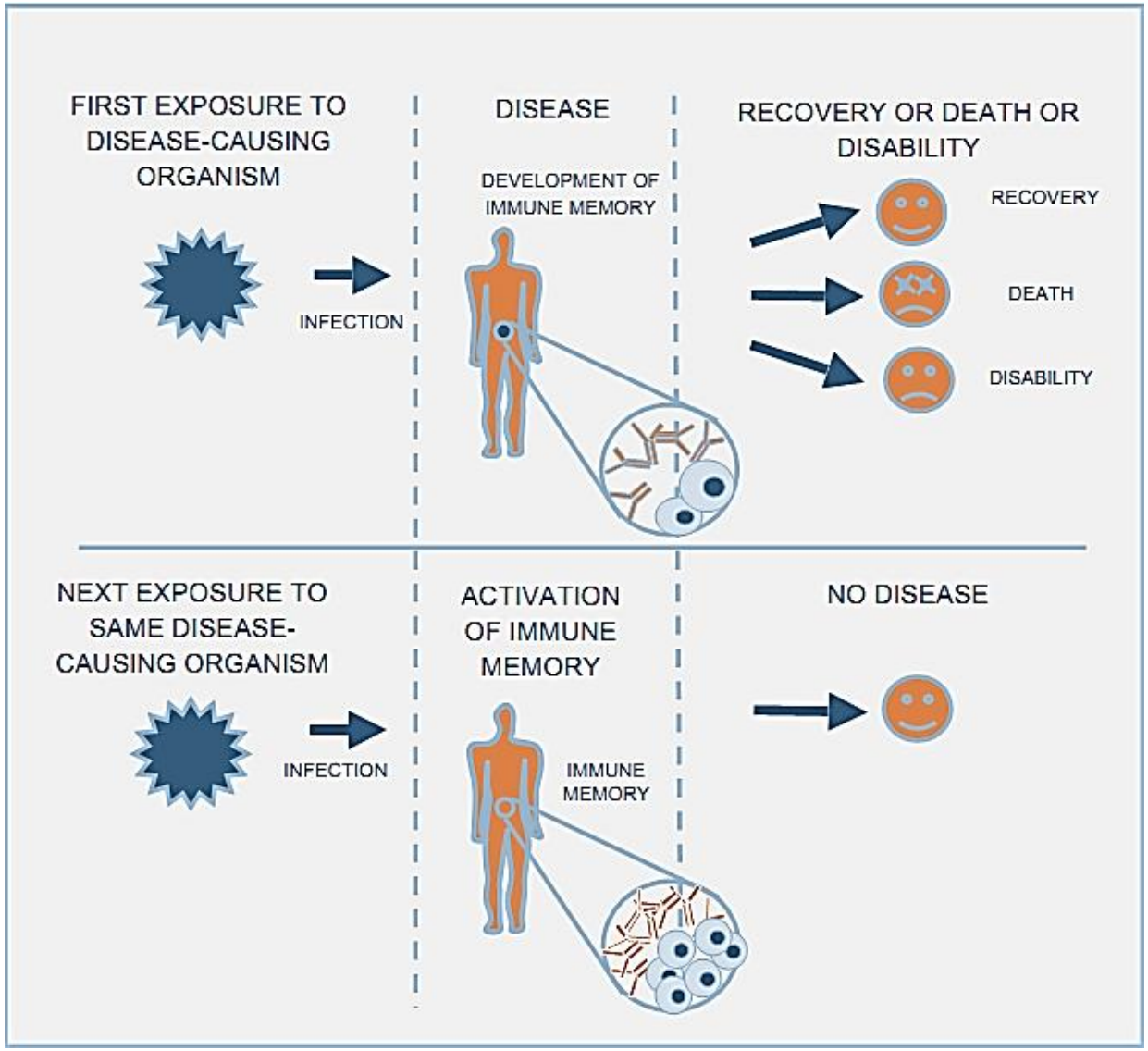
How do vaccines work?



comparison of the immune response to a diseases-causing organism & to a vaccine

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

Cont……



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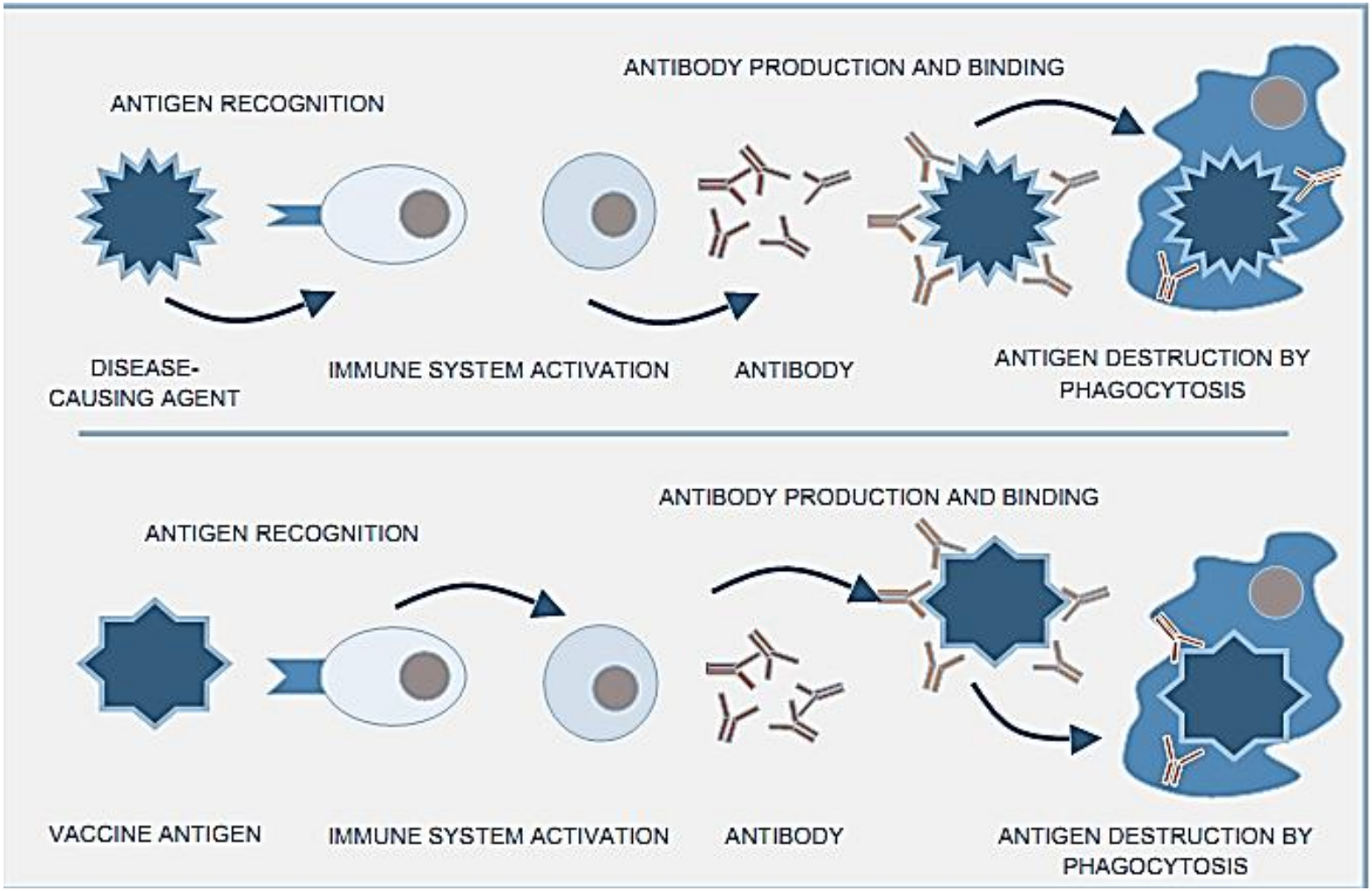
Antibody Destruction of Antigen



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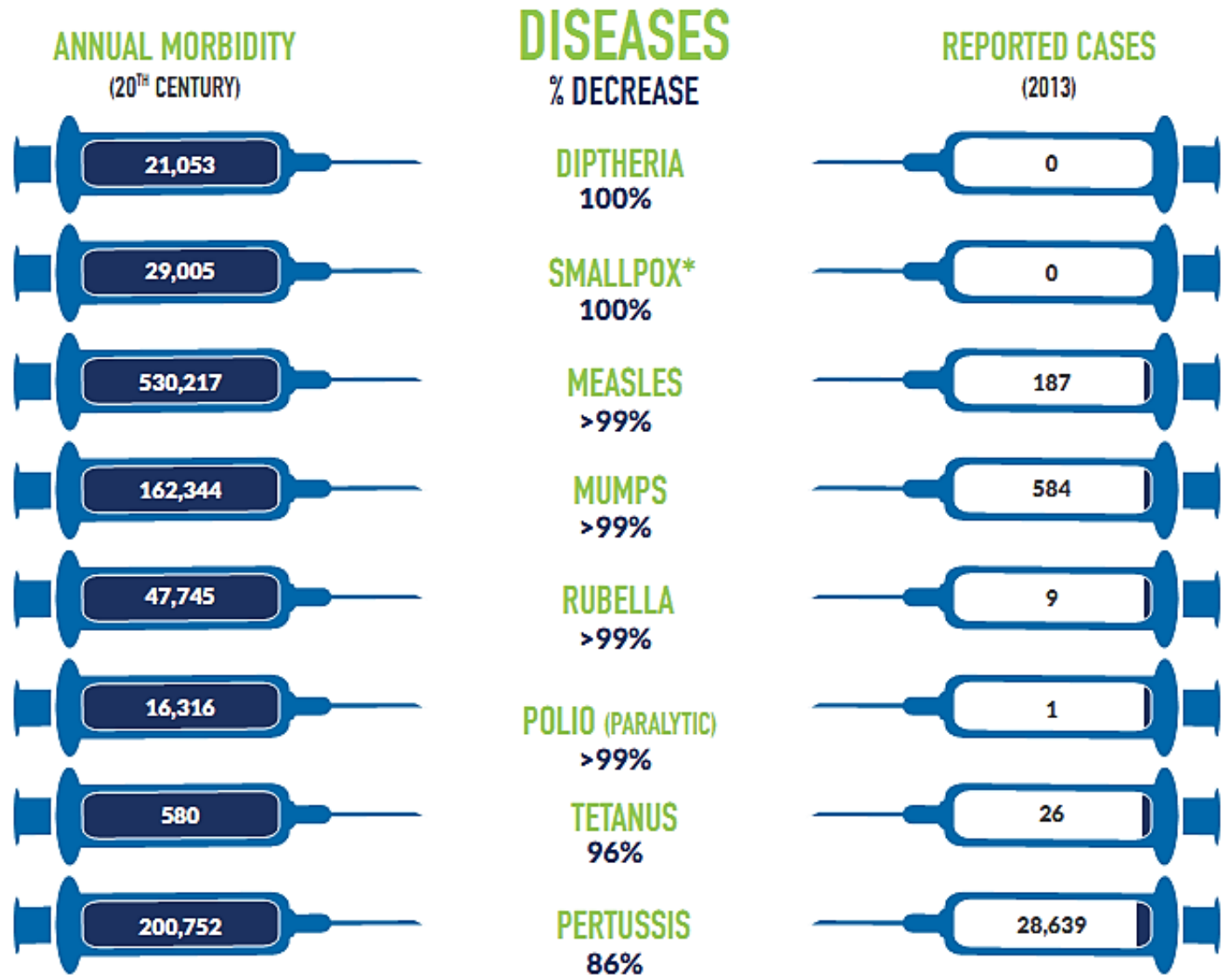
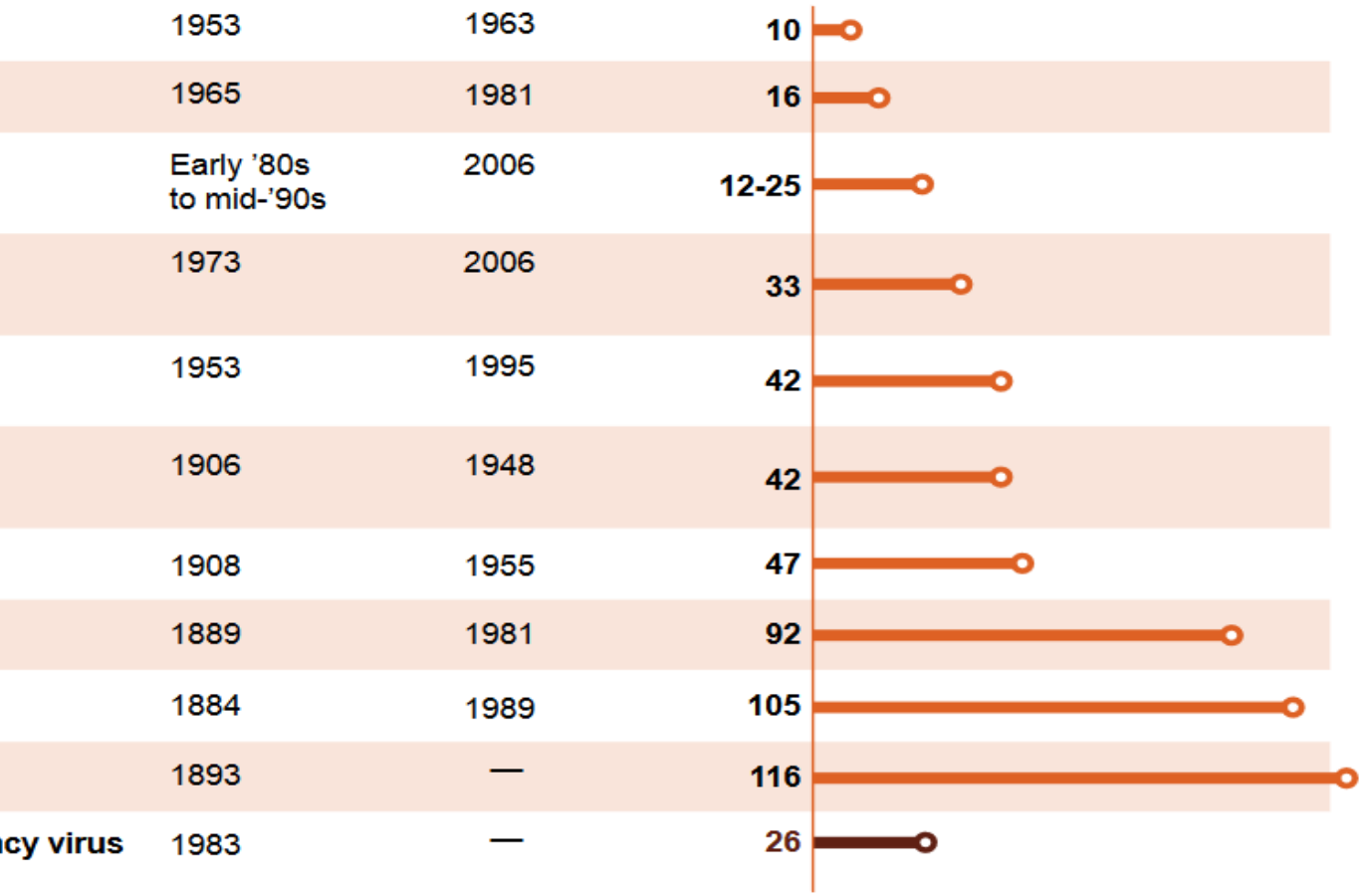
Vaccines: transforming public health in the united states



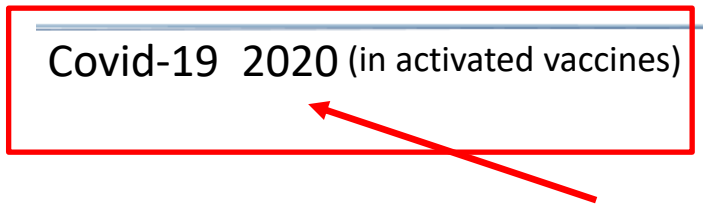
http://phrma-docs.phrma.org/files/dmfile/Vaccines_ReportLong_2017.pdf

Persevere: Vaccines can take decades to develop

INFECTIOUS AGENT (Disease)	AGENT LINKED TO DISEASE IN …	VACCINE LICENSED IN U.S. IN …	YEARS ELAPSED
Measles	1953	1963	10
Hepatitis B	1965	1981	16
Human papilloma virus (cervical cancer)	Early '80s to mid-'90s	2006	12-25
Rotavirus (diarrheal disease)	1973	2006	33
Varicella zoster (chickenpox)	1953	1995	42
Pertussis (whooping cough)	1906	1948	42
Polio	1908	1955	47
Haemophilus influenza	1889	1981	92
Typhoid	1884	1989	105
Malaria	1893	—	116
Human immunodeficiency virus (HIV/AIDS)	1983	—	26

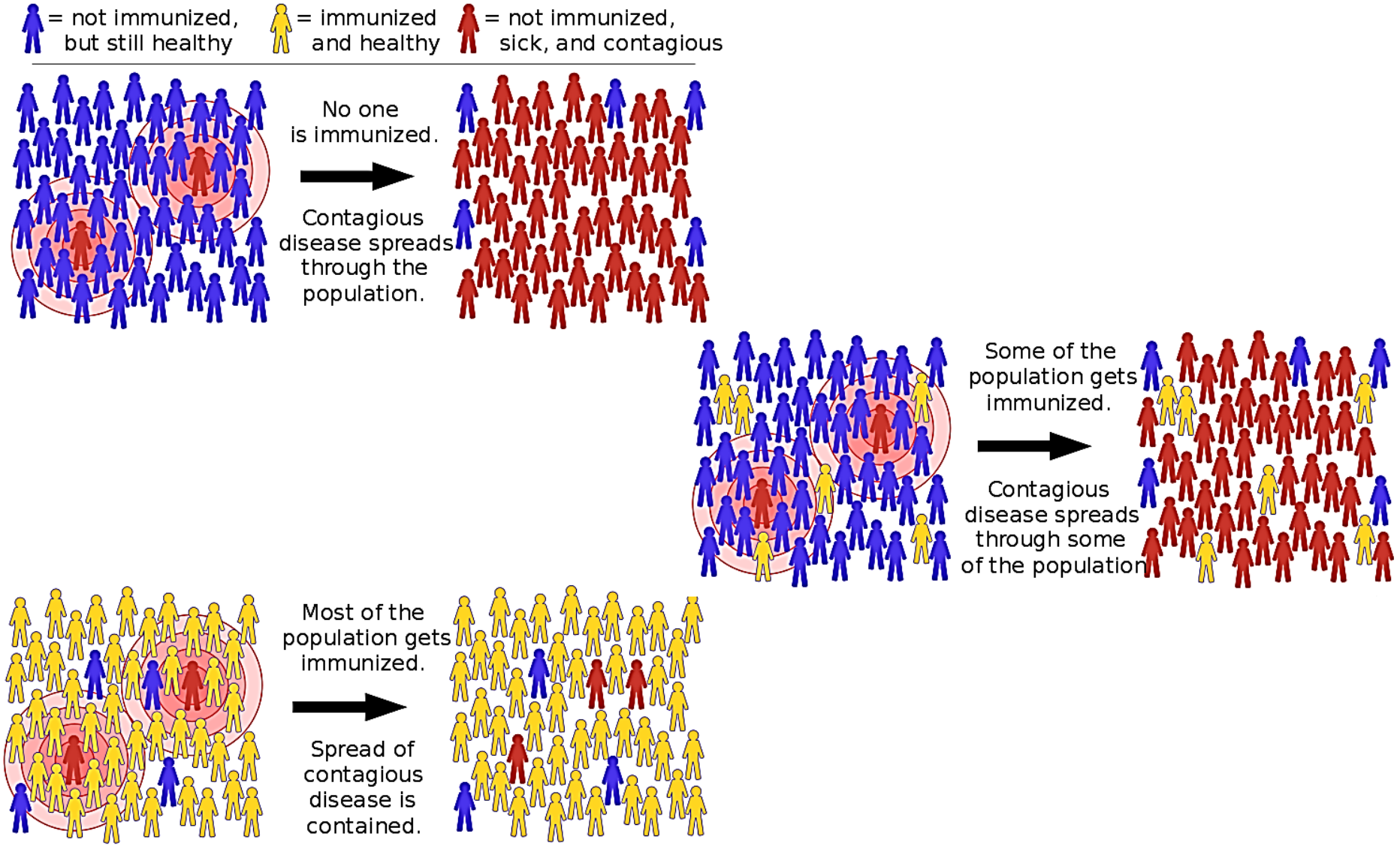


Covid-19 2020 (in activated vaccines)



Herd immunity

(herd effect, community immunity, population immunity, or **social immunity)**



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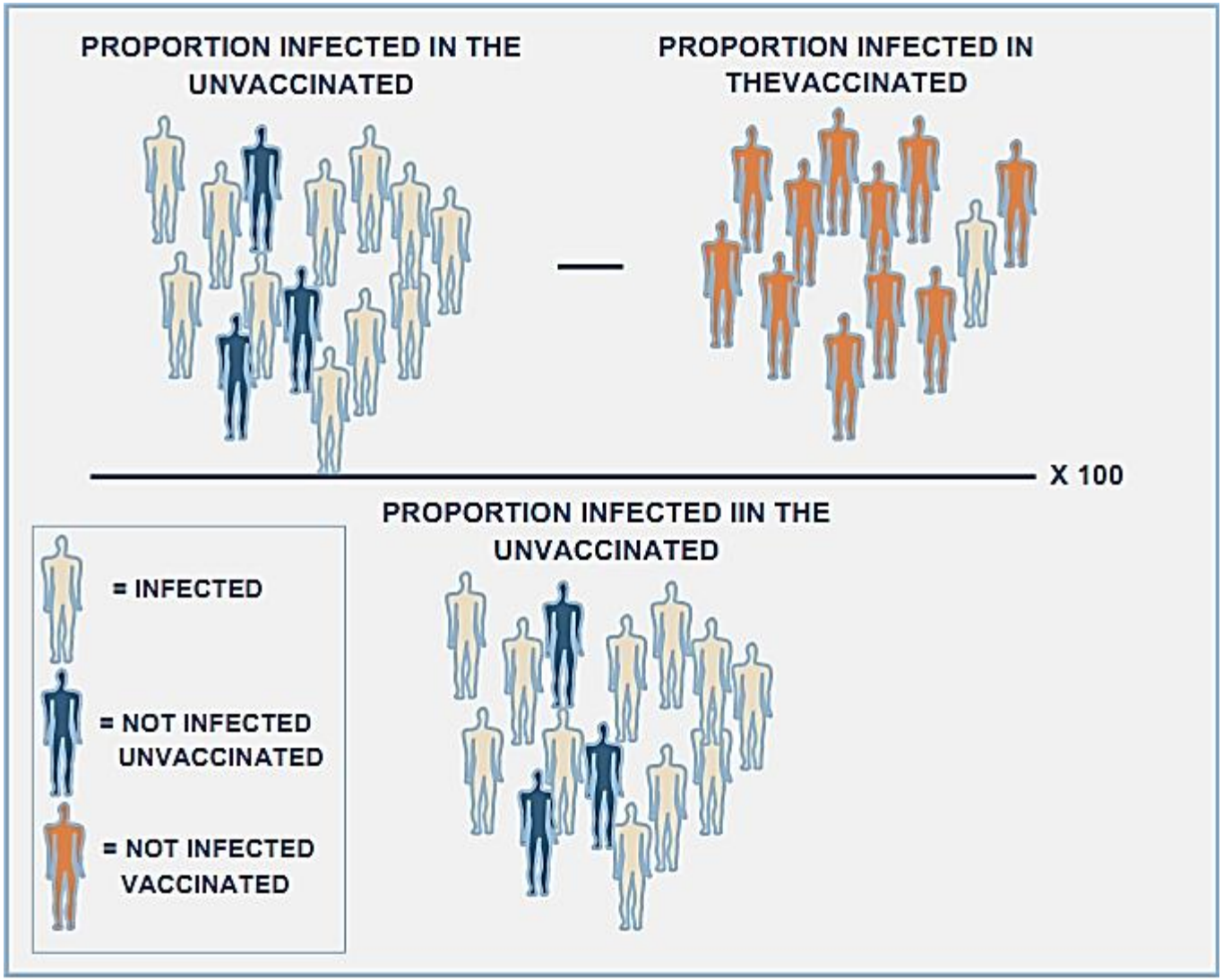
Vaccine Efficacy (VE)



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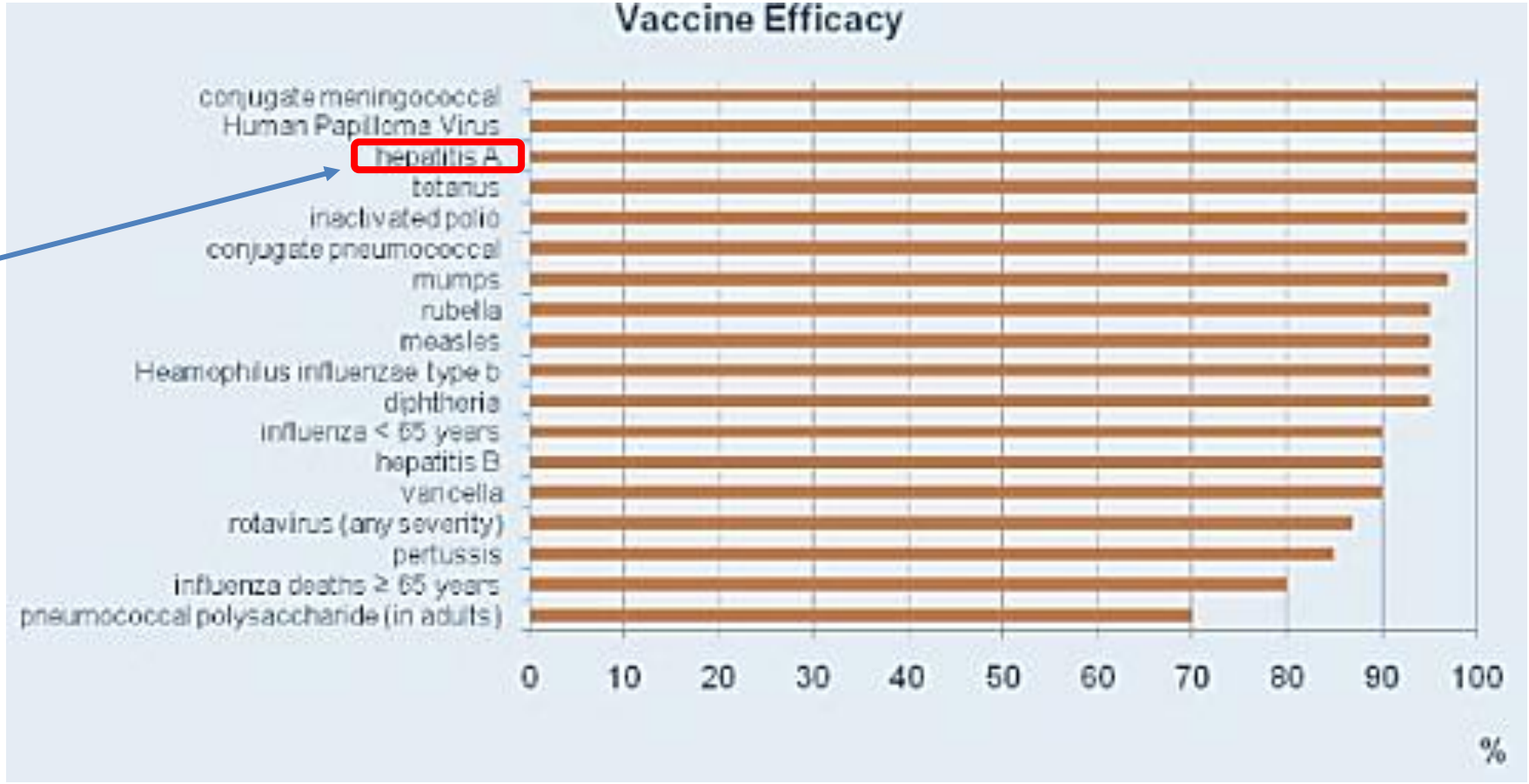
Observed efficacies of some vaccines (maximum values are shown for ranges)



http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

Science

REPORTS

Cite as: A. Wajnberg *et al.*, *Science* 10.1126/science.abd7728 (2020).

Robust neutralizing antibodies to SARS-CoV-2 infection persist for months

Ania Wajnberg[1]*, Fatima Amanat[2,3], Adolfo Firpo[4], Deena R. Altman[5], Mark J. Bailey[1], Mayce Mansour[1], Meagan McMahon[2], Philip Meade[2,3], Damodara Rao Mendu[4], Kimberly Muellers[1], Daniel Stadlbauer[2], Kimberly Stone[1], Shirin Strohmeier[2], Viviana Simon[2], Judith Aberg[5], David L. Reich[6], Florian Krammer[2]*, Carlos Cordon-Cardo[4]*

[1]Department of General Internal Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA. [2]Department of Microbiology, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA. [3]Graduate School of Biomedical Sciences, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA. [4]Clinical Microbiology Laboratory, Department of Pathology, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA. [5]Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA. [6]Department of Anesthesiology, Perioperative and Pain Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA.

*Corresponding author. Email: ania.wajnberg@mountsinai.org (A.W.); florian.krammer@mssm.edu (F.K.); carlos.cordon-cardo@mssm.edu (C.C.-C.)

SARS-CoV-2 has caused a global pandemic with millions infected and numerous fatalities. Questions regarding the robustness, functionality, and longevity of the antibody response to the virus remain unanswered. Here we report that the vast majority of infected individuals with mild-to-moderate COVID-19 experience robust IgG antibody responses against the viral spike protein, based on a dataset of 30,082 individuals screened at Mount Sinai Health System in New York City. We also show that titers are relatively stable for at least a period approximating 5 months and that anti-spike binding titers significantly correlate with neutralization of authentic SARS-CoV-2. Our data suggests that more than 90% of seroconverters make detectible neutralizing antibody responses. These titers remain relatively stable for several months after infection.

CS Dipindai dengan CamScanner

How safe are vaccines?

- Immune reactions that they induce can cause some discomfort
- The vast majority of adverse events are minor & transi
- These are typically pain injection site, or mild fever
- More serious adverse events occur rarely → risk cannot be accurately assessed
- Some serious adverse events may be so rare → once in millions of vaccine doses delivered
- Some individuals may be sensitive to some components or elements in some vaccines, such as eggs, antibiotics, gelatin
- It is believed that rare & very rare adverse events are associated with individual differences in immune responses
- Furthermore, a 10–11 year study of 657,461 children found that the MMR vaccine does not cause **autism** & actually reduced the risk of autism by 7 percent.
- Covid-19 Still developed

Disease Control & Prevention (2018)
March 5, Reuters Updated; 2019 (2019-03-05). "Another study, this one of 657k kids, finds MMR vaccine doesn't cause autism | Montreal Gazette". Retrieved 2019-03-13.

Common reactions to vaccines routinely used in several industrialized countries

Vaccine	Pain, swelling, redness	Fever > 38°C	Systemic symptoms
BCG (against tuberculosis)	90-95%		
Haemophilus influenzae type b	5-15%	2-10%	
Hepatitis B	adults 15% children 5%	1-6%	
Measles / Measles, Mumps, Rubella / Measles, Rubella	~10%	5-15%	5% rash
Oral polio	very rare	< 1%	<1% diarrhea, headache, muscle pains
Tetanus / Tetanus, diphtheria	~10% 50-85% booster doses	~10%	~25% irritability and malaise
Pertussis (whole cell)	up to 50%	up to 50%	up to 55% irritability and malaise

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

Classification of adverse events following immunization (AEFI)

Classification	Frequency
very common	> 1 / 10
common	> 1 / 100 and < 1 / 10
uncommon	> 1 / 1 000 and < 1 / 100
rare	> 1 / 10 000 and < 1 / 1 000
very rare	< 1 / 10 000

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

Innate & Adaptive Immunity

- Innate Immunity/ natural/ native immunity :
  - Essential for defending againts microbes in the first few hours or days after infection
  - Facilitate rapid responses to invading microbes
- Adaptive Immunity/ specific/ acquired immunity :
  - Develops as a response to infection & adapts to the infection
  - Recognizes & react to microbial & non-microbial substances (**antigens**)
  - Stronger & more specialized are capable of eradicating
  - Enhancing the protective mechanism of innate immunity

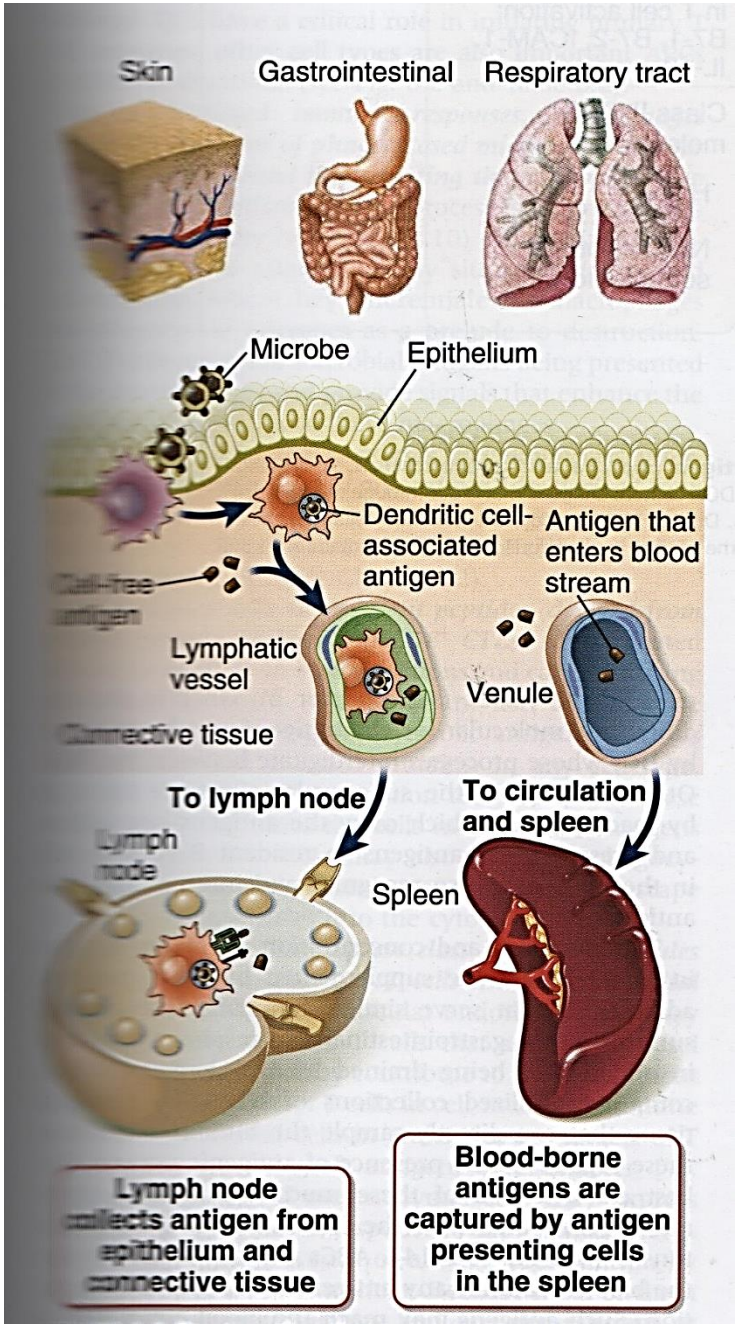
→ Making them more capable of effectively **combating microbes**

(Abbas, 2018)

- The innate immunity system :
  - ✓Maintains physical & chemical defences at epithelial barriers (skin & lining gastrointestinal & respiratory tracts → which block microbial entry)
  - ✓The two major types of protecting reactions → inflammation & antiviral defences

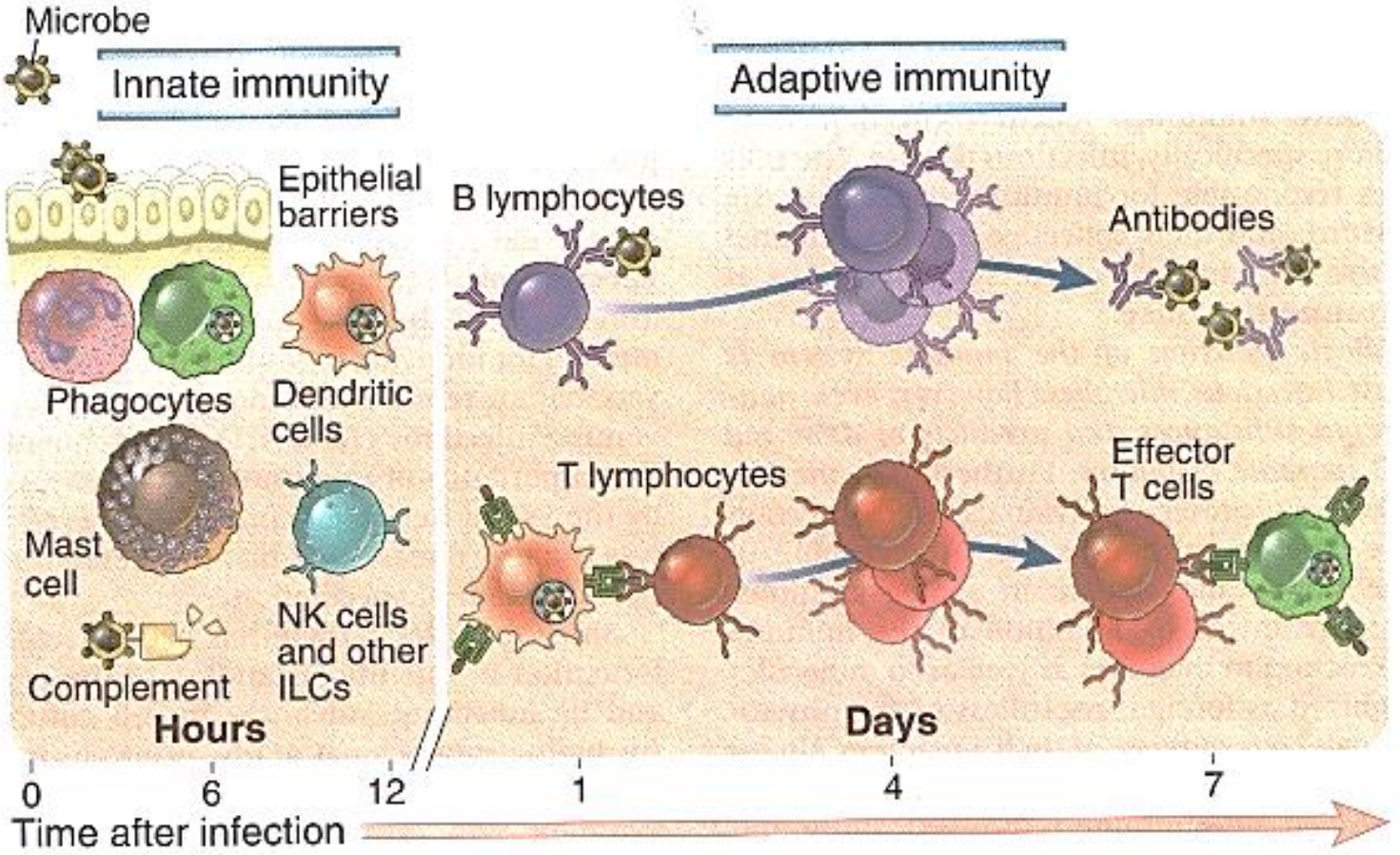
(Abbas, 2018)

Routes of antigen entry



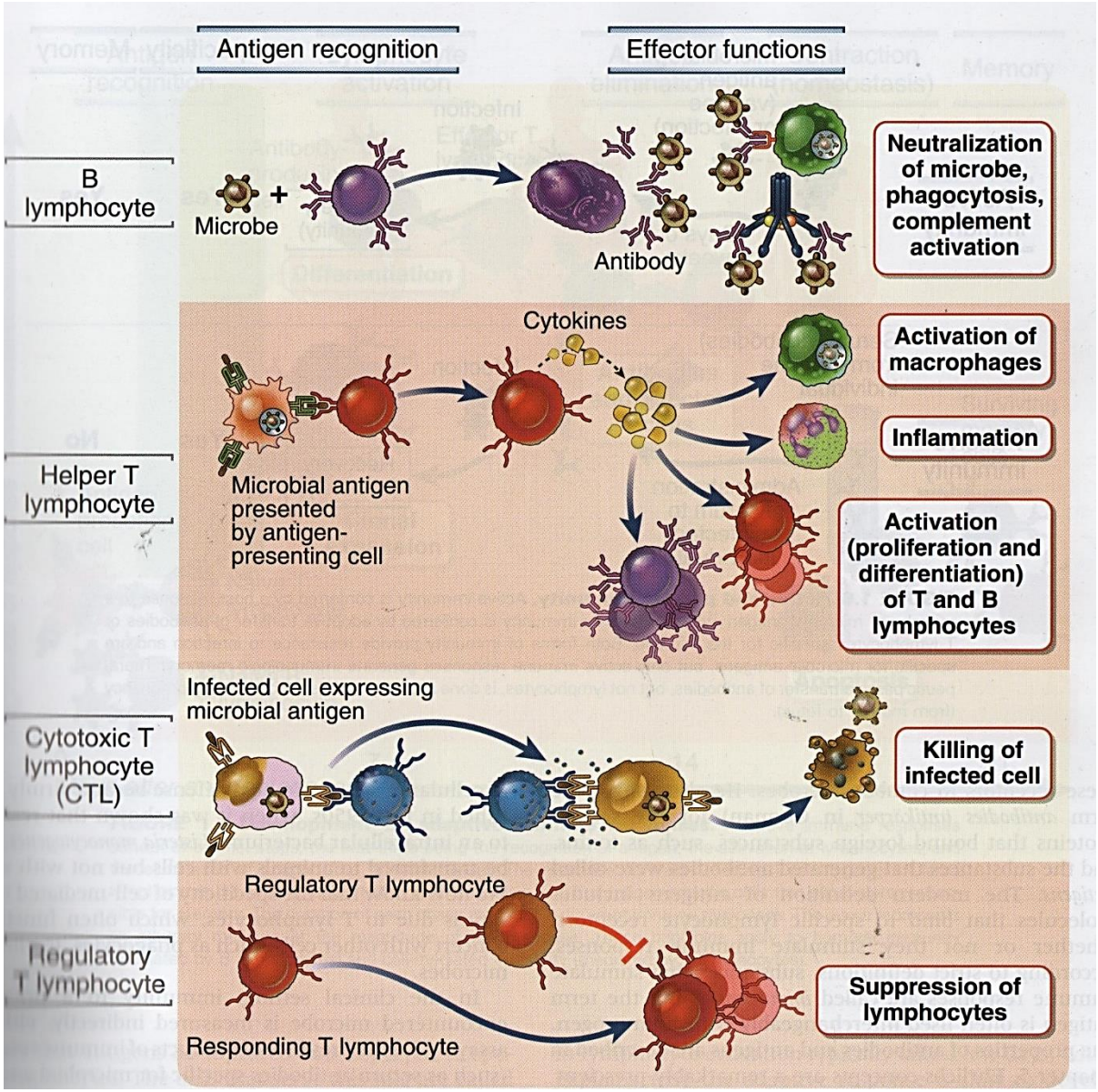
(Abbas, 2018)

Innate & Adaptive Immunity

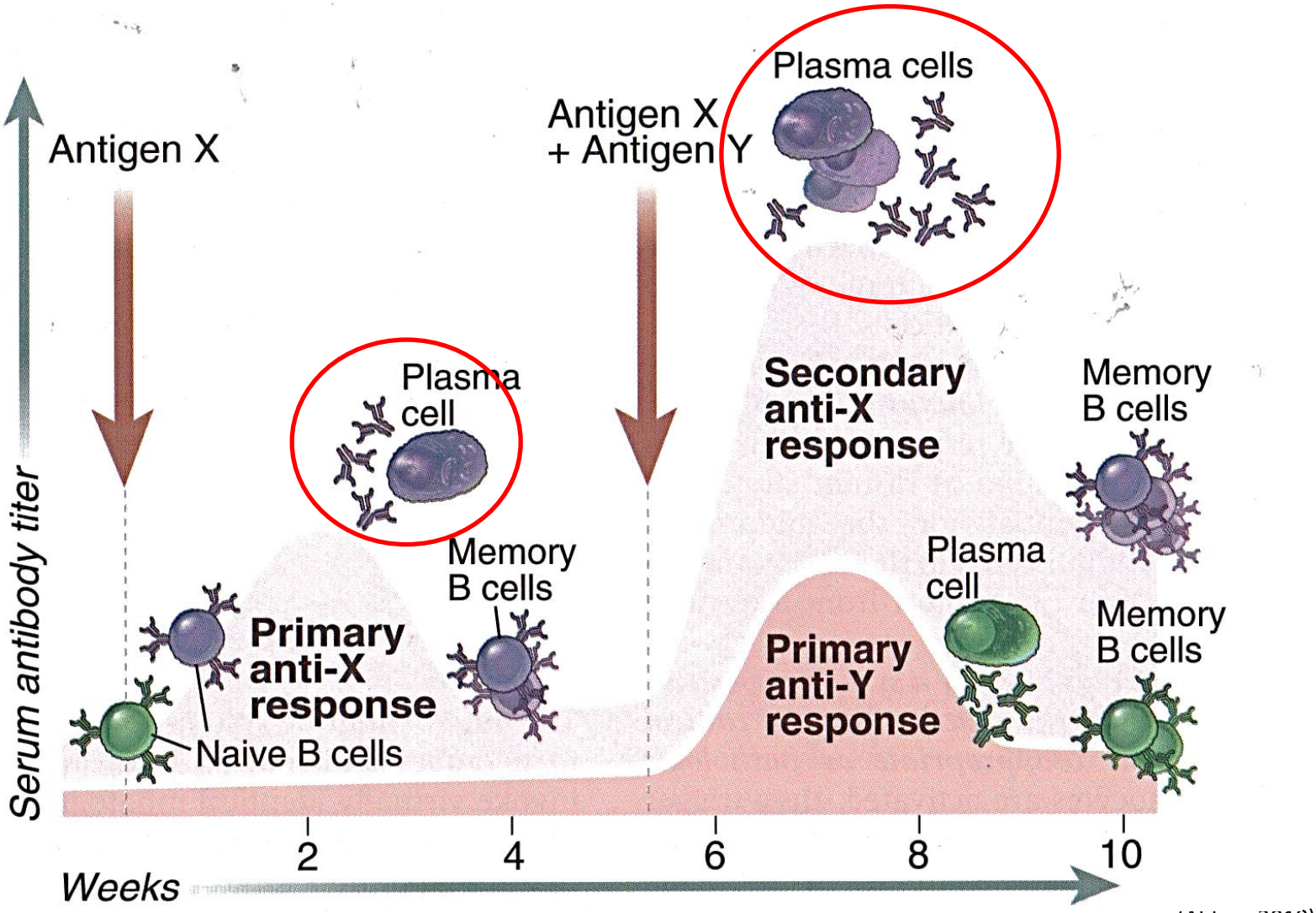


(Abbas, 2018)

Classes of lymphocytes

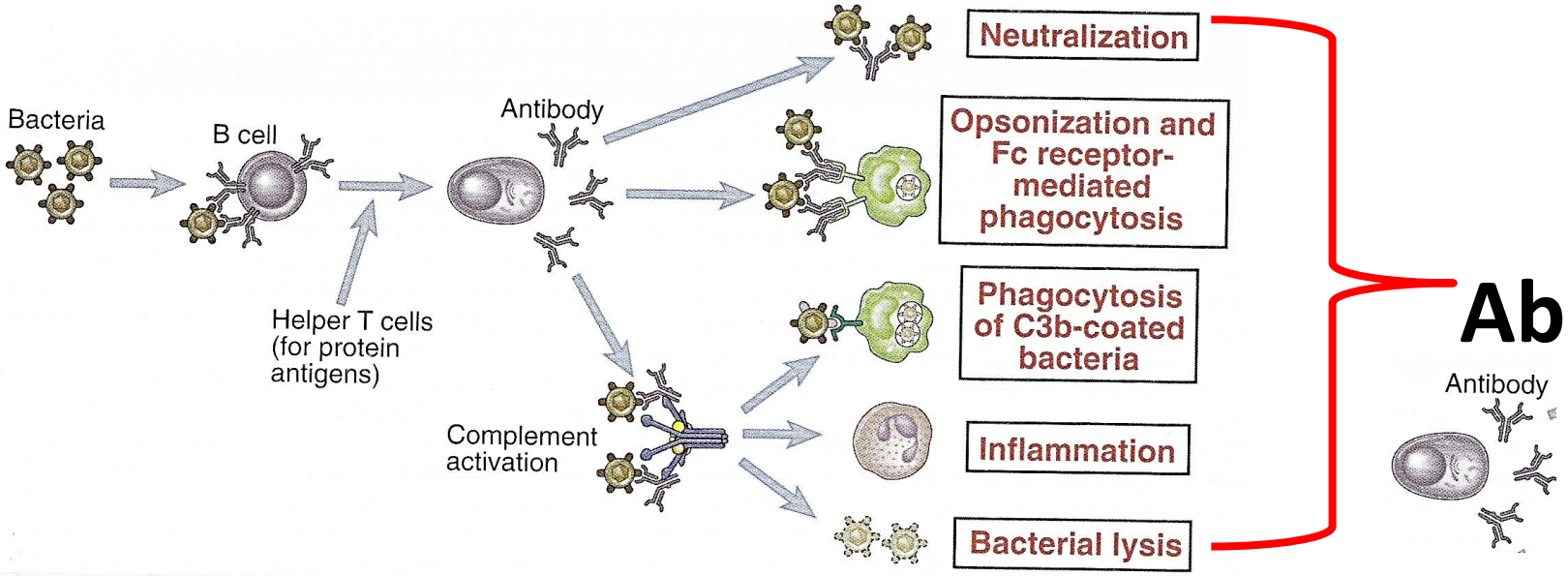


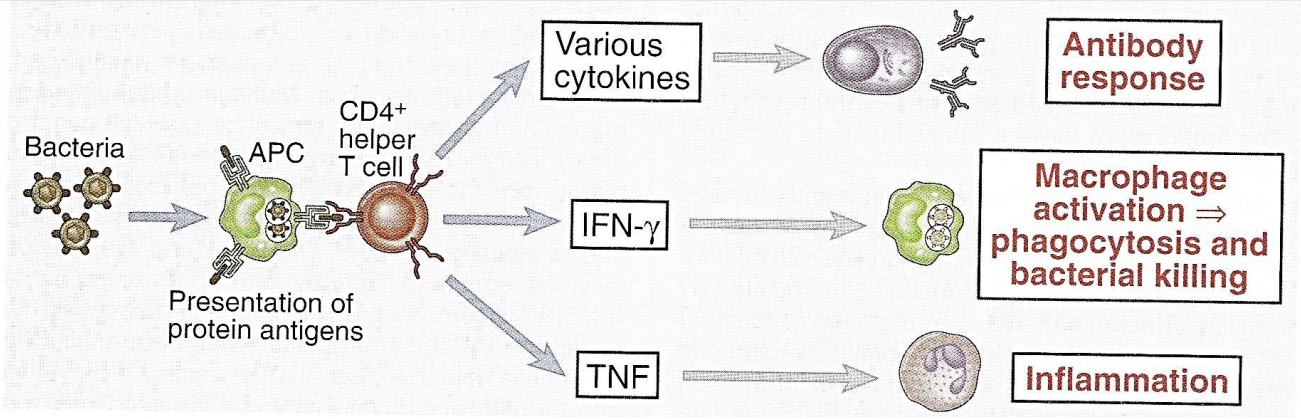
Specificity, memory, & contraction of adaptive immune responses



(Abbas, 2018)

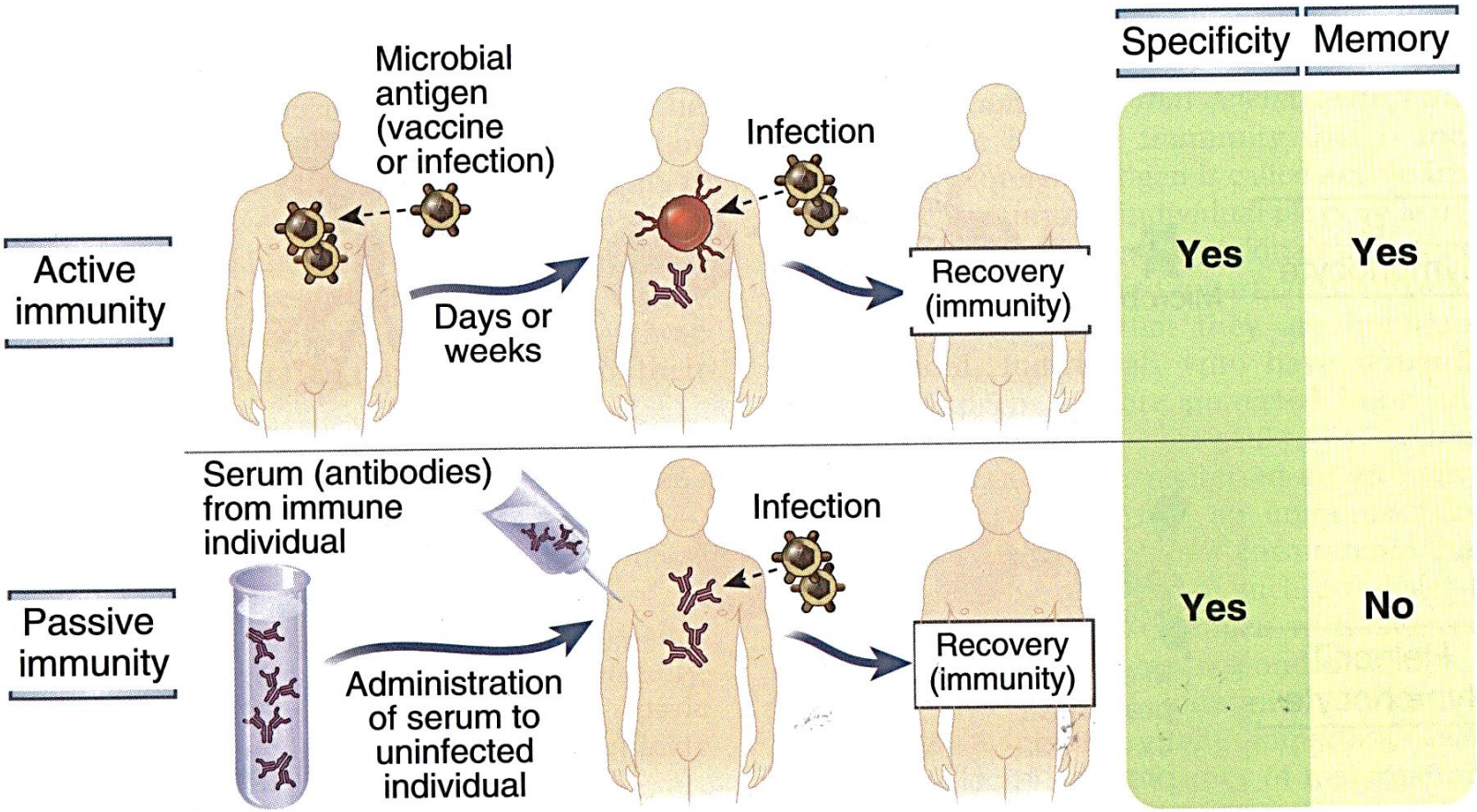
Adaptive immune responses to extracellular microbes





Adaptive immune responses to extracellular microbes, such as bacteria, & their toxins consist of antibody production & the activation of CD4+ helper T cells. Antibodies neutralize & eliminate microbes & toxins by several mechanisms. Helper T cells produce cytokines that stimulate B cell responses, macrophage activation, & inflammation.

Active & passive immunity



(Abbas, 2018)

Vaccine safety surveillance & evaluation

- Since vaccines are typically administered to healthy individuals, tolerance for adverse events is much lower
- Most governments mitigate the investigation of possible adverse events following immunization (AEFIs)
- Before a vaccine is licensed, it is carefully studied for all possible harmful effects
- Testing proceeds in a stepwise approach
- Safety is first evaluated in animals.
- If there is no evidence of harm in animals, testing can begin in a small number of humans.
- If there is no evidence of harm in humans, testing proceeds to increasing numbers of human subjects.

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

In humans, testing proceeds in three phases:

- Phase I clinicaltrials involve a few dozen
- Phase II involve 50 – hundreds
- Phase III involve thousands or tens of thousands **of subjects.**

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

Vaccine injury compensation systems

- Vaccine injury compensation systems → to rapidly award suffer injury from properly produced & administered vaccines
- Designed as no-fault systems, that do not require proof of negligence on the part of the manufacturer (e.g. from improper design)
- As such, punitive damages cannot be sought unless a manufacturer can be shown to have been grossly negligent
- In addition to providing protection from legal action against vaccine manufacturers, vaccine injury compensation systems also provide protection for healthcare providers
- In the absence of protection, healthcare providers might be unwilling to provide immunization services

http://phrma-docs.phrma.org/sites/default/files/pdf/PhRMA_Vaccine_FactBook_2013.pdf

Storing & transporting vaccines

- Once manufactured, vaccines → packaged, stored & delivered → in appropriate conditions.
- Most vaccines require a strict cold-chain to maintain their stability → under refrigeration.
- Exposure to temperatures outside → can reduce the effectiveness of the vaccine.
- Maintaining the cold-chain can be challenging in countries that lack a reliable infrastructure
- So researchers are working on vaccines that do not need to be refrigerated or can be out of refrigeration temporarily.

Kristensen , 2016; Isanaka S, et al. 2017


WE ARE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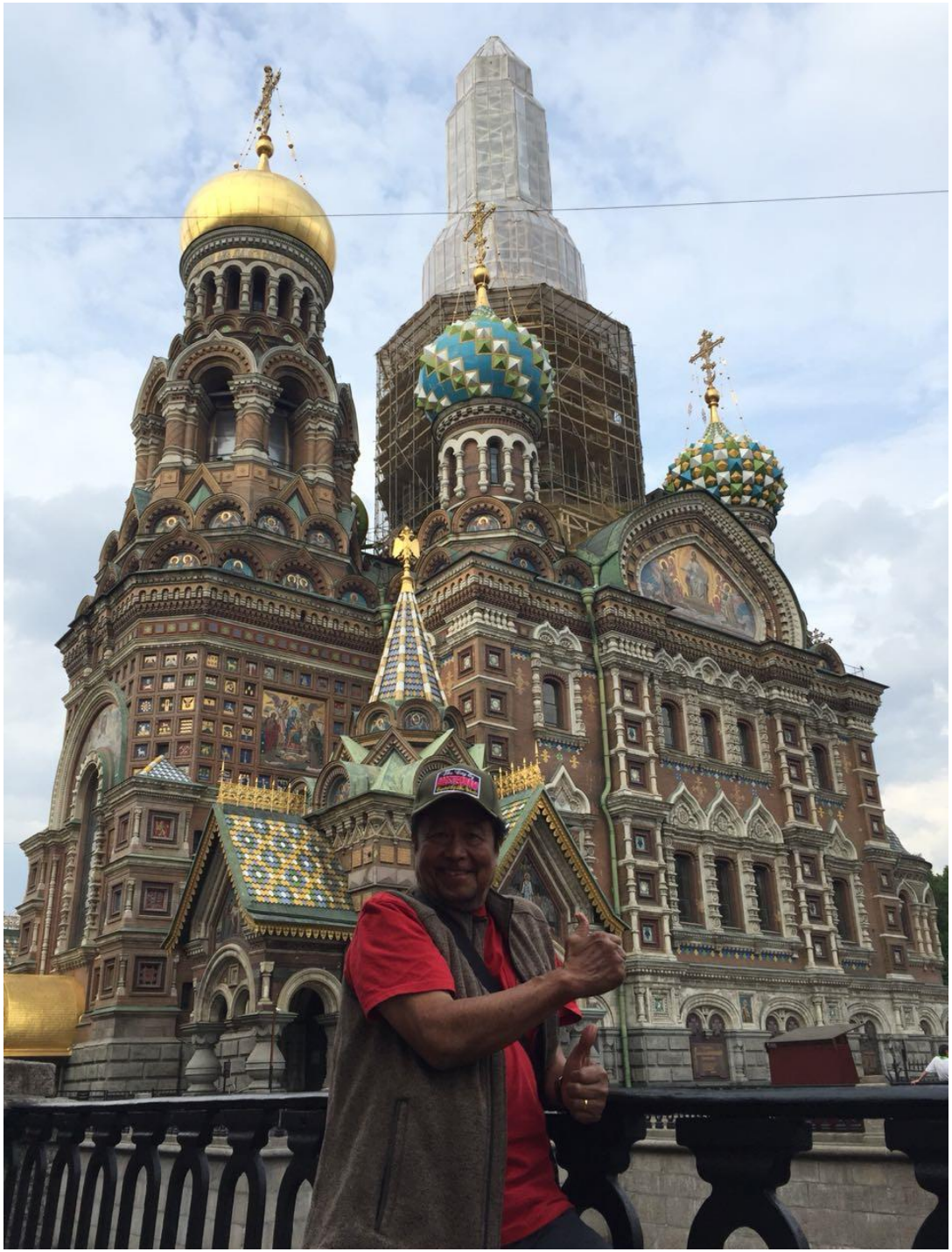

Thank You