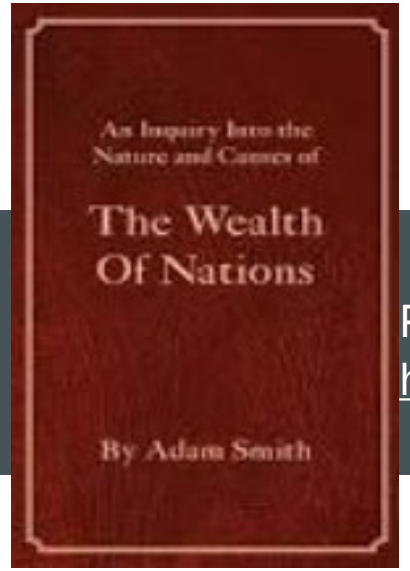
THE HEALTH OF NATIONS

Part I
https://dspace.mit.edu/handle/1721.1/145774



Part II
https://dspace.mit.edu/handle/1721.1/152921

Disclaimer: The scientific evidence presented in this talk is not the outcome of the author's research. The author has compiled publicly available published papers and facts/figures in order to support POV and the call to action.

ACKNOWLEDGEMENTS

Kathleen Hefferon, Cornell University

Anahita Dua, MGH/MGB, Harvard

Andrew Fire, Stanford University

John Carr, Cambridge University

Elliot Meyerowitz, Cal Tech

Katalin Karikó, UPenn

Sanjay Sarma, MIT

Roy Curtiss III, UF

The explicit purpose of the list on the left is to indicate beyond any doubt that the contents of this talk were subjected to quite rigorous verification with respect to the science included as evidence. The scientific rationale of the proposal advocates exploring plant-based oral vaccines (POV), a global solution for nations under economic constraints (which is about 7 billion of the world's population).

Shoumen Palit Austin Datta, Massachusetts General Hospital, Harvard Medical School & Dept of Mechanical Engineering, Massachusetts Institute of Technology

https://dspace.mit.edu/handle/1721.1/145774

https://dspace.mit.edu/handle/1721.1/153283

The ideas in this presentation are not due to the author but based on extrapolations from published research which was not conducted by the author in any capacity, at all. Opinions in this talk may not represent the views of the institutions with which the author is affiliated at present, was affiliated in the past or may be affiliated in the future.

This material was presented on 10-10-2022 to the Global Health Science Sub-Committee members of the EU Political Action Committee (EUPAC) at a private meeting in Gif-sur-Yvette, France (organized by the "Science Valley" institutions). The author was invited to speak by a NGO and was the only speaker without a political affiliation.

REMEDY & RESPONSE: FROM PARADOX TO PARADIGMS ?

Shoumen Palit Austin Datta

MDPnP Lab and Cybersecurity Program, Department of Anesthesiology, Massachusetts General Hospital, Harvard Medical School, Partners Research Building, 65 Landsdowne Street, Cambridge, MA 02139, USA (sdatta8@mgh.harvard.edu) https://mdpnp.mgh.harvard.edu

&

MIT Auto-ID Labs, 35-208, Department of Mechanical Engineering, Massachusetts Institute of Technology 77 Massachusetts Avenue, Cambridge, MA 02139, USA (shoumen@mit.edu) https://autoid.mit.edu/shoumen-datta ▪ http://autoid.mit.edu/people-2

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SHOUMEN PALIT AUSTIN DATTA

https://ilp.mit.edu/node/23302

First Draft created 9/9/2022

https://web.mit.edu/search/?q=Shoumen+Datta

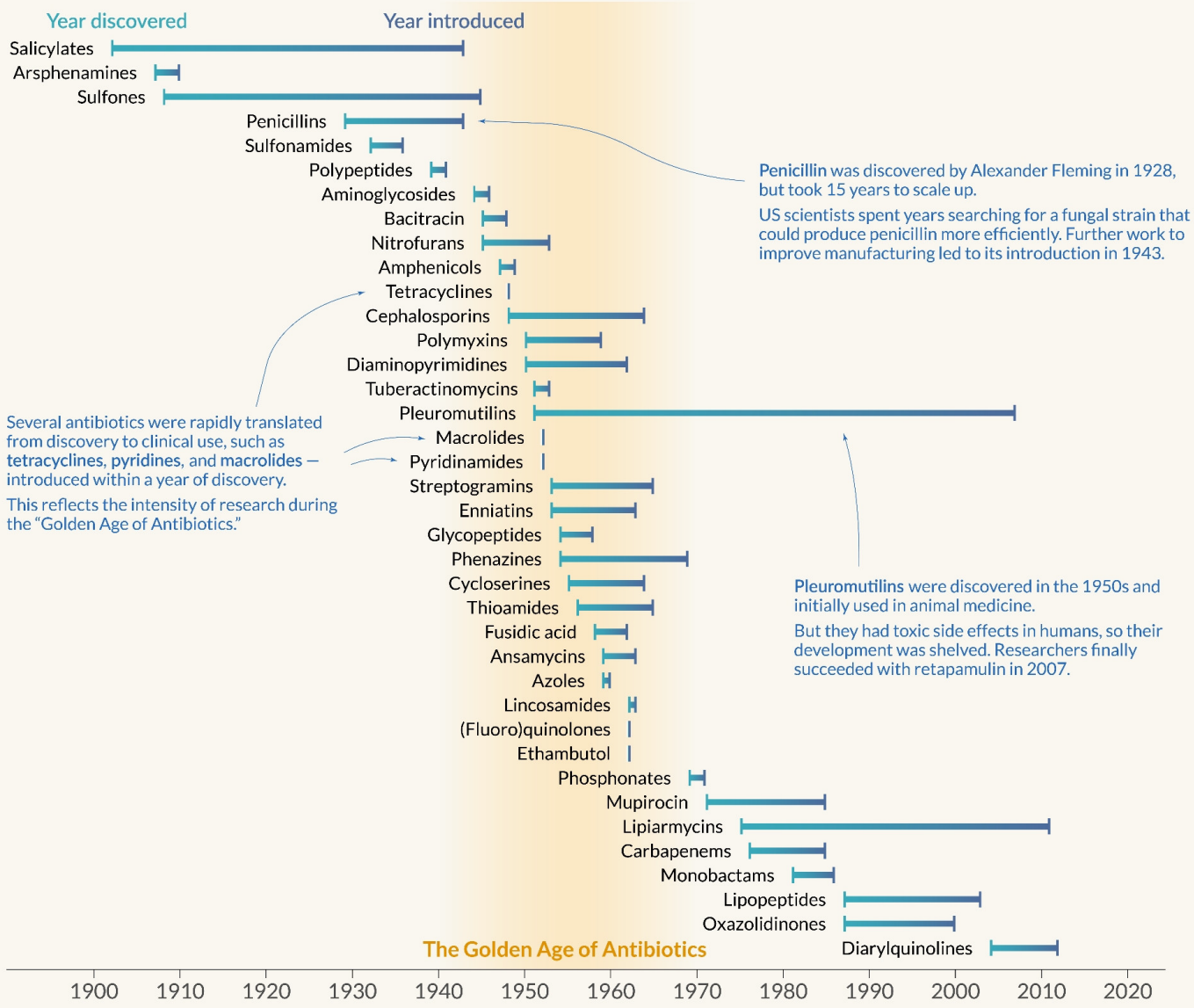
https://bit.ly/Google-Scholar-SD

Bagnulo A, Muñoz Sastre MT, Kpanake L, Sorum PC, Mullet E. ***Why patients want to take or refuse to take antibiotics: an inventory of motives.*** BMC Public Health. 2019 April 27; 19(1): 441 doi: 10.1186/s12889-019-6834-x. PMID: 31029110; PMCID: PMC6487028.

Antibiotics: time from discovery to introduction

Our World in Data

The timespan between when each antibiotic drug class was discovered and when it was first in clinical use.



Source: Hutchings, Truman, Wilkinson (2019) Antibiotics: *Past, present and future.*

Antibiotics, the rage (?) before the age of vaccines ?

Saloni Dattani (2024) "What was the Golden Age of Antibiotics, and how can we spark a new one?" https://ourworldindata.org/golden-age-antibiotics

Enders JF, Weller TH, Robbins FC. Cultivation of the Lansing Strain of Poliomyelitis Virus in Cultures of Various Human Embryonic Tissues. Science. 1949 January 28; 109(2822):85-7. doi: 10.1126/science.109.2822.85. PMID: 17794160.

THE AGE OF VACCINES

A breakthrough occurred in 1949, when poliovirus was successfully cultivated in human tissue by John Enders, Thomas Weller and Frederick Robbins at Boston Children's Hospital. Their pioneering work was recognized with the 1954 Nobel Prize.

Not long afterwards, in the early 1950s, the first successful vaccine was created by US physician Jonas Salk. Salk tested his experimental killed-virus vaccine on himself and his family in 1953, and a year later on 1.6 million children in Canada, Finland and the USA.

The results were announced on 12 April 1955, and Salk's inactivated polio vaccine (IPV) was licensed on the same day. By 1957, annual cases dropped from 58 000 to 5600, and by 1961, only 161 cases remained.

www.nobelprize.org/prizes/medicine/1954/summary/

Salk was committed to equitable access to his vaccine, and understood that elimination efforts would not work without universal low- or no-cost vaccination.

Six pharmaceutical companies were licensed to produce IPV, and Salk did not profit from sharing the formulation or production processes.

In a 1955 interview, when asked who owned the patent for IPV, he replied: "Well, the people, I would say. There is no patent. Could you patent the sun?"

A second type of polio vaccine, the oral polio vaccine (OPV) was developed by physician and microbiologist Albert Sabin.

Sabin's vaccine was live-attenuated (using the virus in weakened form) and could be given orally, as drops or on a sugar cube.

With the Salk vaccine in wide use by the late 1950s, United States interest in testing this new kind of vaccine was low.

www.who.int/news-room/spotlight/history-of-vaccination/history-of-polio-vaccination

At age 33, in 1930, Enders received his Ph.D. from Harvard Medical School for a thesis supervised by Hans Zinsser, which presented evidence that bacterial anaphylaxis and hypersensitivity of the tuberculin type are distinct phenomena. From 1930 until 1946, Enders remained at Harvard as a member of the teaching staff. In 1946, Enders was asked to establish a laboratory for research in infectious diseases at the Children's Medical Center, HMS. John Enders was the Higgins University Professor at Harvard University and Chief of the Research Division of Infectious Diseases of the Children's Hospital, Harvard Medical School, Boston, Massachusetts, U.S.A. John Enders passed away in 1985 (1897-1985).

THE NOBEL PRIZE

Nobel Prizes & laureates About Stories Educational Events & museums

The Nobel Prize in Physiology or Medicine 1954

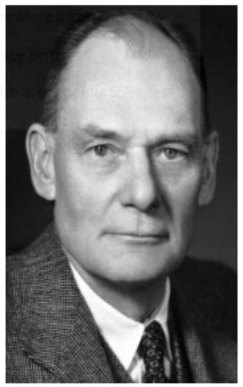


Photo from the Nobel Foundation archive.

John Franklin Enders

Prize share: 1/3

Photo from the Nobel Foundation archive.

Thomas Huckle Weller

Prize share: 1/3

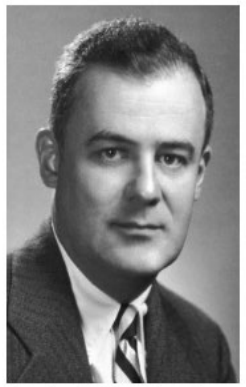


Photo from the Nobel Foundation archive.

Frederick Chapman Robbins

Prize share: 1/3

The Nobel Prize in Physiology or Medicine 1954 was awarded jointly to John Franklin Enders, Thomas Huckle Weller and Frederick Chapman Robbins "for their discovery of the ability of poliomyelitis viruses to grow in cultures of various types of tissue"

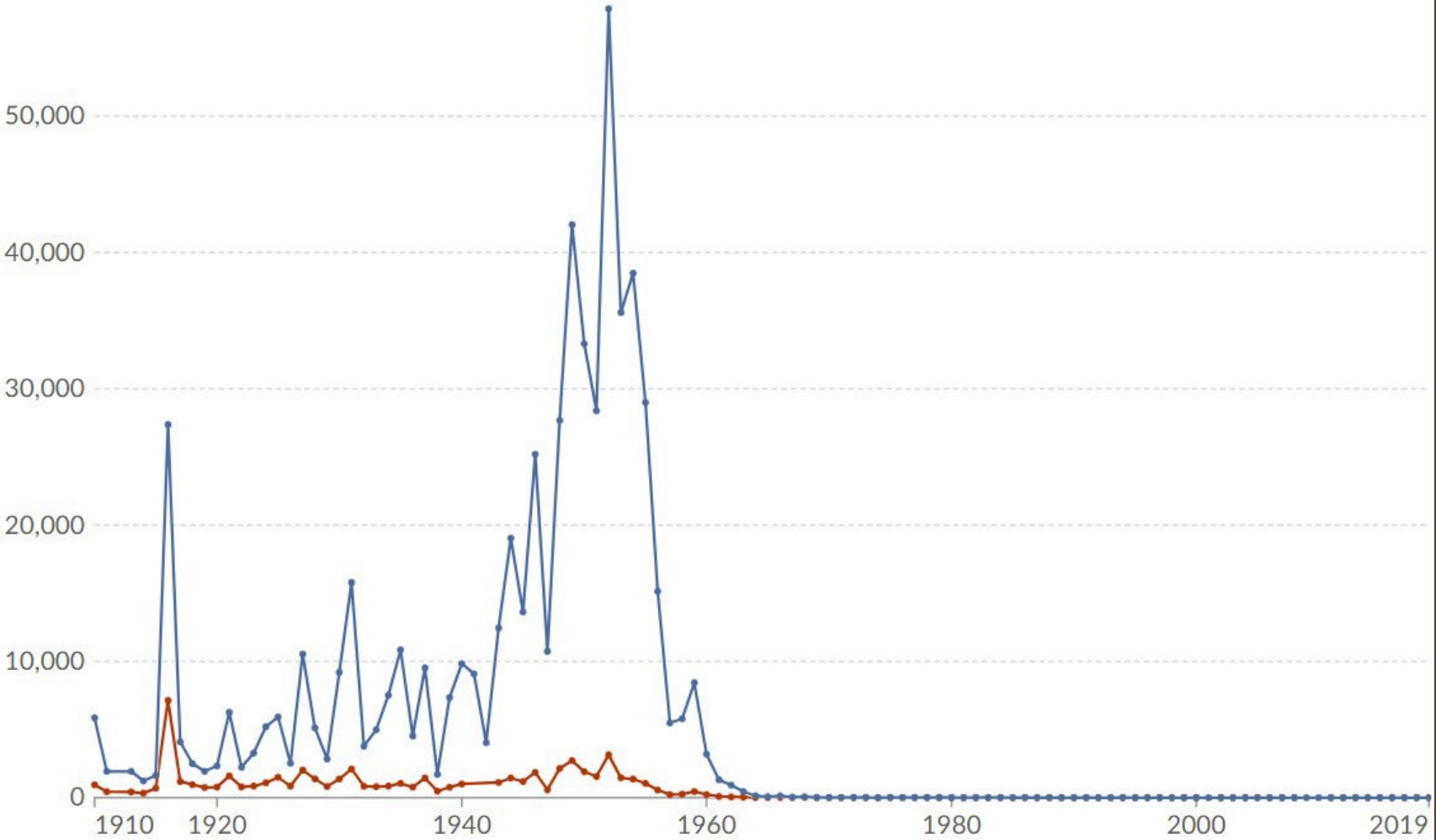
Affiliation at the time of the award: Harvard Medical School, Boston, MA, USA; Research Division of Infectious Diseases, Children's Medical Center, Boston, MA, USA

Prize motivation: “for their discovery of the ability of poliomyelitis viruses to grow in cultures of various types of tissue”

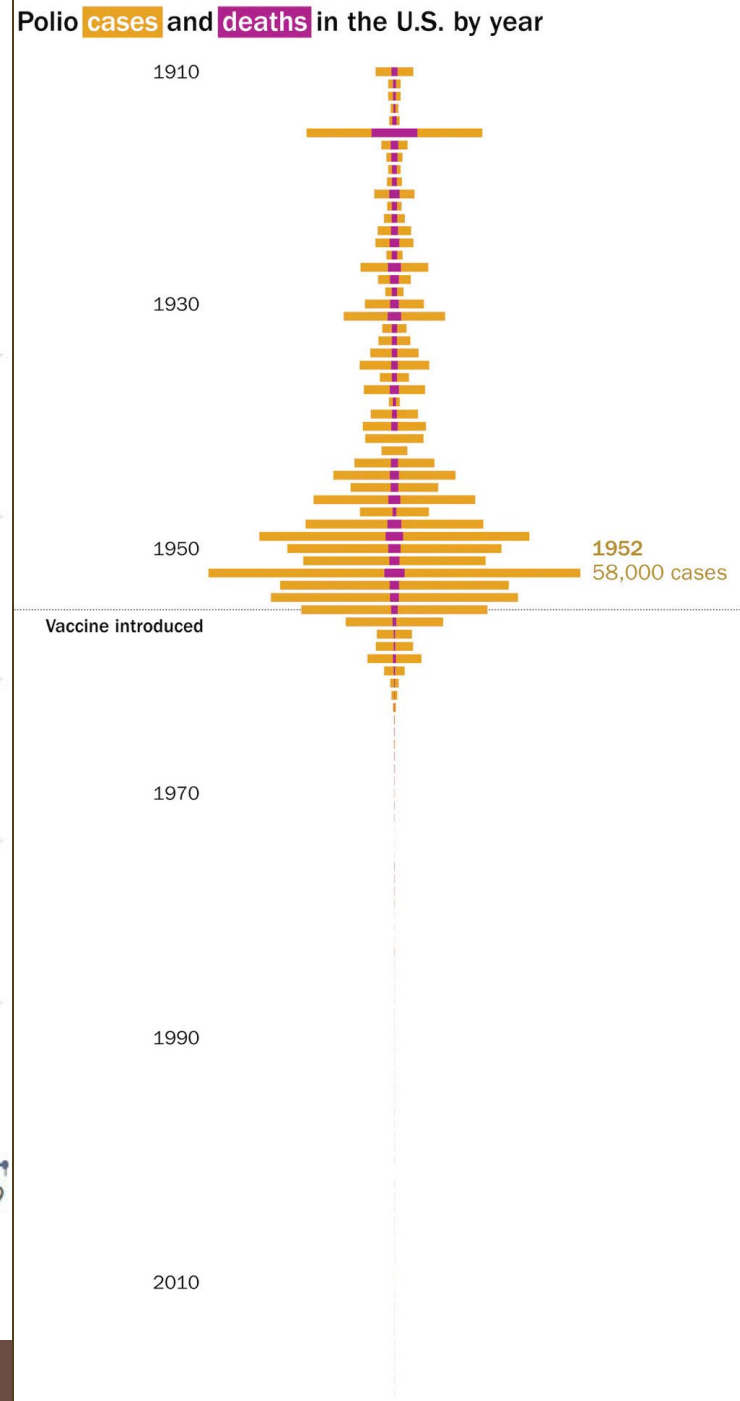
THE AGE OF VACCINES

Reported paralytic polio cases and deaths, United States, 1910 to 2019

The reported figures include both wild-[1] and vaccine-derived poliovirus[2] infections that occurred indigenously and as imported cases.



Data source: Our World In Data based on US Public Health Service; US Center for Disease Control; and WHO
OurWorldinData.org/polio | CC BY



Saloni Dattani, Fiona Spooner, Sophie Ochmann and Max Roser (2017) "Polio." *Our World in Data* (Updated May 2024) https://ourworldindata.org/polio

Jia You (2017) doi: 10.1126/science.aal1107 SCIENCE https://www.science.org/content/article/here-s-visual-proof-why-vaccines-do-more-good-harm

Plant-based Oral Vaccine (POV)

AMAT VICTORIA CURAM

DRAFT

TABLE OF CONTENTS PAGE(S)

RE-VIEW / RE-PRESENT / RE-DISCOVER / RE-EVALUATE / RE-SEARCH

Bio-Engineered Plant-produced Antigens, Self-Administered for Oral Vaccination: A Cottage Industry for Vaccines for Less Affluent Nations?

Shoumen Palit Austin Datta

MIT Auto-ID Labs, Department of Mechanical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, USA (shoumen@mit.edu)
MDPnP Lab, Cybersecurity Program and Center for Smart and Autonomous Medical Systems, Department of Anesthesiology, Massachusetts General Hospital, Mass General Brigham, Harvard Medical School, Research Building, 65 Landsdowne Street, Cambridge, Massachusetts 02139, USA (sdatta8@mgh.harvard.edu)

ABSTRACT

In this unconventional and non-systematic re-view, we re-present published results indicating that transgenic plants engineered to express (foreign) antigens show significant levels of mRNA (from viral coding region) and viral antigen (protein) in plant tissues (leaves). Oral administration of plant-produced antigens were immuno-stimulatory in humans, capable of conferring immunity from the viral infection (specific for the viral antigen bioengineered for expression in plant). Use of antigen-containing plant products for oral (or sublingual) administration does not require purification. The plant "paste" may be sufficient (?) for immunizing humans (and animals). Scientific evidence supports advocacy for oral administration of "raw" plant-based products (sublingual) without purification. Implementing this proposal may accelerate the pace of global vaccination and preventive healthcare for less affluent communities by [0] eliminating the need for purification,[1] eliminating the need for "cold" supply chain logistics, [2] eliminating the dependency on medical professionals for vaccination and [3] eliminating supply chain fulfillment dependencies by growing the antigen-producing "potted plants" in community gardens or at home, as a vaccine cottage industry. Communities may also brew the cottage industry for transgenic plants producing antigens as an entrepreneurial innovation endeavor and/or social business for vaccines. The latter, if built on pillars of ethical profitability, is expected to prioritize science as a service to society to improve access to global public goods with respect to health and healthcare.

The only thing necessary for the triumph of anti-science is for scientists to do nothing.

THE KILLER WITHIN: ANTI-VAXXERS

ANTI-VACCINE MISINFORMATION

HTTPS://WWW.NCBI.NLM.NIH.GOV/PMC/ARTICLES/PMC10398812/PDF/NIHPP-2023.07.12.23292568V2.PDF

AJC Reports: There is No Excuse. Anti-Vaxxers Put Us All at Risk

Ethan Lindenberger is the 18-year-old from Ohio shared his story about growing up in an anti-vaccine household. He spoke at a U.S. Senate hearing on vaccines and the outbreak of preventable diseases. His mother, however well-meaning, never took him to get the standard vaccines that protect against measles, mumps, chickenpox, rubella and other diseases.

Morehouse School of Medicine assistant professor of infectious disease, Austin Chan, M.D., shares why he believes the anti-vaccine movement is incredibly dangerous.

https://www.msm.edu/RSSFeedArticles/2019/March/anti-vaxxers-put-all-risk.php
https://www.politico.com/news/2023/09/24/anti-vaxxers-political-power-00116527

Estimated preventable COVID-19-associated deaths due to non-vaccination in the United States

Katherine M. Jia[1] · William P. Hanage[1] · Marc Lipsitch[1] · Amelia G. Johnson[2] · Avnika B. Amin[2,3] · Akilah R. Ali[2] · Heather M. Scobie[2] · David L. Swerdlow[1]

ncbi.nlm.nih.gov/pmc/articles/PMC10123459/table/Tab1/?report=objectonly

Table 1

Estimated number of preventable COVID-19-associated deaths among unvaccinated adults (aged ≥ 18 years), May 30, 2021–September 3, 2022

	30 jurisdictions[a]	US
Number of individuals aged ≥ 18 years (mean)	159,862,404[b]	233,656,270[c]
Estimated number of preventable COVID-19-associated deaths among unvaccinated adults (aged ≥ 18 years), May 30, 2021–September 3, 2022	158,000[d]	232,000[e]

Jia KM, Hanage WP, Lipsitch M, Johnson AG, Amin AB, Ali AR, Scobie HM, Swerdlow DL. ***Estimated preventable COVID-19-associated deaths due to non-vaccination in the United States.*** Eur J Epidemiol. 2023 Nov; 38(11):1125-1128. doi: 10.1007/s10654-023-01006-3. Epub 2023 April 24. PMID: 37093505; PMCID: PMC10123459. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10123459/pdf/10654_2023_Article_1006.pdf

THE HEALTH OF NATIONS

PART 1 – THE GOLDEN AGE OF VACCINES

PART 1 – The Health of Nations – download from the MIT Library - https://dspace.mit.edu/handle/1721.1/145774

PART 2 – The Health of Nations – download from the MIT Library - https://dspace.mit.edu/handle/1721.1/152921

PART 3 – The Health of Nations – download from the MIT Library - https://dspace.mit.edu/handle/1721.1/153283

The Health of Nations

Shoumen Palit Austin Datta

[1] MDPnP Lab and Cybersecurity Program, Massachusetts General Hospital, Harvard Medical School, Partners Research Building, 65 Landsdowne Street, Cambridge, Massachusetts 02139, USA (sdatta8@mgh.harvard.edu)
[2] MIT Auto-ID Labs, Department of Mechanical Engineering, Massachusetts Institute of Technology, Room 35-206, School of Engineering, 77 Massachusetts Avenue, Cambridge Massachusetts 02139, USA (shoumen@mit.edu)

The requirement for food, agnostic of the economic climate and constraints of individuals, makes plant-based nutrition an overwhelming platform for delivery of preventive and prescriptive therapeutics. The delivery of medicinal value through food and nutrition, for example, prevention of xeropthalmia (blindness) in children using tools of plant biotechnology, is documented through robust scientific research. There is little doubt that the reach of therapeutics can also include vaccines, for the rest of the world which cannot afford the fruits of brilliant but expensive outcomes, for example, mRNA vaccines. This talk lifts the veil over seminal research performed at least a quarter century ago (in the 20th century) which demonstrated the immense potential for global immunization from infectious diseases (for example, Ebola virus) using plant based oral vaccines in food (as well as sublingual and transdermal modes of delivery). Changes in leadership, creative implementation strategies and innovative capacity building are necessary to bring basic health related low-cost solutions to ~7 billion people (~80% of the global population) who are not a part of the affluent world (~1 billion). This talk will also highlight the urgent need for even a modicum of healthcare equity for the down-trodden, forgotten and misbegotten. There is nothing new in this talk but a gentle reminder for the entrepreneurs of social innovation to re-evaluate grand and profound old results, in the context of the post-pandemic world. Is "food" the final frontier in research in plant molecular biology and plant biotechnology research and development?

Table 1 Timeline of rapid development of mRNA vaccines against SARS-CoV-2 in 2020 (based on Barbier et al. 2022)

Date in 2020	Occurrence
12 January	SARS-CoV-2 genomic sequence published
13 January	Moderna: mRNA vaccine sequence designed
12 March	Moderna: first subject doses in phase 1
23 April	*BioNTech-Pfizer*: first subject doses in phases 1–2*
29 May	Moderna: first subject doses in phase 2
27 July	Moderna and *BioNTech-Pfizer*: initiation of phase 3
6 October	Regulatory submissions *BioNTech-Pfizer*: European Medicines Agency
9 October	Regulatory submissions *BioNTech-Pfizer*: Canada
9 November	*BioNTech-Pfizer* publishes interim phase 3 results
16 November	Moderna publishes interim phase 3 results
16 November	Regulatory submissions Moderna: European Medicines Agency
18 November	*BioNTech-Pfizer* publishes phase 3 results
20 November	Regulatory submissions *BioNTech-Pfizer*: USA
30 November	Regulatory submissions Moderna: USA
30 November	Moderna publishes phase 3 results
11 December	*BioNTech*162b2 receives EUA in USA
18 December	Moderna mRNA-1273 receives EUA in USA

The table also shows that the two large pharmaceutical companies are competing not only with time but also with each other

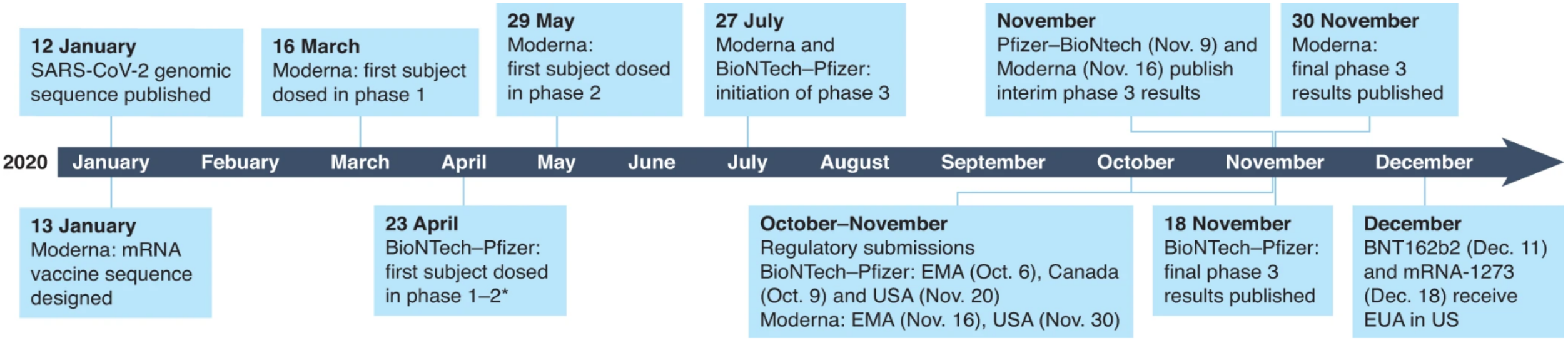
*BNT162 phase 1–2 trial investigated several drug candidates, with BNT162b2 selected for phase 3 trials

Deák C, Pardi N, Miklósi Á. Innovation in the 21st century: following the footsteps of Katalin Karikó. Biol Futur. 2023 Jun;74(1-2):101-108. doi: 10.1007/s42977-023-00161-8. Epub 2023 May 22. PMID: 37213055

Deák C, Pardi N, Miklósi Á. Innovation in the 21st century: following the footsteps of Katalin Karikó. Biol Futur. 2023 Jun ;74(1-2):101-108. doi: 10.1007/s42977-023-00161-8. Epub 2023 May 22. PMID: 37213055

Fig. 1: 2020 timeline showing rapid development of mRNA vaccines against SARS-CoV-2.

From: The clinical progress of mRNA vaccines and immunotherapies



*BNT162 phase 1–2 trial investigated several drug candidates, with BNT162b2 selected for phase 3 trials. EMA, European Medicines Agency.

Barbier AJ, Jiang AY, Zhang P, Wooster R, Anderson DG. The clinical progress of mRNA vaccines and immunotherapies. Nat Biotechnol. 2022 Jun;40(6):840-854. doi: 10.1038/s41587-022-01294-2. Epub 2022 May 9. PMID: 35534554.

Breaking Through isn't just the story of an extraordinary woman. It's an indictment of closed-minded thinking and a testament to one woman's commitment to laboring intensely in anonymity—knowing she might never be recognized in a culture that is driven by prestige, power, and privilege—because she believed that her work would save lives.

https://www.nobelprize.org/prizes/medicine/2023/summary/

The Nobel Prize in Physiology Medicine 2023

Ill. Niklas Elmehed © Nobel Prize Outreach

Katalin Karikó

Prize share: 1/2

Ill. Niklas Elmehed © Nobel Prize Outreach

Drew Weissman

Prize share: 1/2

Send | From: SDATTA8@mgh.harvard.edu

From: Kariko, Katalin <kariko@pennmedicine.upenn.edu>
Sent: Sunday, September 26, 2021 12:05 PM
To: Shoumen Pa Datta <shoumen@mit.edu>
Subject: Re: What we do in life, echoes in eternity.

Dear Shoumen,
Thanks for your kind words,
Kati

From: Shoumen Pa Datta <shoumen@mit.edu>
Sent: Sunday, September 26, 2021 9:03 AM
To: Kariko, Katalin <kariko@pennmedicine.upenn.edu>
Subject: [External] What we do in life, echoes in eternity.

Dear Kati -

Congratulations! See you soon in Stockholm.

Thanks,

from a grateful world!

Regards,

Shoumen

Shoumen Palit Austin Datta
MIT - http://autoid.mit.edu
HARVARD - http://mdpnp.mgh.harvard.edu

2021

2023

www.nobelprize.org/prizes/medicine/2023/press-release

Karikó, K., Buckstein, M., Ni, H. and Weissman, D. Suppression of RNA Recognition by Toll-like Receptors: The impact of nucleoside modification and the evolutionary origin of RNA. *Immunity* **23**, 165–175 (2005).

Karikó, K., Muramatsu, H., Welsh, F.A., Ludwig, J., Kato, H., Akira, S. and Weissman, D. Incorporation of pseudouridine into mRNA yields superior nonimmunogenic vector with increased translational capacity and biological stability. *Mol Ther* **16**, 1833–1840 (2008).

Anderson, B.R., Muramatsu, H., Nallagatla, S.R., Bevilacqua, P.C., Sansing, L.H., Weissman, D. and Karikó, K. Incorporation of pseudouridine into mRNA enhances translation by diminishing PKR activation. *Nucleic Acids Res*. **38**, 5884–5892 (2010).

Katalin Karikó receiving the call from the Nobel Prize Committee (October 3, 2023). Photograph by Béla Francia (husband of Katalin Karikó).

■ 2021 ➔ 2023

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MIT - http://autoid.mit.edu
HARVARD - http://mdpnp.mgh.harvard.edu

The Nobel Prize in Physiology Medicine 2023

Ill. Niklas Elmehed © Nobel Prize Outreach
Katalin Karikó
Prize share: 1/2

Ill. Niklas Elmehed © Nobel Prize Outreach
Drew Weissman
Prize share: 1/2

Three respiratory viruses could make you sick this season – but for the first time, there are vaccines against all of them

By Brenda Goodman, CNN

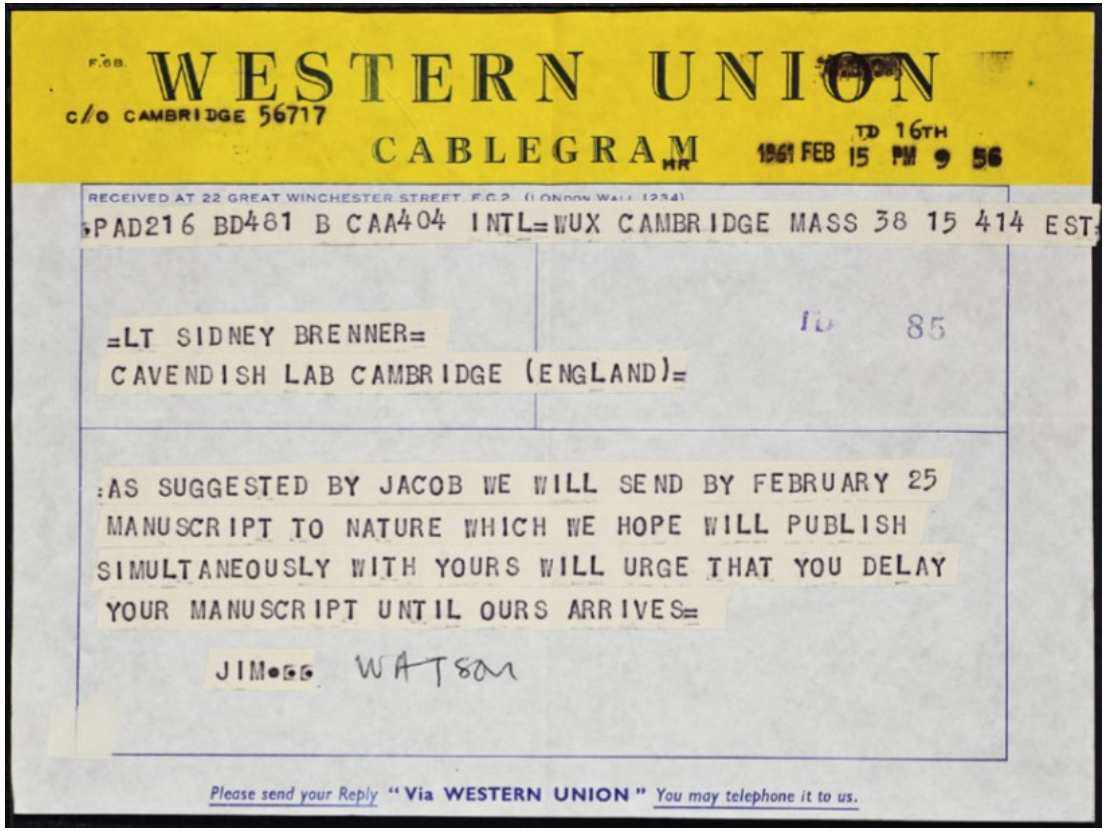
Updated 8:42 AM EDT, Fri August 18, 2023

WHO DISCOVERED MESSENGER RNA TO MAKE IT POSSIBLE TO PRODUCE THE MESSENGER RNA VACCINE FOR COVID-19

SCIENCE AS A SERVICE TO SOCIETY

Matthew Cobb (2015). ***Who discovered mRNA?*** Current Biology 2015 June 29; 25(13):R526-32. doi: 10.1016/j.cub.2015.05.032

- First person: DNA produces RNA which in turn leads to protein synthesis was André Boivin, 1947.
- First suggestion: small RNA molecules move from nucleus to cytoplasm and associate with ribosomes where they drive protein synthesis was made by Raymond Jeener, 1950.
- First reports: what we would now identify as mRNA were from Al Hershey, 1953 and by Volkin and Astrachan, 1956.
- First realization: mRNA might exist - insight of Brenner and Crick; Jacob and Monod claimed to name “m” RNA
- First unambiguous description of mRNA: Brenner, Crick and Meselson; later Jim Watson’s team, see cablegram ➔
- First to prove mRNA’s biological function: Nirenberg and Matthaei (they did not frame their results in these terms).



WESTERN UNION

c/o CAMBRIDGE 56717

CABLEGRAM

1961 FEB 15 PM 9 56

RECEIVED AT 22 GREAT WINCHESTER STREET, E.C.2.

PAD216 BD481 B CAA404 INTL=WUX CAMBRIDGE MASS 38 15 414 EST

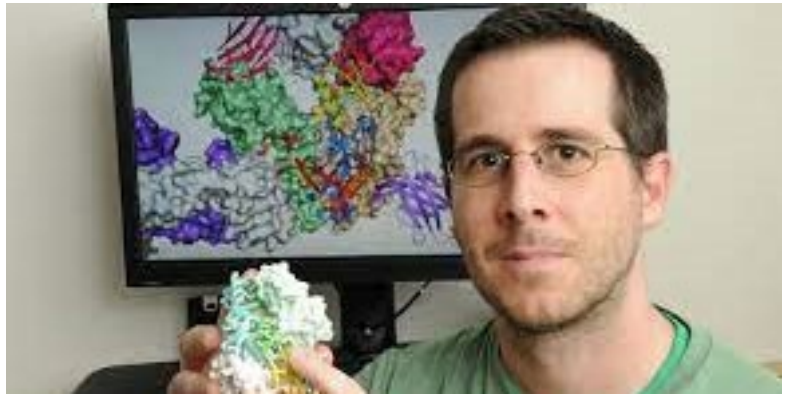
=LT SIDNEY BRENNER=
CAVENDISH LAB CAMBRIDGE (ENGLAND)=

:AS SUGGESTED BY JACOB WE WILL SEND BY FEBRUARY 25
MANUSCRIPT TO NATURE WHICH WE HOPE WILL PUBLISH
SIMULTANEOUSLY WITH YOURS WILL URGE THAT YOU DELAY
YOUR MANUSCRIPT UNTIL OURS ARRIVES=

JIM WATSON

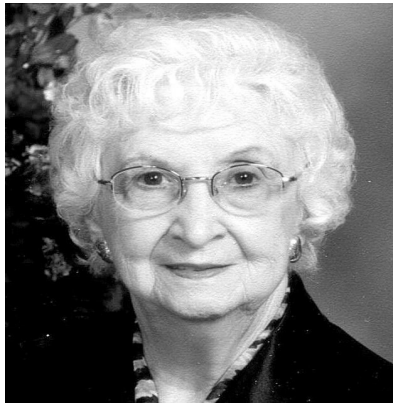
Please send your Reply "Via WESTERN UNION" You may telephone it to us.

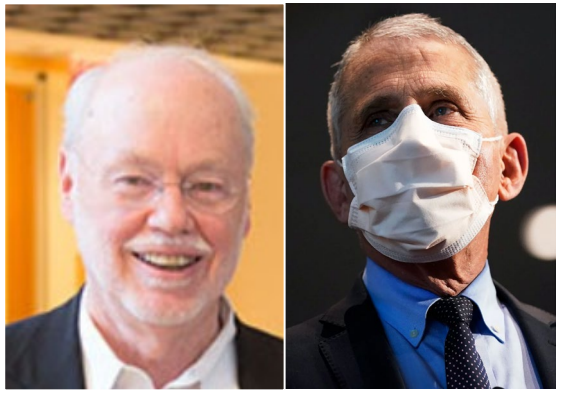
AN ODE TO A FEW OF MANY PIONEERS OF mRNA VACCINE



From top: (Susan Francia) Katalin Kariko, Jason McLellan, Kizzmekia Corbett, Barney Graham

It took almost 50 years, but the grand convergence of basic science research made it possible to produce and implement mRNA vaccines for CoVID-19 in order to immunize humans against SARS-CoV-2[n]. It is a brilliant beacon of research excellence and science in the service of society, when it was needed the most, during the pandemic of the 21st century.

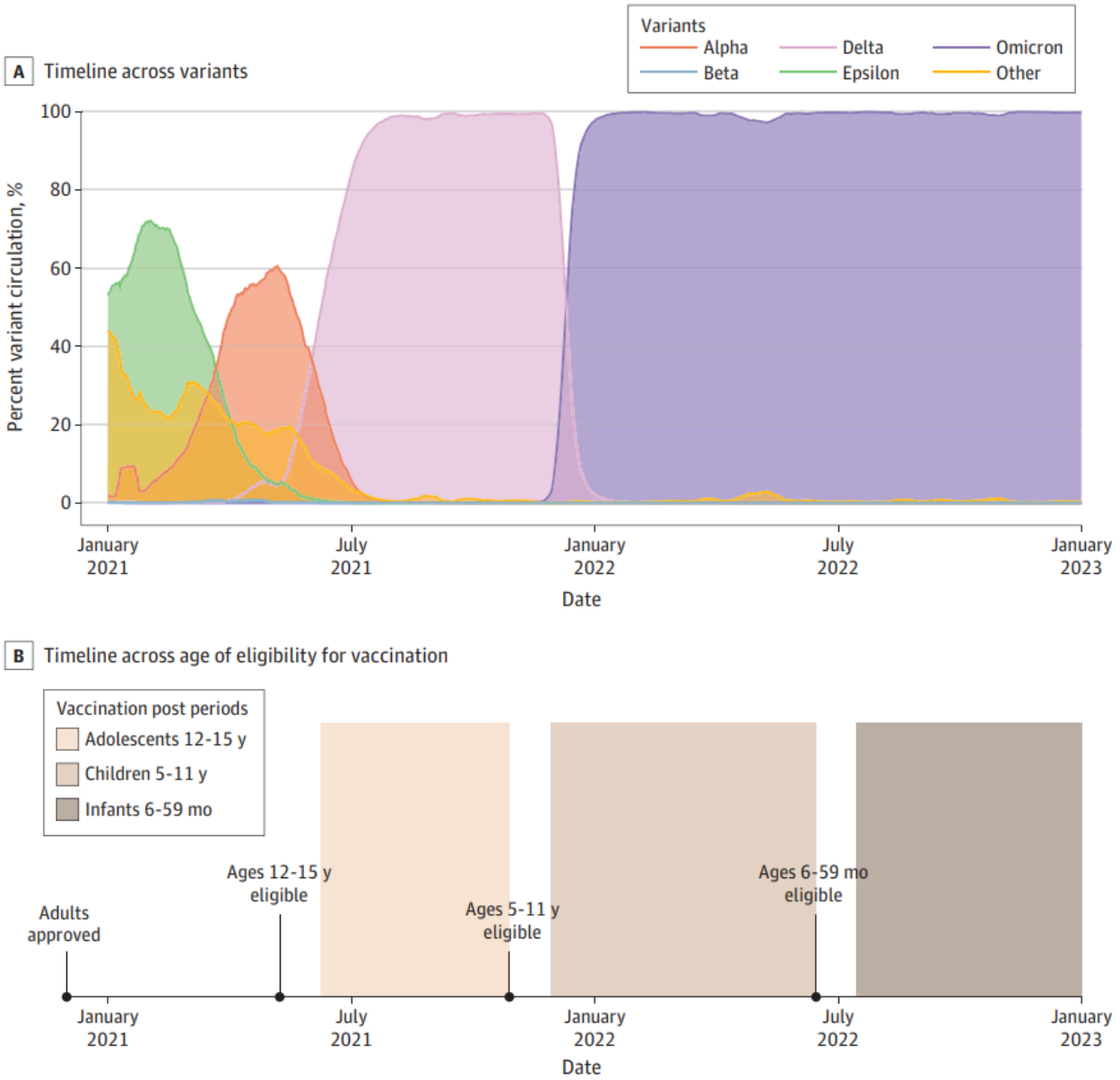




From top: Bob Langer, Marilyn Kozak, Phil Sharp, Anthony Fauci

Analysis of >3.9 million COVID cases in California found that pediatric vaccination averted >375,000 cases of COVID-19 and about 270 hospitalizations in children 6mo-15yrs in the 4 to 7 months following availability of the vaccine.

Figure 1. Timeline of Major Circulating Variants and Vaccine Eligibility by Age Group



Timelines of major circulating variants (A) and eligibility, with the age groups examined shown as shaded rectangles (B).

JAMA Network Open
Original Investigation | Pediatrics

JAMA Netw Open. 2024;7(4):e247822. doi:10.1001/jamanetworkopen.2024.7822

Norman M, Magnus MC, Söderling J, Juliusson PB, Navér L, Örtqvist AK, Håberg S, Stephansson O. ***Neonatal Outcomes After COVID-19 Vaccination in Pregnancy.*** JAMA. 2024 February 6; 331(5):396-407. doi: 10.1001/jama.2023.26945. PMID: 38319332.

Research https://jamanetwork.com/journals/jama/fullarticle/2814537

JAMA | Original Investigation

Neonatal Outcomes After COVID-19 Vaccination in Pregnancy

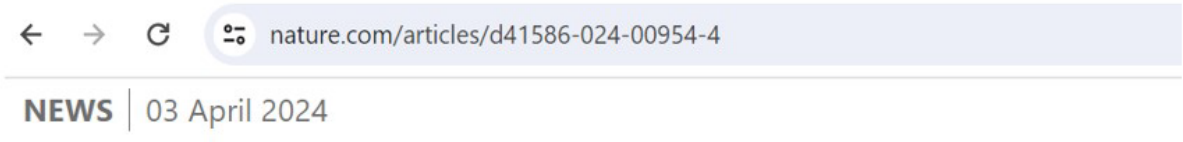
Mikael Norman, MD, PhD; Maria C. Magnus, PhD; Jonas Söderling, PhD; Petur B. Juliusson, MD, PhD; Lars Navér, MD, PhD; Anne K. Örtqvist, MD, PhD; Siri Håberg, MD, PhD; Olof Stephansson, MD, PhD

CONCLUSIONS AND RELEVANCE In this large population-based study, vaccination of pregnant individuals with mRNA COVID-19 vaccines was not associated with increased risks of neonatal adverse events in their infants.

196,470 newborn infants (51.3% male, 93.8% born at term, 62.5% born in Sweden), 94 303 (48.0%) were exposed to COVID-19 vaccination during pregnancy. Exposed infants exhibited no increased odds of adverse neonatal outcomes, and they exhibited lower odds for neonatal nontraumatic intracranial hemorrhage, hypoxic-ischemic encephalopathy and neonatal mortality.

Katalin Karikó's mRNA vaccine for CoVID-19 discovery saved about 50 million lives in its first year of use (from 8 December 2020)
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9537923/pdf/JPC-9999-0.pdf

A drug that uses messenger RNA technology has shown early success in addressing the core deficiency behind a rare genetic disorder. The results have ignited hope that the technology (which first gained attention through its breakthrough use in COVID-19 vaccines) could realize its long-awaited promise of generating therapeutic proteins directly in the body. “This is a first step in the right direction,” says Katalin Karikó, the Nobel prize winning mRNA pioneer affiliated with the University of Szeged in Hungary and the University of Pennsylvania in Philadelphia. Yet challenges remain in the form of side effects, which may complicate the path towards widespread adoption.



NEWS | 03 April 2024

mRNA drug offers hope for treating a devastating childhood disease

Drug trial results show that vaccines aren’t the only use for the mRNA technology behind the most widely used COVID-19 jabs.

https://www.nature.com/articles/d41586-024-00954-4

“Anti-retroviral therapy in the US has prolonged life by an estimated 13 years”

pubmed.ncbi.nlm.nih.gov/16741877/

Comparative Study > J Infect Dis. 2006 Jul 1;194(1):11-9. doi: 10.1086/505147. Epub 2006 Jun 1.

The survival benefits of AIDS treatment in the United States

Rochelle P Walensky [1], A David Paltiel, Elena Losina, Lauren M Mercincavage, Bruce R Schackman, Paul E Sax, Milton C Weinstein, Kenneth A Freedberg

Affiliations – collapse

Affiliation

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PMID: 16741877 DOI: 10.1086/505147

Haitian Patient, before and after Receiving Free Treatment for HIV Infection and Tuberculosis.
The photograph on the left was taken in March 2003, and that on the right in September 2003. Many impoverished patients in rural Haiti and Rwanda now receive comprehensive medical care through public–private partnerships.

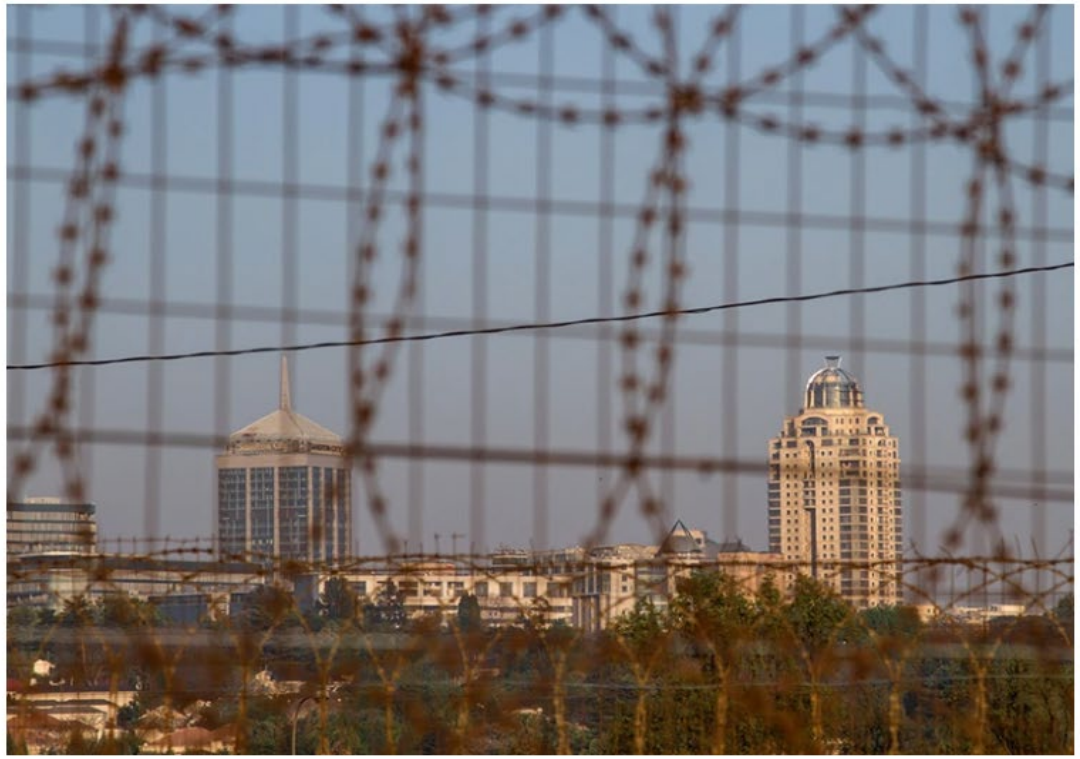
Kim JY, Farmer P. ***AIDS in 2006--moving toward one world, one hope?*** N Engl J Med. 2006 August 17; 355(7):645-647. doi: 10.1056/NEJMp068166
www.nejm.org/doi/pdf/10.1056/NEJMp068166

EDITORIAL | 11 July 2023

The best medicine for improving global health? Reduce inequality

The COVID pandemic knocked back progress towards improving public health. Without addressing the underlying social and economic causes of ill health, it could completely stall.

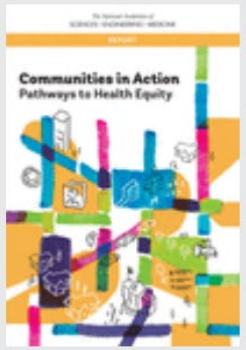
www.nature.com/articles/d41586-023-02251-y.pdf



A barbed wire separates Alexandra, a suburb of Johannesburg, South Africa, from its wealthy neighbour, Sandton. Credit: Dean Hutton/Bloomberg/Getty

The National Academies of SCIENCES ENGINEERING MEDICINE

THE NATIONAL ACADEMIES PRESS



Communities in Action: Pathways to Health Equity

DETAILS

582 pages | 6 x 9 | PAPERBACK
ISBN 978-0-309-45296-0 | DOI: 10.17226/24624

CONTRIBUTORS

James N. Weinstein, Amy Geller, Yamrot Negussie, and Alina Baciu, Editors; Committee on Community-Based Solutions to Promote Health Equity in the United States; Board on Population Health and Public Health Practice; Health and Medicine Division; National Academies of Sciences, Engineering, and Medicine

www.ncbi.nlm.nih.gov/books/NBK425848/pdf/Bookshelf_NBK425848.pdf

The NEW ENGLAND JOURNAL of MEDICINE

nejm.org/doi/full/10.1056/NEJMp2307312

Perspective

RECOGNIZING HISTORICAL INJUSTICES IN MEDICINE AND THE JOURNAL

Explaining Health Inequities — The Enduring Legacy of Historical Biases

David S. Jones, M.D., Ph.D., Evelynn Hammonds, Ph.D., Joseph P. Gone, Ph.D., and David Williams, M.P.H., Ph.D.

February 1, 2024
N Engl J Med 2024; 390:389-395
DOI: 10.1056/NEJMp2307312

This article is part of an invited series by independent historians, focused on biases and injustice that the Journal has historically helped to perpetuate. We hope it will enable us to learn from our mistakes and prevent new ones.

When the Journal was launched in 1812, claims had circulated for centuries about differences in anatomy, physiology, and disease susceptibility between different human populations.[1] Physicians' persistent belief that these differences are innate has long drawn attention away from other possible causes of health inequities. As the *Journal* explores its history and acknowledges its role in voicing and perpetuating racism and discrimination, it must examine how it grappled with the problem of difference.

https://www.nejm.org/doi/full/10.1056/NEJMp2307312

English translation

Lippenbekenntnis

lip service

nature.com/articles/d41586-024-00545-3

COMMENT | 23 February 2024

Save lives in the next pandemic: ensure vaccine equity now

The proposed Pandemic Agreement must ensure that COVID-19 vaccine nationalism is never repeated; 290 scientists call for action.

By the end of 2021, the global distribution of vaccines was highly heterogeneous, with some countries gaining over 90% coverage in adults, whereas others reached less than 2%. In this study, we used an age-structured model of SARS-CoV-2 dynamics, matched to data from 152 countries in 2021, to investigate this inequity. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9671807/pdf/41591_2022_Article_2064.pdf

- Refusal of wealthier nations to cooperate had cost between 200,000 and 1.3 million lives by the end of 2021 in low- and middle-income countries[1,2]. One-third of the world's population has still not received a single dose of CoVID-19 vaccine. The death toll vaccine continues to grow.

www.nature.com/articles/d41586-024-00545-3

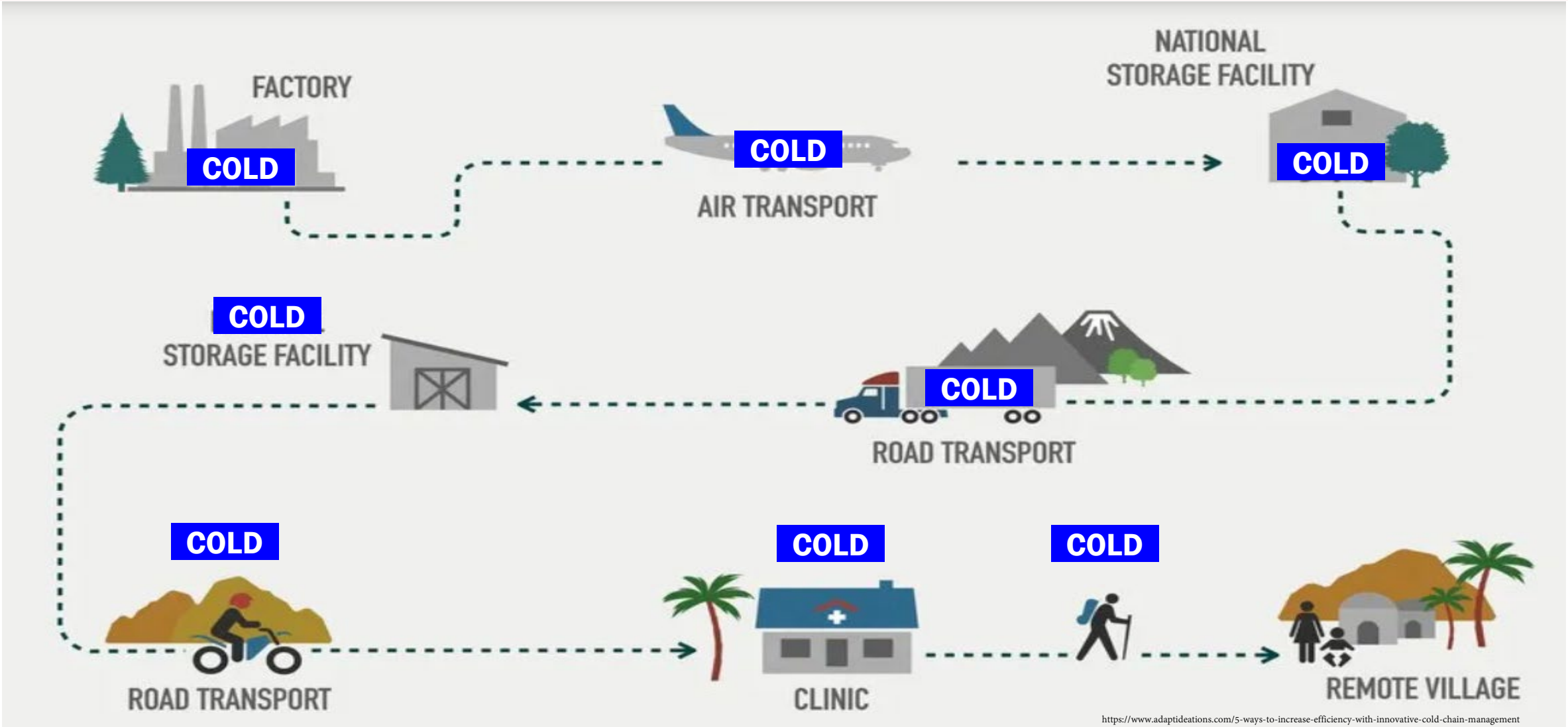
www.ncbi.nlm.nih.gov/pmc/articles/PMC9225255/

Phelan, Alexandra L. **"The World Health Organization's pandemic treaty."** BMJ 2023 Feb 28; 380:463 https://pubmed.ncbi.nlm.nih.gov/36854465/

THE ENEMY OF HEALTHCARE FOR POOR PEOPLE ?

The Greatest Enemy of Preventive Healthcare

COLD CHAIN - SUPPLY CHAIN MANAGEMENT



https://www.adaptideations.com/5-ways-to-increase-efficiency-with-innovative-cold-chain-management

Last-mile delivery increases vaccine uptake in Sierra Leone

https://doi.org/10.1038/s41586-024-07158-w

Received: 13 September 2022

Accepted: 1 February 2024

Niccolò F. Meriggi[1,2,3]✉, Maarten Voors[2], Madison Levine[4], Vasudha Ramakrishna[5], Desmond Maada Kangbai[6], Michael Rozelle[2], Ella Tyler[2], Sellu Kallon[2,7], Junisa Nabieu[2], Sarah Cundy[8] & Ahmed Mushfiq Mobarak[9]✉

To increase uptake, bring vaccines to people

Mobile clinics in rural villages in Sierra Leone sharply boosted the uptake of COVID-19 vaccines compared to villages that did not get the service. When COVID-19 vaccines were first made available, people who live in rural areas had to make, on average, a seven-hour round trip to receive one, at a total cost that could exceed a week's wages, says economist and study co-author Ahmed Mushfiq Mobarak. "When you're starting with a baseline vaccination rate of essentially zero, our research shows that the most cost-effective thing to do is just to show up," Mobarak says. The mobile clinics cost about US$33 per person vaccinated.

Meriggi NF, Voors M, Levine M, Ramakrishna V, Kangbai DM, Rozelle M, Tyler E, Kallon S, Nabieu J, Cundy S, Mobarak AM. ***Last-mile delivery increases vaccine uptake in Sierra Leone.*** Nature. 2024 March 13. doi: 10.1038/s41586-024-07158-w PMID: 38480877.

EACH DOSE OF VACCINE COSTS $33 IN SIERRA LEONE

LUDICROUS ?

RIDICULOUS ?

Compare & Gasp : Cost of each vaccine USD33 to Purchasing Power Parity of USD1.90 per day

Poverty reduction has been slow despite economic growth

3. Is Sierra Leone's poverty rate excessive given its income? We can attempt to answer this question by doing an international comparison of income and poverty rates. **As in other low-income countries, GDP per capita in Sierra Leone is correlated with a high level of extreme poverty.** Many countries achieve lower rates of poverty than predicted by their GDP per capita, likely because they have good economic and social policies and effective institutions. Middle-income countries (often with economies that have started on the path of structural transformation) appear to be especially successful in achieving lower rates of poverty, possibly thanks to enhanced productivity (see Figure 1).

Figure 1: A Comparison of GDP Per Capita (PPP) and Extreme Poverty

In percent of population below PPP $1.9 per day

www.thesierraleonetelegraph.com/wp-content/uploads/2022/12/Sierra-Leone-Poverty-Assessment-FINAL.pdf

hls.harvard.edu/today/using-her-voice-to-address-gender-based-violence-in-the-african-context/

Teaching & Learning

Lifting women up

First Lady of Sierra Leone Fatima Maada Bio is working to end gender-based violence, and empower women

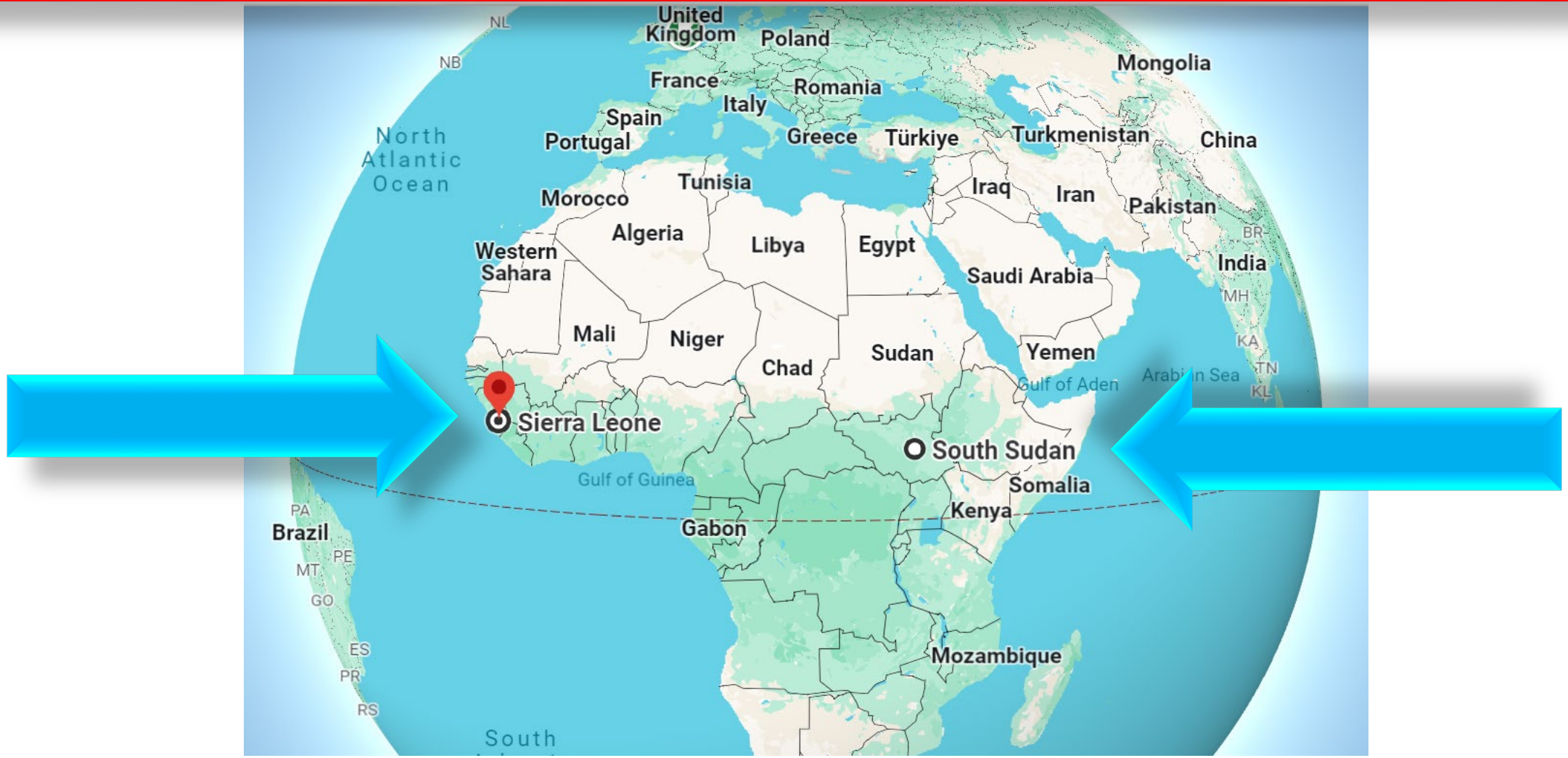
Mar 18, 2024 By Colleen Walsh

Credit: Lorin Granger

According to the 2019 Sierra Leone Demographic and Health Survey, 61% of women and girls between the ages of 15-49 have experienced physical violence since the age 15, and 7% have experienced sexual violence. The non-governmental organization Human Rights Watch has said sexual violence during the nation's civil war from 1991 to 2002, "affected thousands of girls and women of all ages," and was rooted in "the persistent human rights violations that push women into a lower status with limited rights in all spheres of their lives." For more information go to https://dhsprogram.com/pubs/pdf/FR365/FR365.pdf

IS SIERRA LEONE AN EXCEPTION IN TERMS OF POVERTY ?

HOW ABOUT SOUTH SUDAN ON THE CONTINENT OF AFRICA ?



This page is for those who may not have heard of Sierra Leone or has no clue about South Sudan

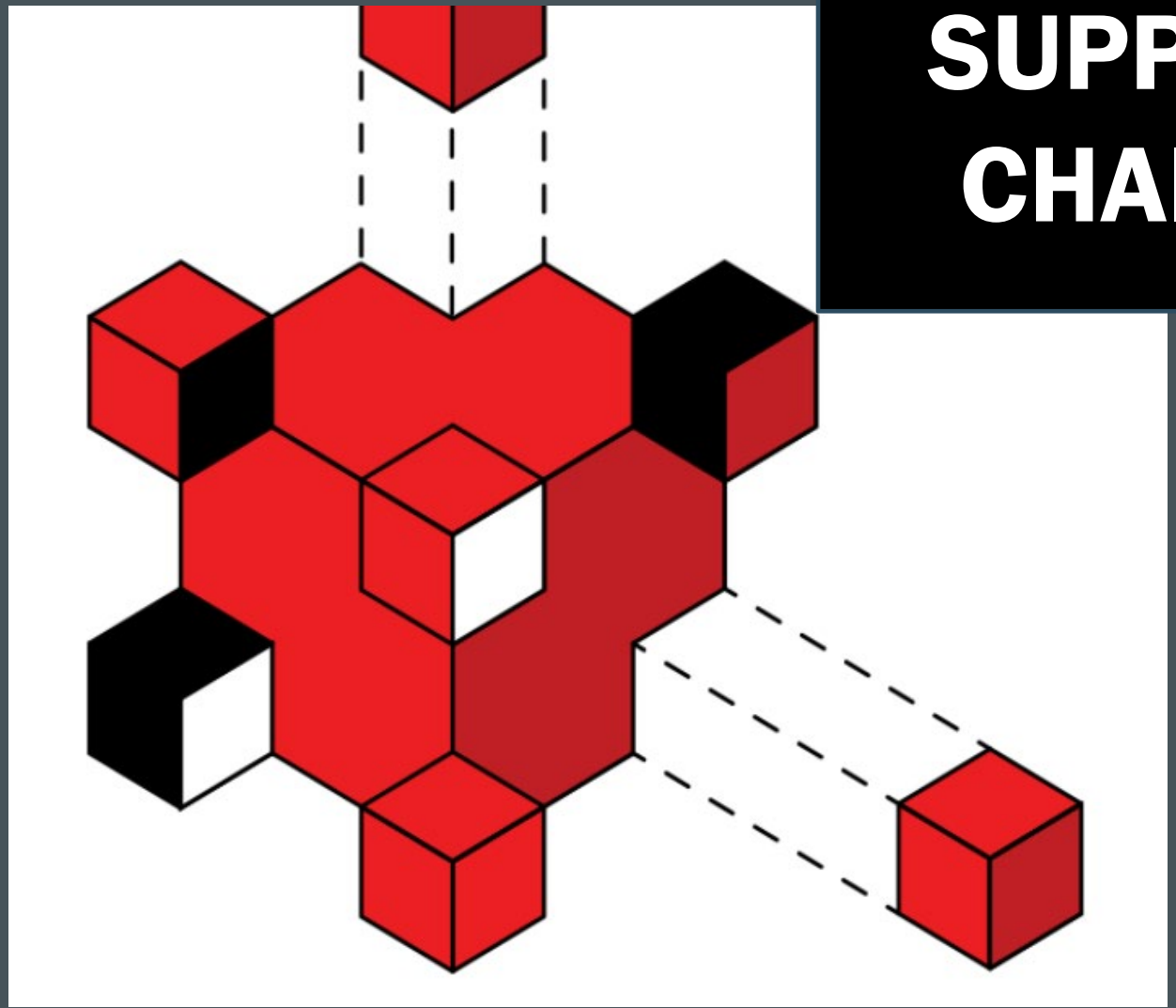
A $1 dollar plate of bean stew costs equivalent of $320 in South Sudan

Oct 30, 2017

THIS PROPOSAL

FOR PREVENTIVE HEALTHCARE AND VACCINATION WILL SHOW HOW TO DEMOLISH THE COLD CHAIN OF SUPPLY CHAIN MANAGEMENT

ELIMINATE THE COLD SUPPLY CHAIN



BUT SUPPLY CHAIN IS THE BEDROCK OF OPERATIONS

DO I KNOW WHAT I AM TALKING ABOUT ?

from EVOLUTION ... 1 / 65 | − 175% + | ⛶ ⟲ ⬇

Chapter 1

ADAPTIVE VALUE NETWORKS

*Convergence of Emerging Tools, Technologies and Standards as Catalytic Drivers**

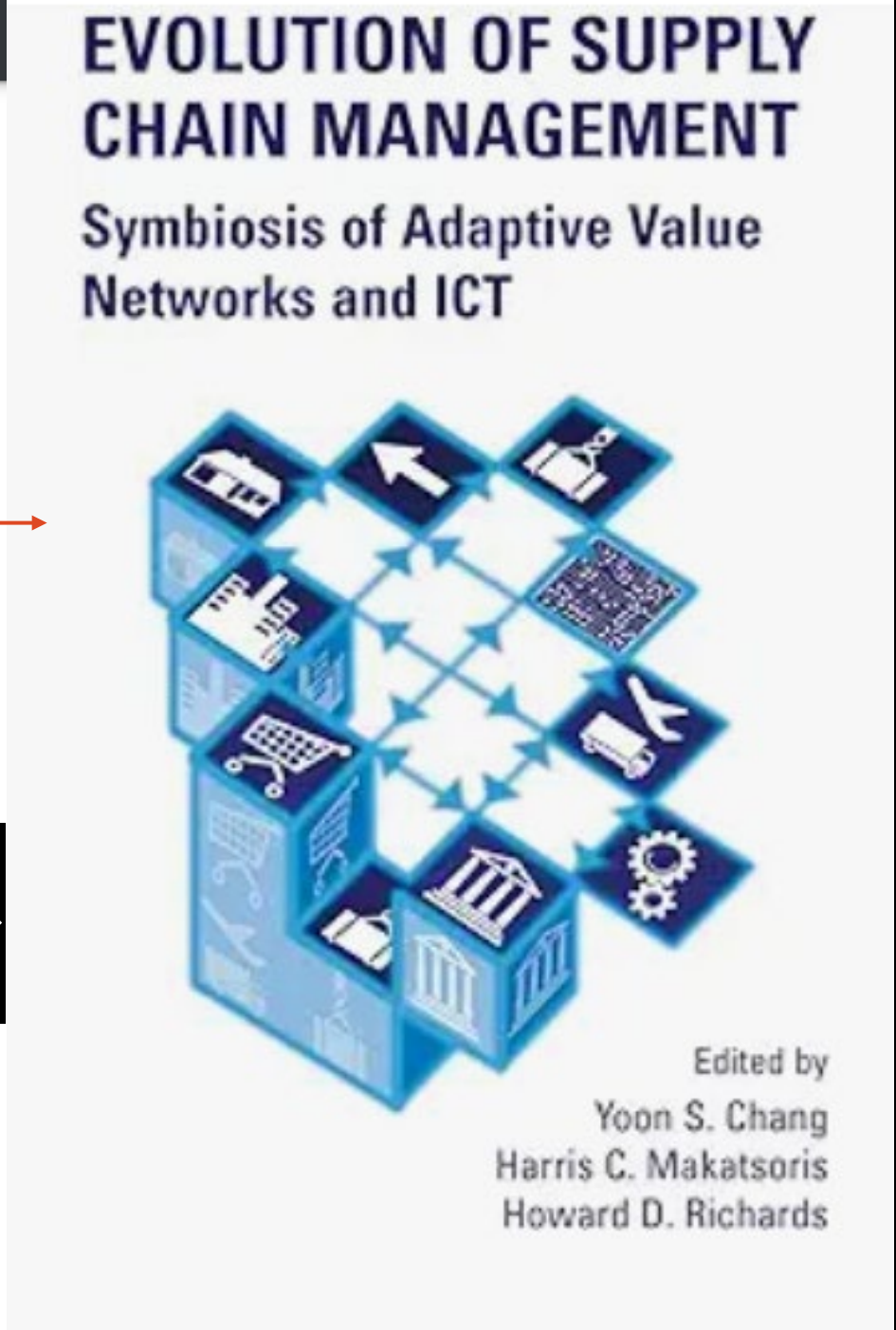
Shoumen Datta[1], Bob Betts[2], Mark Dinning[3], Feryal Erhun[4], Tom Gibbs[5], Pinar Keskinocak[6], Hui Li[1], Mike Li[1], Micah Samuels[7]

Massachusetts Institute of Technology[1], Timogen Inc.[2], Dell Corporation[3], Stanford University[4], Intel Corporation[5], Georgia Institute of Technology[6], Amazon.com[7]

- I have some idea, I think ...

ISBN-10 1402078129

ISBN-13 978-1402078125



Plant-based Oral Vaccines for Global Health: *Is it the light at the end of the tunnel?*

Unless prevented by vaccination, global economic loss from future pandemics may exceed $250 trillion. The jaw-dropping estimate is based on economic disaster data due to CoVID-19[1] and the long list of microbes/viruses with pandemic potential[2] which may erupt. Human mortality[3] due to CoVID-19 may be triple or quadruple the number of reported deaths (~15 million lives[4]). Governments invested ~$50 billion[5] to produce vaccines against SARS-CoV-2 (~13 billion doses, mostly for affluent[6] nations). For >80% of the global population, vaccines will be out of reach at $130 per dose[7] due to malicious corporate[8] greed. To prevent healthcare mediated global economic meltdown due to natural causes (microbes), the concept of vaccines must be extended biologically and geographically to include less affluent nations (**The Health of Nations**[9]) home to ~7 billion people (of ~8 billion global population). Preventive vaccination is key to reducing infectious disease transmission.

OBJECTIVE

EXECUTIVE SUMMARY

We propose an alternative vaccine form for preventive healthcare, based on credible scientific results (published evidence presented in **The Health of Nations**). The central thesis of this proposal begins with the confirmation[10] that Hepatitis B virus surface antigen (HBsAg) mRNA and protein were detected in plant (transgenic tobacco leaf). HBsAg from tobacco leaves elicited HBsAg-specific antibodies in mice[11] as proof of immunogenicity. **Human study**[12] with transgenic lettuce plant, expressing hepatitis B virus surface antigen, developed specific serum-IgG response to plant produced HBsAg. **Human study**[13] with potato-expressed E. coli labile toxin B subunit (LT-B) resulted in toxin neutralizing serum IgG antibodies (10/11) as late as day 59 (ingestion of raw potato expressing LT-B on day 0, 7, 21). **Human study**[14] with potato-expressed capsid protein of Norwalk virus (enteric pathogen) reported 95% of subjects (19/20) showing increases in antibody-secreting cells (IgA).

Taken together, transgenic plants expressing recombinant vaccine immunogens offer an attractive and potentially inexpensive alternative to industrial vaccine production, purification, packaging, storage, distribution and the "last mile" administration by injection (requires trained medical personnel). Plants and edible produce can be grown locally, anywhere. Sublingual[15] consumption of leaf paste or raw produce may be less palatable but does not require any specialized training. Eliminating downstream supply chain of vaccines and "last mile" delivery problems will facilitate access and availability of healthcare products (plants) for self-vaccination, worldwide. Developing immunity is the first step in prevention of infection.

EXECUTIVE SUMMARY - THE HEALTH OF NATIONS

1-Page Extended Summary "POV" may be downloaded from the MIT Library https://dspace.mit.edu/handle/1721.1/145774

Dr Shoumen Palit Austin Datta, Massachusetts General Hospital, Harvard Medical School and Department of Mechanical Engineering, Massachusetts Institute of Technology

Are you too busy designing the next gen mRNA vaccine, small molecules or nanobodies for the next pandemic?

Then you won't have the time to peruse this power-point doc.

Too bad, you wouldn't know what's here, proven and can be delivered, now, to prevent the 22nd century pandemic(s).

OK then …

SCIENCE & SOCIETY

https://www.nature.com/articles/d41586-024-00476-z

6. Remember that changing the world is hard

Timing and chance play a part in whether and how much a researcher can have an impact, says Cairney. For example, a set of results might become influential because it emerges at just the moment that a related policy is being revamped.

Abhijit Banerjee, an economist at the Massachusetts Institute of Technology in Cambridge who shared the 2019 Nobel economics prize for his research on fighting global poverty , has attributed his own career to a series of happy accidents – the first being that he was born to two economists. Because chance events have a hand in our lives, Banerjee is cautious about being too directive in telling young people to enter one field or another. "A lot of it is accidents that make us who we are," he says, and sometimes we learn something about ourselves as a result of them.

Whatever you do, he says, be willing to work hard. The work of Banerjee and his collaborators has touched the lives of an estimated 600 million people, but he's also been open about working long hours. Banerjee has a warning for those who think they can change the world while making lots of money. "I'm not saying it's impossible, but don't fool yourself – it's often hard," he says. "Changing the world might be a full-time job by itself."

www.nobelprize.org/prizes/economic-sciences/2019/banerjee/facts/

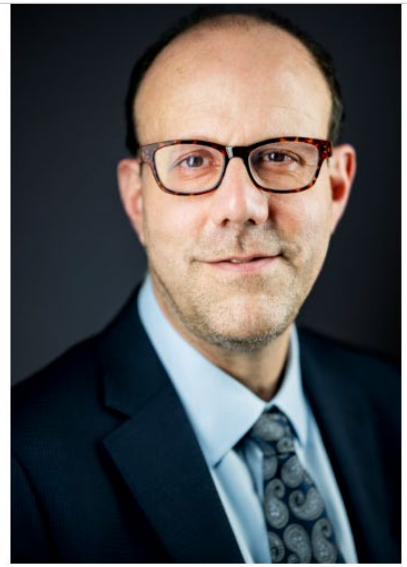
'Randomistas' who used controlled trials to fight poverty win economics Nobel

Abhijit Banerjee, Esther Duflo and Michael Kremer have been awarded the prize for their experimental approach to alleviating poverty.

Prize in Economic Sciences 2019 | Abhijit Banerjee - Facts

© Nobel Media. Photo: A. Mahmoud
Abhijit Banerjee

© Nobel Media. Photo: A. Mahmoud
Esther Duflo



© Nobel Media. Photo: A. Mahmoud
Michael Kremer

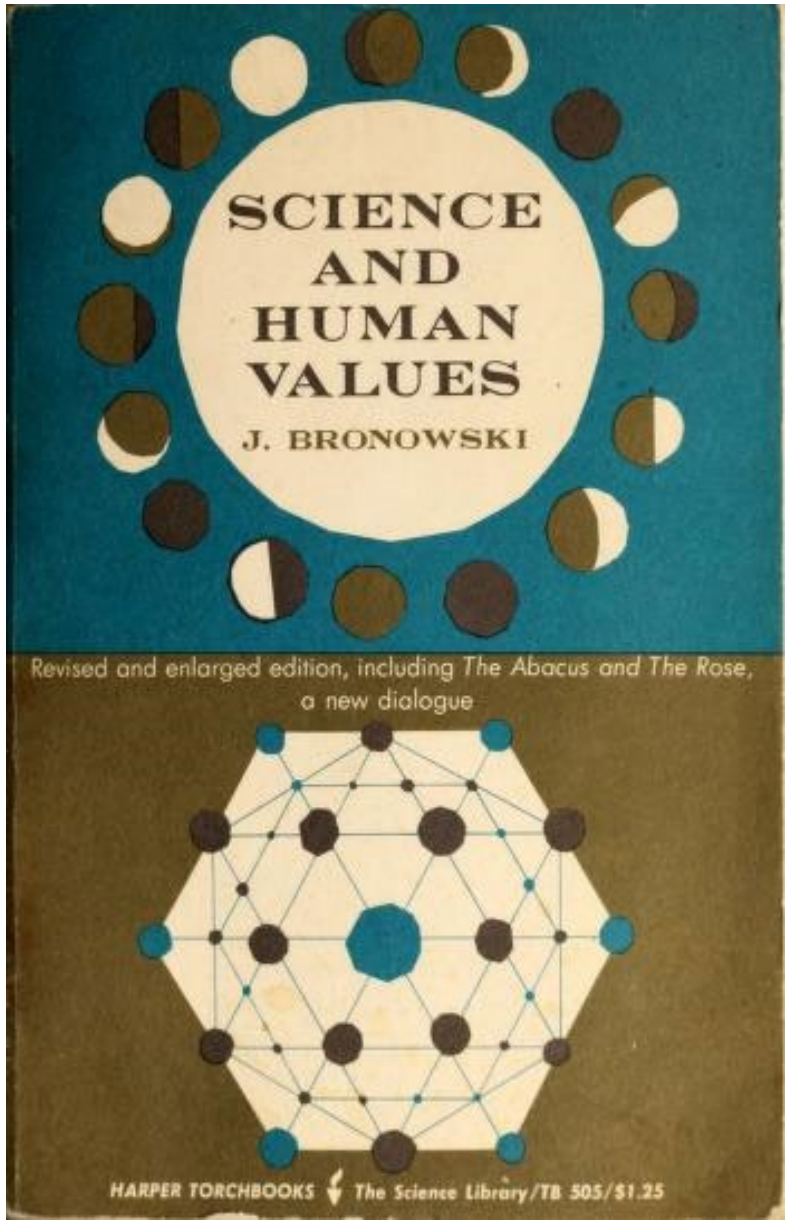
https://news.mit.edu/2019/esther-duflo-abhijit-banerjee-win-2019-nobel-prize-economics-1014

Abhijit Banerjee was born in Mumbai, India. Both of his parents were professors of economics. After studying at the University of Calcutta and Jawaharlal Nehru University in Delhi, he earned his doctorate at Harvard University in the United States in 1998. He taught at Harvard University and Princeton University before becoming a professor at the Massachusetts Institute of Technology, where he now works. Abhijit Banerjee married his fellow researcher, Esther Duflo, with whom he also shared the Economics Prize.

SCIENCE & SOCIETY

IN PRAISE OF IMPERFECTION

- It took almost ~50 years, but the grand convergence of basic science research made it possible to produce and implement the mRNA vaccine for CoVID-19 in order to immunize humans against SARS-CoV-2[n]. It is a brilliant beacon of research excellence and translating science to be of service to society, when it was most needed, during the pandemic of the 21st century, which went viral.



https://sciencepolicy.colorado.edu/students/envs_5110/bronowski_1956.pdf

Those who do not learn from history are doomed to repeat it.

ESTHER NAKKAZI SCIENCE OCT 18, 2022 7:00 AM

Ebola Is Back—and Vaccines Don't Work Against It

Public health officials are racing to contain an outbreak in Uganda. It's an urgent warning to the rest of the world.

September 15, 2022. A 24-year-old man, suffering from high fever and convulsions, was admitted to Mubende Regional Referral Hospital, Uganda. He was bleeding from his eyes, blood-stained vomit and diarrhea. The man died on September 19, 2022. The next day, tests confirmed the infection by Ebola. By October 16, 2022, the Ministry of Health had reported 60 confirmed cases of Ebola (11 new cases in the previous 2 weeks). In total, 24 deaths have been confirmed, including 4 among health workers, along with 24 recoveries.

www.wired.com/story/uganda-ebola-outbreak-vaccine

www.science.org/doi/epdf/10.1126/science.ado7079

A SPIKING FEVER

Long neglected, Lassa fever is surging in West Africa. Researchers want to know why

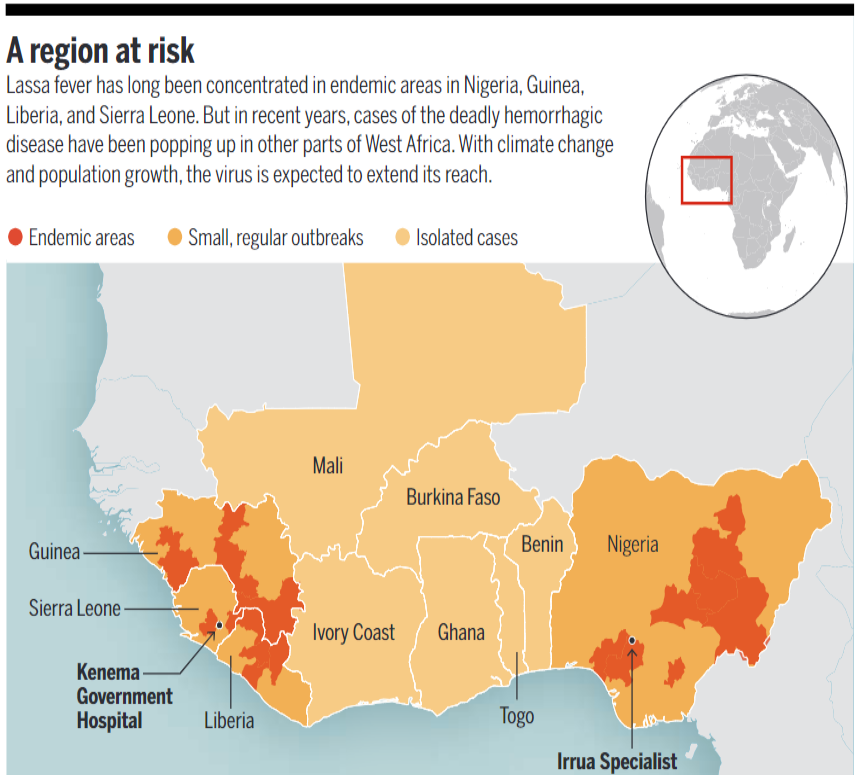
Sitting on a bench outside the Irrua Specialist Teaching Hospital (ISTH) in Edo state in southwestern Nigeria in September 2023, Muhammed Luqman Dagana recounted his ordeal earlier in the year with Lassa fever, a deadly hemorrhagic disease of West Africa. At first the 33-year-old wasn't alarmed—his fever, headache, body aches, and cough were innocuous enough. A doctor at his local clinic gave him antibiotics for typhoid fever and antimalarial drugs. But his symptoms persisted, so he tried another clinic. Again, the diagnosis was malaria and typhoid.

By **Leslie Roberts**, *in Irrua, Nigeria, and Kenema, Sierra Leone; Photography by* **Apochi Owoicho**

Reporting for this story was supported by the Pulitzer Center.

https://www.who.int/health-topics/lassa-fever

Corrected 26 February 2024. See full text.



Lassa virus, member of the arenavirus family.
www.who.int/health-topics/lassa-fever

https://www.science.org/content/article/deadly-viral-illness-exploding-west-africa-researchers-are-scrambling-figure-out-why

Lassa fever kills far more people than Ebola — 10,000 or more annually, although no one knows for sure. Identified only half a century ago, the rodent-borne disease, which can be transmitted between people via body fluids, affects the rural poor, who live far from any health center. A record-shattering epidemic in 2018 in Nigeria, the hardest hit country, put Lassa fever on the map, prompting both the World Health Organization and Nigeria to declare a public health emergency. Confirmed cases (25 to 100 in previous outbreak years) reached 633, 171 people died, including 45 health care workers.

Laissez Faire Lippenbekenntnisses ?

Prof Ira M. Longini (bio-statistician at University of Florida, Gainesville, FL, MARVAC member) says that if the Rwandan outbreak continues, the plan is to trial one vaccine as ring vaccination. The approach showed effectiveness of an Ebola vaccine in Guinea (2014–2016 West African outbreak) which involves immunizing contacts of an infected individual.

nature.com/articles/d41586-024-03218-3

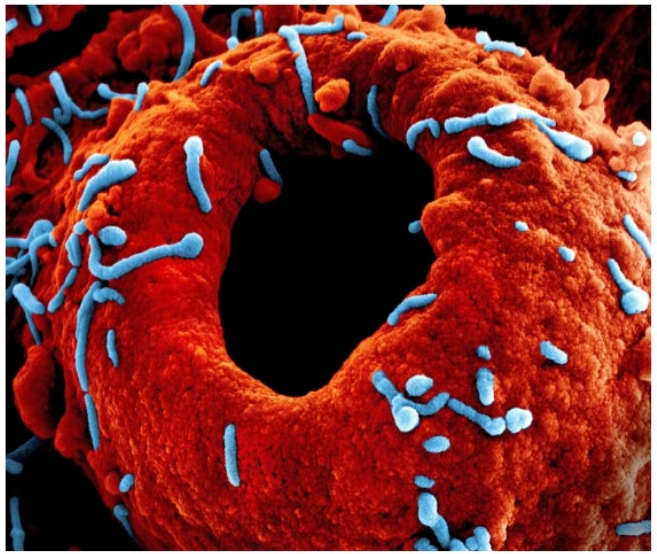
https://doi.org/10.1038/d41586-024-03275-8

NEWS | 01 October 2024

Deadly Marburg virus: scientists race to test vaccines in outbreak

There are no approved treatments for the Ebola-like haemorrhagic fever, which is spreading in Rwanda.

By Ewen Callaway



Marburg virus particles (blue) on the surface of an infected cultured cell (red). Credit: NIAID/SPL

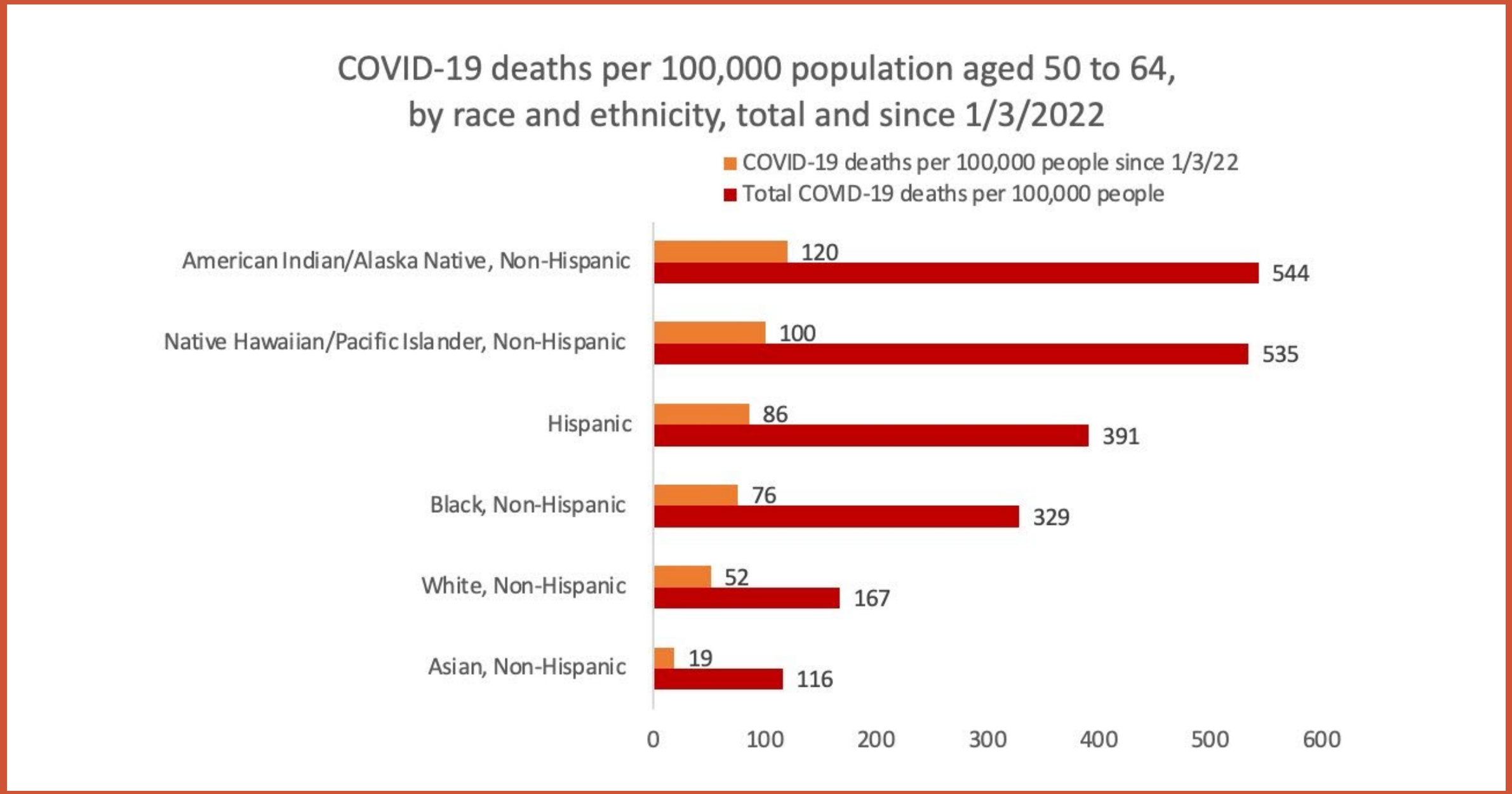
Researchers are in a race against time to deploy vaccines and treatments against a deadly virus that has exploded in Rwanda.

The fact that clinical-trial plans are in place and that other groundwork has been laid increases the odds that Marburg vaccines and treatments will be used in Rwanda, says Nancy Sullivan, a viral immunologist at Boston University, Boston, MA. It's likely that data on Marburg vaccines and treatments will be needed from multiple outbreaks before conclusions can be drawn about their effectiveness.
"The idea now is that you just move forward and don't worry that the outbreak will end before trial enrolment is complete," Sullivan adds. "It's just a piece of the overall trial."

Nature **634**, 278 (2024)
https://doi.org/10.1038/d41586-024-03218-3

Hamer *et al* (2023) ***Safety, tolerability, immunogenicity of the chimpanzee adenovirus type 3-vectored Marburg virus (cAd3-Marburg) vaccine in healthy adults in USA: irst-in-human, phase 1, open-label, dose-escalation trial***. **Lancet.** 2023 January 28; 401(10373):294-302. doi: 10.1016/S0140-6736(22)02400-X. PMID: 36709074; PMCID: PMC10127441. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10127441/pdf/nihms-1871339.pdf

Those who cannot remember the past are condemned to repeat it. [George Santayana]

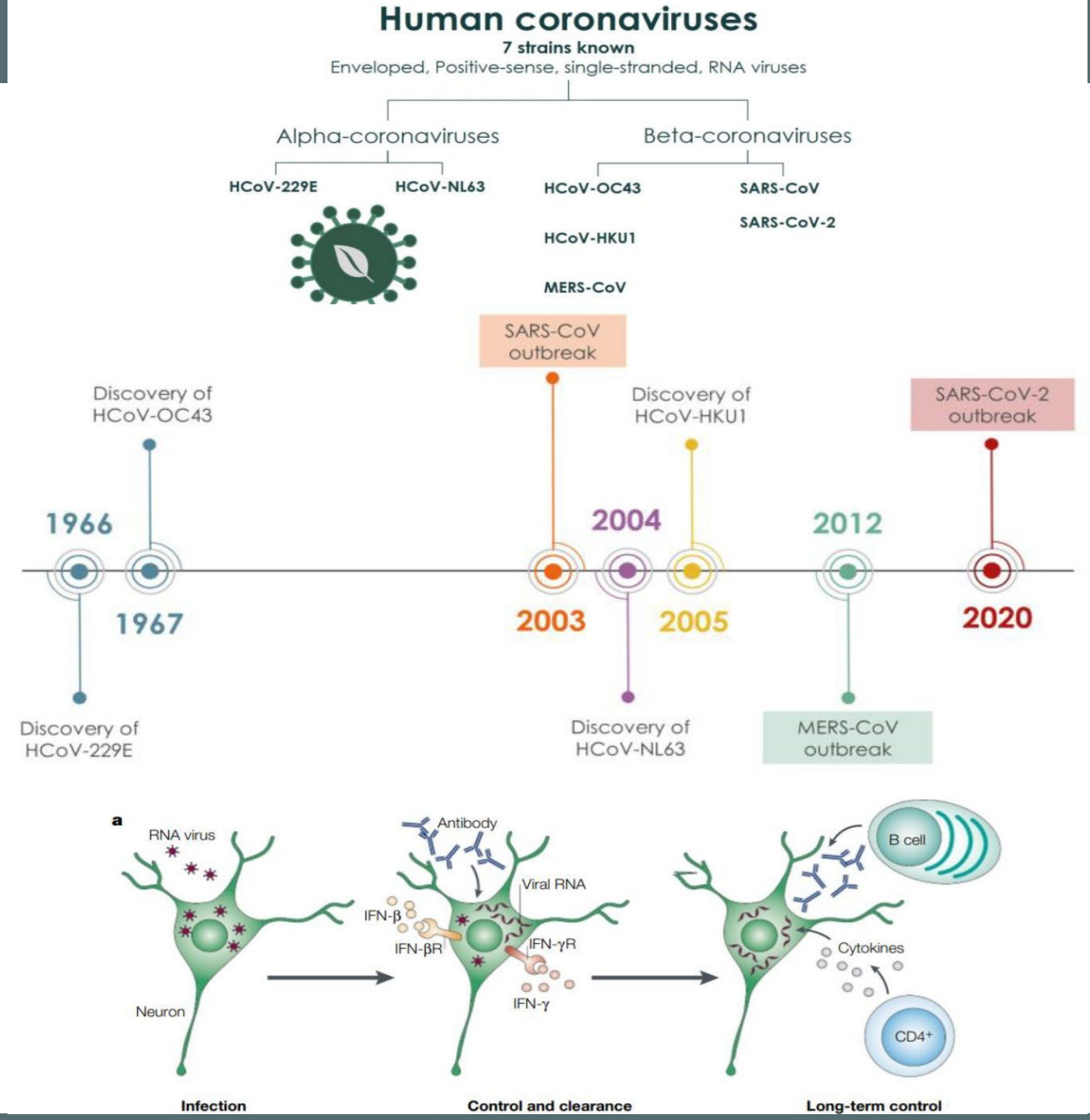


Bassett MT, Chen JT, Krieger N (2020) Variation in racial/ethnic disparities in COVID-19 mortality by age in US: A cross-sectional study. PLoS Med 17(10): e1003402. https://journals.plos.org/plosmedicine/article/file?id=10.1371/journal.pmed.1003402&type=printable

It is so crucial to grasp why chronic long-term morbidity is far worse for society than mortality (death).

21st century viral outbreaks were caused by pathogenic coronaviruses: SARS-CoV-1 (2003), MERS-CoV (2012) and SARS-CoV-2 (2019). Over 3,000 strains of coronavirus have been discovered, but only 7 have crossed the species barrier and spilled over to humans from a zoonotic source. In addition to 3 pathogenic strains, four (OC43, NL63, 229E, HKU1) are endemic in human populations (cause mild respiratory symptoms, contributing to 15-30% of cases of common cold). But, all 7 strains of human coronaviruses are capable of infecting the human brain, presenting an immense risk of chronic long-term morbidity (brain is constantly infected and colonized with numerous microorganisms, some of which can induce substantial pathogenesis). This complex interaction was neglected in the past and one critical reason why vaccination/immunization is crucial against viral/bacterial infections (not only for those with pandemic potential). The transsynaptic spread of SARS-CoV-2 and other human coronaviruses throughout the olfactory path would explain the fast presentation of symptoms such as anosmia (loss of sense of smell). Multiple molecular mechanisms are likely to be involved for brain infection and induced behavioral alterations by microorganisms (e.g., SARS-CoV-2). It will take decades to understand the extent of damage due to neuroinvasive potential of microbes. Long-term outcomes may be grave and grim. Hence, preventive measures (vaccination, immunization) are quintessential to reduce risk of morbidity rather than relying on future discoveries for better treatment (e.g. patients with acute and chronic COVID-19 sequelae).

Dr. Danielle Beckman, California National Primate Research Center, University of California (Davis, CA) dbeckman@ucdavis.edu ▪ https://www.daniellebeckman.com


Human coronaviruses
7 strains known
Enveloped, Positive-sense, single-stranded, RNA viruses
Alpha-coronaviruses
Beta-coronaviruses
HCoV-229E
HCoV-NL63
HCoV-OC43
HCoV-HKU1
SARS-CoV
SARS-CoV-2
MERS-CoV
SARS-CoV outbreak
Discovery of HCoV-OC43
Discovery of HCoV-HKU1
SARS-CoV-2 outbreak
1966
1967
2003
2004
2005
2012
2020
Discovery of HCoV-229E
Discovery of HCoV-NL63
MERS-CoV outbreak
a
RNA virus
Antibody
Viral RNA
IFN-β
IFN-βR
IFN-γR
IFN-γ
Neuron
B cell
Cytokines
CD4+
Infection
Control and clearance
Long-term control

Zika, dengue transmission expected to rise with climate change

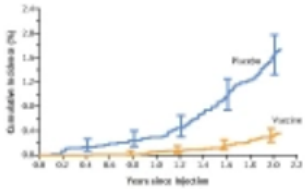
by **Luís Patriani** on 9 August 2023 | Translated by **Maya Johnson**

- *A new study foresees a 20% increase in cases of viruses like dengue, Zika and chikungunya over the next 30 years due to climate change.*
- *Higher temperatures are already causing the diseases carried by the Aedes aegypti mosquito to spread in cooler regions like southern Brazil and southern Europe.*
- *Deforestation also favors the spread of these illnesses because biodiversity-rich forests with more predators tend to inhibit mosquito populations.*

The number of deaths in Brazil due to dengue hit a record high in 2022, with 1,016 — the first time in history the number had surpassed four digits.

Van Wyk H, Eisenberg JNS, Brouwer AF. Long-term projections of the impacts of warming temperatures on Zika and dengue risk in four Brazilian cities using a temperature-dependent basic reproduction number. PLoS Negl Trop Diseases. 2023 April 27; 17(4):e0010839. doi: 10.1371/journal.pntd.0010839
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10138270/pdf/pntd.0010839.pdf

Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults



E.G. Kallás and Others

CME

Kallás et al. recently published a report of the efficacy and safety findings after 2 years of follow-up of an ongoing phase 3 trial in Brazil that is evaluating a single dose of Butantan–Dengue Vaccine for the prevention of symptomatic, virologically confirmed dengue infection in children, adolescents, and adults regardless of their history of dengue exposure.

Clinical Pearls

What regions of the world have the largest burden of dengue disease?

Four serotypes of dengue virus (DENV) circulate worldwide, causing an estimated 390 million infections annually. The largest burden of dengue disease occurs in Southeast Asia and Central and South America. In Brazil, DENV is hyperendemic, with varying incidence across the country. Although most primary DENV infections are asymptomatic or subclinical, DENV can result in severe disease, particularly with secondary heterotypic infection.

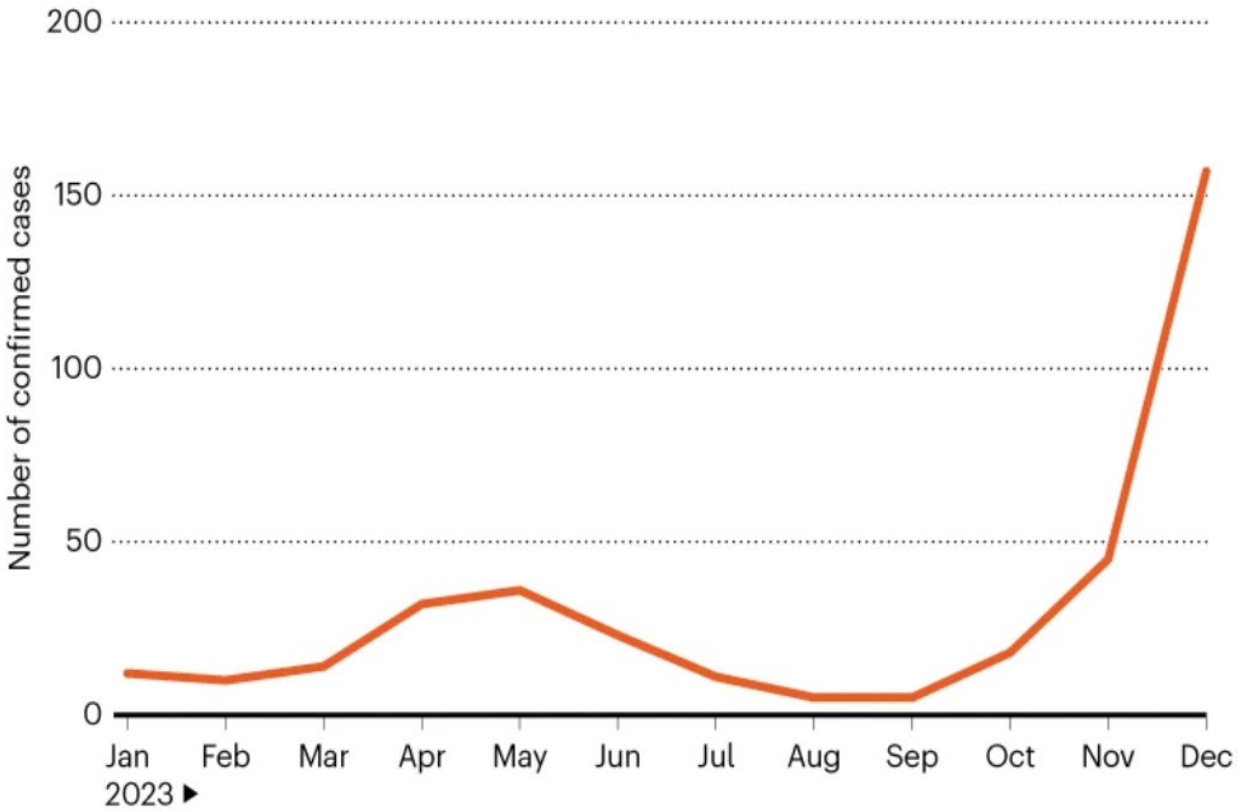
Kallás EG, Cintra MAT, Moreira JA, Patiño EG, Braga PE, Tenório JCV, Infante V, Palacios R, de Lacerda MVG, Batista Pereira D, da Fonseca AJ, Gurgel RQ, Coelho IC, Fontes CJF, Marques ETA, Romero GAS, Teixeira MM, Siqueira AM, Barral AMP, Boaventura VS, Ramos F, Elias Júnior E, Cassio de Moraes J, Covas DT, Kalil J, Precioso AR, Whitehead SS, Esteves-Jaramillo A, Shekar T, Lee JJ, Macey J, Kelner SG, Coller BG, Boulos FC, Nogueira ML. **Live, Attenuated, Tetravalent Butantan-Dengue Vaccine in Children and Adults.** New England J Med. 2024 February 1; 390(5):397-408. doi: 10.1056/NEJMoa2301790. PMID: 38294972.

Measles outbreaks cause alarm: what the data say

A drastic rise in infections in the United Kingdom and Europe follows a drop in vaccine uptake.

MEASLES SURGE

There have been more than 200 confirmed cases of measles in England since October 2023, prompting health authorities to declare a national incident.



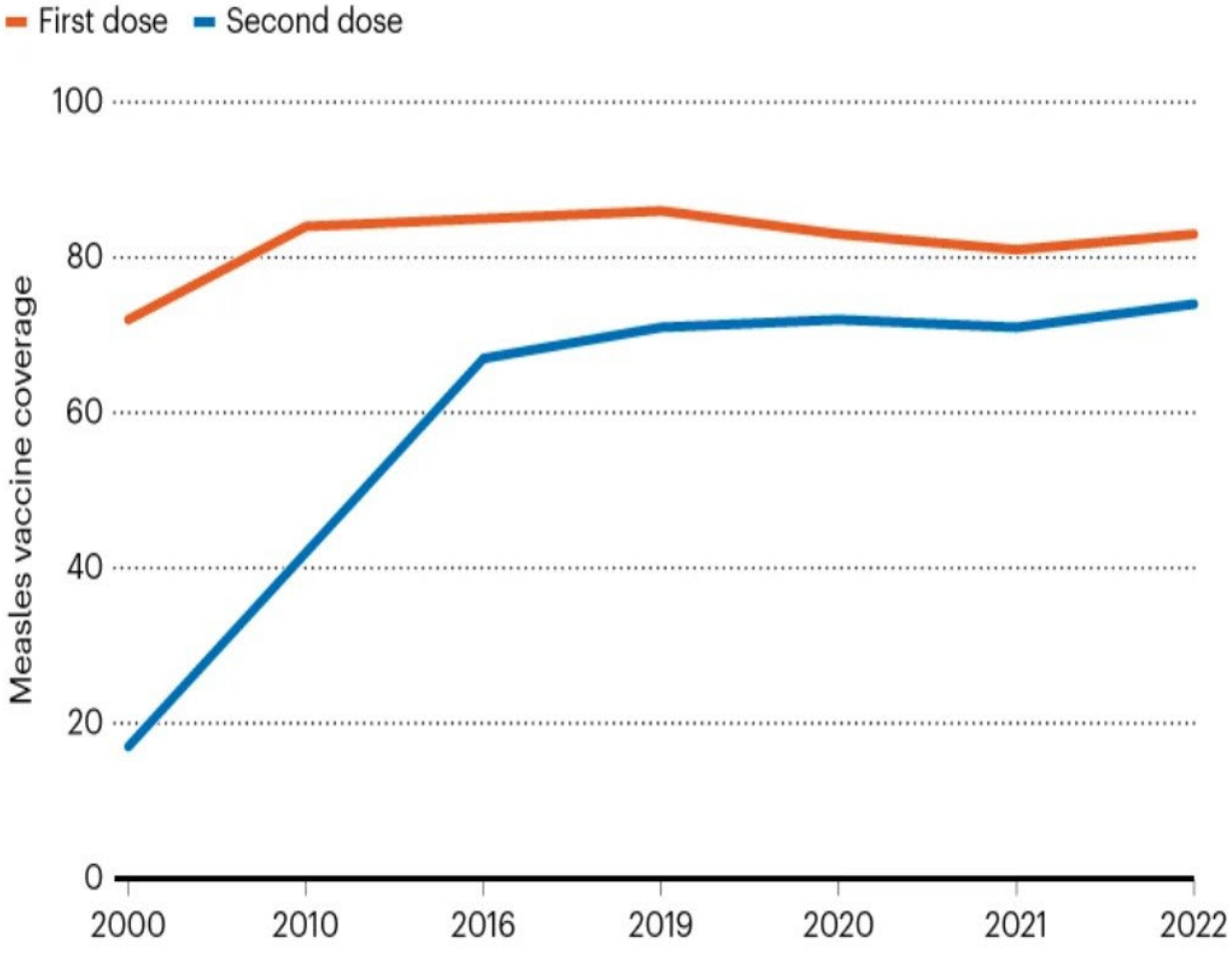
https://www.nature.com/articles/d41586-024-00265-8

Source: UK government

Europe is facing an alarming situation: 45-fold rise in measles from 2022 to 2023. In 2023, the region reported 42,200 measles cases, up from fewer than 1,000 in 2022. Globally, the number of measles cases increased by 18% between 2021 and 2022, and deaths from measles increased by 43%, according to a WHO report (November, 2023).

JABS NEEDED

The proportion of people globally who have received their first and second doses of measles-containing vaccines falls short of the World Health Organization's recommended level of 95%, which achieves 'herd immunity'.



THE STATE OF GLOBAL HEALTH AND HEALTHCARE DEPENDS ON

F E W S

F	FOOD
E	ENERGY
W	WATER
S	SANITATION

The shorter the FEWS, the longer the healthcare burden

FEWS

S

SANITATION

• Approximately half a billion people defecate in the open (on streets, open sewers, bushes, fields, bodies of water - streams, ponds, lakes)

World Health Organization

•Over 1.5 billion people do not have access to basic sanitation facilities, toilets or latrines.

•In 2022, ~ half of the global population (~4 billion people) did not have any managed sanitation service.

https://www.who.int/news-room/fact-sheets/detail/sanitation

https://doi.org/10.1038/d41586-024-00886-z

FEWS

W

WATER

https://sdgs.un.org/conferences/water2023

United Nations

UN 2023 Water Conference

22 – 24 Mar 2023, New York

2 billion people do not have access to clean and safe drinking water, according to UN (United Nations World Water Development Report on 22 March 2023).

NATURE ■ https://www.nature.com/articles/d41586-024-02621-0

FEWS

W

WATER

‘Unacceptable’: a staggering 4.4 billion people lack safe drinking water, study finds

New estimate doubles the previous figure, raising questions about which is correct and highlighting gaping data holes.

4.4 billion people do not have access to safe drinking water (2024).

SCIENCE ■ https://www.science.org/doi/pdf/10.1126/science.adh9578

FEWS

E

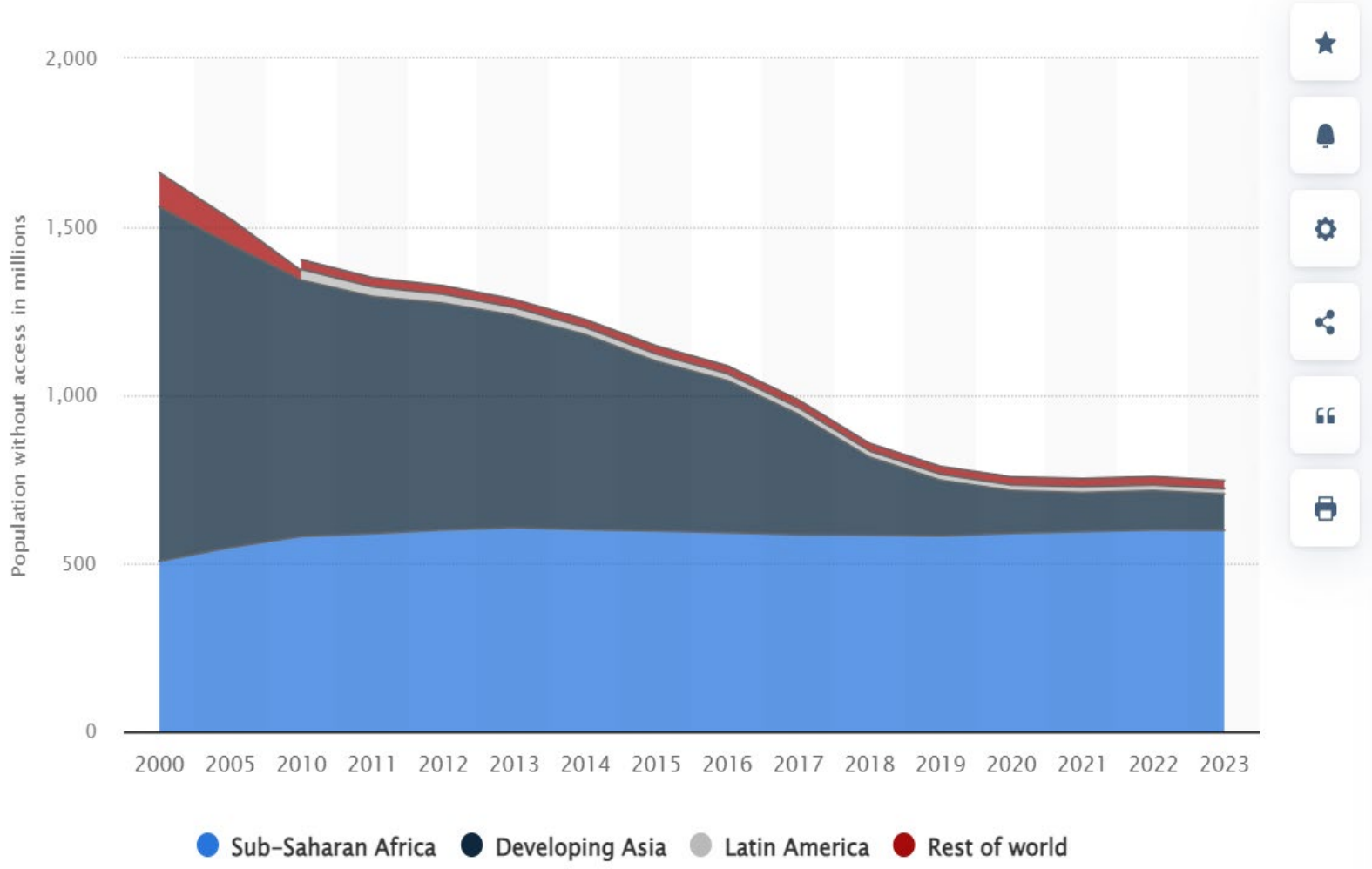
ENERGY

https://unstats.un.org/sdgs/report/2023/Goal-07

Energy & Environment › Energy www.statista.com/statistics/829803/number-of-people-without-access-to-electricity-by-region/

Number of people without access to electricity worldwide 2023, by region

(in millions)



FEWS

E

ENERGY

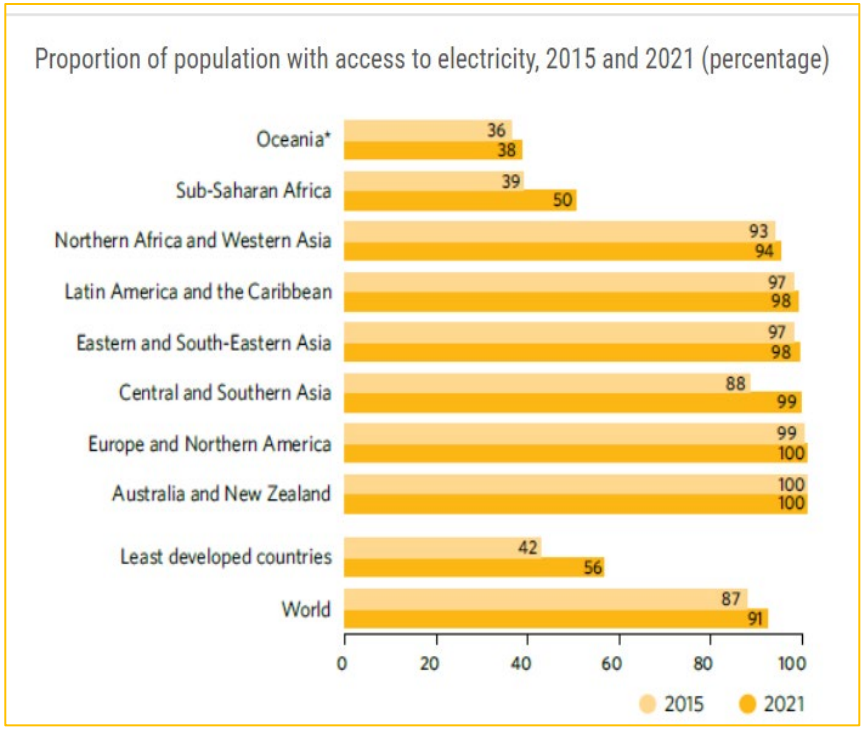
https://ourworldindata.org/energy-access

Access to Energy

Access to electricity and clean cooking fuels are vital for a good standard of living and good health.

By: Hannah Ritchie, Pablo Rosado and Max Roser

This page was first published in September 2019 and last revised in January 2024.



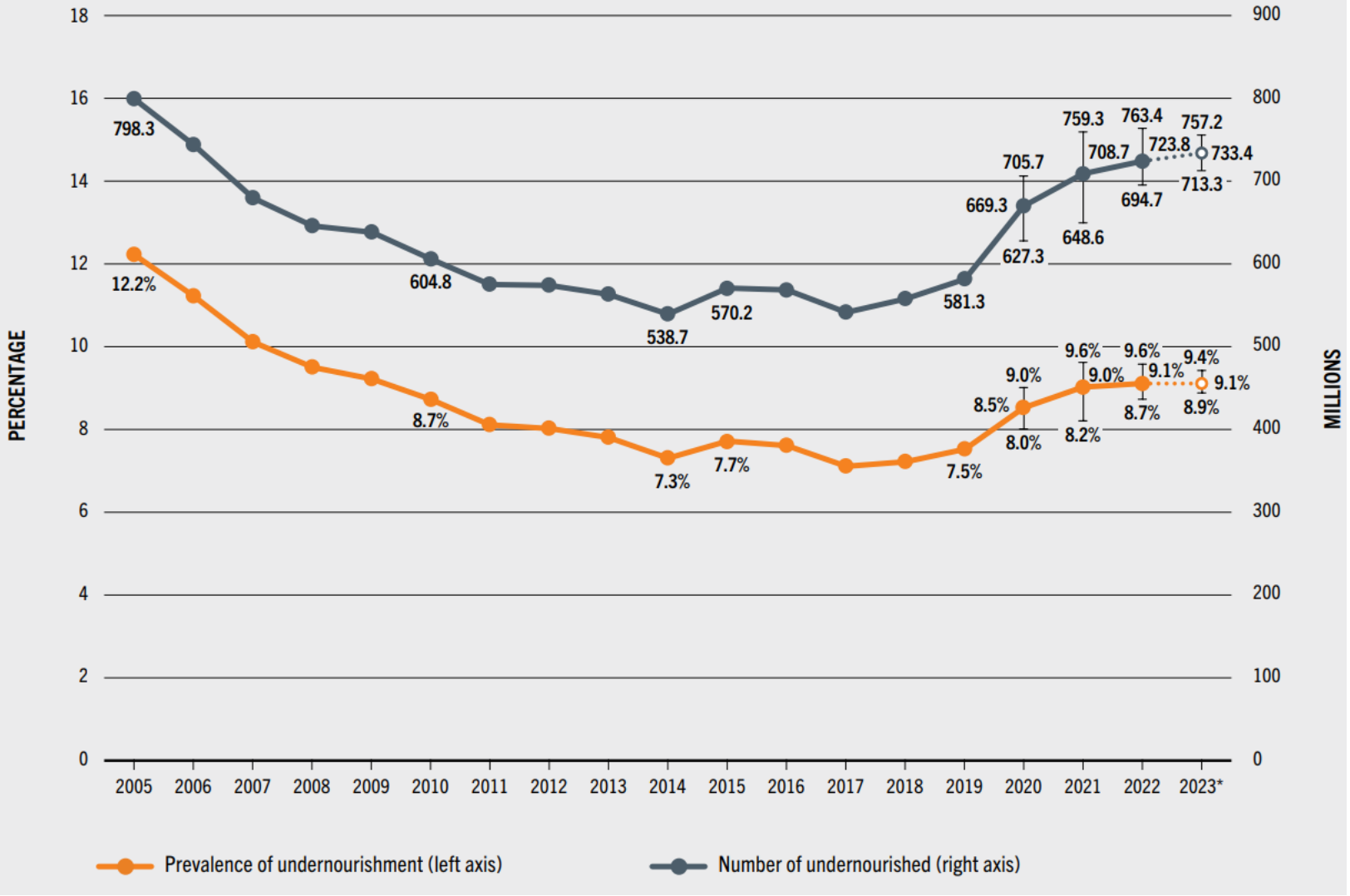
FAO, IFAD, UNICEF, WFP, WHO. 2024. The State of Food Security and Nutrition in the World 2024 – Financing to end hunger, food insecurity and malnutrition in all its forms.

FEWS

F

FOOD

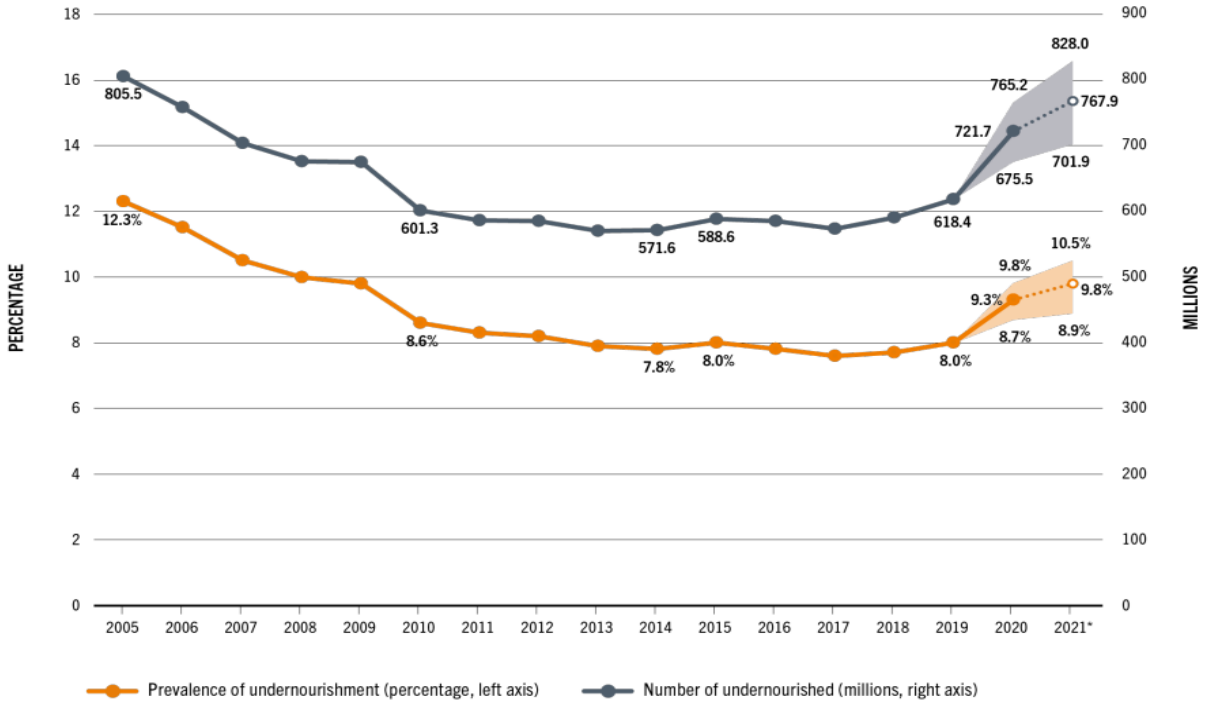
FIGURE 1 GLOBAL HUNGER ROSE SHARPLY FROM 2019 TO 2021 AND PERSISTED AT THE SAME LEVEL TO 2023



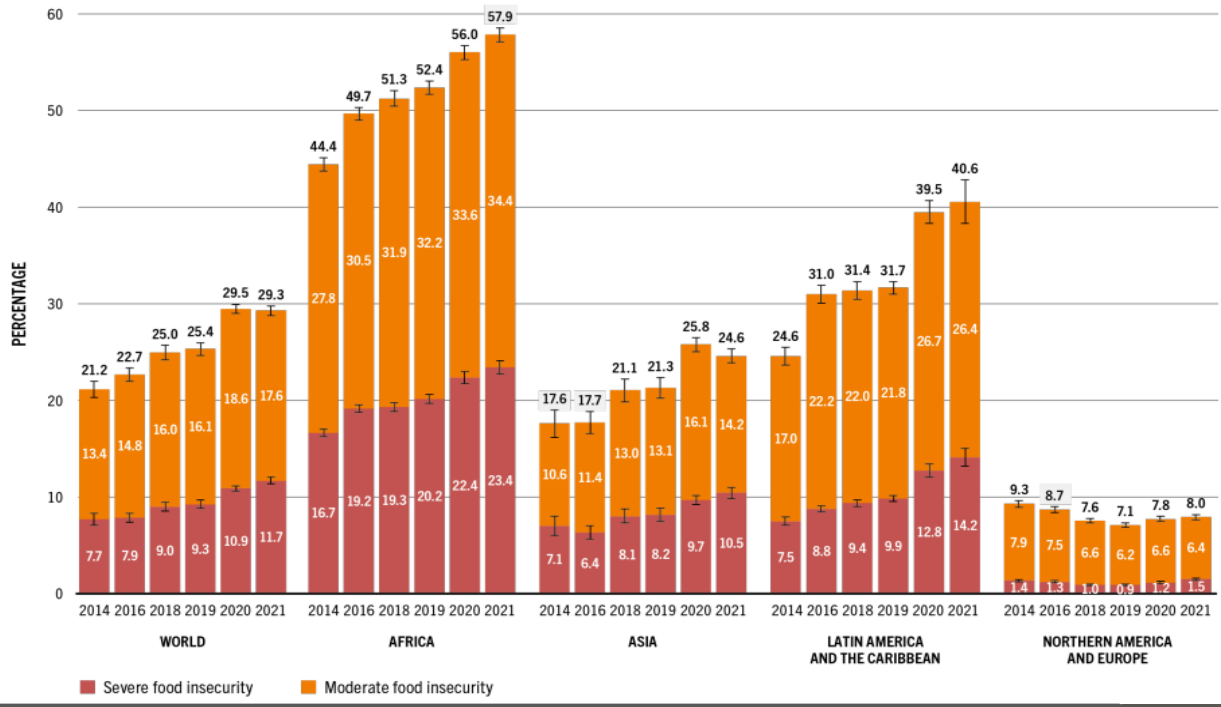
https://doi.org/10.4060/cd1254en

https://openknowledge.fao.org/server/api/core/bitstreams/5750b9e9-a74c-4b0e-8c76-1f7568874e4a/content

~1 Billion people in the world: Facing Hunger, 2021



~2 Billion people in the world: Food Insecurity, 2021



FAO, IFAD, UNICEF, WFP and WHO. 2022. *The State of Food Security and Nutrition in the World 2022. Repurposing food and agricultural policies to make healthy diets more affordable*. Rome, FAO.
https://doi.org/10.4060/cc0639en
https://www.fao.org/3/cc0879en/cc0879en.pdf
https://www.fao.org/3/cc0639en/cc0639en.pdf

Food Waste Index Report 2024. Think Eat Save: Tracking Progress to Halve Global Food Waste (UNEP, 2024)
https://sdg2advocacyhub.org/wp-content/uploads/2024/03/food_waste_index_report_2024.pdf

https://doi.org/10.4060/cd1254en

29% of the global population is food insecure.

Food loss and waste (FLW) is about one third (1.3 billion tonnes) of total food produced. In 2022, 13% of all food produced was lost, and 19% of food available to consumers was wasted at retail, food service and households. The highest FLW shares are seen in the case of fruits and vegetables (45%), followed by fish and seafood (35%), cereals (30%), dairy products (20%), and meat and poultry (20%).

https://www.nature.com/articles/s43016-024-01041-7.epdf

www.ncbi.nlm.nih.gov/books/NBK597352/

FEWS

F

FOOD

Global estimation of dietary micronutrient inadequacies: a modelling analysis

Simone Passarelli*, Christopher M Free*, Alon Shepon, Ty Beal, Carolina Batis, Christopher D Golden

Summary

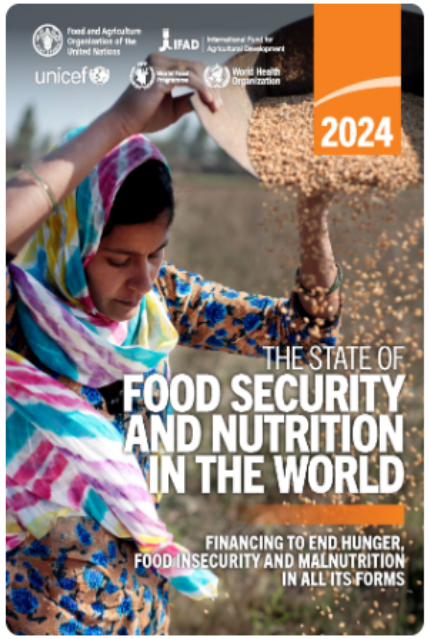
Background Inadequate micronutrient intakes and related deficiencies are a major challenge to global public health.

About two-thirds of the global population (~5 billion people) do not consume enough iodine (68% of the global population), vitamin E (67%), and calcium (66%). More than 4 billion people do not consume enough iron (65%), riboflavin (55%), folate (54%), and vitamin C (53%). Within the same country and age groups, estimated inadequate intakes were higher for women than for men for iodine, vitamin B12, iron, and selenium and higher for men than for women for magnesium, vitamin B6, zinc, vitamin C, vitamin A, thiamin, and niacin.

The Lancet Global Health, August 29, 2024
DOI: 10.1016/S2214-109X(24)00276-6

https://www.thelancet.com/action/showPdf?pii=S2214-109X%2824%2900276-6

fao.org/publications/home/fao-flagship-publications/the-state-of-food-security-and-nutrition-in-the-world/en



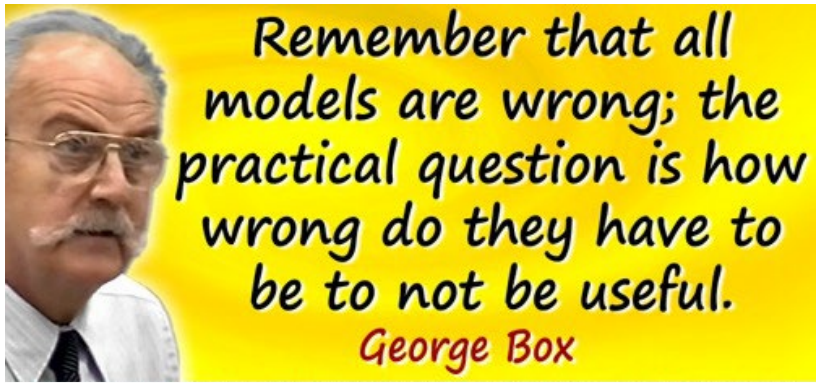
JUST RELEASED

The State of Food Security and Nutrition in the World 2024

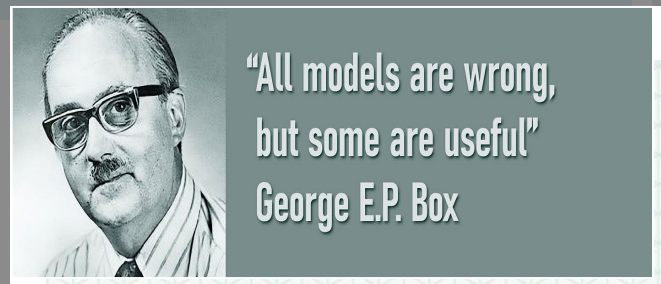
Financing to end hunger, food insecurity and malnutrition in all its forms

This year's report provides timely and relevant recommendations regarding the efficient use of innovative financing tools and reforms to the food security and nutrition financing architecture. Establishing a common ground on how food security and nutrition financing is defined, along with methods for its tracking, measurement and implementation, is an important first step towards sustainably increasing the financing flows needed to end hunger, food insecurity and all forms of malnutrition, and to ensure access to healthy diets for all, today and tomorrow. To this end, insights of this report are particularly important in light of the next Summit of the Future in September 2024 and the Fourth International Conference on Financing for Development in June and July 2025.

https://openknowledge.fao.org/server/api/core/bitstreams/31af4e18-aaeb-4164-991e-2431fe9d41ca/content



https://en.wikipedia.org/wiki/George_E._P._Box



FOOD: WHOLE LOT OF BLAH…BLAH…BLAH

What would making our food systems inclusive, health-enhancing and environmentally sustainable entail? This report draws on extensive research undertaken by the Food System Economics Commission from 2020 to 2023: is such a global transformation economically viable? What are the policy levers? And what obstacles could block its way?

https://foodsystemeconomics.org/wp-content/uploads/FSEC-Global_Policy_Report.pdf

ISN'T FEWS INCOMPLETE WITHOUT HEALTHCARE?

ADD 'H'

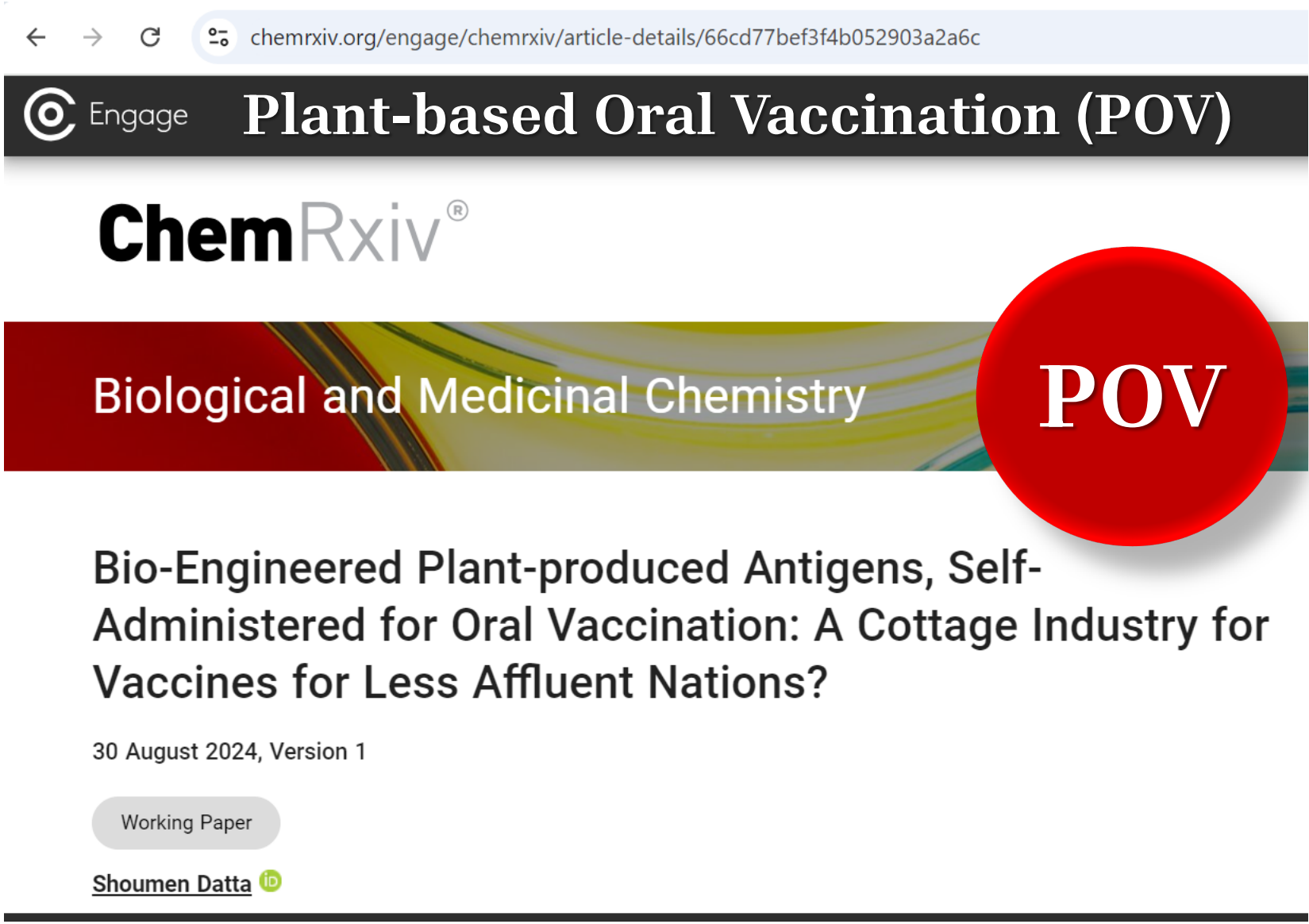
Datta, S. *Bio-Engineered Plant-produced Antigens, Self-Administered for Oral Vaccination: A Cottage Industry for Vaccines for Less Affluent Nations?* . ChemRxiv. 2024; doi:10.26434/chemrxiv-2024-9zvtr Download https://chemrxiv.org/engage/chemrxiv/article-details/66cd77bef3f4b052903a2a6c

FEWSH

Food
Energy
Water
Sanitation
Healthcare

H

HEALTHCARE



POV FOR THE HEALTH OF NATIONS

Halabi, Sam, and George L. O'Hara. "Preparing for the Next Pandemic — Expanding and Coordinating Global Regulatory Capacity." *New England J of Medicine*, vol. 391, no. 6, August 2024, pp. 484–487 https://doi.org/10.1056/NEJMp2406390 https://www.nejm.org/doi/pdf/10.1056/NEJMp2406390

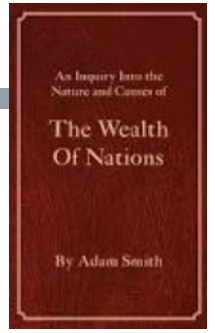
Pandemic Regulatory Capacity.*

Country	Regulatory Authority	Maturity Level	Scope of Products
China	National Medical Products Administration (NMPA)	3	Vaccines (producing)
Egypt	Egyptian Drug Authority (EDA)	3	Vaccines (producing)
Ghana	Food and Drugs Authority (FDA)	3	Medicines; vaccines (nonproducing)
India	Central Drugs Standard Control Organization (CDSCO)	3	Vaccines (producing)
Indonesia	National Agency of Drug and Food Control (BADAN POM)	3	Vaccines (producing)
Nigeria	National Agency for Food and Drug Administration and Control (NAFDAC)	3	Medicines; vaccines (nonproducing)
Saudi Arabia	Saudi Food and Drug Authority (SFDA)	4	Medicines; vaccines (producing)
Serbia	Medicines and Medical Devices Agency of Serbia (ALIMS)	3	Vaccines (producing)
Singapore	Health Sciences Authority (HSA)	4	Medicines; vaccines (nonproducing)
South Africa	South African Health Products Regulatory Authority (SAHPRA)	3	Vaccines (producing)
South Korea	Ministry of Food and Drug Safety (MFDS)	4	Medicines; vaccines (producing)
Tanzania	Tanzania Medicines and Medical Devices Authority (TMDA)	3	Medicines; vaccines (nonproducing)
Thailand	Food and Drug Administration (FDA)	3	Vaccines (producing)
Turkey	Turkish Medicines and Medical Devices Agency (TITCK)	3	Medicines; vaccines (producing)
Vietnam	Vaccine regulatory system involving the Drug Administration of Vietnam (DAV); the Administration of Science, Technology, and Training (ASTT); the National Institute for the Control of Vaccines and Biologicals (NICVB); and the General Department of Preventive Medicine (GDPM)	3	Vaccines (producing)

* Information is from the World Health Organization (https://www.who.int/publications/m/item/list-of-nras-operating-at-ml3-and-ml4).

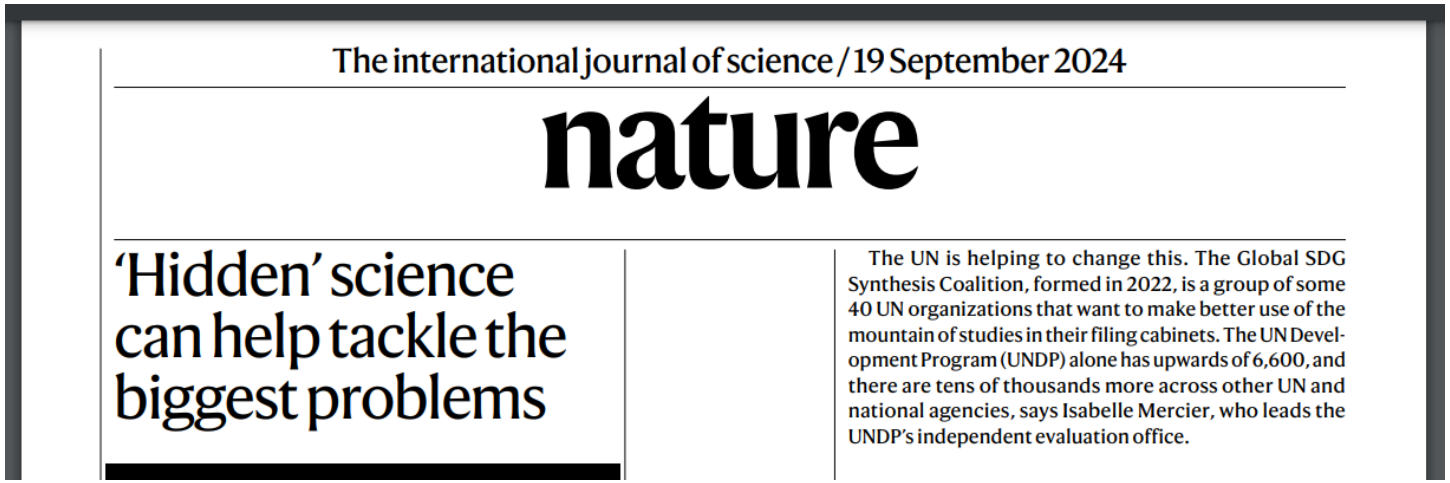
IGNORING OR IGNORANT OF POV ??

THE HEALTH OF NATIONS



The requirement for food, agnostic of the economic climate of individuals, makes nutrition an overwhelming platform of choice for delivery of preventive and prescriptive therapeutics. Willful ignorance peddled by a few disenfranchised groups continue their march of unreason by sowing socio-economic morbidity. It has plagued the delivery of medicinal value through food and nutrition, for example, prevention of xeropthalmia in children. The unbounded global transmissibility of prions, viruses and bacteria has exposed the chasm between the affluent nations and resource constrained communities in terms of access to healthcare and public health practices. There is little doubt that the reach of therapeutics (vaccines) are stringently controlled by corporate greed and gluttony, under the protection of legal frameworks. The latter makes a mockery of health as a human right and perpetrates the myth of irremediable injustices. Are they irremediable? Radical changes in research leadership and strategy are necessary to bring health related remedies and solutions to >80% of the global population (~8 billion) who are not a part of the affluent world (~1 billion). Is “food” the final frontier in scientific research in our plight to usher even a modicum of healthcare equity for the down-trodden, forgotten and misbegotten? This talk will not present any new ideas but revisit grand and profound old results, with renewed analyses through my old eyes.

Shoumen Palit Austin Datta, Massachusetts General Hospital, Harvard Medical School and Department of Mechanical Engineering, Massachusetts Institute of Technology



The international journal of science / 19 September 2024

nature

‘Hidden’ science can help tackle the biggest problems

The UN is helping to change this. The Global SDG Synthesis Coalition, formed in 2022, is a group of some 40 UN organizations that want to make better use of the mountain of studies in their filing cabinets. The UN Development Program (UNDP) alone has upwards of 6,600, and there are tens of thousands more across other UN and national agencies, says Isabelle Mercier, who leads the UNDP’s independent evaluation office.

nature.com/articles/d41586-024-02991-5

nature

nature › editorials › article

EDITORIAL | 17 September 2024

Unearthing ‘hidden’ science would help to tackle the world’s biggest problems

https://www.nature.com/articles/d41586-024-02991-5

PREPARE FOR POV

Can we trigger immune response in humans to foreign antigens by sublingual administration of raw leaf “paste” from plants expressing foreign proteins?

ABSTRACT

FDA approval of a form of glucocerebrosidase purified from and produced in plants (carrot cells) unleashed the potential for plant-derived therapeutic molecules to accelerate access to healthcare for resource constrained communities. The pandemic has increased the demand for delivery of antigens to vulnerable populations in remote corners of the world who cannot afford vaccines marketed by US corporations. Global public health challenge from viruses with pandemic potential (e.g., Ebola) requires the convergence of virologists, molecular biologists and plant geneticists to construct vectors expressing viral antigens detectable in leaves and stems of fast-growing transgenic plants (e.g., *Arabidopsis thaliana*). The ubiquitous availability of these plants (each expressing one or more viral antigens or epitopes) and eliminating the need for purification of the viral protein product from the plant, are key catalysts. A low-cost crude leaf “paste” made by using a mortar and pestle, may be used directly under the tongue to allow the viral antigens to enter the bloodstream through the bed of capillaries under the mucosal membranes (sublingual). This review discusses this hypothetical proposal and analyzes why the optimism may not be irrational.

HYPOTHESIS

SELF-VACCINATION USING (ORAL) SUBLINGUAL EDIBLE RAW LEAF PASTE

Raw leaf “paste” from transgenic plants, harboring recombinant foreign antigens (for example, Ebola Virus “Spike” protein – EBOV), can deliver foreign antigen(s) to the bloodstream of humans through sublingual administration. The presence of foreign antigen in the human bloodstream will trigger a healthy immune system to mount humoral (antibodies) and cellular (T-Lymphocytes) response. Thus, plants (raw leaf paste) can be a very low-cost vehicle for self-vaccination which can immunize billions of people in less affluent nations (>80% of the global population). This hypothesis is only about DELIVERY of the *optimized antigen* through a low-cost and ubiquitous vehicle (plant, food).

BASIC SCIENCE

Vaccines are a generic term. Delivery of one or more foreign antigen(s) is a more appropriate term. CoVID-19 vaccine was not a conventional attenuated virus vaccine. CoVID-19 vaccine delivered a “blueprint” (mRNA) for a target antigen (Spike protein of SARS-CoV-2). If a healthy human can receive (vaccinated, immunized) the foreign antigen prior to exposure to infectious particles (prions, virus, bacteria, fungi, parasites) then a healthy immune system can naturally defend the body by mounting immune responses (antibodies, T-lymphocytes). Delivering the foreign antigen is key.

Streatfield SJ, Karczewski J, Yusibov V. Introduction. Vaccine. 2017 October 4;35(41):5435-5436. doi: 10.1016/j.vaccine.2017.08.032. Epub on 2017 August 18. PMID: 28826749; PMCID: PMC7130944. www.ncbi.nlm.nih.gov/pmc/articles/PMC7130944/pdf/main.pdf

HELPS TO UNDERSTAND THE NATURE & TYPES OF VACCINES

Vaccine Types https://www.hhs.gov/immunization/basics/types/index.html
https://www.pfizer.com/news/articles/understanding_six_types_of_vaccine_technologies
Humoral Immunity (Antibodies) https://www.ncbi.nlm.nih.gov/books/NBK10752/
Cellular Immunity (T-Lymphocytes) https://www.ncbi.nlm.nih.gov/books/NBK10762/

THE PROPOSAL

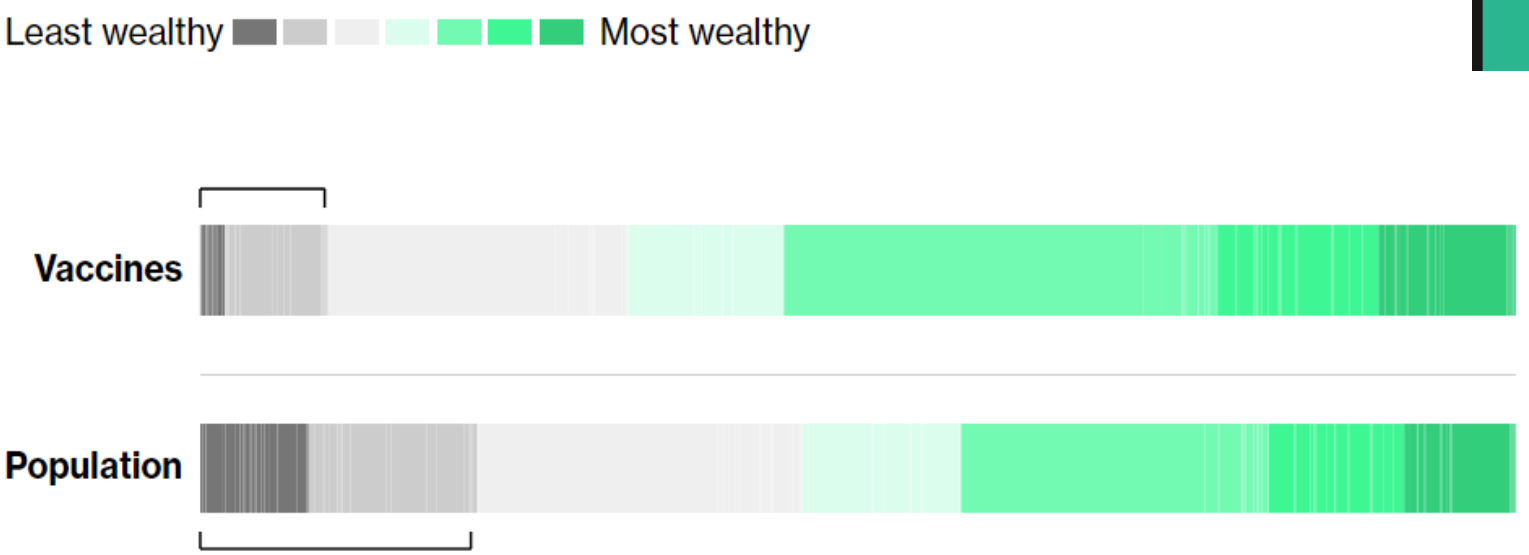
WHY THIS SUGGESTION? WHO MAY BENEFIT? HOW?

THIS IS NOT A NEW OR NOVEL SUGGESTION. THIS TALK IS MERELY HIGHLIGHTING RESEARCH RESULTS SPANNING 30 YEARS.

In the first two years after a pandemic was declared, a dozen new vaccines were developed and more than 10 billion doses were administered. The rollout was unprecedented in its speed and scope, but distribution has been lopsided. Countries with the highest incomes have been vaccinated 10 times faster than those with the lowest.

Delivering billions of additional doses to some of the world's least-equipped nations remains one of the biggest challenges for global health.

Uneven Access to Vaccines

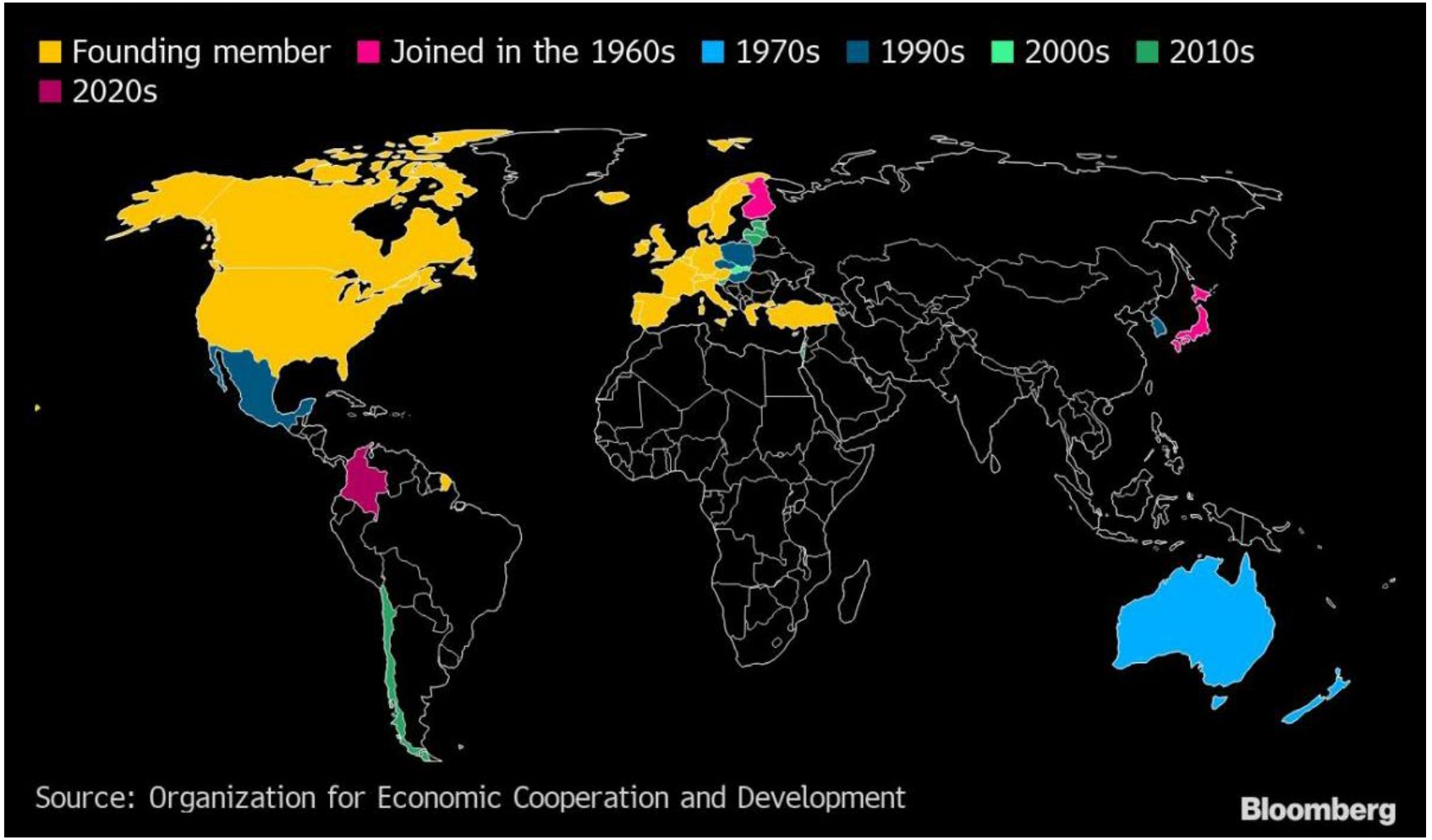


Note: Countries and regions are ordered by GDP per capita (PPP).

https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/

raison d'être

THE WEALTH OF NATIONS



This suggestion may not benefit the founding members of the "Club"

CHANGE

WHY IS THIS IMPORTANT ? WHO MAY BENEFIT? **HOW?**

IMAGINE, INVENT, INNOVATE TO CHANGE THESE THREE PROCESSES

- ANTIGEN-VACCINE MANUFACTURING
- MATERIAL STORAGE, DISTRIBUTION, LOGISTICS
- ACT OF VACCINATION (IMPLEMENTATION OF IMMUNIZATION)

IS DEMOCRATIZATION OF THE PROCESS THE ANSWER ?

ANTIGEN-VACCINE MANUFACTURING CORPORATIONS

SINGLE MOST IMPORTANT RATE LIMITING FACTOR (BOTTLE NECK). PROCESS OWNED BY CORPORATIONS CONTROLLING ACCESS.

Company	Location	Plant	Bioproduct
Kentucky BioProcessing LLC (KBP)	Owensboro, KY, USA	Tobacco, potato	Norovirus VP1 Ebola virus antibody (ZMapp)
Sigma-Aldrich Fine Chemicals	St. Louis, MO, USA	Maize	Trypsin
Medicago Inc.	Quebec, Canada	*Nicotiana benthamiana*	Influenza HA-VLP
Protalix	Carmiel, Israel	Carrot cells, tobacco cells	Alphataliglicerase
Caliber Biotherapeutics LLC	Byran, TX, USA	Tobacco	Influenza HA
Fraunhofer CMB USA	Newark, DE, USA	*Nicotiana benthamiana*	Influenza HA
Fraunhofer IME	Aachen, Germany	Tobacco	Antibody (for HIV)
National Institute of Advanced Industrial Science and Technology	Hokkaido, Japan	Strawberry	Canine interferon alpha
Institute of Medical Science, The University of Tokyo	Tokyo, Japan	Rice	Cholera toxin B subunit

www.pfizer.com/news/press-release/press-release-detail/pfizer_and_protalix_biotherapeutics_announce_fda_approval_of_elelyso_taliglucerase_alfa_for_the_treatment_of_gaucher_disease

May 1, 2012 - US Food & Drug Administration (FDA) approves first plant cell-expressed ELELYSO™ (taliglucerase alfa*), an enzyme replacement therapy for adults with type 1 Gaucher disease. ELELYSO is derived from Protalix's proprietary manufacturing system, using genetically engineered carrot cells as bio-reactors to produce a form of human lysosomal enzyme, glucocerebrosidase.

www.nature.com/articles/nbt0612-472
www.drugs.com/history/elelyso.html

10+ years ago

* Shaaltiel Y, Bartfeld D, Hashmueli S, Baum G, Brill-Almon E, Galili G, Dym O, Boldin-Adamsky SA, Silman I, Sussman JL, Futerman AH, Aviezer D. (2007) Production of glucocerebrosidase with terminal mannose glycans for enzyme replacement therapy of Gaucher's disease using a plant cell system. Plant Biotechnol J. 2007 September; 5(5):579-590. doi: 10.1111/j.1467-7652.2007.00263.x. Epub 2007 May 24. PMID: 17524049. https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1467-7652.2007.00263.x

Daniell H, Singh ND, Mason H, Streatfield SJ. (2009) Plant-made vaccine antigens and biopharmaceuticals. Trends Plant Sci. 2009 December; 14(12):669-679. doi: 10.1016/j.tplants.2009.09.009. Epub 2009 October 14. PMID: 19836291; PMCID: PMC2787751. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2787751/pdf/main.pdf

Kwon KC, Verma D, Singh ND, Herzog R, Daniell H. (2013) Oral delivery of human biopharmaceuticals, autoantigens and vaccine antigens bioencapsulated in plant cells. Adv Drug Deliv Rev. 2013 June 15; 65(6):782-799. doi: 10.1016/j.addr.2012.10.005. Epub 2012 October 23. PMID: 23099275; PMCID: PMC3582797. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3582797/pdf/nihms417004.pdf

Shaaltiel Y, Gingis-Velitski S, Tzaban S, Fiks N, Tekoah Y, Aviezer D. (2015) Plant-based oral delivery of β-glucocerebrosidase as an enzyme replacement therapy for Gaucher's disease. Plant Biotechnol J. 2015 October; 13(8):1033-40. doi: 10.1111/pbi.12366. Epub 2015 April 1. PMID: 25828481. https://onlinelibrary.wiley.com/doi/epdf/10.1111/pbi.12366

PLANTS, NATURALLY

NATURAL BIO-MIMETIC MANUFACTURING PROCESS

PLANTS ☑ CARROTS AS PROPRIETARY BIOREACTORS

NOT NEW. CLINICAL TRIALS ARE IN PROGRESS WITH PLANT-BASED COVID-19 VACCINE. BUT THERE IS AN IMMENSE CONTROL FACTOR - PRODUCTION IS FOLLOWED BY PURIFICATION OF SARS-COV-2 VLP (VIRUS LIKE PARTICLES) FOR USE AS AN ANTIGEN.

REFERENCE HTTPS://WWW.NATURE.COM/ARTICLES/S41591-021-01370-1

CLINICAL TRIAL HTTPS://CLINICALTRIALS.GOV/CT2/SHOW/NCT03739112

REVIEW HTTPS://WWW.NCBI.NLM.NIH.GOV/PMC/ARTICLES/PMC8473425/

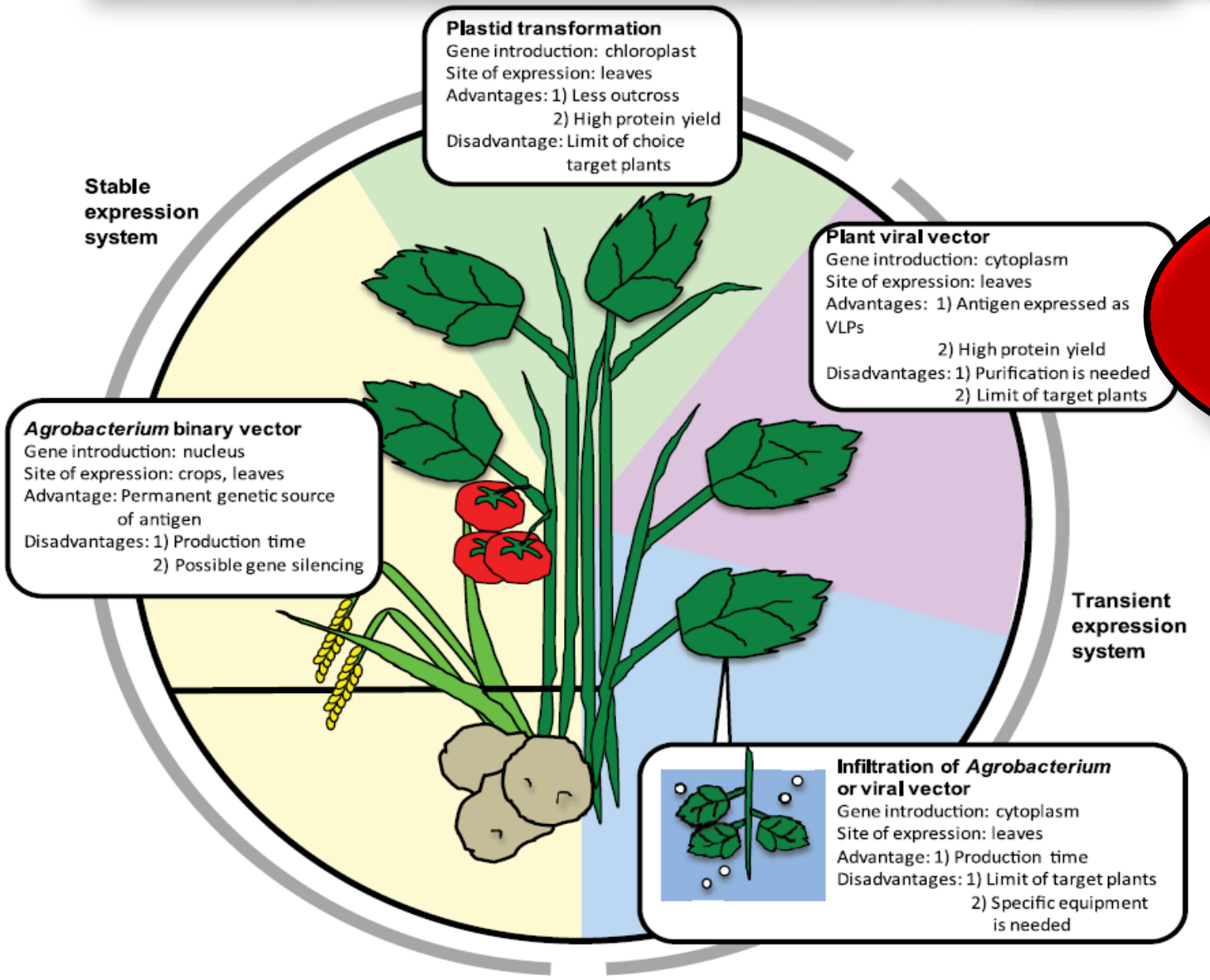
CORPORATE PURIFICATION OF PLANT BASED VLP ROBS THE BIO-MIMICRY OF THE MANUFACTURING PROCESS (PLANTS). AGAIN RE-INTRODUCES INSURMOUNTABLE BARRIERS (ACCESS), INCREASES COST (FOCUS ON SHAREHOLDER PREMIUM NOT HUMAN VALUE) AND CONTROL OF PRODUCT DEVELOPMENT RE-CREATES THE NIGHTMARE OF LOGISTICS BEFORE IT REACHES HUMANS.

SHOULD WE PRAISE IMPURITIES WITH IMPUNITY ?

THE RADICAL PART IN THIS HYPOTHETICAL SUGGESTION

CAN WE ELIMINATE THE PURIFICATION STEP ???

IN PRAISE OF IMPERFECTION



DO NOT PURIFY

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4667769/pdf/10.1177_2051013615613272.pdf

WE HAVE BEEN PRAISING IMPURITIES WITH IMPUNITY

https://www.youtube.com/watch?v=ebTrfbaAOFE

https://www.youtube.com/watch?v=aOpTFCVN_Ok

https://www.youtube.com/watch?v=RdRNxXf_WXw

Indians still use neem stem as a tooth-brush cum tooth paste, for astringent tooth cleaning. It is an old practice in India (and Asia, Africa) since time immemorial. People pluck and use neem stems as traditional tooth-brushes for tooth cleaning. The fact that the “brush” is a natural plant product helps to bypass corporate greed.

IS PURIFICATION A “WESTERN” CONCEPT ?

THE RADICAL PART IN THIS SUGGESTION IS A COMMON PRACTICE

DO THESE WORDS HOLD THE KEY? RAW? SUBLINGUAL?

THIS SUGGESTION - PLEASE CONSIDER LEAF "PASTE"

ANTIGEN PRODUCED IN A PLANT (IN LEAF)

*SUBLINGUAL DELIVERY (RAW LEAF PASTE)

* 2007 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2234198/pdf/zpq1644.pdf
* 2010 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2950356/pdf/0536-10.pdf
* 2011 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3206068/pdf/pone.0026973.pdf
* 2018 https://doi.org/10.1016/j.vaccine.2018.07.073

ARE WE PROPOSING TO DO WHAT HAS BEEN DONE BEFORE?

EDIBLE RAW PLANT PRODUCTS/EXTRACTS ARE QUITE COMMON IN LESS AFFLUENT NATIONS. 80% OF WORLD

AYURVEDIC MEDICINE RELIES ON PLANTS AND PLANT PRODUCTS WHICH ARE LOCAL, GROWS WITHOUT MUCH ATTENTION, AND USED BY BILLIONS OF PEOPLE FOR THOUSANDS OF YEARS IN INDIA. USE OF MEDICINAL PLANTS IS COMMON IN CHINA.

YES

CAN WE PRODUCE VIRAL ANTIGENS IN PLANTS?

YES.

PUBLISHED 30 YEARS AGO (1992).

ROGER THAT

CAN WE PRODUCE VIRAL ANTIGENS IN FOOD?

YES.

PUBLISHED 25+ YEARS AGO (1996).

AFFIRMATIVE

CAN VIRAL ANTIGENS IN FOOD INDUCE IMMUNITY ??

YES.

HIGH TITERS OF ANTIBODIES IN MICE.

PUBLISHED 25 YEARS AGO (SINCE 1996).

STILL WAITING FOR GODOT ?

WHAT ARE WE WAITING FOR ??

LEADERSHIP IN SCIENTIFIC RESEARCH ??

SCIENCE FOR THE SERVICE OF SOCIETY.

INFECT THE WORLD WITH MAGNANIMITY.

DRUM ROLL

HERE ARE THE EVIDENCE

45 years ago

- SOMATOSTATIN IN BACTERIA

SCIENCE ● December 1977

198 (4321):1056-1063

doi: 10.1126/science.412251.

- INSULIN IN BACTERIA ● June 1978

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC392859/pdf/pnas00020-0197.pdf

- INSULIN IN BACTERIA ● October 1978

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC382885/pdf/pnas00001-0114.pdf

Proc. Natl. Acad. Sci. USA
Vol. 75, No. 8, pp. 3727–3731, August 1978
Biochemistry

A bacterial clone synthesizing proinsulin

(rat preproinsulin/cDNA cloning/solid-phase radioimmunoassay/DNA sequence/fused proteins)

LYDIA VILLA-KOMAROFF*, ARGIRIS EFSTRATIADIS*, STEPHANIE BROOME*, PETER LOMEDICO*, RICHARD TIZARD*, STEPHEN P. NABER†, WILLIAM L. CHICK†, AND WALTER GILBERT*

* Biological Laboratories, Harvard University, Cambridge, Massachusetts 02138; and † Elliot P. Joslin Research Laboratory, Harvard Medical School, and the Peter Bent Brigham Hospital, Boston, Massachusetts 02215

Contributed by Walter Gilbert, June 9, 1978

Expression in *Escherichia coli* of a Chemically Synthesized Gene for the Hormone Somatostatin

Abstract. *A gene for somatostatin, a mammalian peptide (14 amino acid residues) hormone, was synthesized by chemical methods. This gene was fused to the* Escherichia coli *β-galactosidase gene on the plasmid pBR322. Transformation of* E. coli *with the chimeric plasmid DNA led to the synthesis of a polypeptide including the sequence of amino acids corresponding to somatostatin. In vitro, active somatostatin was specifically cleaved from the large chimeric protein by treatment with cyanogen bromide. This represents the first synthesis of a functional polypeptide product from a gene of chemically synthesized origin.*

Proc. Natl. Acad. Sci. USA
Vol. 76, No. 1, pp. 106–110, January 1979
Biochemistry

Expression in *Escherichia coli* of chemically synthesized genes for human insulin

(plasmid construction/*lac* operon/fused proteins/radioimmunoassay/peptide purification)

DAVID V. GOEDDEL*†, DENNIS G. KLEID*, FRANCISCO BOLIVAR*, HERBERT L. HEYNEKER*, DANIEL G. YANSURA*, ROBERTO CREA*‡, TADAAKI HIROSE‡, ADAM KRASZEWSKI‡, KEIICHI ITAKURA‡, AND ARTHUR D. RIGGS†‡

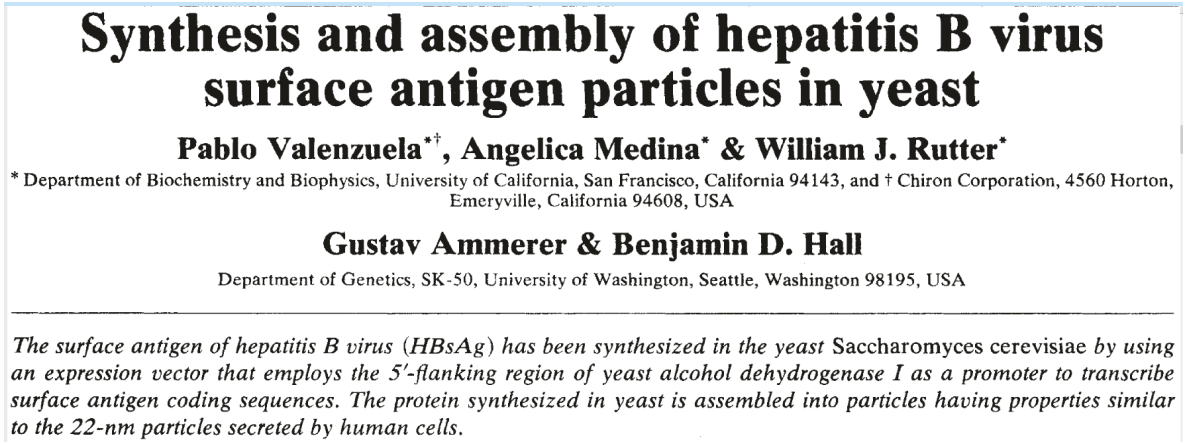
*Division of Molecular Biology, Genentech, Inc., 460 Point San Bruno Boulevard, South San Francisco, California 94080; and ‡Division of Biology, City of Hope National Medical Center, Duarte, California 91010

Communicated by Ernest Beutler, October 3, 1978

Dr. Lydia Villa-Komaroff - https://amysmartgirls.com/20for2020-dr-78d197fdbf3c

>40 years ago

40 years ago at UCSF… a catalyst… Bill Rutter's HepB antigen in yeast…



Synthesis and assembly of hepatitis B virus surface antigen particles in yeast

Pablo Valenzuela*†, Angelica Medina* & William J. Rutter*

* Department of Biochemistry and Biophysics, University of California, San Francisco, California 94143, and † Chiron Corporation, 4560 Horton, Emeryville, California 94608, USA

Gustav Ammerer & Benjamin D. Hall

Department of Genetics, SK-50, University of Washington, Seattle, Washington 98195, USA

The surface antigen of hepatitis B virus (HBsAg) has been synthesized in the yeast Saccharomyces cerevisiae *by using an expression vector that employs the 5′-flanking region of yeast alcohol dehydrogenase I as a promoter to transcribe surface antigen coding sequences. The protein synthesized in yeast is assembled into particles having properties similar to the 22-nm particles secreted by human cells.*

Valenzuela P, Medina A, Rutter WJ, Ammerer G, Hall BD. (1982) Synthesis and assembly of hepatitis B virus surface antigen particles in yeast. Nature. 1982 July 22;298(5872):347-350. doi: 10.1038/298347a0. PMID: 7045698.

Bill Rutter https://oac.cdlib.org/view?docId=kt7q2nb2hm&query=&brand=oac4

Nature. 1989 Nov 2;342(6245):76-8. doi: 10.1038/342076a0.

Production of antibodies in transgenic plants

A Hiatt [1], R Cafferkey, K Bowdish

Affiliations

Affiliation

1 Department of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, California 92037.

PMID: 2509938 DOI: 10.1038/342076a0

Production of antibodies in transgenic plants

Andrew Hiatt, Robert Cafferkey & Katherine Bowdish

Department of Molecular Biology, The Research Institute of Scripps Clinic, 10666 North Torrey Pines Road, La Jolla, California 92037, USA

WHERE IS THE EVIDENCE ?

HTTPS://WWW.NATURE.COM/ARTICLES/342076A0.PDF

33 years ago

WHERE IS THE EVIDENCE ?

patentscope.wipo.int/search/en/detail.jsf?docId=WO1990002484

Publication Number
WO/1990/002484

Publication Date
22.03.1990

International Application No.
PCT/US1989/003799

International Filing Date
05.09.1989

Chapter 2 Demand Filed
21.03.1990

IPC
A61K 39/00 2006.1 | C07K 14/245 2006.1 | C07K 14/315 2006.1 | C12N 9/10 2006.1 | C12N 9/24 2006.1 | C12N 15/82 2006.1

CPC
A01H 5/00 | A61K 39/00 | C07K 14/245 | C07K 14/315 | C07K 2319/00 | C12N 15/8258
View more classifications

Applicants
WASHINGTON UNIVERSITY [US]/[US]
1 Brookings Drive St. Louis, MO 63130, US

Inventors
CURTISS, Roy, III
CARDINEAU, Guy, A.

Title
(EN) ORAL IMMUNIZATION BY TRANSGENIC PLANTS
(FR) IMMUNISATION PAR VOIE ORALE A L'AIDE DE PLANTES TRANSGENIQUES

Abstract
(EN) The invention is directed to transgenic plants expressing colonization and/or virulence antigens specified by genes from pathogenic microorganisms. It is also directed to the use of such transgenic plants for oral immunization of humans and other animals to elicit a secretory immune response which inhibits colonization of or invasion by such pathogenic microorganisms through a mucosal surface of humans or other animals.
(FR) L'invention concerne des plantes transgéniques exprimant des antigènes de colonisation et/ou de virulence spécifiés par des gènes provenant de microorganismes pathogènes. Elle concerne également l'utilisation de telles plantes transgéniques pour l'immunisation par voie orale de l'homme et de l'animal, afin de provoquer une réponse immunitaire sécrétoire inhibant la colonisation ou l'invasion par lesdits microorganismes pathogènes, à travers une surface muqueuse humaine ou animale.

Related patent documents
EP0433372 AU1989043172 CA1339307 JP1992501801 AT218797 ZA1989/06803 KR1019900701152 US5654184 US5679880 US5686079 JP2000166411

https://patentscope.wipo.int/search/en/detail.jsf?docId=WO1990002484

↑ 33 years ago
3 years ago ↓

Ma F, Zhang E, Li Q, Xu Q, Ou J, Yin H, Li K, Wang L, Zhao X, Niu X, Li X, Zhang S, Wang Y, Deng R, Zhou E, Zhang G. (2020) *A Plant-Produced Recombinant Fusion Protein-Based Newcastle Disease Subunit Vaccine and Rapid Differential Diagnosis Platform.* Vaccines (Basel). 2020 March 9; 8(1):122. doi: 10.3390/vaccines8010122. www.ncbi.nlm.nih.gov/pmc/articles/PMC7157242/pdf/vaccines-08-00122.pdf

Proc. Natl. Acad. Sci. USA
Vol. 89, pp. 11745–11749, December 1992
Immunology

Expression of hepatitis B surface antigen in transgenic plants

(oral vaccine/foreign genes/plants)

HUGH S. MASON*†, DOMINIC MAN-KIT LAM*‡, AND CHARLES J. ARNTZEN†§

*AgriStar Inc., 100 Hawthorn, Conroe, TX 77301; †Institute of Biosciences and Technology, Center for Plant Biotechnology, Texas A&M University, Houston, TX 77030-3303; and ‡LifeTech Industries, Ltd., 100 Hawthorn, Conroe, TX 77301

Contributed by Charles J. Arntzen, September 16, 1992

WHERE IS THE EVIDENCE ?

HTTPS://WWW.NCBI.NLM.NIH.GOV/PMC/ARTICLES/PMC50633/PDF/PNAS01098-0106.PDF

30 years ago

Proc. Natl. Acad. Sci. USA
Vol. 92, pp. 3358–3361, April 1995
Immunology

Immunogenicity of transgenic plant-derived hepatitis B surface antigen

(plant-derived antigens/antibody production/T-cell proliferation)

Y. THANAVALA*, Y.-F. YANG*, P. LYONS†, H. S. MASON†, AND C. ARNTZEN†

*Department of Molecular Immunology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263; and †Alkek Institute of Biosciences and Technology, Texas A&M University, 2121 Holcombe Boulevard, Houston, TX 77030-3303

Contributed by C. Arntzen, January 6, 1995

WHERE IS THE EVIDENCE ?

HTTPS://WWW.NCBI.NLM.NIH.GOV/PMC/ARTICLES/PMC42165/PDF/PNAS01492-0291.PDF

27 years ago

Production of hepatitis B surface antigen in transgenic plants for oral immunization

Liz J. Richter[1], Yasmin Thanavala[2], Charles J. Arntzen[1], and Hugh S. Mason[1]*

*[1]Boyce Thompson Institute for Plant Research, Inc., Tower Rd., Ithaca, NY 14853-1801. [2]Department of Immunology, Roswell Park Cancer Institute, Elm and Carlton Streets, Buffalo, NY 14263. *Corresponding author (HSM7@cornell.edu).*

Received 24 January 2000; accepted 27 June 2000

WHERE IS THE EVIDENCE ?

HBSAG POTATO HTTPS://WWW.NATURE.COM/ARTICLES/NBT1100_1167.PDF

22 years ago

Human Immune Responses to a Novel Norwalk Virus Vaccine Delivered in Transgenic Potatoes

Carol O. Tacket,[1] Hugh S. Mason,[3]
Genevieve Losonsky,[1] Mary K. Estes,[2]
Myron M. Levine,[1] and Charles J. Arntzen[3]

[1]*Center for Vaccine Development, University of Maryland School of Medicine, Baltimore;* [2]*Baylor College of Medicine, Division of Molecular Virology, Houston, Texas;* [3]*Boyce Thompson Institute for Plant Research, Ithaca, New York*

A new approach for delivering vaccine antigens is the use of inexpensive, plentiful, plant-based oral vaccines. Norwalk virus capsid protein (NVCP), assembled into virus-like particles, was used as a test antigen, to determine whether immune responses could be generated in volunteers who ingested transgenic potatoes. Twenty-four healthy adult volunteers received 2 or 3 doses of transgenic potato ($n = 20$) or 3 doses of wild-type potato ($n = 4$). Each dose consisted of 150 g of raw, peeled, diced potato that contained 215–751 μg of NVCP. Nineteen (95%) of 20 volunteers who ingested transgenic potatoes developed significant increases in the numbers of specific IgA antibody–secreting cells. Four (20%) of 20 volunteers developed specific serum IgG, and 6 (30%) of 20 volunteers developed specific stool IgA. Overall, 19 of 20 volunteers developed an immune response of some kind, although the level of serum antibody increases was modest.

WHERE IS THE EVIDENCE ?

NORO VLP IN POTATO HTTPS://ACADEMIC.OUP.COM/JID/ARTICLE/182/1/302/884350

22 years ago

JOURNAL OF VIROLOGY, Aug. 2003, p. 8702–8711 Vol. 77, No. 16
0022-538X/03/$08.00+0 DOI: 10.1128/JVI.77.16.8702–8711.2003

Oral Immunogenicity of Human Papillomavirus-Like Particles Expressed in Potato

Heribert Warzecha,[1]† Hugh S. Mason,[1]‡ Christopher Lane,[2] Anders Tryggvesson,[1] Edward Rybicki,[3] Anna-Lise Williamson,[3] John D. Clements,[4] and Robert C. Rose[2]*

Boyce Thompson Institute for Plant Research, Ithaca, New York 14850[1]; Department of Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York 14642[2]; Department of Medical Microbiology, University of Cape Town, Cape Town, South Africa[3]; and Department of Microbiology and Immunology, Tulane University Health Sciences Center, New Orleans, Louisiana 70118[4]

Received 10 January 2003/Accepted 13 May 2003

Human papillomavirus-like particles (HPV VLPs) have shown considerable promise as a parenteral vaccine for the prevention of cervical cancer and its precursor lesions. Parenteral vaccines are expensive to produce and deliver, however, and therefore are not optimal for use in resource-poor settings, where most cervical HPV disease occurs. Transgenic plants expressing recombinant vaccine immunogens offer an attractive and potentially inexpensive alternative to vaccination by injection. For example, edible plants can be grown locally and can be distributed easily without special training or equipment.

WHERE IS THE EVIDENCE ?

HTTPS://WWW.NCBI.NLM.NIH.GOV/PMC/ARTICLES/PMC167207/PDF/0052.PDF

~ 20 years ago

Samuel Taylor Coleridge (1772-1834) in *The Rime of the Ancient Mariner* (1798).

"water, water everywhere, nor any drop to drink"

Su H, Yakovlev IA, van Eerde A, Su J, Clarke JL. (2021) Plant-Produced Vaccines: Future Applications in Aquaculture. Front Plant Sci. 2021 August 12;12:718775. doi: 10.3389/fpls.2021.718775. PMID: 34456958; PMCID: PMC8397579. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8397579/pdf/fpls-12-718775.pdf

EMBARRASSMENT OF RICHES (EVIDENCE)

POVERTY OF IMPLEMENTATION

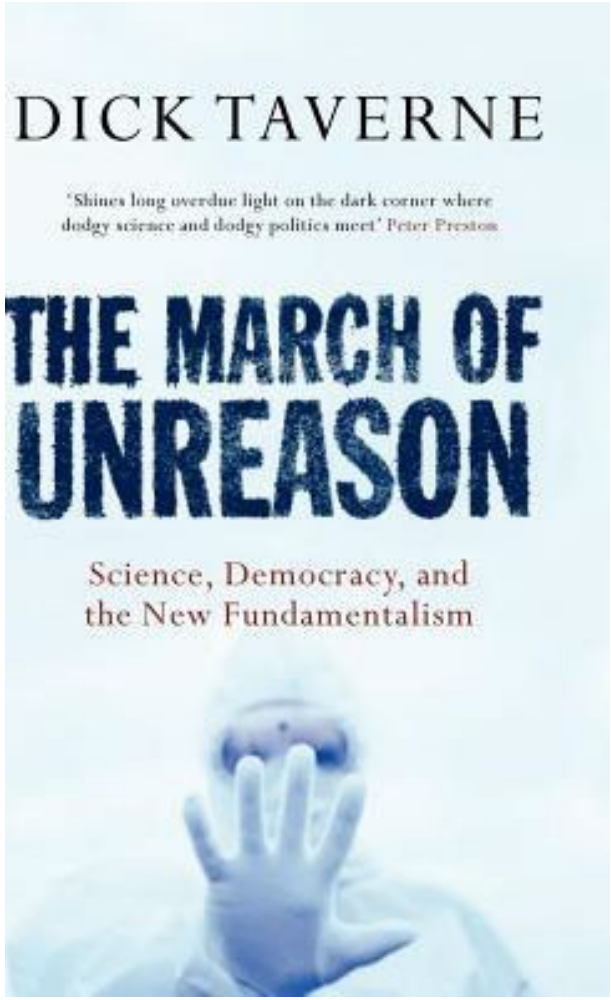
DON'T ASK "WHY?"… ASK "WHY NOT?" ■ THE TRIUMPH OF REASON

PURIFICATION

&

PHOBIA

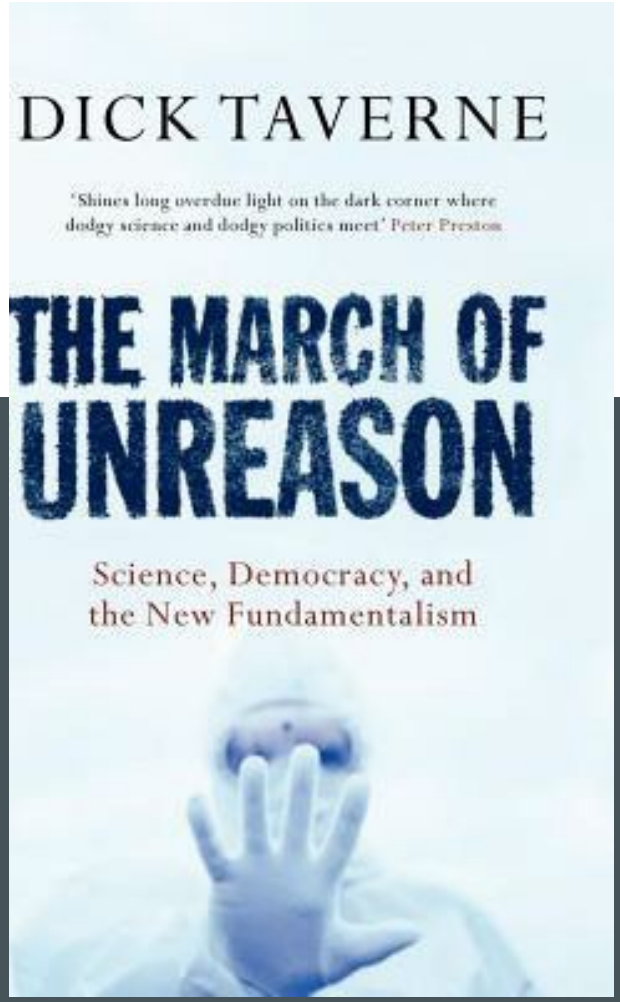
https://ccc.bc.edu/content/ccc/blog-home/2011/07/blog-2011-07-don-t-ask--why---ask--why-not-.html



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC558032/pdf/bmj33001214.pdf

IRRATIONAL EXUBERANCE OR EGREGIOUS ERRORS ?

PHOBIA ABOUT TRANSGENIC PLANTS IS KILLING PEOPLE, STARVING NATIONS AND FUELS ANARCHY BECAUSE OF WILLFUL IGNORANCE OF A FEW, ABOUT SCIENCE. PLANTS/FOOD CAN STOP SPREAD OF INFECTIOUS DISEASE.



Vitamin A deficiency (VAD) has killed millions of children in less-developed countries for at least the last three decades—roughly 2 million annually in the early 1990s alone (1–4). Although the number is declining, it was estimated to be 266,200 (4) at the start of the millennium.

The consumption of the genetically modified rice variety known as Golden Rice (GR) offers a potent and

https://www.pnas.org/doi/epdf/10.1073/pnas.2120901118
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8713968/pdf/pnas.202120901.pdf

Widespread consumption of the genetically modified rice variety known as Golden Rice offers a potent and cost-effective strategy to combat vitamin A deficiency. Image credit: International Rice Research Institute; photo licensed under CC BY 2.0.

Wu F, Wesseler J, Zilberman D, Russell RM, Chen C, Dubock AC. (2021) ***Opinion: Allow Golden Rice to save lives.*** Proc Natl Acad Sci USA. 2021 Dec 21; 118(51): e2120901118. doi: 10.1073/pnas.2120901118.

PNAS PNAS

COMMENTARY

Vaccines are for dinner

David W. Pascual*

Department of Veterinary Molecular Biology, Montana State University, Bozeman, MT 59717-3610

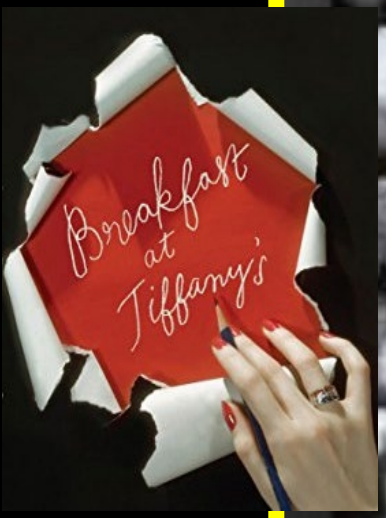
Transgenic plants have been sought not only as bioreactors but also as potential scaffolds for oral vaccines.

Table 1. Edible transgenic plant vaccines

Vaccine	Edible plant	Ref.
Norwalk virus particle	Potato	3
	Tomato	4
Heat-labile enterotoxin B subunit	Potato	5
	Maize	6
	Soybean	20
Cholera toxin B subunit	Rice	14
	Potato	21
Enterotoxigenic *Escherichia coli* fimbrial subunit	Soybean	11
Japanese cedar pollen peptide	Rice	19

Pascual DW (2007) *Vaccines are for dinner.* Proc Natl Acad Sci U S A. 2007 June 26; 104(26):10757-8. doi: 10.1073/pnas.0704516104. PMID: 17581867; PMCID: PMC1904143. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1904143/pdf/zpq10757.pdf

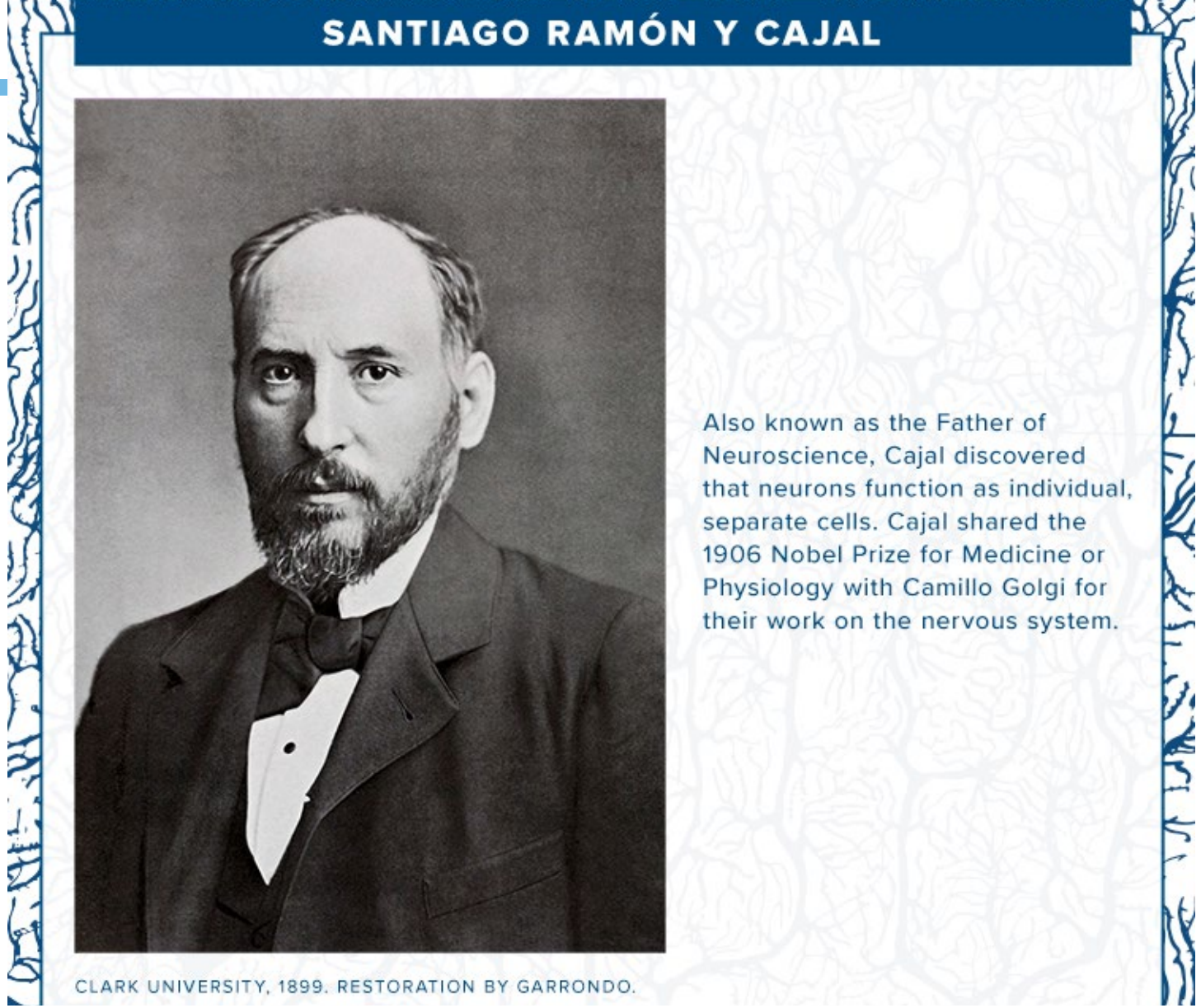
Breakfast at Vaxine's



Bistro Maxine
PARIS IN PALO ALTO

SANTIAGO RAMÓN Y CAJAL (IN 1899)

"Every disease has two causes. The first is pathophysiological; the second, political."

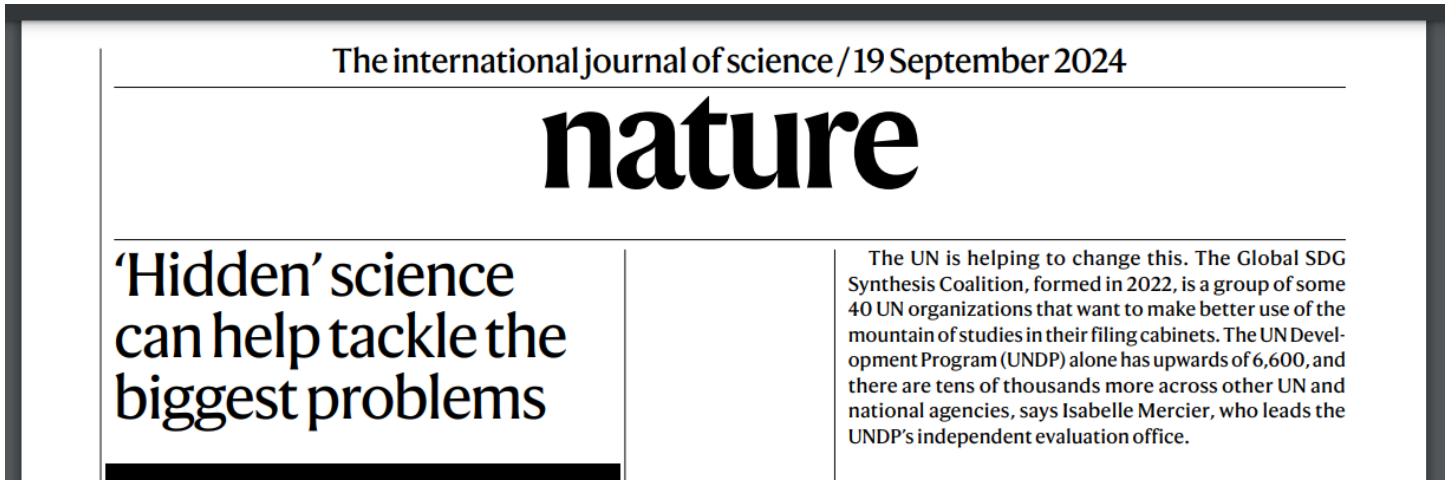


Moss, William J. (2022) "The Seeds of Ignorance - Consequences of a Booming Betel-Nut Economy." *New England Journal of Medicine*, September 2022, p. NEJMp2203571. https://doi.org/10.1056/NEJMp2203571. https://www.nejm.org/doi/pdf/10.1056/NEJMp2203571?articleTools=true

RE-SEARCH WHAT WAS ONCE RESEARCHED AND FOUND

RE-DISCOVER THE SEMINAL RESEARCH RESULTS

SIMPLIFY WHAT WE KNOW FROM CHARLES ARNTZEN



The international journal of science / 19 September 2024

nature

‘Hidden’ science can help tackle the biggest problems

The UN is helping to change this. The Global SDG Synthesis Coalition, formed in 2022, is a group of some 40 UN organizations that want to make better use of the mountain of studies in their filing cabinets. The UN Development Program (UNDP) alone has upwards of 6,600, and there are tens of thousands more across other UN and national agencies, says Isabelle Mercier, who leads the UNDP’s independent evaluation office.

nature.com/articles/d41586-024-02991-5

nature

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EDITORIAL | 17 September 2024

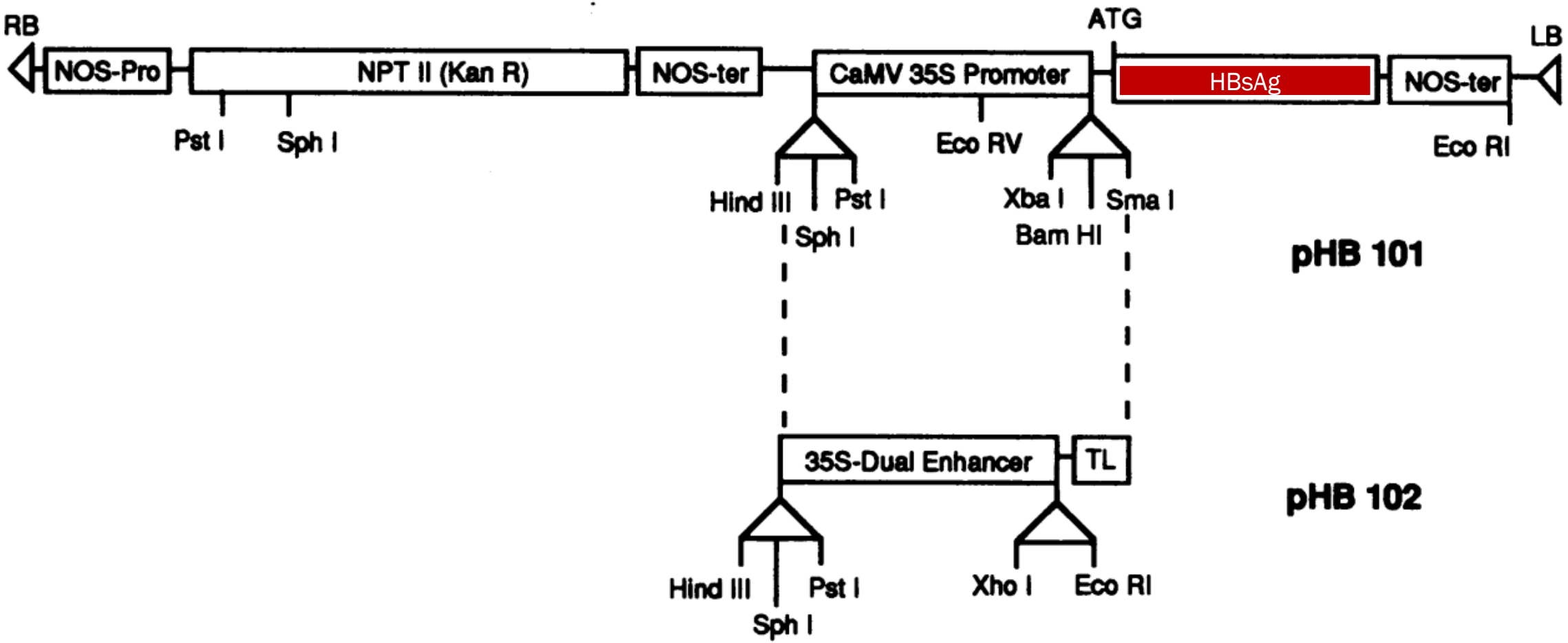
Unearthing ‘hidden’ science would help to tackle the world’s biggest problems

https://www.nature.com/articles/d41586-024-02991-5

THE MEANING

UNDERSTAND THE SIGNIFICANCE OF THE EXPERIMENTAL RESULTS

RECOMBINANT HEPATITIS B SURFACE ANTIGEN (HBsAG) IN TOBACCO PLANTS

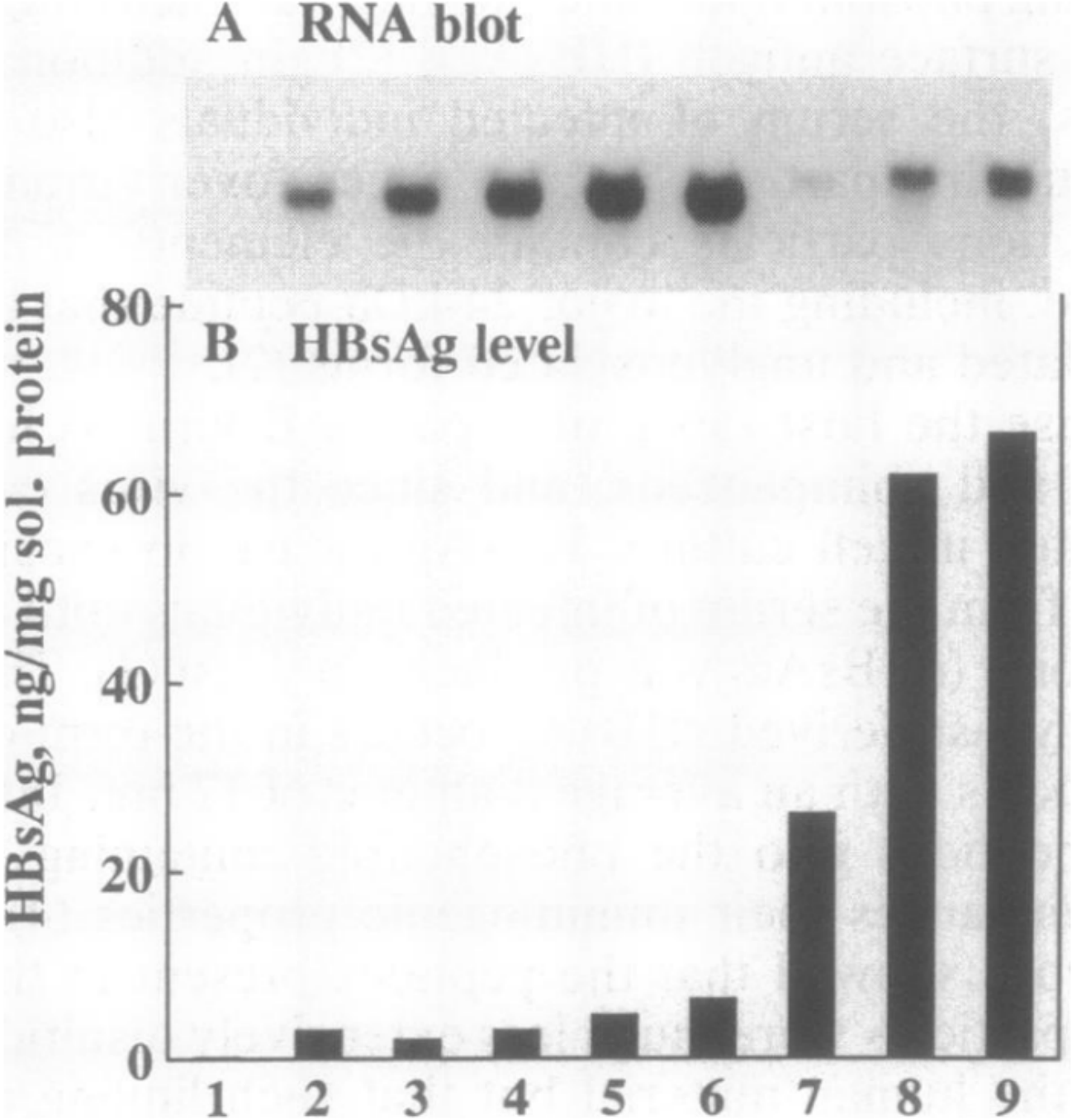


Mason HS, Lam DM, Arntzen CJ. (1992) Expression of hepatitis B surface antigen in transgenic plants. PNAS 1992 December 15; 89(24): 11745-11749. doi: 10.1073/pnas.89.24.11745 www.ncbi.nlm.nih.gov/pmc/articles/PMC50633/pdf/pnas01098-0106.pdf

UNDERSTAND THE SIGNIFICANCE - EXPERIMENTAL RESULT IN FIG 2

FROM CHARLES ARNTZEN (MASON ET AL, 1992)

FIG. 2. HBsAg mRNA and protein levels in transgenic tobacco plants. (A) Total RNA from wild-type untransformed or independent transgenic tobacco lines carrying either the pHB101 or the pHB102 construct was hybridized with a probe specific for the HBsAg coding region. (B) Protein extracts from the same leaves were tested for HBsAg with the Auszyme monoclonal kit (Abbott), and HBsAg levels were quantified using a standard curve of human serum derived HBsAg. Numbers: 1, wild-type control plant; 2-6, independent transformants harboring the construct in pHB101; 7-9, independent transformants harboring pHB102 (dual enhancer).

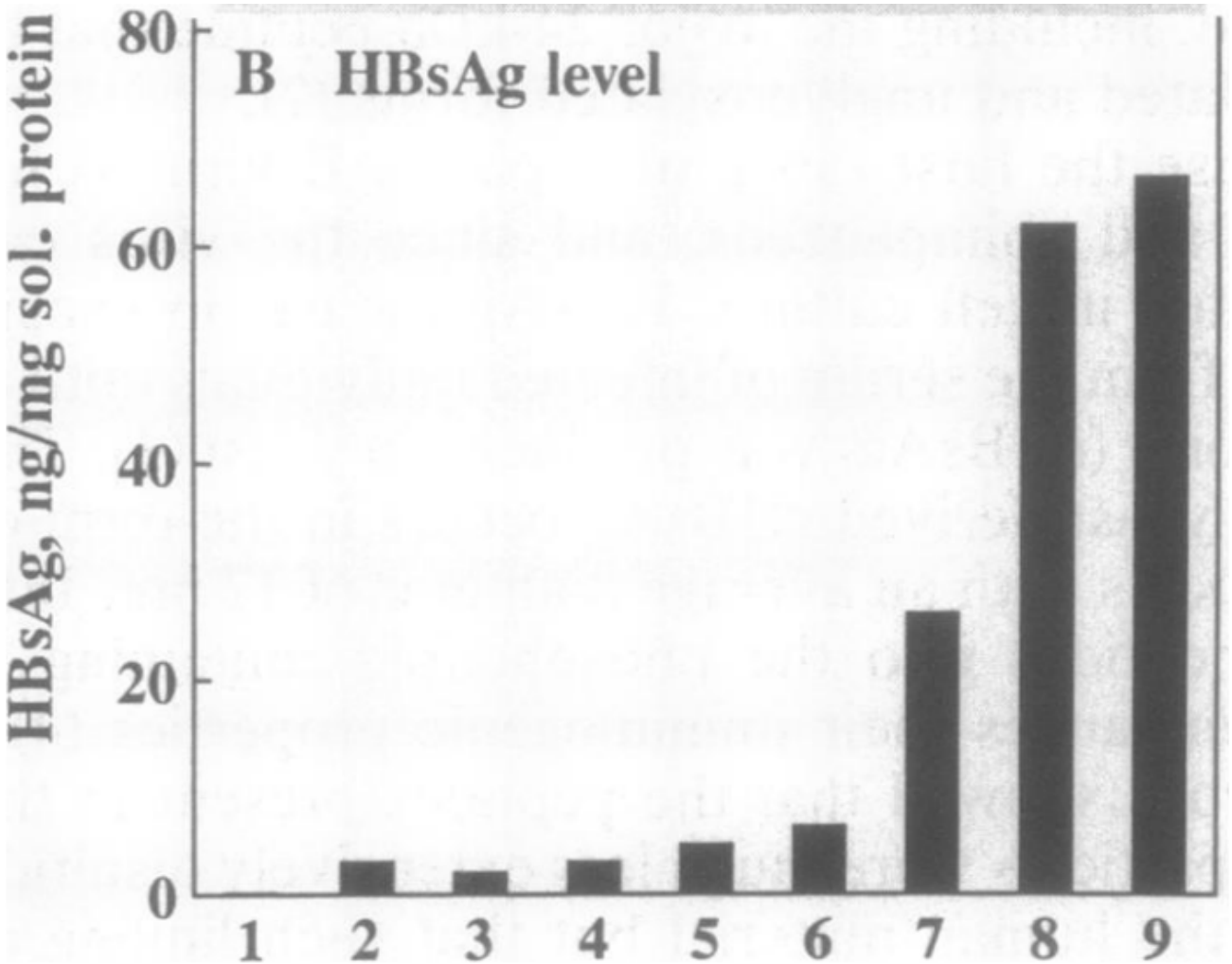


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC50633/pdf/pnas01098-0106.pdf

THIS EXPERIMENTAL RESULT MAY UNLOCK POTENTIAL FOR GLOBAL VACCINATION AT LOW COST, FOR 80% OF THE WORLD'S POPULATION

HepatitsB antigen was detected in the leaves of the plant (as it should, see 2-9). This or other plant can be grown almost anywhere in the world, the leaves can be mashed up in a mortar and pestle to make a paste (contains the antigen). This paste (may not be tasty) may be placed under the tongue (sublingual route by which substances diffuse directly into the blood through tissues under the tongue). The "expectation" is that the antigen (protein molecules) will diffuse out of the paste and enter the blood of the person. Antigen then triggers the immune system. Hence, the person is vaccinated (hypothetical).

(Charles Arntzen et al, 1992) Data from Fig 2



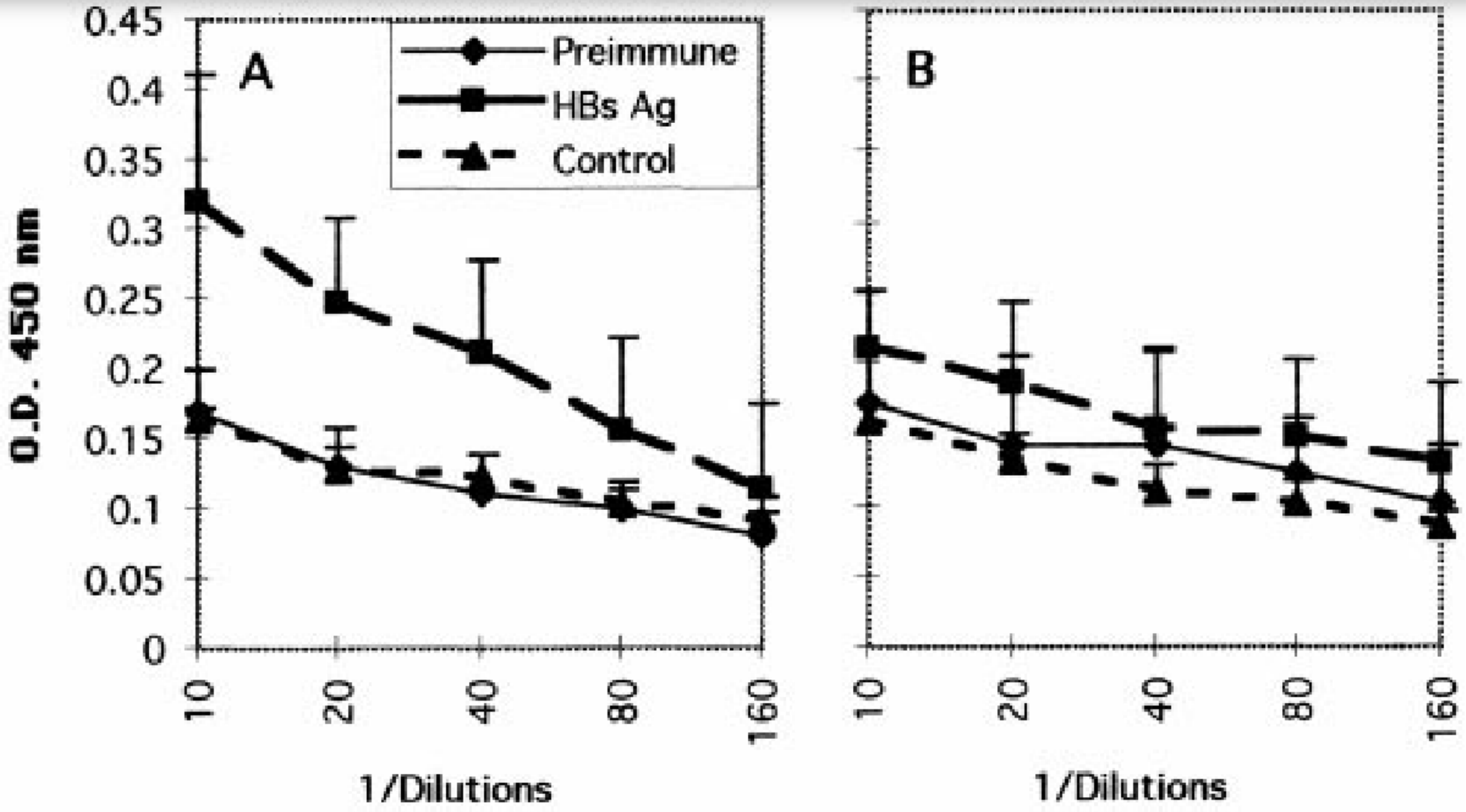
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC50633/pdf/pnas01098-0106.pdf

WHAT DOES THIS MEAN IN TERMS OF IMMUNOGENICITY IN HUMANS ?

WHAT DOES THIS MEAN IN TERMS OF IMMUNOGENICITY IN HUMANS ?

The ability of the body to differentiate between the “edible” plant proteins (e.g., should not produce an immune response to lettuce leaves, potatoes, watercress) and the foreign antigen in the transgenic plant product (e.g., bioengineered lettuce leaves, potatoes or watercress expressing foreign antigen) lies at the heart of the anticipated specificity of antigen-induced immunogenicity in humans. Induction of immunity by foreign antigens (sufficient as a protection from infection) in healthy individuals is the ultimate “litmus” test for recombinant antigens produced in plants. The choice of administration of the plant product (oral “edible” products or sublingual administration for rapid absorption in the blood stream) may influence the intensity (titer) and duration (prevalence of titer) of the immune response.

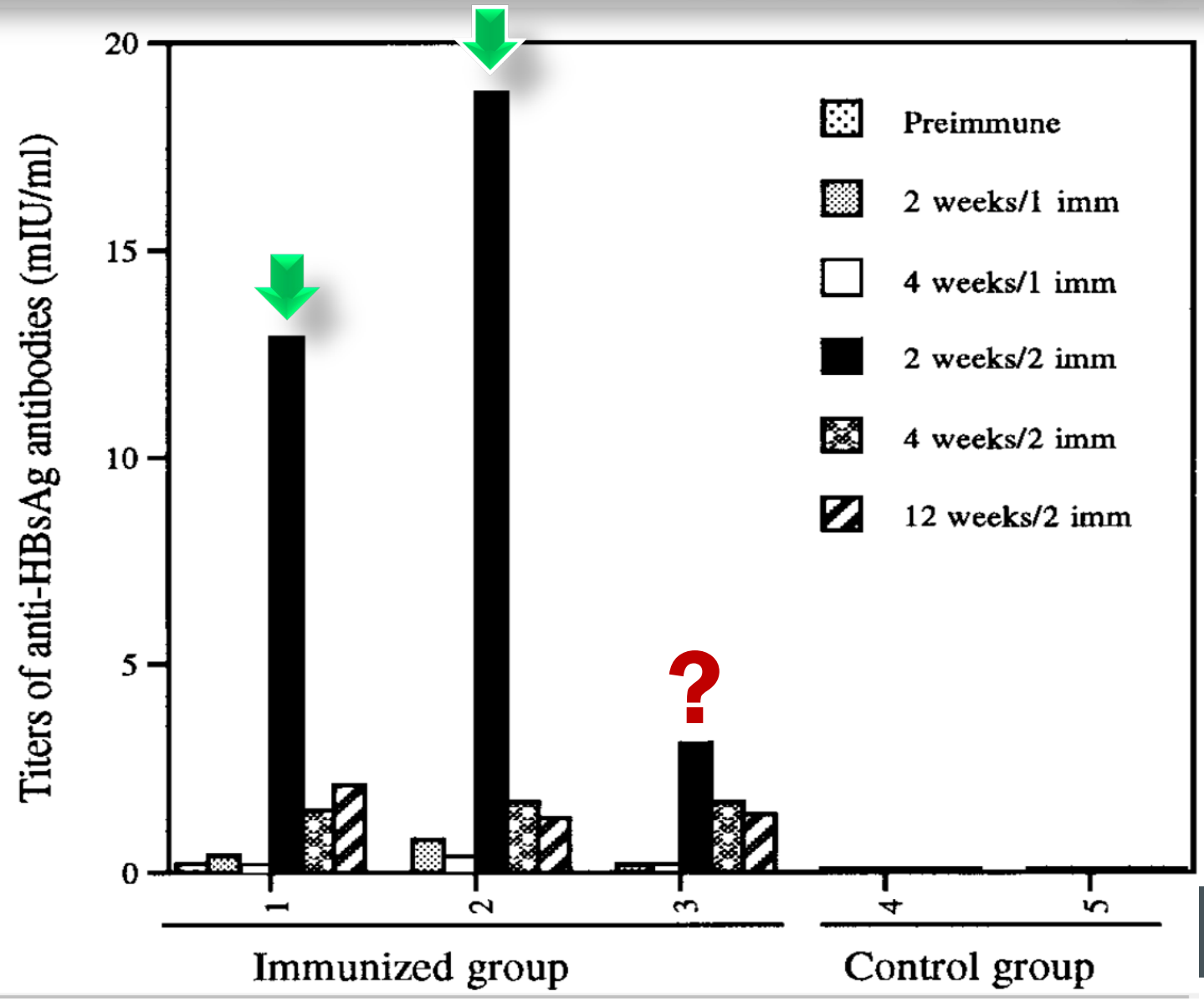
IMMUNOGENICITY OF PLANT PRODUCED HEPATITIS VIRUS ANTIGEN IN HUMANS



Titer of antibodies [A] 3 individuals immunized orally with transgenic lettuce engineered to express Hepatitis B surface antigen (HBsAg). [B] Control (2 individuals fed with lettuce without bioengineered expression of HBsAg).

Kapusta *et al* (1999) Plant-derived edible vaccine against hepatitis B virus. FASEB J. 13: 1796-1799. https://doi.org/10.1096/fasebj.13.13.1796

IMMUNOGENICITY OF PLANT PRODUCED HBsAg IN HUMANS



Kapusta *et al* (1999) Plant-derived edible vaccine against hepatitis B virus. FASEB J. 13: 1796-1799. https://doi.org/10.1096/fasebj.13.13.1796

WAS IT NECESSARY TO PURIFY THE ANTIGEN BEFORE ORAL USE TO INDUCE IMMUNOGENICITY IN HUMANS?

Tacket *et al*, 1998, fed human volunteers with genetically modified raw (uncooked) potatoes expressing the enterotoxigenic *Escherichia coli* LT-B (B subunit of the *E. coli* enterotoxin is related to the B subunit of cholera toxin). Healthy adult volunteers (n=14) ingested either 100 g of transgenic potato, 50 g of transgenic potato, or 50 g of wild-type potato. *E. coli* enterotoxin LT-B subunit protein in the potato was estimated to be 3.7-15.7 µg per gram. The amount of *E. coli* enterotoxin LT-B subunit protein ingested per 50g or 100 g dose ranged from 0.4mg to 1.1mg per dose (mean 0.75 mg/dose).

Table 1 Antibody secreting cell (ASC) responses among volunteers who ingested transgenic or wild-type potatoes on days 0, 7 and 21

doi: 10.1038/nm0598-607
PMID: 9585236

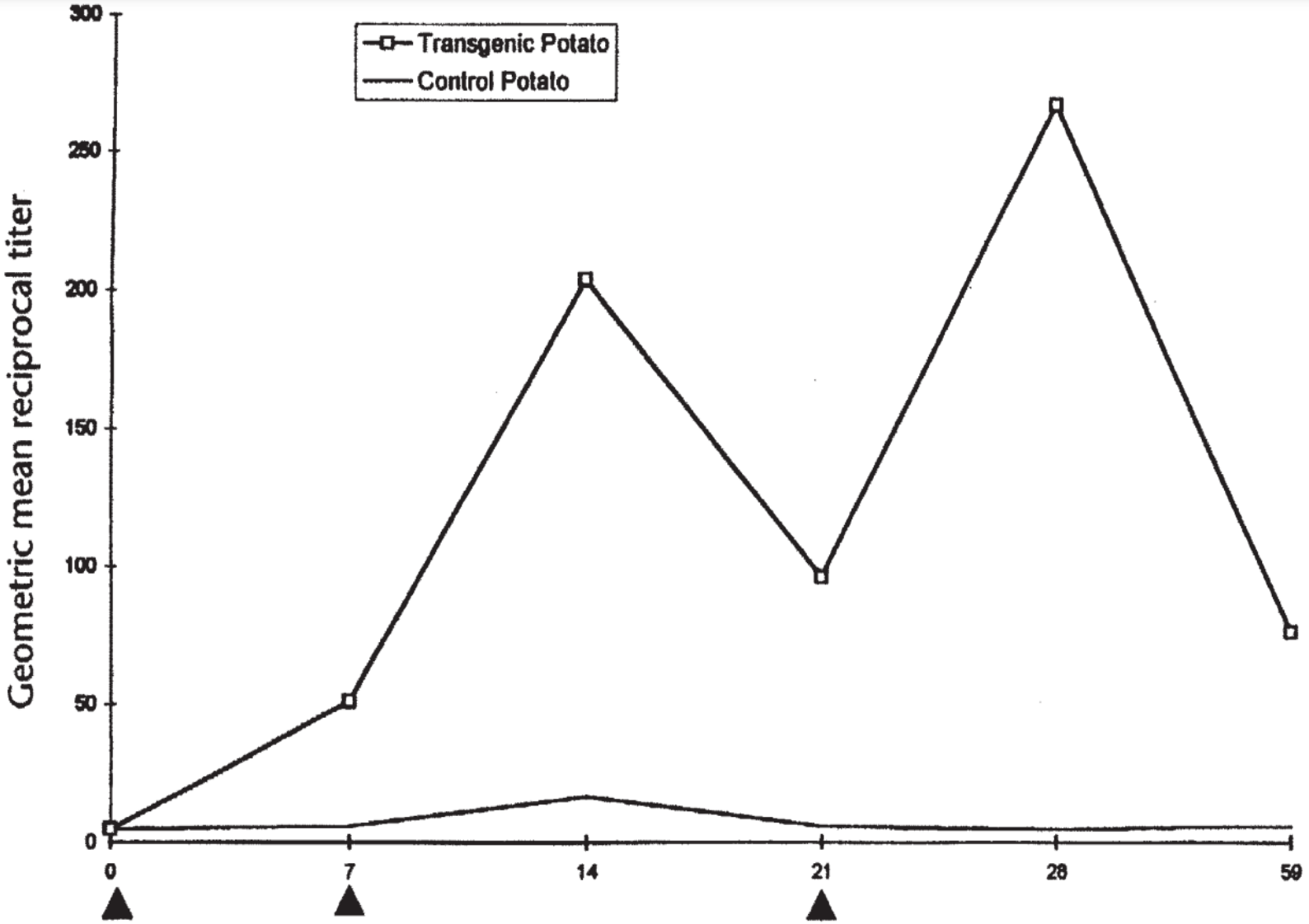
	Geometric mean IgA anti-LT ASC per 10^6 PBMC*					Geometric mean IgG anti-LT ASC per 10^6 PBMC				
	Day 0	Day 7	Day 14	Day 21	Day 28	Day 0	Day 7	Day 14	Day 21	Day 28
Transgenic potato (*n*=11)	0.1	18.4	6.6	0.8	19.1	0	13.5	5.7	0.7	7.2
Wild-type potato (*n*=3)	0	0	0.7	0.3	2.4	0	0	1.8	0.4	0.6

IMMUNOGENICITY OF PLANT PRODUCED BACTERIAL TOXIN (NON-TOXIC B SUBUNIT)

ENTEROTOXIGENIC *ESCHERICHIA COLI* LT-B B SUBUNIT OF TOXIN IN TRANSGENIC POTATOES

Tacket *et al* Immunogenicity in humans of a recombinant bacterial antigen delivered in a transgenic potato. Nat Med. 1998 May; 4(5):607-09

IMMUNOGENICITY IN HUMANS: POTATOES PRODUCING Enterotoxin *E. coli* LT-B ANTIGEN



Tacket *et al*, 1998
doi: 10.1038/nm0598-607 PMID: 9585236

Geometric mean LT-B neutralizing antibody titers in volunteers who ingested LT-B transgenic potatoes (n = 11) or wild-type potatoes (n = 3). Potatoes were ingested on days 0, 7 and 21 (arrows).

WAS IT NECESSARY TO PURIFY THE ANTIGEN BEFORE ORAL USE TO INDUCE IMMUNOGENICITY IN HUMANS?

Tacket *et al*, 2000, explored immunization against **NOROVIRUS** (causative agent for gastroenteritis, commonly referred to as stomach flu) using plant-based oral vaccine (POV). The first norovirus outbreak occurred in Norwalk, Ohio, USA, in a school in 1968. For this reason, the first strain of norovirus is also known as the Norwalk virus. Tacket *et al*, 2000, used "Norwalk virus capsid protein (NVCP), assembled into virus-like particles (VLP), as a test antigen, to determine whether immune responses could be generated in volunteers who ingested transgenic potatoes. Healthy adult volunteers (n = 24) received 2 or 3 doses of transgenic potato (n=20) or 3 doses of wild-type potato (n=4). Each dose consisted of 150g of uncooked, raw, peeled, diced potato that contained 215–751mg of NVCP. 19 (95%) of 20 volunteers who ingested transgenic potatoes developed significant increases in the numbers of specific IgA antibody–secreting cells (ASC). 4 (20%) of 20 volunteers developed specific serum IgG, and 6 (30%) of 20 volunteers developed specific stool IgA. Overall, 19 of 20 volunteers (95%) developed an immune response of some kind, although the level of serum antibody increases was modest."

Immune responses to Norovirus - transgenic potatoes expressing Norwalk virus capsid protein (NVCP) versus control (wild-type potatoes). Tacket *et al*, 2000.

Immunoassay	Transgenic potatoes			Wild-type potatoes,
	3 doses (n = 10)	2 doses (n = 10)	Total (n = 20)	3 doses (n = 4)
IgA ASC anti-NVCP response rate	9/10 (90%)	10/10 (100%)	19/20 (95%)	0/4
Geometric mean peak ASCs per 10^6 PBMC[a]	32	26	28	—
Range IgA ASCs per 10^6 PBMC[a]	6–245	6–280	6–280	—
IgG ASC anti-NVCP response rate	2/10 (20%)	4/10 (40%)	6/20 (30%)	0/4
Geometric mean peak ASCs per 10^6 PBMC[a]	103	34	49	0
Range IgG ASCs per 10^6 PBMC[a]	92–115	25–62	25–115	0
Serum IgG anti-NVCP response rate	3/10 (30%)	1/10 (10%)	4/20 (20%)	0/4
IgG peak geometric mean titer[a]	1:468	1:3200	1:757	—
Mean peak fold rise[a]	13.3	8	12	—
Serum IgM anti-NVCP response rate	4/10 (40%)	0/10 (0%)	4/20 (20%)	0/4
IgM peak geometric mean titer[a]	1:100	—	1:100	—
Mean peak fold rise[a]	7	—	7	—
Stool IgA response rate	4/10 (40%)	2/10 (20%)	6/20 (30%)	0/4
Stool IgA peak geometric mean titer[a]	1:48	1:38	1:45	—
Mean peak fold rise[a]	17.8	16.6	17.4	—

NOTE. ASC, antibody-secreting cell; PBMC, peripheral blood mononuclear cells.
[a] Among responders.

Tacket CO, Mason HS, Losonsky G, Estes MK, Levine MM, Arntzen CJ. (2000) Human immune responses to a novel norwalk virus vaccine delivered in transgenic potatoes. Journal of Infectious Diseases 2000 July; 182(1):302-305. doi: 10.1086/315653
https://academic.oup.com/jid/article-pdf/182/1/302/17999637/182-1-302.pdf

WAS IT NECESSARY TO PURIFY THE ANTIGEN BEFORE ORAL USE TO INDUCE IMMUNOGENICITY IN HUMANS?

PURIFICATION IS UNNECESSARY FOR ORAL USE OF EDIBLE PLANT ANTIGENS TO INDUCE IMMUNOGENICITY IN HUMANS.

IF PURIFICATION IS UNNECESSARY

FOR ORAL ADMINISTRATION OF PLANT-PRODUCED ANTIGENS TO INDUCE IMMUNOGENICITY IN HUMANS, THEN WHY THE CLAMOR TO ADD THE PURIFICATION STEP ??

IF PURIFICATION IS UNNECESSARY

FOR ORAL ADMINISTRATION OF PLANT-PRODUCED ANTIGENS TO INDUCE IMMUNOGENICITY IN HUMANS,

THEN WHY THE CLAMOR TO ADD THE PURIFICATION STEP ??

IN THIS CASE, PURIFICATION IS PURELY FOR PECUNIARY PURPOSES for CORPORATE PROFIT and CORPORATE CONTROL to LIMIT ACCESS to BASIC HEALTHCARE FOR ~7 BILLION POOR PEOPLE WHO MAY BENEFIT IN LESS AFFLUENT NATIONS.

Plant-based Oral Vaccines (POV) is a SASSY (Science As a Service for SocietY) Project

Implementation of POV will be a win for ethical globalization. A small step to enable the delivery of global public goods to reduce disparity and inequity in healthcare services. An example of collaborative action rather than *lippenbekenntnis*. A tiny domain where the mighty Hermes may not be able to fully exert his influence and may fail to exercise his pecuniary interests. A human triumph?

Asclepius, the god of healing and his three daughters, Meditrina (medicine), Hygieia (hygiene), and Panacea (healing). The staff and single snake of Asclepius should not be confused with the twin snakes and caduceus of Hermes, the deified trickster and god of commerce, who is viewed with disdain.

Plate from Aubin L Millin, *Galerie Mythologique* (1811)

Wilkinson, Ian, ed. *Oxford Handbook of Clinical Medicine*. 10th edition. Oxford University Press, 2017. ISBN 9780199689903

DOES SCIENCE/EVIDENCE SUGGEST PLANT-BASED ORAL (RAW) ANTIGENS ARE IMMUNOGENIC IN HUMANS?

YES

KEEP IT SIMPLE ▪PLANT MUSH UNDER TONGUE DAILY, (HOME) TEST (SENSOR) TO DETECT ANTIBODY IN BLOOD. VOILA! VACCINATED!

RESEARCH STUDY – REPEAT ARNTZEN'S 1992 SEMINAL WORK WITH EBOLA VIRUS SURFACE GLYCOPROTEIN EBOV (BINDS HUMAN TIM-1)

To get started follow the Arntzen Way (1992)

- Use EBOV or TIM-1 binding epitopes of EBOV?
- Can we detect EBOV protein in sap, stem, leaves?
- Is the sap, stem, leaf *mush* safe from side effects?
- Assay human blood sample for EBOV on day 0
- Sublingual administration of "mush" 2-3 times/day
- Assay blood for EBOV and EBOV-ab every few days
- Titer of EBOV-ab is KPI (key performance indicator).

Ebola Marburg Receptor TIM-1 https://www.pnas.org/doi/pdf/10.1073/pnas.1019030108

KEEP IT SIMPLE ▪PLANT MUSH UNDER TONGUE DAILY, (HOME) TEST (SENSOR) TO DETECT ANTIBODY IN BLOOD. VOILA! VACCINATED!

RESEARCH STUDY – REPEAT ARNTZEN'S 1992 SEMINAL WORK WITH EBOLA VIRUS SURFACE GLYCOPROTEIN EBOV (BINDS HUMAN TIM-1)

Tobacco - The Arntzen Way

- Use EBOV or TIM-1 binding epitopes of EBOV?
- Can we detect EBOV protein in sap, stem, leaves?
- Is the sap, stem, leaf *mush* safe from side effects?
- Assay human blood sample for EBOV on day 0
- Sublingual administration of "mush" 2-3 times/day
- Assay blood for EBOV and EBOV-ab every few days
- Titer of EBOV-ab is KPI (key performance indicator).

Also: Arabidopsis, Rose, Tulip, Potato, Orange

- Arabidopsis can be transfected by dipping leaves
- Use Arntzen's CaMV vectors, A. tumefaciens, etc.
- Can we find a way to create EBOV in Rose, Tulip?
- Rose/Tulip vectors: Rose Rosette Virus, Potyviruses
- Expectation: EBOV in rose / tulip (petals are edible)
- Food: Arntzen's potato, lettuce, carrot, citrus*
- KPI (outcome) high EBOV-ab titer detected in blood

Ebola (and Marburg Virus) Receptor Human TIM-1 https://www.pnas.org/doi/pdf/10.1073/pnas.1019030108

*CITRUS https://patentimages.storage.googleapis.com/2a/ad/8a/0eb4420eea4fc7/US20130125254A1.pdf

Play it again, Sam

REPEAT THIS PROTOCOL WITH ANY (VIRAL*) ANTIGEN

THIS IS A “PLATFORM” APPROACH TO VACCINATION.

IMMUNIZATION WITHOUT CORPORATE CONTROL AND MEDICAL STAFF MAY IMPROVE “WELLNESS” ACCESS

* Graham BS, Sullivan NJ. Emerging viral diseases from a vaccinology perspective: preparing for the next pandemic. Nat Immunol. 2018 Jan; 19(1):20-28 www.ncbi.nlm.nih.gov/pmc/articles/PMC7097586/pdf/41590_2017_Article_7.pdf

WHO WILL CONSTRUCT VECTOR WITH ANTIGEN, TRANSFECT, CREATE THE CONDITIONS FOR GROWING THE PLANT?

NEED A SCIENTIFIC TEAM, OPEN COMMUNICATIONS, CENTRAL REPOSITORY FOR DISTRIBUTING MATERIALS, ANTIBODY TESTING AND ASSOCIATED MATERIALS/SENSORS, DATA SYSTEMS, DATA TRANSMISSION USING MOBILE PHONE APPS.

TABLE 6 Event Information Site bulletins published, by disease, condition or hazard, 2018–2022

No.	Disease/Condition/Hazard	Annually					Five-year period 2018–2022
		2018	2019	2020	2021	2022	
1	Acute gastrointestinal syndrome	—	—	—	1	—	1
2	Acute haemorrhagic fever syndrome	—	3	—	2	—	5
3	Acute hepatitis E	3	—	1	4	—	8
4	Acute hepatitis of unknown aetiology	—	—	—	—	1	1
5	Antibiotic-resistant bacterial infection	—	2	—	—	—	2
6	Arenaviral haemorrhagic fever	—	—	1	—	—	1
7	Argentine haemorrhagic fever	—	—	1	—	—	1
8	Chikungunya virus disease	2	1	1	—	—	4
9	Cholera	8	3	1	4	13	29
10	COVID-19/SARS-CoV-2	—	—	90	—	—	90
11	Crimean–Congo haemorrhagic fever	—	—	—	—	1	1
12	Dengue fever	3	10	3	2	7	25
13	Diphteria	1	—	—	—	—	1
14	Dracunculiasis	—	—	1	—	—	1
15	Ebola virus disease	7	1	4	5	4	21

Ebola Virus

World Health Organization. (2023). Global public health intelligence report 2022. World Health Organization. https://apps.who.int/iris/handle/10665/372054
ISBN ▪ 9789240073579 (electronic version) ▪ 9789240073586 (print version) https://apps.who.int/iris/bitstream/handle/10665/372054/9789240073579-eng.pdf

MARBURG, EBOLA, HANTA, LASSA, JUNIN, NORO

PLANT-BASED TECHNOLOGIES TO ENABLE RAPID RESPONSE TO EBOLA OUTBREAK

Jerzy Karczewski, Fraunhofer CMB, Newark, Delaware, USA

Vidadi Yusibov, Fraunhofer CMB, Newark, Delaware, USA

June 12-17, 2016

PRIORITIZE DEADLY VIRUSES FOR VACCINE TARGETS

HTTPS://DC.ENGCONFINTL.ORG/VACCINE_VI/44/

HTTPS://DC.ENGCONFINTL.ORG/CGI/VIEWCONTENT.CGI?FILENAME=0&ARTICLE=1043&CONTEXT=VACCINE_VI&TYPE=ADDITIONAL

Hefferon, Kathleen Laura (2012) Plant virus expression vectors set the stage as production platforms for biopharmaceutical proteins. Virology. 2012 November 10; 433(1):1-6. doi: 10.1016/j.virol.2012.06.012. PMID: 22979981. https://www.sciencedirect.com/science/article/pii/S004268221200314 5?via%3Dihub

Loh HS, Green BJ, Yusibov V. (2017) Using transgenic plants and modified plant viruses for the development of treatments for human diseases. Curr Opin Virol. 2017 October; 26:81-89. doi: 10.1016/j.coviro.2017.07.019. Epub 2017 August 8. PMID: 28800551; PMCID: PMC7102806. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7102806/pdf/main.pdf

IS MEASURABLE SUCCESS STILL JUST AN IMAGINARY MIRAGE ?

Ponndorf D, Meshcheriakova Y, Thuenemann EC, Dobon Alonso A, Overman R, Holton N, Dowall S, Kennedy E, Stocks M, Lomonossoff GP, Peyret H. (2021) Plant-made dengue virus-like particles produced by co-expression of structural and non-structural proteins induce a humoral immune response in mice. Plant Biotechnol J. 2021 April; 19(4):745-756. doi: 10.1111/pbi.13501. Epub 2020 Nov 22. PMID: 33099859; PMCID: PMC8051607.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8051607/pdf/PBI-19-745.pdf

www.nature.com/articles/nbt0306-233

USDA approves the first plant-based vaccine

In what could be a milestone for veterinary as well as human vaccine research, the US Department of Agriculture (USDA) on January 31, 2006, announced it had issued the first market license ever issued to a veterinary vaccine produced in plant cells. The vaccine, made by Dow AgroSciences of Indianapolis, Indiana, a wholly owned subsidiary of the Dow Chemical Company, has proven safe and effective in protecting chickens from illness caused by the Newcastle disease virus, according to the USDA's Center for Veterinary Biologics. The subunit vaccine was produced using modified tobacco plant cells in an indoor, biocontained production system, eliminating environmental or consumer concerns about pharmaceuticals produced in food crops or open fields. Although Dow may decide not to sell the now-approved chicken vaccine because of market concerns, the company called the license a "regulatory milestone," allowing it to develop a range of other veterinary vaccines. Using the same production system for human vaccines is "a real possibility," the company said. Charles Arntzen, a biotech researcher at Arizona State University in Phoenix, who has been pushing plant-based vaccines for many years, welcomes the approval. "It shows that large companies are investing product-development resources in plant-derived pharmaceuticals, [and] that the [USDA] is receptive to the new strategy," Arntzen says. *PV*

USDA approves the first plant-based vaccine

January 2006 · Nature Biotechnology 24(3):233-234

DOI:10.1038/nbt0306-233

16 years ago

Parry G, Provart NJ, Brady SM, Uzilday B; Multinational Arabidopsis Steering Committee. Current status of the multinational Arabidopsis community. Plant Direct. 2020 August 2; 4(7):e00248. doi: 10.1002/pld3.248. PMID: 32775952; PMCID: PMC7396448.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7396448/pdf/PLD3-4-e00248.pdf
https://arabidopsis.info/static/info/masc_2020.pdf

BOTTOM LINE – CAN WE FAST FORWARD TO ARABIDOPSIS ?

Meyerowitz EM. (2001) Prehistory and history of Arabidopsis research. Plant Physiol. 2001 January; 125(1):15-19. doi: 10.1104/pp.125.1.15. PMID: 11154286; PMCID: PMC1539315.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1539315/pdf/hw0015.pdf

Somerville, C.R. and Meyerowitz, E.M. (eds.) The Arabidopsis Book. Am Soc of Plant Biologists, Rockville, 2003.
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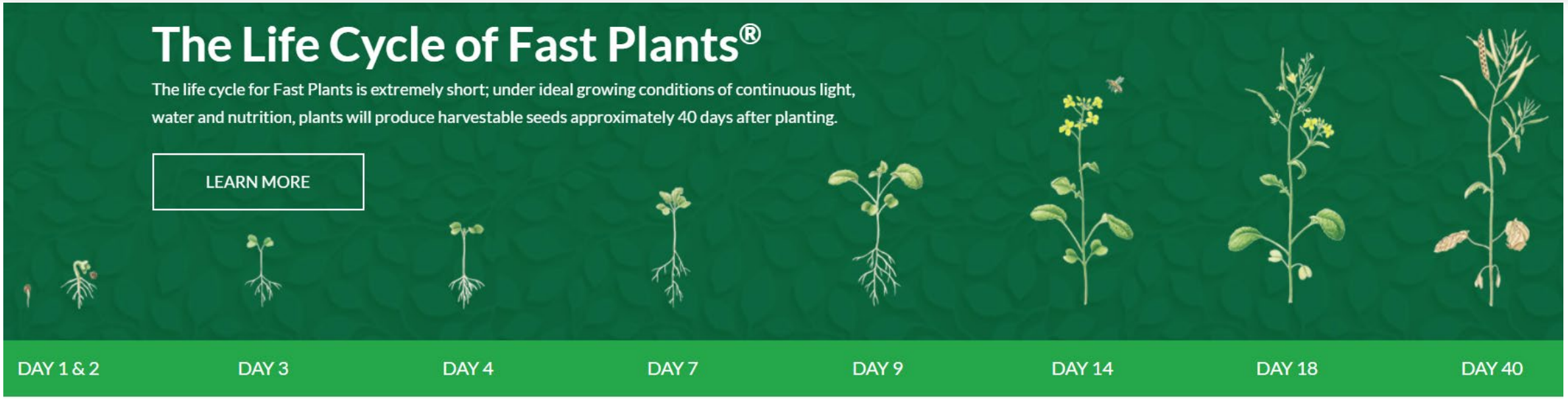
https://www.ncbi.nlm.nih.gov/pmc/journals/1655/

Chang C, Bowman JL, Meyerowitz EM. (2016) Field Guide to Plant Model Systems. Cell. 2016 October 6; 167(2): 325-339. doi: 10.1016/j.cell.2016.08.031. PMID: 27716506; PMCID: PMC5068971.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5068971/pdf/nihms-819752.pdf

FASTER, CHEAPER? LEAVES IN 4 DAYS, SEEDS IN 40 DAYS



Fast Plants (*Brassica rapa*) were developed by Paul H. Williams of University of Wisconsin-Madison. https://fastplants.org/origin/

WHY FAST FORWARD TO ARABIDOPSIS ?

Arabidopsis thaliana, small dicotyledonous species, is a member of the Brassicaceae family. *Arabidopsis* requires light, air, water and few minerals to complete its fast life cycle (seeds in ~ 40 days). It produces numerous self progeny, requires limited space, and is easily grown in a greenhouse or indoor growth. https://www.nsf.gov/pubs/2002/bio0202/model.htm

Brassica rapa

Brassica rapa is a plant species growing in various widely cultivated forms including the turnip; Komatsuna, napa cabbage, bomdong, bok choy, and rapini. Brassica rapa subsp. oleifera is an oilseed which has many common names, including rape, field mustard, bird's rape, and keblock. The term rapeseed oil is a general term for oil from Brassica species. Food grade oil made from the seed of low-erucic acid Canadian-developed strains is also called canola oil, while non-food oil is called colza oil. Canola oil is sourced from three species of Brassica plants: Brassica rapa and Brassica napus are commonly grown in Canada, while Brassica juncea is a minor crop for oil production.

Wikipedia

https://en.wikipedia.org › wiki › Arabidopsis_thaliana

Arabidopsis thaliana | Wikipedia

Arabidopsis thaliana, the **thale cress**, mouse-ear **cress** or arabidopsis, is a small plant from the mustard family (Brassicaceae), ... Like most Brassicaceae species, A. thaliana is **edible** by humans in a salad or cooked, but it does not enjoy widespread use as a spring vegetable. [24]

How “far” is thale cress from the idea of watercress / yellowcress (*Nasturtium officinale*) as a choice for transgenic plant vaccines?

PLATFORM ARABIDOPSIS THALIANA (THALE CRESS IS AN EDIBLE PLANT FOR HUMANS)

References 1-18 included in the following 4 pages

Arabidopsis has a rich scientific history[1] and its genetics[2] continues to be an active[3] field of plant research with potential for applications in medicine[4] as well as improving our understanding of basic science[5], food and nutrition. Hence, the Arabidopsis system is a suitably informed platform to explore the expression of recombinant proteins[6] in vegetables[7] and cereals[8] by creatively[9] re-constructing or modifying available[10] viral[11] vectors (RNA[12] or DNA[13] based) which are safe[14] for the environment. Success[15] of Arabidopsis as a platform[16] and the potential for paradigm shift[17] may translate into tangible results[18] of immense human value.

[1] Kertbundit S, De Greve H, Deboeck F, Van Montagu M, Hernalsteens JP. In vivo random beta-glucuronidase gene fusions in Arabidopsis thaliana. Proc Natl Acad Sci U S A. 1991 June 15; 88(12):5212-6. doi: 10.1073/pnas.88.12.5212. PMID: 2052601; PMCID: PMC51842.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC51842/pdf/pnas01062-0155.pdf

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32 years ago

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dspace.mit.edu/handle/1721.1/128017

Author(s)
Datta, Shoumen

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BACKGROUND, MILESTONES: A COLLECTION OF PAPERS

PAPERS ON PLANT-BIOLOGICS RELATED MATERIAL IN A ZIPPED FOLDER (~230MB)

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WORK IN PROGRESS ??

Plant-based human vaccines in clinical trials.

Pathogen or disease	Antigen	Plant	Expression system	Administration route	Clinical trial	Reference
Enterotoxigenic *E. coli*	LTB	Potato	Transgenic	Oral	Phase I	Tacket *et al.* [1998]
Enterotoxigenic *E. coli*	LTB	Maize	Transgenic	Oral	Phase I	Tacket *et al.* [2004]
Norovirus	Capsid protein	Potato	Transgenic	Oral	Phase I	Tacket *et al.* [2000]
Hepatitis B virus	Viral major surface protein	Lettuce	Transgenic	Oral	Phase I	Kapusta *et al.* [1999]
Hepatitis B virus	Viral major surface protein	Potato	Transgenic	Oral	Phase I	Thanavala *et al.* [2005]
Rabies virus	Glycoprotein and nucleoprotein (fusion)	Spinach	Viral vector (transient)	Oral	Phase I	Yusibov *et al.* [2002]
Influenza virus (H5N1)	HA	*Nicotiana benthamiana*	Launch vector (transient)	Intramuscular	Phase I	Chichester *et al.* [2012]
Influenza virus (H1N1; 2009 pandemic)	HA	*Nicotiana benthamiana*	Launch vector (transient)	Intramuscular	Phase I	Cummings *et al.* [2014]
Influenza virus (H5N1)	HA (H5; VLP)	*Nicotiana benthamiana*	Agrobacterial binary vector (transient)	Intramuscular	Phase IPhase II	D'Aoust *et al.* [2008] Landry *et al.* [2010]
Influenza virus (H7N9)	HA (H7; VLP)	*Nicotiana benthamiana*	Agrobacterial binary vector (transient)	Intramuscular	Phase I	Medicago Inc. (http://www.medicago.com)
Influenza virus	HA (VLP) (seasonal; quadrivalent)	*Nicotiana benthamiana*	Agrobacterial binary vector (transient)	Intramuscular	Phase I	Medicago Inc. (http://www.medicago.com)
Cholera	CTB	Rice	Transgenic	Oral	Phase I	Nochi *et al.* [2009] Yuki *et al.* [2013]

Takeyama N, Kiyono H, Yuki Y. Plant-based vaccines for animals and humans: recent advances in technology and clinical trials. Ther Adv Vaccines. 2015 Sept; 3(5-6):139-54. doi: 10.1177/2051013615613272. PMID: 26668752; PMCID: PMC4667769.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4667769/pdf/10.1177_2051013615613272.pdf
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4550766/pdf/AV2015-936940.pdf (Pit Sze Liew and Mohd Hair-Bejo ▪ Email mdhair@upm.edu.my)

Cereals for cattle? Can wheat pastures provide immune protection from farm animal diseases?

- **Some 60% of emerging infectious diseases that are reported globally come from animals, both wild and domestic. Over 30 new human pathogens have been detected in the last 3 decades, 75% of which have originated in animals.** www.who.int/news-room/fact-sheets/detail/one-health

https://www.nal.usda.gov/animal-health-and-welfare/farm-animal-diseases
http://agtoday.wpengine.com/wp-content/uploads/2016/12/Jourdans-photo.jpg
https://agrilifetoday.tamu.edu/2016/12/07/winter-wheat-management-critical-spring-production/
https://www.hpj.com/crops/the-best-ways-to-utilize-wheat-pasture-for-cattle/article_07bf9f28-ee88-11e9-aa66-9b267ae8f7b4.html

A sheep with bluetongue disease caused by the viral strain BTV-8 is treated in France 8/8/24. A more virulent strain, BTV-3, is ravaging farms in northwest Europe.

Livestock virus hits Europe with a vengeance

Bluetongue spreads rapidly in sheep and cattle in six countries despite the use of three new vaccines

20 AUG 2024 · 5:45 PM ET · BY ERIK STOKSTAD

www.science.org/content/article/livestock-virus-hits-europe-vengeance

Table 3. Plant-based vaccines for veterinary use.

Host	Pathogen	Antigen	Plant	Administration route	Treated animal	Reference
Chicken	Newcastle disease	Hemagglutinin-neuraminidase	Tobacco suspension cells	Subcutaneous	Chicken	Vermij *et al.* [2006]
Chicken	Newcastle disease	F protein	Maize	Oral	Chicken	Approved by USDA Guerrero-Andrade *et al.* [2006]
Chicken	Newcastle disease	F protein	Rice	Oral	Mice	Yang *et al.* [2007]
Chicken	IBV	S1 glycoprotein	Potato	Oral	Chicken	Zhou *et al.* [2004]
Chicken	IBDV	VP2	Rice	Oral	Chicken	Wu *et al.* [2007]
Pig	ETEC	Fimbriae (F4)	Tobacco (chloroplast)	N/D	Pig (in vitro assay in intestines)	Kolotilin *et al.* [2012]
Pig	ETEC	Fimbriae (F4)	Alfalfa	Oral	Piglet	Joensuu *et al.* [2006]
Pig	ETEC	Cholera toxin B subunit	Rice	Oral	Pig	Takeyama et.al. [2015]
Pig	ETEC	Fimbriae (F4)	Barley	Subcutaneous	Mice	Joensuu *et al.* [2006]
Pig	Foot and mouth disease virus	VP1	*Nicotiana bentamiana*	Intramuscular	Pig	Yang *et al.* [2007]
Pig	TGEV	S protein	Tobacco	Intramuscular	Pig	Tuboly *et al.* [2000]
Cattle	Bovine Herpesvirus	gD protein	Tobacco	Intramuscular and subcutaneous	Cattle	Pérez Filgueira *et al.* [2003]
Cattle	Bovine Viral Diarrhea Virus	E2 protein	Alfalfa	Intramuscular	Cattle	Peréz Aguirreburualde *et al.* [2013]
Cattle	Rinderpest virus	Hemagglutinin	Peanut	Oral	Cattle	Khandelwal *et al.* [2003]

Guerrero-Andrade O, Loza-Rubio E, Olivera-Flores T, Fehérvári-Bone T, Gómez-Lim MA. (2006) Expression of the Newcastle disease virus fusion protein in transgenic maize and immunological studies. Transgenic Res. 2006 August; 15(4):455-463. PMID: 16906446. doi: 10.1007/s11248-006-0017-0.

https://link.springer.com/content/pdf/10.1007/s11248-006-0017-0.pdf

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4667769/pdf/10.1177_205101361561327 2.pdf

Transplant paradoxes with paradigms ?

Tacket CO. (2009) Plant-based oral vaccines: results of human trials. Curr Top Microbiol Immunol. 2009; 332:103-17. doi: 10.1007/978-3-540-70868-1_6.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7121496/pdf/978-3-540-70868-1_Chapter_6.pdf

IS THIS THE HEART OF THE PROBLEM?

Finally, we need to define the procedures for manufacturing and processing of plant-based pharmaceuticals. The challenge is to facilitate the procedures without compromising quality, which is a prerequisite for manufacturing plant-based human and animal vaccines.

Takeyama N, Kiyono H, Yuki Y. Plant-based vaccines for animals and humans: recent advances in technology and clinical trials. Ther Adv Vaccines. 2015 Sept; 3(5-6):139-54. doi: 10.1177/2051013615613272. PMID: 26668752; PMCID: PMC4667769.

IS THIS SCIENCE IN THE SERVICE OF SOCIETY ?

ARABIDOPSIS ANTIGEN DELIVERY PLATFORM ?

LOGICAL STEPS FOR AN EBOLA ANTIGEN ?

THE MINIMUM PROOF OF CONCEPT IS …

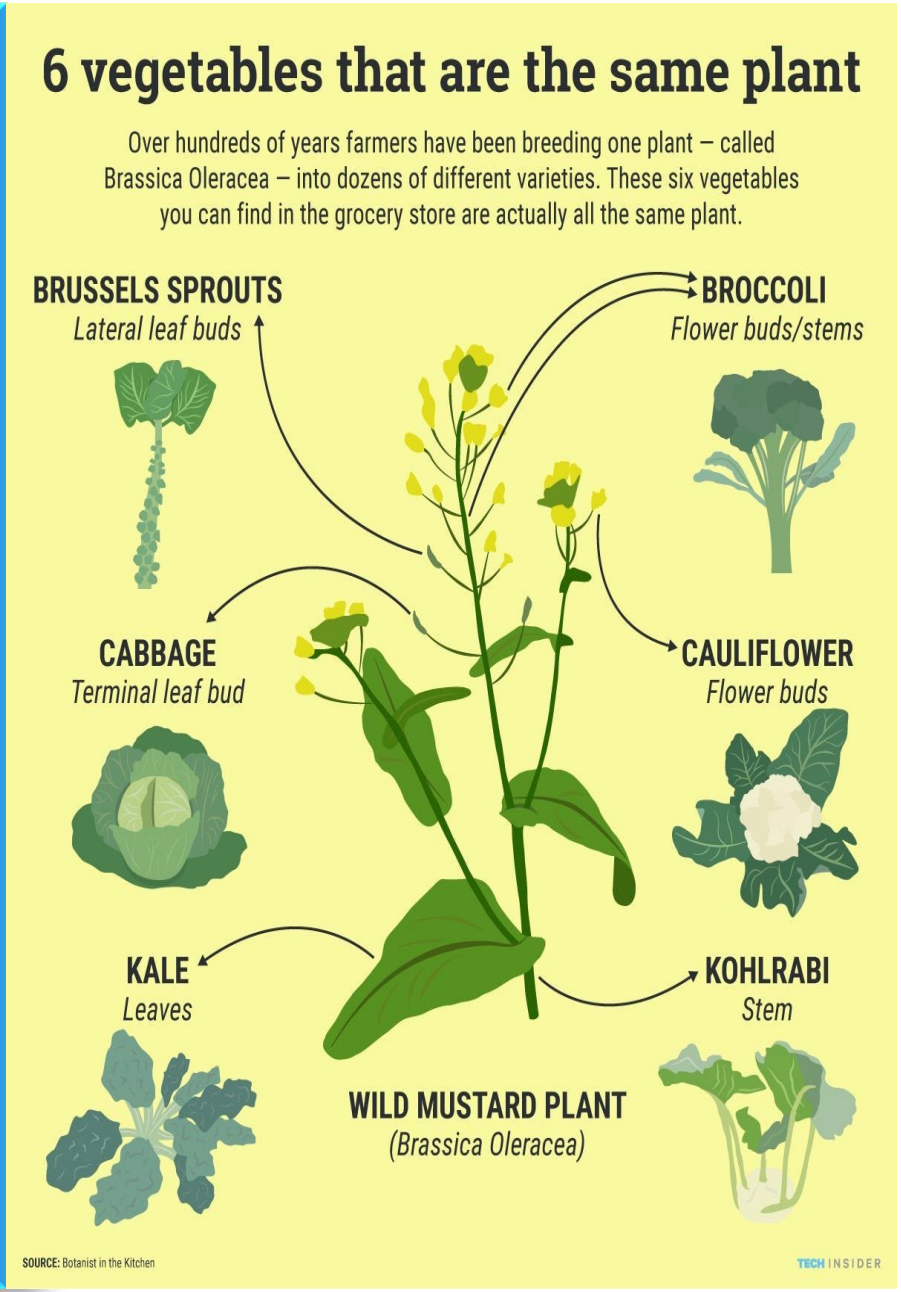
- Re-construct available viral vector(s) with EBOV
- Transfect Arabidopsis with EBOV-containing vector
- Assay for EBOV protein (antigen) in stem/leaf
- Test sublingual stem/leaf “paste” in humans
- Detect EBOV antigens / antibodies in blood

https://www.botanic.cam.ac.uk/learning/trails/dnatrail/arabidopsis/

Arabidopsis thaliana, the thale cress, mouse-ear cress or arabidopsis, is a small flowering plant native to Eurasia and Africa. A. thaliana is considered a weed; it is found along the shoulders of roads and in disturbed land.

Transplant paradoxes with paradigms ?

With just one plant.



PROBLEMS, ISSUES, QUESTIONS AND THE CONTEXT OF REMEDIABLE INJUSTICES VS TOLERABLE DISCOMFORTS NECESSARY FOR GLOBAL ACCESS TO IMMUNIZATION

- BIO-AVAILABILITY of antigens [1] through the sublingual route: will the plant "paste" release sub-cellular proteins? [2] if antigens enter the bloodstream, will it suffice (critical mass, threshold) to trigger a robust immune response?
- Why it may work: Crushing garlic in a mortar and pestle releases alliinase which converts alliin into allicin, the sulfur-containing molecule which provides garlic its signature odour (cannot be detected if the cells fail to rupture/break).
- Why it may work: Salivary amylase in saliva can reach amyloplasts (sub-cellular organelles) to hydrolyze starch in potato. Hence, proteins (antigens) should be available (a theoretical expectation) for sublingual extraction.
- Pre-treatment of "paste" with non-denaturing agents and/or non-proteolytic enzymes to partially loosen/break the cellulose scaffolds and/or cell walls, provides opportunity for proteins from sub-cellular compartments to escape.
- Uncooked plant "paste" (from tobacco leaves, potato/carrot slices, orange juice) may contain other proteins or small molecules (alkaloids) which may structurally or functionally interfere with the antigen expected to be delivered. What if other proteins in the "paste" also trigger immune responses? The Pandora's Box of "paste" related potential contraindications justifies purification of antigen prior to administration to humans but increases control and cost.
- VLPs are not suggested (but should be) partly because the dimensions (~100nm) may be a magnitude larger than antigens (proteins). Small molecules have a higher probability of diffusing through the mucous membranes and absorbed into the bed of capillaries under the tongue. Sublingual route is commercially (www.biolingus.ch) viable.

TRANSFORM PARADOXES TO PARADIGMS (TP-TOP)

DISCLAIMER AND HYPOTHETICAL RESERVATIONS

The cautious suggestion in this document to explore plants as a source of foreign antigen for self-vaccination and immunization of humans (and animals) is NOT A PANACEA solution for all ills and illnesses. It may be a low-cost tool in our "tool-box" of mitigation strategies for future public health catastrophes, epidemics and pandemics.

The concept of TP-TOP (pronounced "*tipee-top*") may face scientific limitations which may render the overtly simple idea impractical, inefficient and untenable as a vehicle for low-cost implementation of immunization.

The reliance on virologists, molecular biologists and plant geneticists to create recombinant vectors and the transgenic plants may lead to economic and IP challenges. Organisms evolve through mutations which causes antigenic drift (affects virulence?). The latter may introduce insurmountable biological barriers due to unknown unknowns. The current SARS-CoV-2 pandemic highlights the importance of *a priori* molecular engineering in RSV which unleashed the critical need to insert two Prolines (2P by Jason McClellan) to prepare the prefusion stabilized SARS-CoV-2 Spike glycoprotein which was used as the antigen template for the mRNA (by Katalin Kariko) vaccine.

The molecular biology and protein chemistry of the antigen is quintessential for efficacy of any hypothetical immune response. This hypothesis is about DELIVERY of the *optimized antigen* through a low-cost ubiquitous vehicle (plant).

Bio-Engineered Plant-Produced Antigens, Self-Administered (BEPASA) for oral immunization

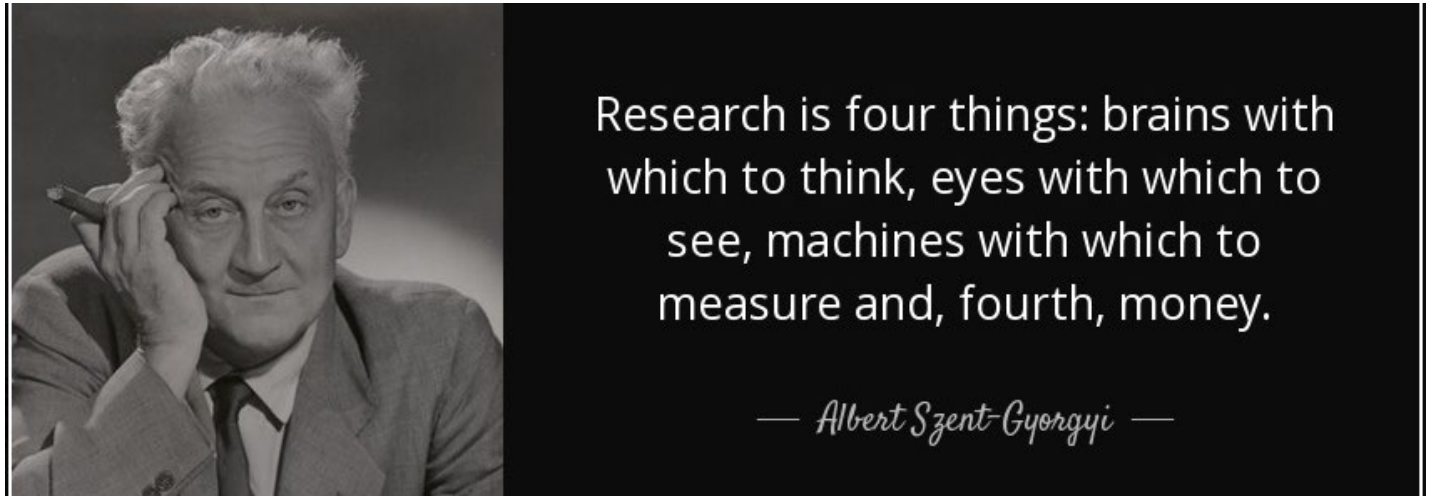
YOU ARE WELCOME

TO DEMOLISH THIS

BIT TOO OPTIMISTIC

HYPOTHESIS WITH

A SLEDGE HAMMER.



1. Money from grant or philanthropic contribution to lead without IP
2. Recombinant vector lab (molecular biology) and a plant bio lab
3. Few enthusiastic molecular biology students & plant bio students
4. Create EBOV vector, transfect, harvest leaves, make “paste”
5. Administer RAW LEAF “paste” – sublingual and/or oral (S. Datta)
6. Check volunteer’s blood for EBOV antigen and EBOV antibodies

https://www.salk.edu/about/history-of-salk/jonas-salk

CHALLENGE THE

VOLUNTEER (S. DATTA)

WITH LIVE EBOLA VIRUS.

IF VOLUNTEER (S. DATTA)

SURVIVES UNINFECTED,

THEN BEPASA IS USEFUL

FOR SUBLINGUAL OR

ORAL IMMUNIZATION.

STEP 7

BEPASA for oral immunization

1. Money from grant or philanthropic contribution to lead without IP
2. Recombinant vector lab (molecular biology) and a plant bio lab
3. Few enthusiastic molecular biology students & plant bio students
4. Create EBOV vector, transfect, harvest leaves, make “leaf paste”
5. Administer RAW LEAF “paste” – sublingual and/or oral (S. Datta)
6. Check volunteer’s blood for EBOV antigen and EBOV antibodies

STEP 7

IS NOT ESSENTIAL FOR POV

1. Money from grant or philanthropic contribution to lead without IP
2. Recombinant vector lab (molecular biology) and a plant bio lab
3. Few enthusiastic molecular biology students & plant bio students
4. Create EBOV vector, transfect, harvest leaves, make “leaf paste”
5. Administer RAW LEAF “paste” – sublingual and/or oral (S. Datta)
6. Check volunteer’s blood for EBOV antigen and EBOV antibodies

FOR IMPLEMENTING POV

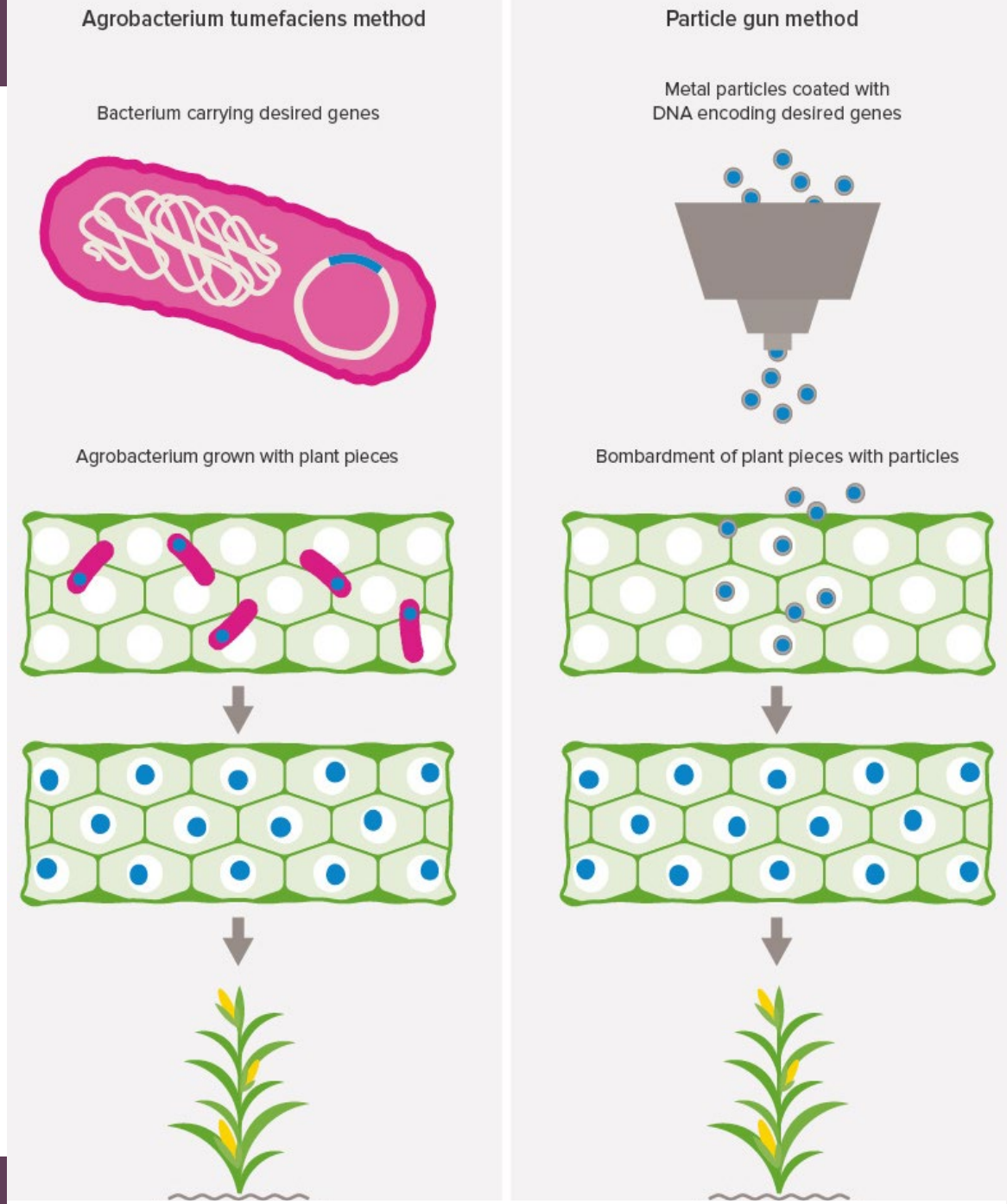
FOCUS ON STEP 4

CREATE EBOV (any gene, specific for the antigen)

VECTOR, TRANSFECT

STEP 4:

Create EBOV vector, transfect



https://royalsociety.org/news-resources/projects/gm-plants/what-is-gm-and-how-is-it-done/

1984

National Research Council (US) Board on Agriculture. Genetic Engineering of Plants: Agricultural Research Opportunities and Policy Concerns. National Academies Press (US); 1984. Gene Transfer. https://www.ncbi.nlm.nih.gov/books/NBK216398/

2004

National Research Council (US) Committee on Identifying and Assessing Unintended Effects of Genetically Engineered Foods on Human Health. Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects. Washington (DC): National Academies Press (US); 2004. Chapter 2: Methods and Mechanisms for Genetic Manipulation of Plants, Animals, and Microorganisms. https://www.ncbi.nlm.nih.gov/books/NBK215771/

2022

https://food.ec.europa.eu/plants/genetically-modified-organisms_en

2023

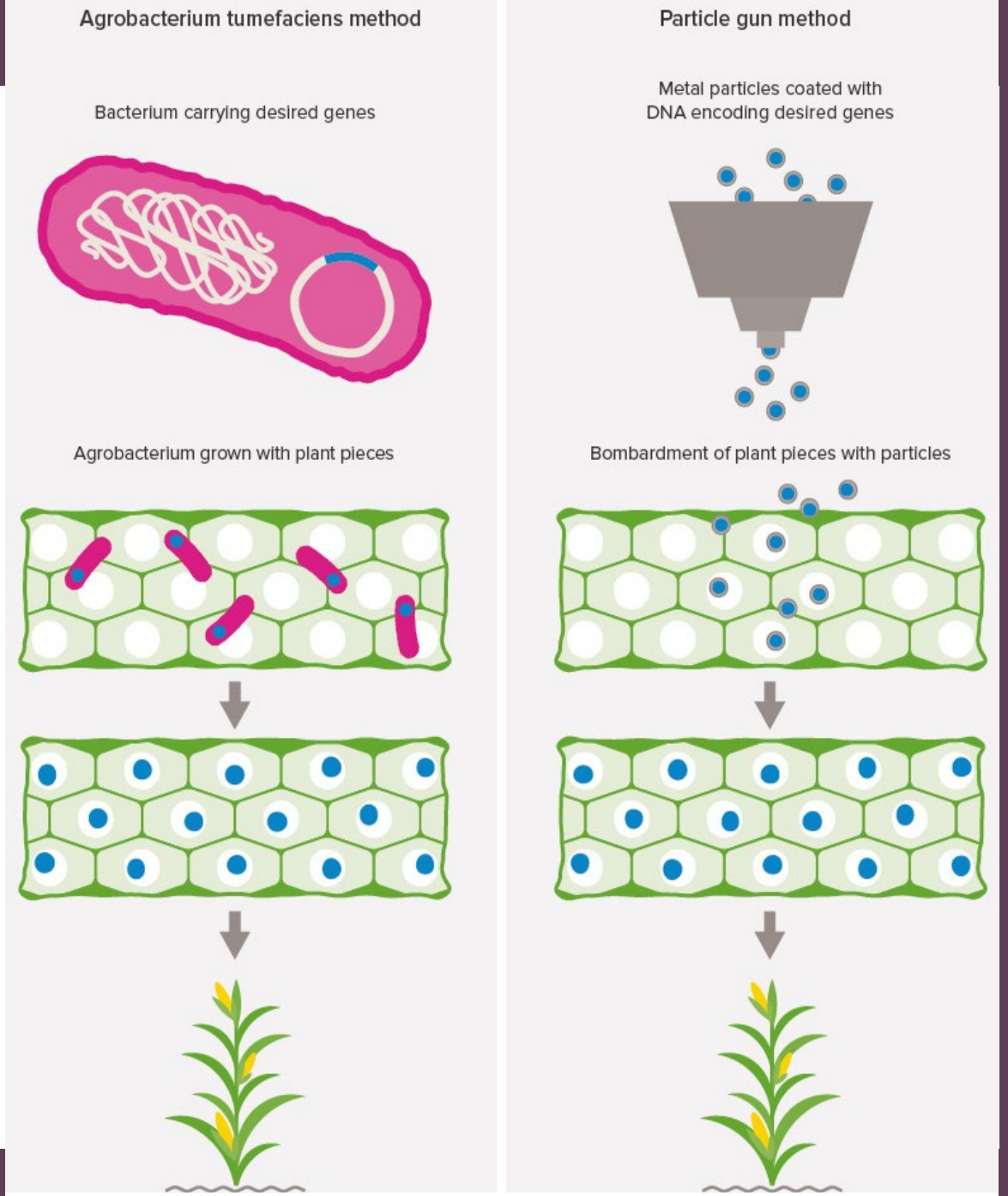
https://crsreports.congress.gov/product/pdf/R/R47683/2

Any poor nation can make their own vaccines !!

STEP 4 - BREAKS ALL THE BARRIERS

If the vector is made available – the vectors for specific viral genes (e.g., EBOV for Ebola) are available because these vectors were used in the published research papers.

If the transfected plant/seed is made available.



https://royalsociety.org/news-resources/projects/gm-plants/what-is-gm-and-how-is-it-done/

STEPS 1-6 must proceed without any delay due to translational science related efforts. We must implement POV. The risk from exposure to deadly viruses far outweigh the risks due to ingestion of potatoes or watercress or mustard greens as a source of PDA (transgenic plant derived recombinant antigens) even without any standard protocol or dietary guide for induction of immunity (IgG titers in blood). While we work in labs, locals must not be kept waiting to benefit from this proven solution (steps 1-6). ***Even low levels of IgG may reduce mortality*** and morbidity (severity/acuity of infection). Should the luxury of pursuing translational science prevent us from implementing POV and deliver potential death sentences for billions of people?

CONCERNS

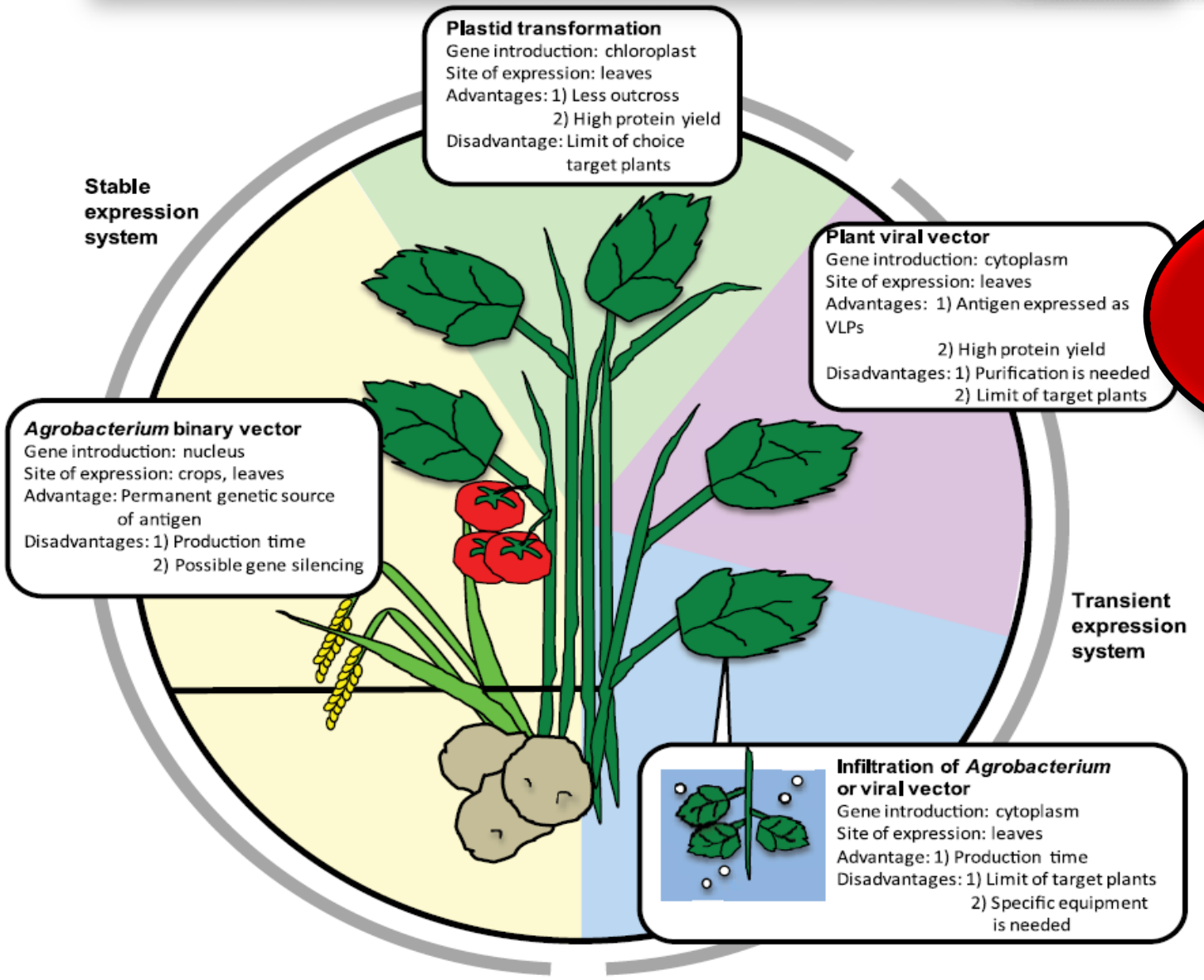
Analyses of possible negative effects of plant-based antigens (PDA) include people who may unknowingly eat such plants and will be exposed (without consent) to material that will trigger an immune response. It may result in negative effects such as induction of autoimmunity or chronic inflammation. Reasonable caution by labelling plant products producing foreign antigen, prevention of uncontrolled spread and assessment of potential side effects are prudent safety measures.

Few may not share the enthusiasm for administering Ebola virus to a volunteer (S. Datta, author) in step 7 and in that instance perhaps US FDA safety regulations/criteria may apply. Should we test, first, in animals? To mitigate unknown health risks due to POV, edible plant-based antigen (ePDA) administration in humans may begin testing a virus that is widespread, already, so that the relative effectiveness of the vaccine can be assessed with minimal harm (e.g., for CoVID vaccines). Testing in humans demand prior knowledge of "sterilizing" immunity. Establishing serum IgG levels for sterilizing immunity proportional to "dose" depends on determining the number of infectious particles (e.g. virions). Estimating the number of particles (10^n) at the *initial point of infection* could be quite error prone (where n = {0, …,10}, if n=0, then it is 1 particle; n=1 indicates 10 particles; n=10 is10 billion particles at the initial point of infection). Thus, any claim for individual "sterilizing" immunity data may be of little value if overwhelmed by the number of infectious virions. The infectious does will outweigh the individual's immune preparedness to accept a certain challenge dose of infectious particles.

STERILIZING IMMUNITY

PERFECT IS THE ENEMY OF GOOD

IN PRAISE OF IMPERFECTION



DO NOT PURIFY

- PERFECT
- IS THE
- ENEMY
- OF
- GOOD

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4667769/pdf/10.1177_2051013615613272.pdf

WE HAVE BEEN PRAISING IMPURITIES WITH IMPUNITY

https://www.youtube.com/watch?v=ebTrfbaAOFE

https://www.youtube.com/watch?v=aOpTFCVN_Ok

https://www.youtube.com/watch?v=RdRNxXf_WXw

Indians still use neem stem as a tooth-brush cum tooth paste, for astringent tooth cleaning. It is an old practice in India (and Asia, Africa) since time immemorial. People pluck and use neem stems as traditional tooth-brushes for tooth cleaning. The fact that the “brush” is a natural plant product helps to bypass corporate greed.

IS PURIFICATION A “WESTERN” CONCEPT ?

THE RADICAL PART IN THIS SUGGESTION IS A COMMON PRACTICE

SHOULD WE PRAISE IMPURITIES WITH IMPUNITY ?

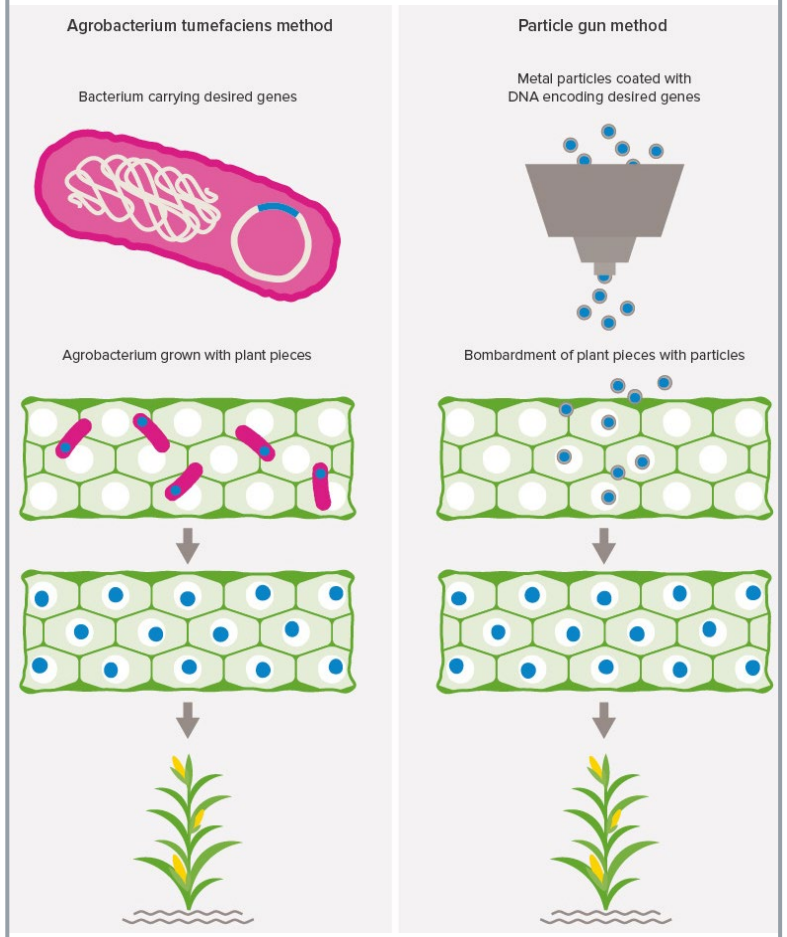
THE RADICAL PART IN THIS HYPOTHETICAL SUGGESTION

CAN WE ELIMINATE THE PURIFICATION STEP ???

PURIFICATION IS UNNECESSARY FOR ORAL USE OF EDIBLE PLANT ANTIGENS TO INDUCE IMMUNOGENICITY IN HUMANS.

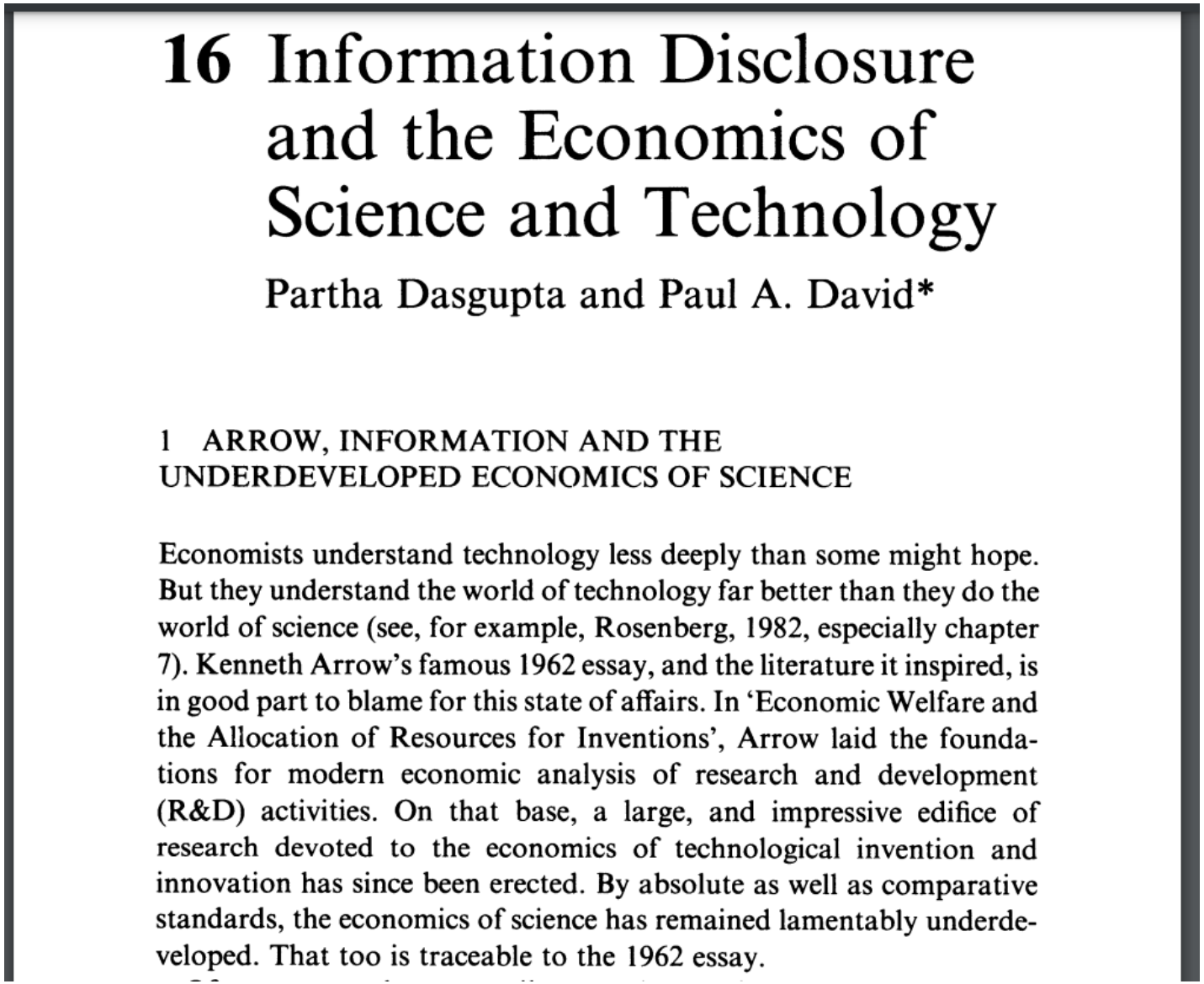
The nightmare of cold chain Supply Chain Management

There is no need for any cold chain



David, P. A. (1990). The Dynamo and the Computer: An Historical Perspective on the Modern Productivity Paradox. *The American Economic Review*, *80*(2), 355–361. http://www.jstor.org/stable/2006600 and David, P.A. & Wright, G. A. (1999) https://www.nuffield.ox.ac.uk/economics/history/paper31/a4.pdf

ISN'T THE ECONOMICS OF TECHNOLOGY IN FAVOR OF PLANT -BASED VACCINES?



16 Information Disclosure and the Economics of Science and Technology

Partha Dasgupta and Paul A. David*

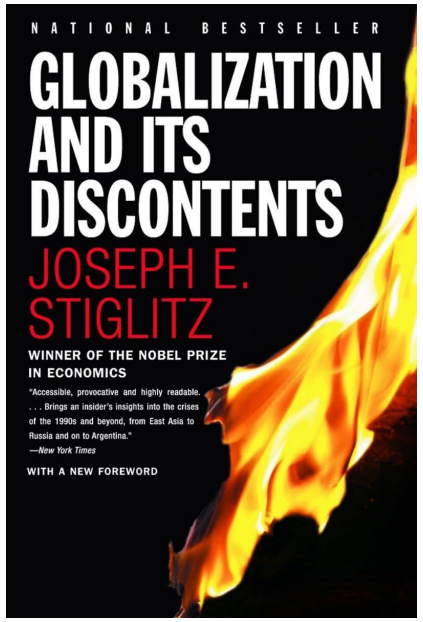
1 ARROW, INFORMATION AND THE UNDERDEVELOPED ECONOMICS OF SCIENCE

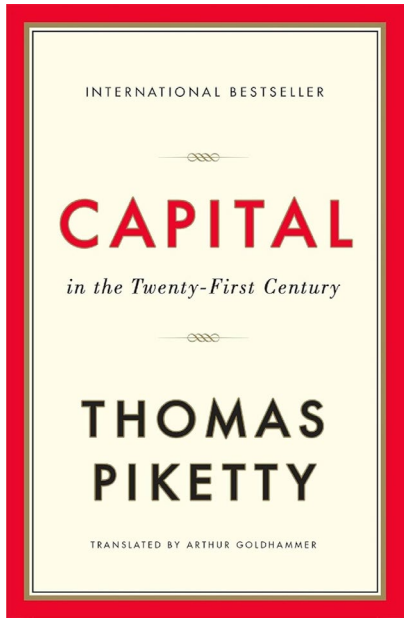
Economists understand technology less deeply than some might hope. But they understand the world of technology far better than they do the world of science (see, for example, Rosenberg, 1982, especially chapter 7). Kenneth Arrow's famous 1962 essay, and the literature it inspired, is in good part to blame for this state of affairs. In 'Economic Welfare and the Allocation of Resources for Inventions', Arrow laid the foundations for modern economic analysis of research and development (R&D) activities. On that base, a large, and impressive edifice of research devoted to the economics of technological invention and innovation has since been erected. By absolute as well as comparative standards, the economics of science has remained lamentably underdeveloped. That too is traceable to the 1962 essay.

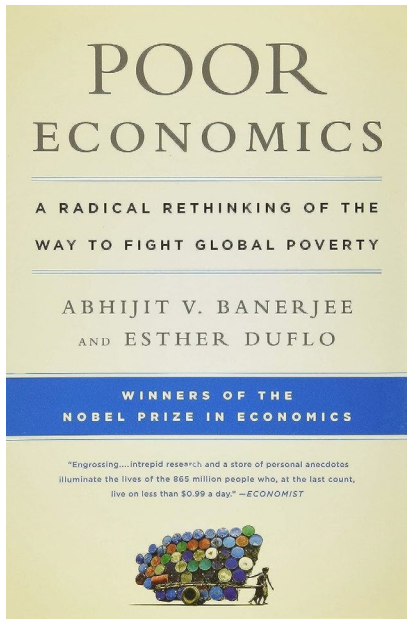
Dasgupta, P., David, P.A. (1987). Information Disclosure and the Economics of Science and Technology. In: Feiwel, G.R. (eds) Arrow and the Ascent of Modern Economic Theory. Palgrave Macmillan, UK. https://doi.org/10.1007/978-1-349-07239-2_16

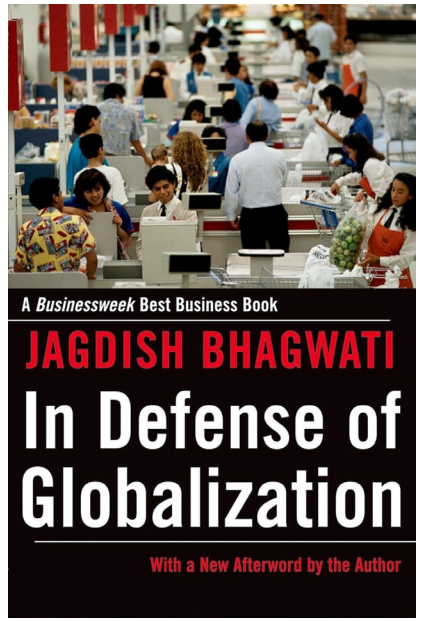
WHY CAN'T LESS AFFLUENT NATIONS FIND/PROVIDE THE LEADERSHIP FOR GLOBALIZATION OF PLANT-BASED VACCINES ?

THE ONLY THING NECESSARY FOR THE TRIUMPH OF ANTI-SCIENCE IS FOR SCIENTISTS TO DO NOTHING.









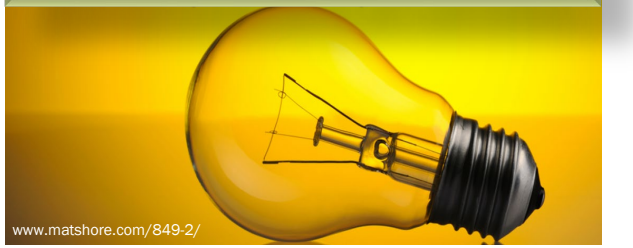
WHY LESS AFFLUENT NATIONS CAN'T PROVIDE THE LEADERSHIP TO GLOBALIZE PLANT-BASED VACCINE

In Business Outsiders Innovate ?
Faux naïveté in its purest distillate ?

Outsiders innovate ??

NBC didn't change media. YouTube did. NASA didn't reinvent space exploration. SpaceX did. GM didn't innovate electric car. Tesla did. AT&T didn't create smart phones. Apple did. Walmart could not innovate retail. Amazon did. Pfizer did not create CoVID-19 mRNA vaccine. *BioNTech did.

The electric bulb didn't result from incremental improvement of candles.



https://yourstory.com/2013/09/silcon-valley-legend-vinod-khosla-plans-slowdown-next-25-years

Healthcare is NOT a Business
Patients are NOT Customers

Why? The "information asymmetry" between patients and doctors.
https://www.nobelprize.org/prizes/economic-sciences/2001/summary/

Outsiders innovate ??

*BioNTech was created by scientists who were original inventors. Plant based oral vaccines (POV) is a science-based effort in need of scientific knowledge and leadership as well as wisdom for implementing POV to use science to benefit society. Greed has no place but ethical profitability is possible.

https://pristina.mfa.gov.hu/eng/news/katalin-kariko-has-been-awarded-the-2023-nobel-prize-in-medicine

Walmart Health Is Closing

April 30, 2024 | 3 Min. Read | Business

BENTONVILLE, Ark., April 30, 2024 – Back in 2019, we launched Walmart Health centers.

innovate ??

CVS Health to lay off nearly 3,000 workers primarily in 'corporate' roles

Gabe Hauari USA TODAY

Published 11:57 a.m. ET Oct. 1, 2024 | Updated 11:57 a.m. ET Oct. 1, 2024

Healthcare is NOT a Business

Businesses have FAILED to provide healthcare services for "greed" only.

FAILED BUSINESS

Walgreens Shutters 160 VillageMD Clinics after $6 Billion Loss

https://corporate.walmart.com/news/2024/04/30/walmart-health-is-closing

https://www.aha.org/aha-center-health-innovation-market-scan/2024-04-09-walgreens-shutters-160-villagemd-clinics-after-6-billion-loss

www.vcloudinfo.com/2011/08/rip-google-health-another-cloud-service.html

https://www.nytimes.com/2014/06/17/upshot/apples-healthkit-probably-wont-bring-a-new-age.html

https://www.fiercehealthcare.com/health-tech/amazon-care-shutting-down-end-2022-tech-giant-said-virtual-primary-care-business-wasnt

https://www.usatoday.com/story/money/2024/10/01/cvs-layoffs-2024/75466456007/

Amazon Care is shutting down at the end of 2022. Here's why

SENSE OF FUTURE THINKING

SOFT

for

HARD

Healthcare-Associated Research & Development

Moderna and BioNTech/Pfizer are "saints" compared to https://magazine.ucsf.edu/corporate-strategy-national-tragedy

OPULENCE OF OPTIMISM

We may not abandon the hope that conventional and more recent vaccine technologies can be streamlined and localized so that every country can possess the capability to produce safe and effective formulations. Perhaps recombinant protein production can be franchised to the point where different agencies/countries can execute the recipes. The same is likely true of mRNA vaccines and it may not be just wishful thinking that this technology may be off-the-shelf in a few decades (few years?). More research is necessary to better understand what makes a good RNA sequence (or protein sequence) for a vaccine. We need to know with precision and accuracy the range of factors that can lead to unwanted effects. Some vaccines may become a part of our daily lives (routine, safe) while others may be used when there is an urgency. Some examples of the ability of individual non-OECD nations to develop superior public health and vaccine infrastructures have been evident during the pandemic (e.g., Cuba). Sharing technologies and information about pathogens is key. The latter (pathogen information, particularly emerging pathogens) is possible with internet/sequencing/cooperation. There will always be some conflicts over intellectual property (Moderna has been particularly aggressive with lawsuits against both BioNTech/Pfizer and the US Government). Are these events transient theatrics by heavy handed venture capitalists or more ominous than meets the eye? The diffusion of technology (which in reality is fairly common in the biomedical world) must be supported.

UCSF MAGAZINE

One slide told drug sales reps to reach out to youths "early," at the "elementary school level," and to use wording that a 6-year-old could understand: "Pain is your body telling you something important." Bullet points even suggested that salespeople connect with respected channels, like Little League coaches and school nurses, and essentially turn them into mouthpieces for the merits of medicated relief.

https://magazine.ucsf.edu/corporate-strategy-national-tragedy

Bad Influencers

Opioid manufacturers sought to recruit coaches and school nurses to encourage kids to use opioids. The bottom slide is from a meeting of the Pain Coalition, a group of leaders in pain management and Janssen professionals that aimed to influence how children, veterans, and other vulnerable groups perceive pain. The document directly below is from an internal Janssen presentation that identified target groups for an unbranded initiative.

While criticizing BioNTech/Pfizer and Moderna for enforcing profit as a key element of their CoVID-19 mRNA vaccine, one must recognize that these behemoths saved millions of lives in affluent nations. On the other hand, the opioid gang, (Purdue Pharma, Janssen and uncivil actions by McKinsey) are responsible for over a million deaths due to their diabolical greed, gluttony and avarice.
www.cdc.gov/opioids/basics/epidemic.html

HUMAN INTEREST

Corporate Strategy, National Tragedy

Fudging numbers. Targeting children. Paying professors. UCSF's industry archives expose the marketing tactics that fueled the opioid epidemic.

By Robin Buller · UCSF Magazine · Winter 2024

English translation

Lippenbekenntnis

lip service

nature.com/articles/d41586-024-00545-3

COMMENT | 23 February 2024

Save lives in the next pandemic: ensure vaccine equity now

The proposed Pandemic Agreement must ensure that COVID-19 vaccine nationalism is never repeated; 290 scientists call for action.

By the end of 2021, the global distribution of vaccines was highly heterogeneous, with some countries gaining over 90% coverage in adults, whereas others reached less than 2%. In this study, we used an age-structured model of SARS-CoV-2 dynamics, matched to data from 152 countries in 2021, to investigate this inequity. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9671807/pdf/41591_2022_Article_2064.pdf

- Refusal of wealthier nations to cooperate had cost between 200,000 and 1.3 million lives by the end of 2021 in low- and middle-income countries[1,2]. Today, one-third of the world's population has still not received a single dose, and the death toll vaccine continues to grow.

www.nature.com/articles/d41586-024-00545-3

www.ncbi.nlm.nih.gov/pmc/articles/PMC9225255/

Phelan, Alexandra L. **"The World Health Organization's pandemic treaty."** BMJ 2023 Feb 28; 380:463 https://pubmed.ncbi.nlm.nih.gov/36854465/

English translation

Lippenbekenntnis

lip service

https://www.nature.com/articles/d41586-023-02251-y.pdf

The best medicine for improving global health? Reduce inequality

But then the pandemic hit, taking millions of lives, leaving millions of people living with disability and disrupting health-care systems worldwide. There were indirect, as well as direct, effects. With world leaders focusing on the pandemic, global spending on tuberculosis services dropped by 10%, from US$6 billion in 2019 to $5.4 billion in 2021; over the same period, deaths from tuberculosis rose from 1.4 million to about 1.6 million. Malaria-associated deaths rose by 12%, from 558,000 in 2019 to 627,000 in 2020. Childhood vaccination rates against diphtheria, tetanus and pertussis fell between 2019 and 2021.

STILL OPTIMISTIC? TOO LATE, FOR TOO FEW, AT A COST TOO HIGH

Wu RL, Idris AH, Berkowitz NM, Happe M, Gaudinski MR, Buettner C, Strom L, Awan SF, Holman LA, Mendoza F, Gordon IJ, Hu Z, Campos Chagas A, Wang LT, Da Silva Pereira L, Francica JR, Kisalu NK, Flynn BJ, Shi W, Kong WP, O'Connell S, Plummer SH, Beck A, McDermott A, Narpala SR, Serebryannyy L, Castro M, Silva R, Imam M, Pittman I, Hickman SP, McDougal AJ, Lukoskie AE, Murphy JR, Gall JG, Carlton K, Morgan P, Seo E, Stein JA, Vazquez S, Telscher S, Capparelli EV, Coates EE, Mascola JR, Ledgerwood JE, Dropulic LK, Seder RA; VRC 614 Study Team. (2022) Low-Dose Subcutaneous or Intravenous Monoclonal Antibody to Prevent Malaria. New England Journal of Medicine 2022 August 4; 387(5):397-407. doi: 10.1056/NEJMoa2203067. PMID: 35921449. https://www.nejm.org/doi/pdf/10.1056/NEJMoa2203067?articleTools=true

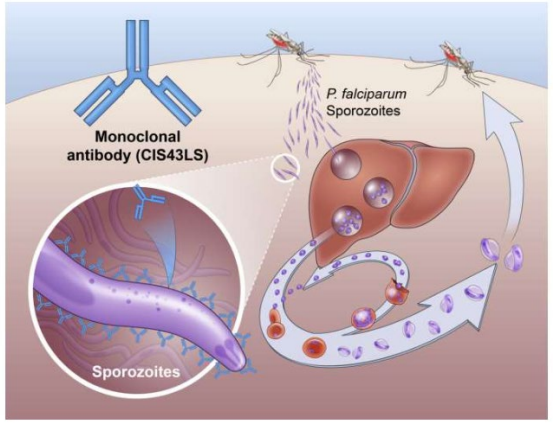
ESTABLISHED IN 1812 AUGUST 4, 2022 VOL. 387 NO. 5

Low-Dose Subcutaneous or Intravenous Monoclonal Antibody to Prevent Malaria

R.L. Wu, A.H. Idris, N.M. Berkowitz, M. Happe, M.R. Gaudinski, C. Buettner, L. Strom, S.F. Awan, L.S.A. Holman, F. Mendoza, I.J. Gordon, Z. Hu, A. Campos Chagas, L.T. Wang, L. Da Silva Pereira, J.R. Francica, N.K. Kisalu, B.J. Flynn, W. Shi, W.-P. Kong, S. O'Connell, S.H. Plummer, A. Beck, A. McDermott, S.R. Narpala, L. Serebryannyy, M. Castro, R. Silva, M. Imam, I. Pittman, S.P. Hickman, A.J. McDougal, A.E. Lukoskie, J.R. Murphy, J.G. Gall, K. Carlton, P. Morgan, E. Seo, J.A. Stein, S. Vazquez, S. Telscher, E.V. Capparelli, E.E. Coates, J.R. Mascola, J.E. Ledgerwood, L.K. Dropulic, and R.A. Seder, for the VRC 614 Study Team*

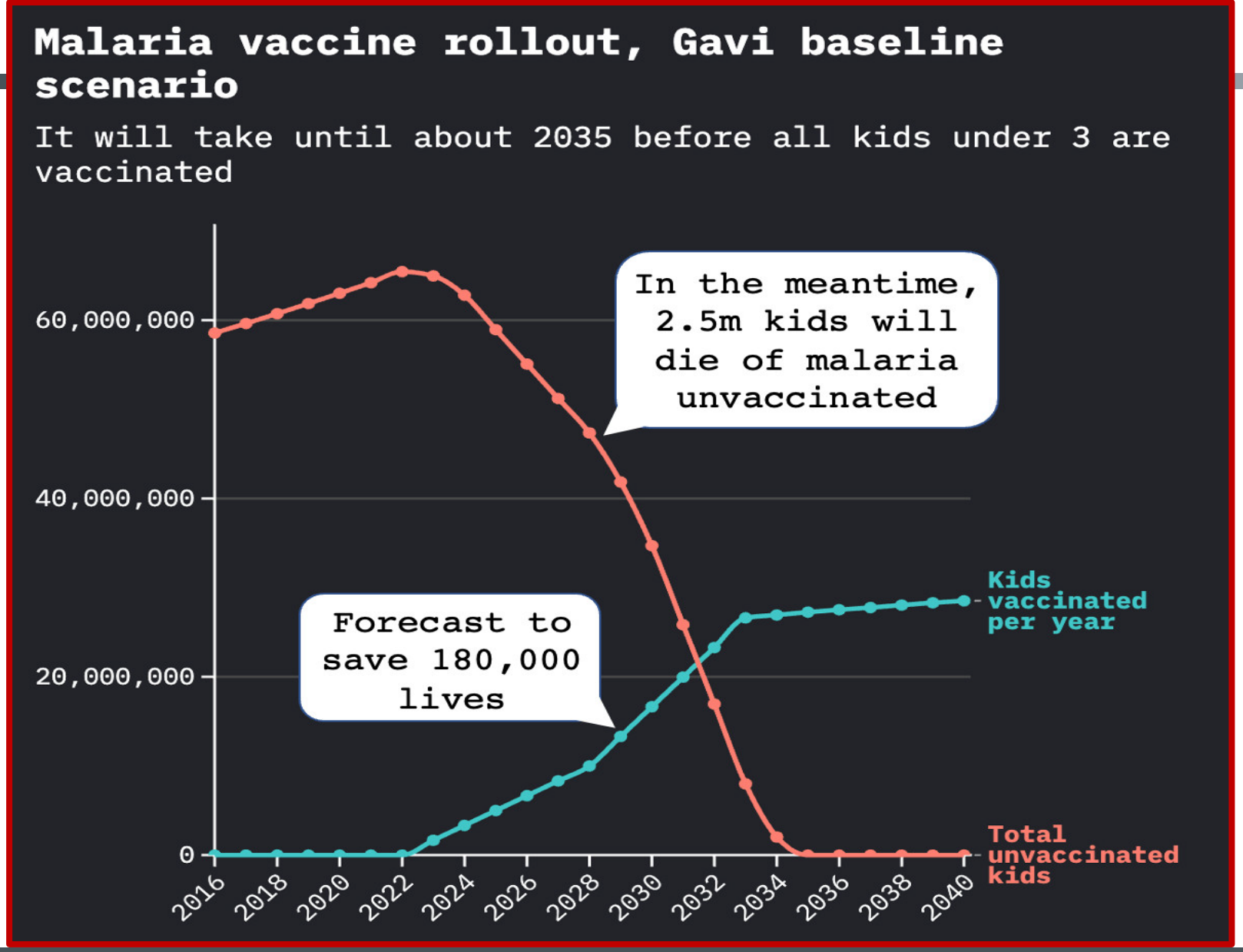
Monoclonal antibody prevents malaria infection in African adults

by NIH/National Institute of Allergy and Infectious Diseases



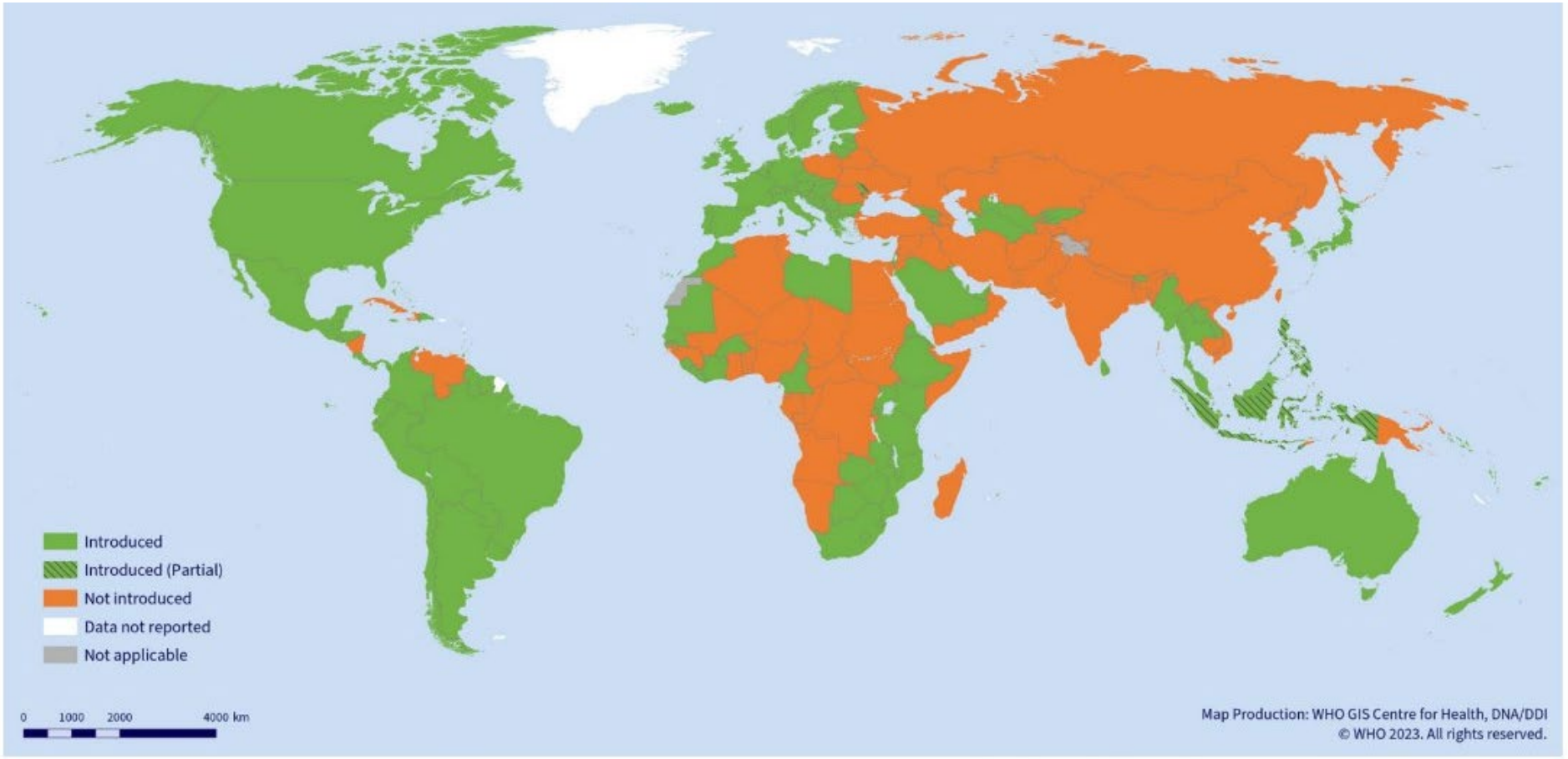
An antibody drug called CIS43LS prevents malaria infection

Gaudinski MR, Berkowitz NM, Idris AH, Coates EE, Holman LA, Mendoza F, Gordon IJ, Plummer SH, Trofymenko O, Hu Z, Campos Chagas A, O'Connell S, Basappa M, Douek N, Narpala SR, Barry CR, Widge AT, Hicks R, Awan SF, Wu RL, Hickman S, Wycuff D, Stein JA, Case C, Evans BP, Carlton K, Gall JG, Vazquez S, Flach B, Chen GL, Francica JR, Flynn BJ, Kisalu NK, Capparelli EV, McDermott A, Mascola JR, Ledgerwood JE, Seder RA; VRC 612 Study Team. (2021) A Monoclonal Antibody for Malaria Prevention. New England Journal of Medicine. 2021 August 26; 385(9):803-814. doi: 10.1056/NEJMoa2034031. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8579034/pdf/nihms-1751179.pdf



www.cgdev.org/sites/default/files/avoiding-another-lost-decade-malaria-vaccines.pdf

Do we still think corporate controlled vaccination is the global solution?



Source: WHO HPV Vaccine Introduction Clearing House: HPV dashboard. Immunization, Vaccines and Biologicals (who.int). Accessed 17 July 2023.

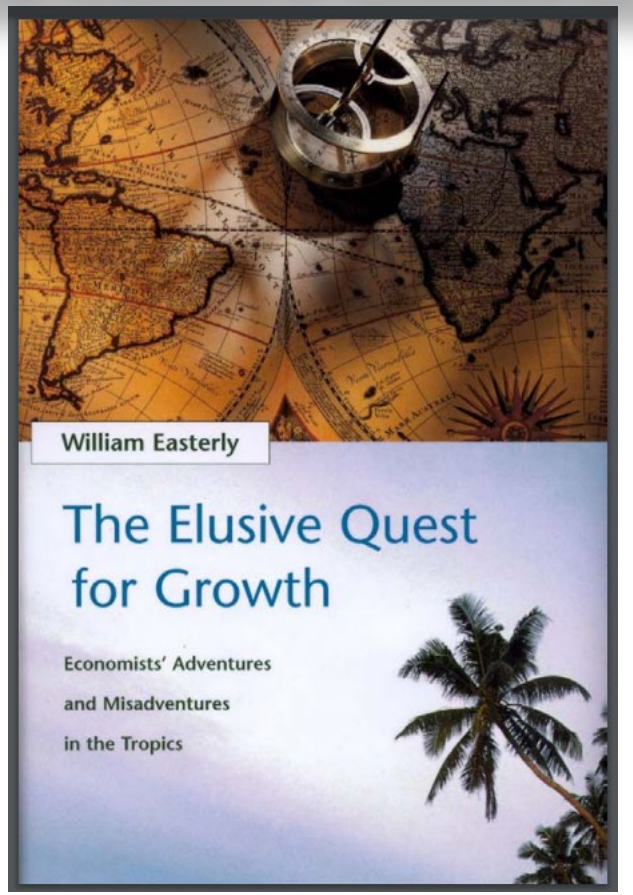
Frazer IH. The HPV Vaccine Story. ACS Pharmacol Transl Sci. 2019 May 29;2(3):210-212. doi: 10.1021/acsptsci.9b00032 www.ncbi.nlm.nih.gov/pmc/articles/PMC7089001/pdf/pt9b00032.pdf
Mammas IN, Sourvinos G, Spandidos DA. The paediatric story of human papillomavirus (Review). Oncol Lett. 2014 Aug;8(2):502-506. doi: 10.3892/ol.2014.2226
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4081157/pdf/ol-08-02-0502.pdf

IS FINANCIAL INCENTIVE THE KEY TO LIFT MANY BOATS ?

PLANT BASED SELF-VACCINATION

AND MASS IMMUNIZATION WILL

IMPROVE THE GLOBAL ECONOMY.



Plant based vaccination as a cottage industry and social business opportunity to improve financial health.

https://sociologiadeldesarrolloi.files.wordpress.com/2014/11/245593638-william-r-easterly-the-elusive-quest-for-growth-bookzz-org-pdf.pdf

https://www.hsph.harvard.edu/news/magazine/public-health-economy-election

- Over the period 1996 to 2020, the economic benefits for those using GM technology increased by $261.3 billion US dollars. In terms of investment, for each extra dollar invested in GM crop seeds (relative to conventional seed cost), farmers gained an average US $3.76 extra income. In developing countries, the average return was $5.22 for each extra dollar invested in GM crop and in developed countries the average return was $3.00.

https://www.tandfonline.com/doi/pdf/10.1080/21645698.2022.2105626?needAccess=true

Farm income and production impacts use of genetically modified (GM) crop technology 1996-2020

Graham Brookes

Pages 171-195 | Received 09 May 2022, Accepted 20 Jul 2022, Published online: 19 Aug 2022

Download citation https://doi.org/10.1080/21645698.2022.2105626 Check for updates

https://www.brookings.edu/blog/future-development/2020/07/21/how-investing-in-health-has-a-significant-economic-payoff-for-developing-economies/

https://sites.google.com/forteprotein.com/forteprotein/blog?authuser=0

Viewpoint: After years of misreporting, NY Times embraces safety and efficacy of GMOs — but still stumbles on nuance and key facts

Henry Miller, Kathleen Hefferon | October 13, 2021

Viewpoint: Farm-to-Fork plan suggests Europe wants sustainable farming. So why do EU politicians ignore the 'green' benefits of GM crops?

Henry Miller, Kathleen Hefferon | May 24, 2021

23 July 2021, Los Baños, PHILIPPINES – Filipino farmers will become the first in the world to be able to cultivate a variety of rice enriched with nutrients to help reduce childhood malnutrition, after receiving the green light from regulators.

Golden Rice was developed by the Department of Agriculture-Philippine Rice Research Institute (DA-PhilRice) in partnership with the International Rice Research Institute (IRRI) to contain additional levels of beta-carotene, which the body converts into vitamin A.

Around one in five children from the poorest communities in the Philippines suffer from vitamin A deficiency (VAD), which affects an estimated 190 million children worldwide. The condition is the most common cause of childhood blindness, as well as a contributing factor to a weakened immune system.

“This milestone puts the Philippines at the global forefront in leveraging agriculture research to address the issues of malnutrition and related health impacts in a safe and sustainable way” said Dr. Jean Balié, Director General of IRRI, a CGIAR research centre.

Resipiscence

https://www.irri.org/news-and-events/news/philippines-becomes-first-country-approve-nutrient-enriched-golden-rice

Kenya approves GMOs after 10-year ban

Joseph Maina | Cornell Alliance for Science | October 14, 2022

In an effort to reduce corn stem-borer infestations, corporate and public researchers partner to develop GMO varieties suitable for Kenya. Credit: Dave Hoisington via PLoS

Resipiscence

THE PRACTICE OF DECEPTION by ANTI-PEOPLE, ANTI-SCIENCE, ANTI-GMO CULTS & CLANS.

What if we knew that a plant or crop may resemble canonical cancer or a cancerous form (if the same criteria were applied to humans and animals)? Should we eat "cancerous" plants or plant products?

The truth, hidden (deliberately?) in plain sight, is that ***we eat, we crave*** and we will be in trouble without that specific plant. Acknowledging the science (genetics) of our daily bread[53] made from wheat (*Triticum-Aegilops* group) reveals that chromosomal multiplication (polyploidy) in wheat is a fact known to science[54] for ~100 years. Chromosomal aberrations (ploidy[55]) are a natural phenomenon in *many* edible plants. Genomic[56] changes and ploidy are associated with cancer[57] in humans (pathological somatic aneuploidy[58]) or indicates risk[59] of cancer[60] (neosis[61] leading to PGCC[62] or polyploid giant cancer cells). Hence, it appears that human cancer scenarios (chromosomal aberrations) are *preserved* in wheat. But, the obstreperous raconteurs in the anti-GM / anti-science cults are not concerned about the state of "cancer" of the wheat in our daily bread-basket. *Is it willful ignorance or just garden variety hypocrisy?*

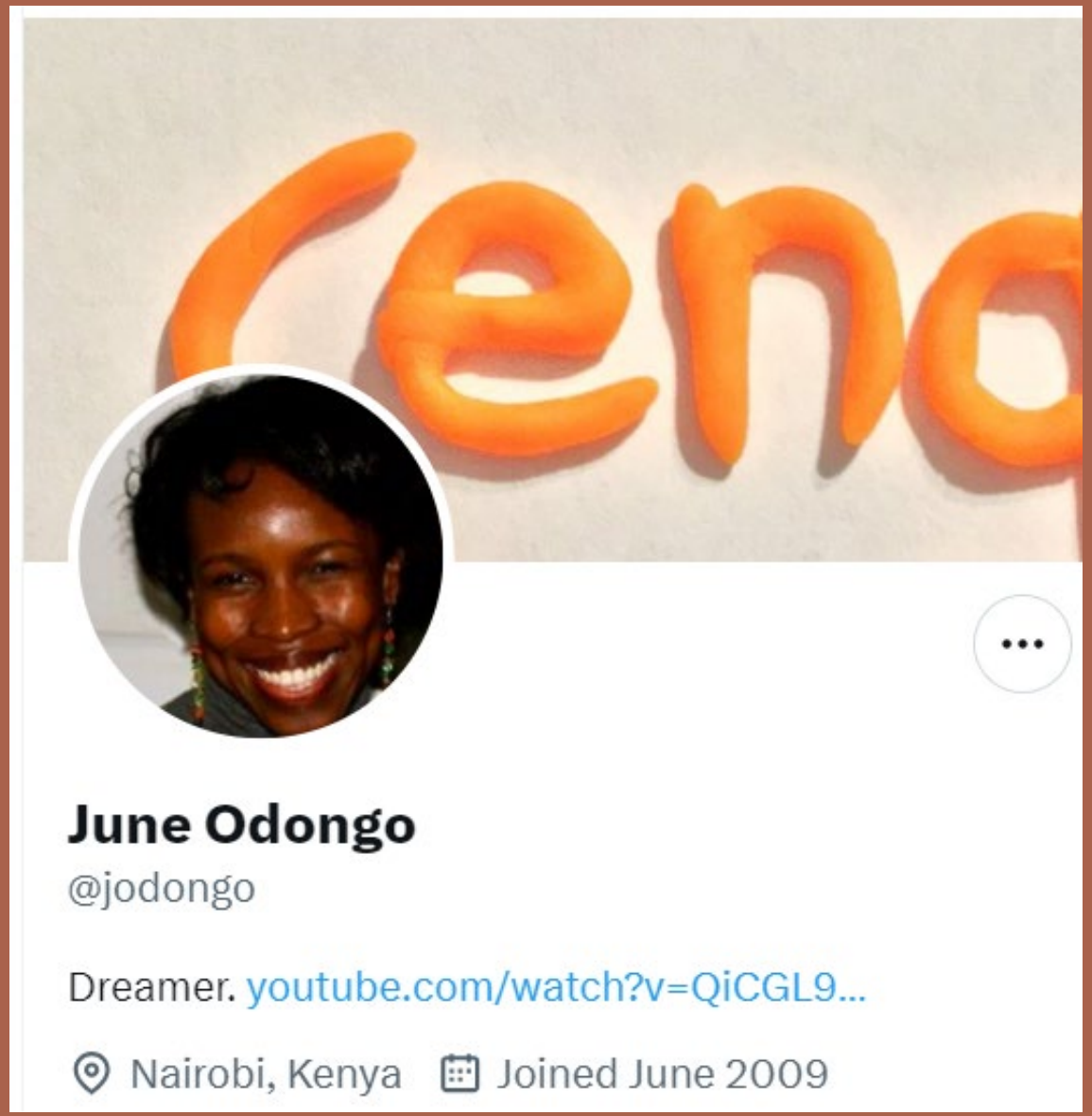
Therefore, the science of genetic modifications behind the evolution of wheat "cancer" is of no consequence (required edible food) for the anti-GM and anti-science aficionados. But, the same "anti" jihadists are up in arms to burn, kill, and prevent access to healthcare, if transgenic plants (e.g. golden rice) may serve as vaccines for the ~7 billion poor people, mostly forgotten and generally down-trodden.

Evolutionary[63] dynamics[64] uses many tools to address "fit" with chaotic[65] non-binary outcomes due to punctuated equilibria[66]. Ploidy-based "cancer" of the wheat is a *positivism* quintessential for our civilization. Exploring[67] ploidy in humans reveal ploidy as a diagnostic[68] tool for cancer prognosis but it also offers certain protective[69] functions and may help in stress response for plants[70] and humans[71].

Taken together, the ill-informed pseudo-science driving the anti-GM collusion is laden with misgivings and incomplete information arbitrage designed to selectively suppress the facts of science. Transgenic plants created by humans use tools which *mimic* the natural genetic processes to insert and delete genetic material (discovery of transposons[72] by Barbara[73] McClintock[74] in the 1920's-1930's and restriction endonucleases by Werner Arber, Daisy Dussoix[75] and Hamilton Smith[76] in the 1960's[77]).

Source: https://dspace.mit.edu/handle/1721.1/145774

THE ONLY THING NECESSARY FOR THE TRIUMPH OF ANTI-SCIENCE IS FOR SCIENTISTS TO DO NOTHING.



June Odongo

@jodongo

Dreamer. youtube.com/watch?v=QiCGL9...

Nairobi, Kenya Joined June 2009

June Odongo @jodongo · Nov 19, 2022

Since GMO is a hot topic again this week, some useful links for learning more (thanks @majiwater). Most citizens eat GMO everyday. Your banana is most likely GMO.

allianceforscience.cornell.edu/blog/2018/03/f...

bayer.com/en/agriculture...

allianceforscience.cornell.edu/blog/2022/11/m...

> **June Odongo** @jodongo · Oct 8, 2022
>
> I think that GMO-hate deserves more empathy & science education; it's universal & at some point, it was reasonable to be against GMOs as, after all, some of the big GMO companies were untrustworthy. However, the World Health Organization found years ago that GMOs are safe. x.com/reubenmuhindi/...

Genetically modified banana resistant to Panama disease given approval for Australian consumption

QLD Country Hour / By Lydia Burton

Posted Fri 16 Feb 2024 at 1:21am

Resipiscence

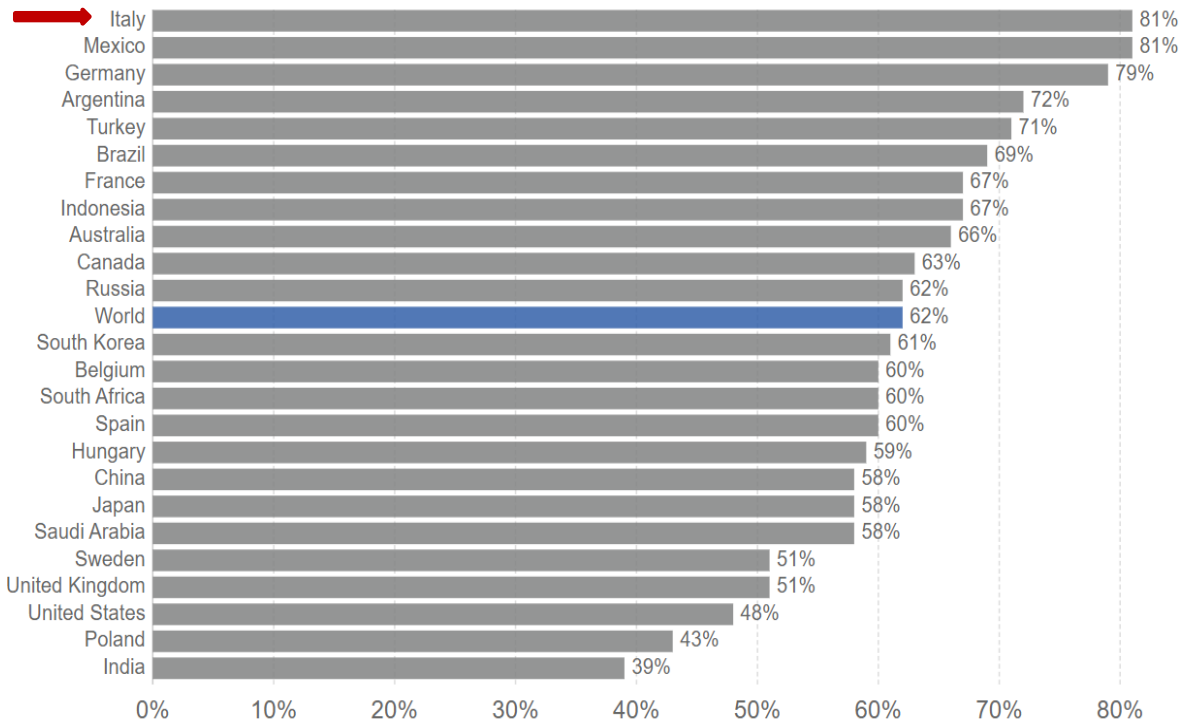
A genetically-modified (GM) banana is a step closer to commercial reality as Queensland scientists gain regulatory approval to release a GM variety of Cavendish banana for humans to eat. Scientists say the QCAV-4 variety is the world's first genetically modified banana and will be the first GM fruit approved for growing in Australia.

https://www.abc.net.au/news/2024-02-16/australia-approves-first-genetically-modified-banana-panama-tr4/103476986

Resipiscence

Public opposition to nuclear energy production

Share of the public who oppose the nuclear energy as a means of electricity production in 2011, following the Fukushima disaster. This constitutes the sum of respondents who stated they were either "somewhat opposed" or "strongly opposed" to nuclear energy.



ECONOMY • NUCLEAR ENERGY

Italy takes another step toward new nuclear plants

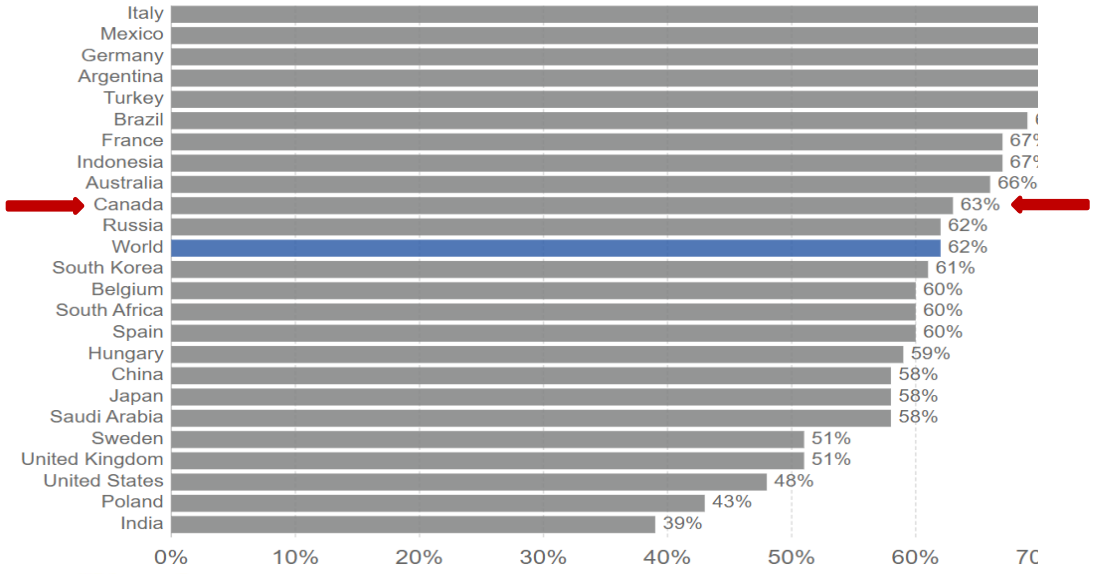
A motion requesting the return of nuclear power to Italian territory was approved by the Chamber of Deputies on Tuesday, strengthening Prime Minister Giorgia Meloni's pro-nuclear stance.

By Allan Kaval (Rome (Italy) correspondent) and Adrien Pécout

Published on May 11, 2023, at 11:33 am (Paris), updated on May 11, 2023, at 11:33 am · 2 min. · Lire en français

Public opposition to nuclear energy production

Share of the public who oppose the nuclear energy as a means of electricity production in 2011, following the Fukushima disaster. This constitutes the sum of respondents who stated they were either "somewhat opposed" or "strongly opposed" to nuclear energy.



world nuclear news

Energy & Environment | New Nuclear | Regulation & Safety | Nuclear Policies | Corporate | Uranium & Fuel |

Canada offers CAD3 billion finance for nuclear in Romania

20 September 2023

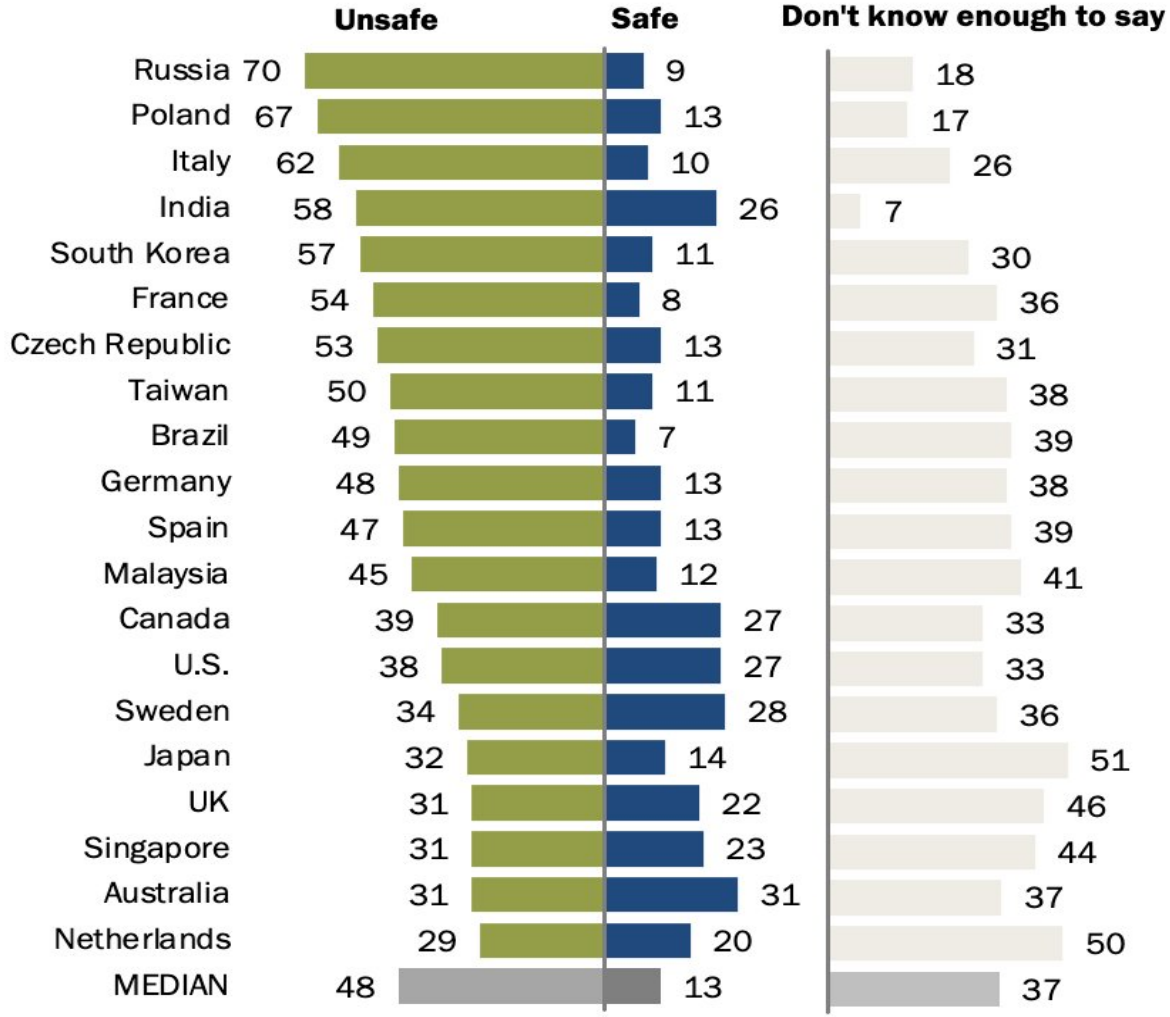
https://world-nuclear-news.org/Articles/Canada-offers-CAD3-billion-finance-for-new-nuclear

Share

The Canadian Minister of Energy and Natural Resources Jonathan Wilkinson has announced CAD3 billion (USD2.2 billion) of export financing to Nuclearelectrica to support the building of two CANDU-6 reactors at the Cernavoda nuclear power plant in Romania.

Widespread skepticism about the safety of genetically modified foods

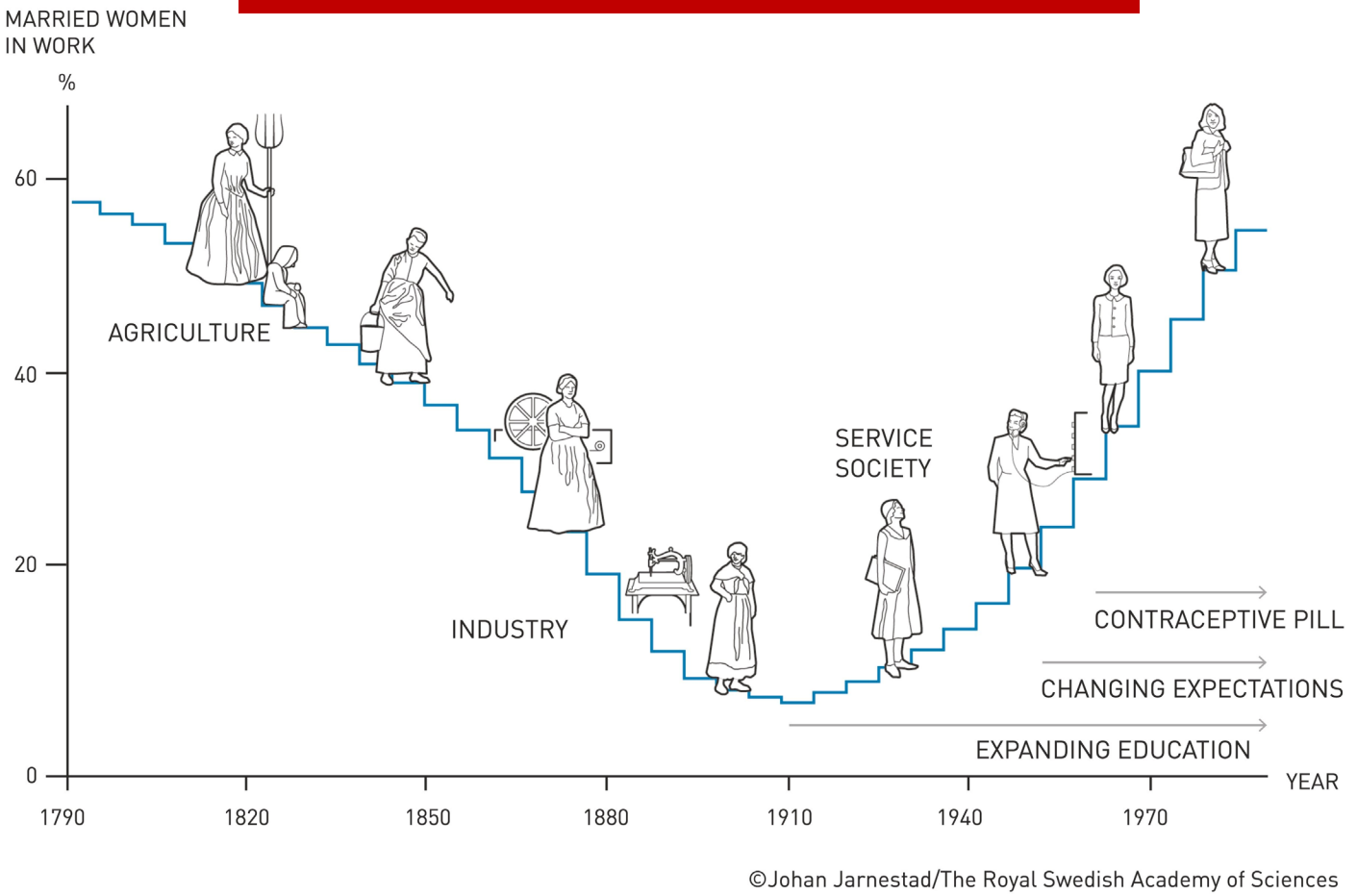
% who say genetically modified foods are generally ____ to eat



Note: Respondents who did not give an answer are not shown.
Source: International Science Survey 2019-2020. Q20.
"Science and Scientists Held in High Esteem Across Global Publics"

PEW RESEARCH CENTER

Resipiscence



Businesses had been banning married women from work since at least the 1880s. Marriage bars were designed not only to reserve employment opportunities for men, but to ensure that unmarried women without families to support were kept in the lowest paying, least prestigious positions.
Claudia Goldin www.nber.org/papers/w2747

India, the "pharmacy of the world"?

Should not the pharma industry set its own house in order?

http://eassarma.in/

E A S Sarma

Former Secretary to Government of India

Inaugurating the first Global Innovation Summit of the pharmaceuticals sector in November, 2021, Prime Minister Modi, in his characteristic triumphant style, said, "*the global trust earned by the Indian healthcare sector* (in recent times) *has led to the nation being called the "pharmacy of the world*" (https://www.business-standard.com/article/current-affairs/india-is-now-being-called-pharmacy-of-the-world-says-pm-modi-121111801288_1.html).

It is true that the Indian pharmaceutical sector meets 50% of the global demand for various vaccines, 40% of generic demand in the US and 25% of all medicine in the UK. The domestic pharmaceutical industry includes a network of 3,000 drug companies and around 10,500 manufacturing units. India therefore occupies an important position in the global pharmaceuticals sector (https://www.ibef.org/industry/pharmaceutical-india) The country has a large supporting pool of scientists and engineers, who should primarily take credit for this.

Recent setbacks:

Is there a pharmacy where we can buy plant-based oral vaccines?

http://eassarma.in/v1/sites/default/files/public/India-the-Pharmacy-of-the-world.pdf

COST IN USA

$530,000

NEWS | 21 March 2024 https://www.nature.com/articles/d41586-024-00809-y

Cutting-edge CAR-T cancer therapy is now made in India — at one-tenth the cost

The treatment, called NexCAR19, raises hopes that this transformative class of medicine will become more readily available in low- and middle-income countries.

COST IN INDIA

$30,000

A single treatment of NexCAR19, manufactured by Mumbai-based ImmunoACT, costs between US$30,000 and $40,000. The first CAR-T therapy was approved in the United States in 2017, and commercial CAR-T therapies in the US cost between $370,000 and $530,000, not including hospital fees and drugs to treat side effects. These treatments have also shown promise in treating autoimmune diseases and brain cancer. “It’s a dream come true,” says Alka Dwivedi, an immunologist who helped to develop NexCAR19 and is now at the US National Cancer Institute (NCI, NIH) in Bethesda, MD. These are people for whom all other treatments have failed, says Dwivedi. There is a “tremendous patient need”, says Nirali Shah, a paediatric oncologist at NCI, NIH who is also an academic collaborator of the researchers at ImmunoACT. “It’s positive news,” says Renato Cunha, a haematologist at the Grupo Oncoclínicas in São Paulo, Brazil. He says the Indian product could pave the way for making advanced cellular therapies accessible to other low- and middle-income countries. “Hope is the word that comes to mind.”

WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

VACCINATION AND IMMUNIZATION NOT ONLY REDUCES THE RISK FROM IMMEDIATE INFECTION AND TRANSMISSIBILITY OF THE INFECTION BUT ALSO REDUCES THE LONG TERM RISK OF OTHER (EVEN MORE SERIOUS) AFFLICTIONS WITH FAR GREATER SCOPE FOR MORBIDITY.

INFECTIOUS AGENTS, ESPECIALLY VIRUSES, INTERACTS WITH THE GENETIC MATERIAL OF CELLS, DIRECTLY OR INDIRECTLY. VIRUSES ARE KNOWN TO INFLICT CELLULAR DAMAGES. THE CUMULATIVE DETRIMENTAL EFFECT OF SUCH DAMAGES ARE UNCERTAIN. IT MAY MANIFEST IN THE FUTURE AS A DYSFUNCTION OR TRIGGER DORMANT CONDITIONS WHICH MAY BE UNTREATABLE AND AFFECT THE QUALITY OF LIFE.

Estimated preventable COVID-19-associated deaths due to non-vaccination in the United States

Katherine M. Jia[1] · William P. Hanage[1] · Marc Lipsitch[1] · Amelia G. Johnson[2] · Avnika B. Amin[2,3] · Akilah R. Ali[2] · Heather M. Scobie[2] · David L. Swerdlow[1]

US COVID-19 DEATHS DUE TO ANTI-VAXXERS

232,000

Jia KM, Hanage WP, Lipsitch M, Johnson AG, Amin AB, Ali AR, Scobie HM, Swerdlow DL. ***Estimated preventable COVID-19-associated deaths due to non-vaccination in the United States.*** Eur J Epidemiol. 2023 Nov; 38(11):1125-1128. doi: 10.1007/s10654-023-01006-3. Epub 2023 April 24. PMID: 37093505; PMCID: PMC10123459. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10123459/pdf/10654_2023_Article_1006.pdf

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ncbi.nlm.nih.gov/pmc/articles/PMC10123459/table/Tab1/?report=objectonly

Table 1 THE KILLER WITHIN: ANTI-VAXXERS

Estimated number of preventable COVID-19-associated deaths among unvaccinated adults (aged ≥ 18 years), May 30, 2021–September 3, 2022

	30 jurisdictions[a]	US
Number of individuals aged ≥ 18 years (mean)	159,862,404[b]	233,656,270[c]
Estimated number of preventable COVID-19-associated deaths among unvaccinated adults (aged ≥ 18 years), May 30, 2021–September 3, 2022	158,000[d]	232,000[e]

Jia KM, Hanage WP, Lipsitch M, Johnson AG, Amin AB, Ali AR, Scobie HM, Swerdlow DL. ***Estimated preventable COVID-19-associated deaths due to non-vaccination in the United States.*** Eur J Epidemiol. 2023 Nov; 38(11):1125-1128. doi: 10.1007/s10654-023-01006-3. Epub 2023 April 24. PMID: 37093505; PMCID: PMC10123459. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10123459/pdf/10654_2023_Article_1006.pdf

Farmed fur animals harbour viruses with zoonotic spillover potential

https://doi.org/10.1038/s41586-024-07901-3

Received: 12 December 2023

Accepted: 1 August 2024

Published online: 04 September 2024

Jin Zhao[1,13], Wenbo Wan[1,13], Kang Yu[1,2,13], Philippe Lemey[3,13], John H.-O. Pettersson[4,5,6,13], Yuhai Bi[7,13,14], Meng Lu[1], Xinxin Li[8], Zhuohang Chen[1], Mengdi Zheng[8], Ge Yan[2], JianJun Dai[2], Yuxing Li[1], Ayidana Haerheng[1], Na He[1], Changchun Tu[9], Marc A. Suchard[10], Edward C. Holmes[11,12,13,14], Wan-Ting He[2,14] ✉ & Shuo Su[1,14] ✉

Animals such as raccoon dogs, mink and muskrats are farmed for fur and are sometimes used as food or medicinal products[1,2], yet they are also potential reservoirs of emerging pathogens[3]. Here we performed single-sample metatranscriptomic sequencing of internal tissues from 461 individual fur animals that were found dead due to disease. We characterized 125 virus species, including 36 that were novel and 39 at potentially high risk of cross-species transmission, including zoonotic spillover. Notably, we identified seven species of coronaviruses, expanding their known host range, and documented the cross-species transmission of a novel canine respiratory coronavirus to raccoon dogs and of bat HKU5-like coronaviruses to mink, present at a high abundance in lung tissues. Three subtypes of influenza A virus—H1N2, H5N6 and H6N2—were detected in the lungs of guinea pig, mink and muskrat, respectively. Multiple known zoonotic viruses, such as Japanese encephalitis virus and mammalian orthoreovirus[4,5], were detected in guinea pigs. Raccoon dogs and mink carried the highest number of potentially high-risk viruses, while viruses from the *Coronaviridae*, *Paramyxoviridae* and *Sedoreoviridae* families commonly infected multiple hosts. These data also reveal potential virus transmission between farmed animals and wild animals, and from humans to farmed animals, indicating that fur farming represents an important transmission hub for viral zoonoses.

We performed single-sample metatranscriptomic sequencing of internal tissues from 461 individual fur animals that were dead due to disease. We characterized 125 virus species, including 36 that were novel and 39 at potentially high risk of cross-species transmission, including zoonotic spillover.

Stay far away from fur and fur farms

www.nature.com/articles/s41586-024-07901-3.pdf

The Southern house mosquito (*Culex quinquefasciatu*) can transmit Oropouche virus to humans, but the vector is midge *Culicoides paraensis*.

nature.com/articles/d41586-024-02746-2

Mysterious Oropouche virus is spreading: what you should know

The virus is endemic to the Amazon but is now spreading outside the region — and has been linked to human deaths for the first time.

By Mariana Lenharo

https://www.nature.com/articles/d41586-024-02746-2

Wastewater COVID-19

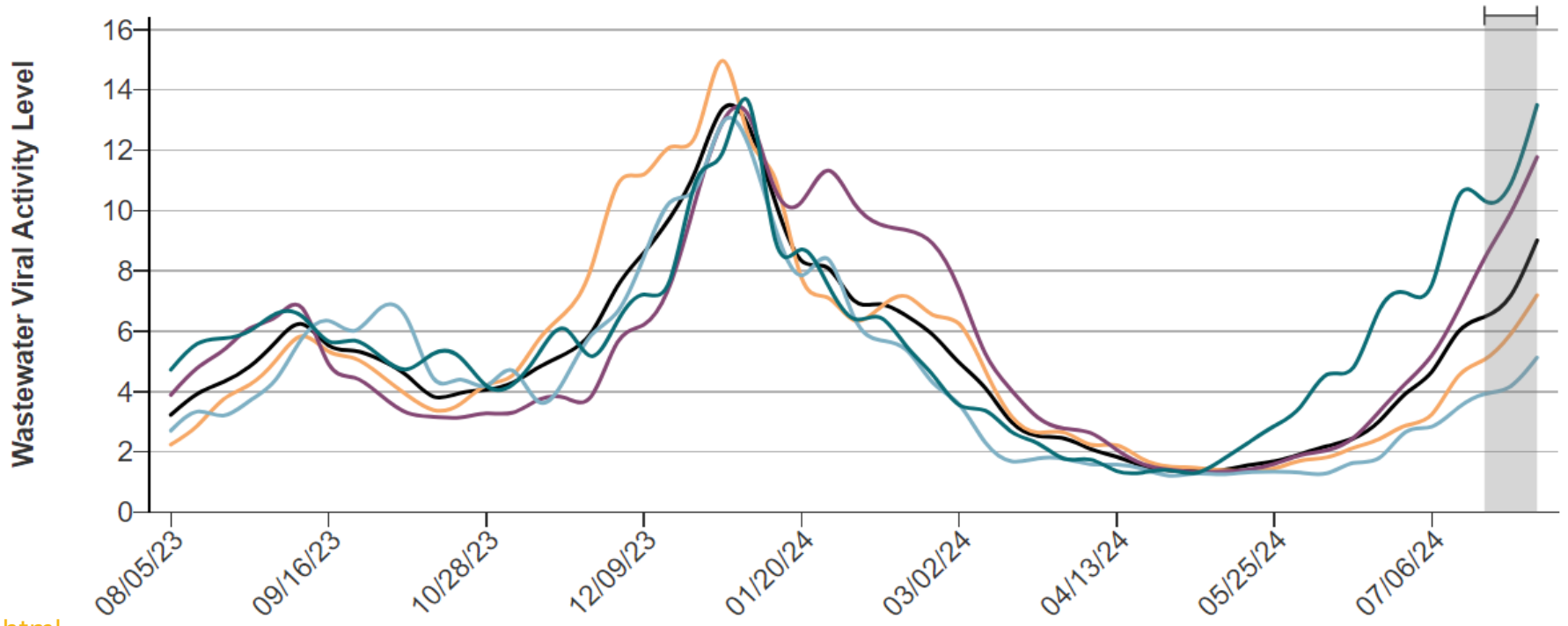
cdc.gov/nwss/rv/COVID19-nationaltrend.html

About Wastewater Data

This chart shows national and regional trends of SARS-COV-2 viral activity levels in wastewater.

Make a selection from the filters to change the visualization information.

1 Year



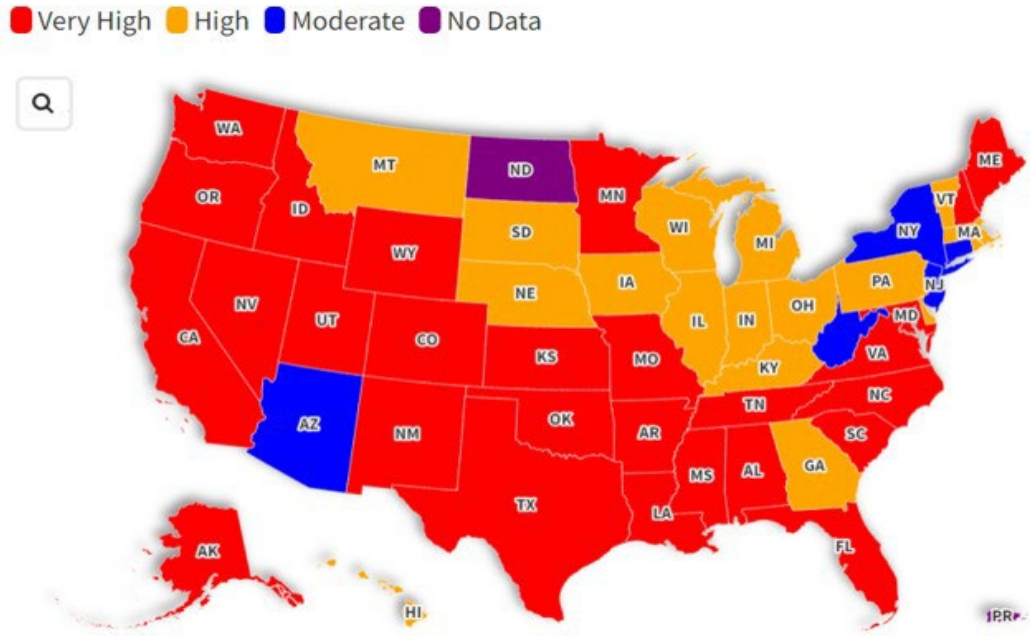
Wastewater Data as of Aug 9, 2024

www.cdc.gov/nwss/rv/COVID19-nationaltrend.html

WASTEWATER DATA as of AUGUST 9TH, 2024

MAP: These 27 states at 'very high' COVID wastewater levels

BY JEREMY TANNER - 08/13/24 8:24 PM ET



Source: U.S. Census Bureau 2021 boundaries , CDC

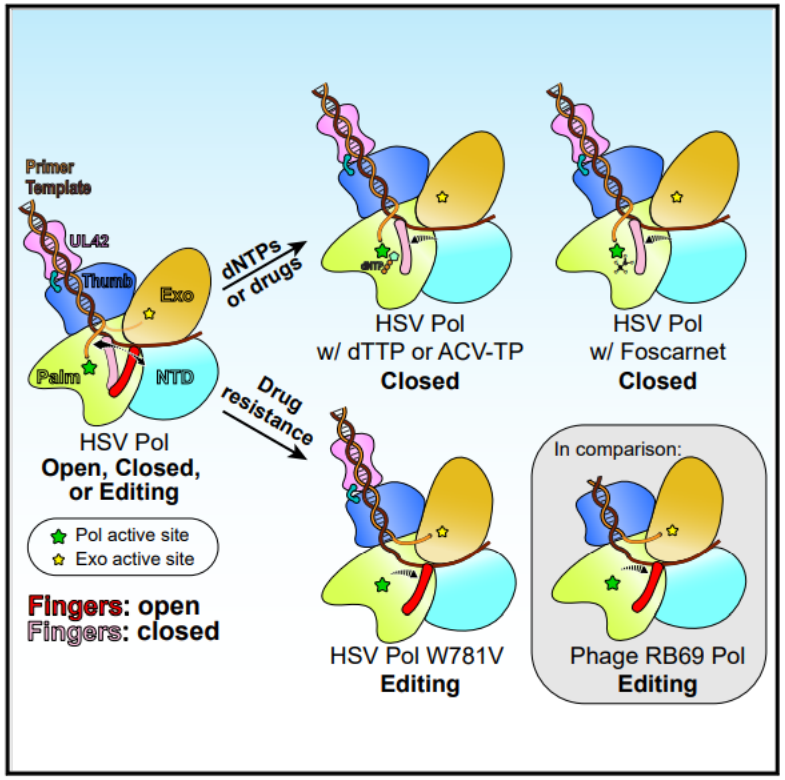
The states with the lowest detected level (moderate) of SARS-CoV-2 were Arizona, West Virginia, New York, New Jersey, the District of Columbia and Connecticut.

What Enables Herpes Simplex Virus To Become Impervious to Drugs?

Findings about how cold sore virus evades treatment offer broader clues on drug resistance

Viral DNA polymerase structures reveal mechanisms of antiviral drug resistance

Graphical abstract



Authors

Sundaresh Shankar, Junhua Pan, Pan Yang, ..., Mrinal Shekhar, Donald M. Coen, Jonathan Abraham

Correspondence

jonathan_abraham@hms.harvard.edu

In brief

High-resolution cryo-EM structures of a fully assembled DNA- and drug-bound herpes simplex virus polymerase holoenzyme complex, in a number of conformations, characterize the mechanisms that drive drug selectivity and resistance profiles of this DNA polymerase.

Published August 26, 2024 ◆ DOI: https://doi.org/10.1016/j.cell.2024.07.048

Case Series of Patients with Marburg Virus Disease, Equatorial Guinea, 2023

https://www.nejm.org/doi/pdf/10.1056/NEJMc2313181

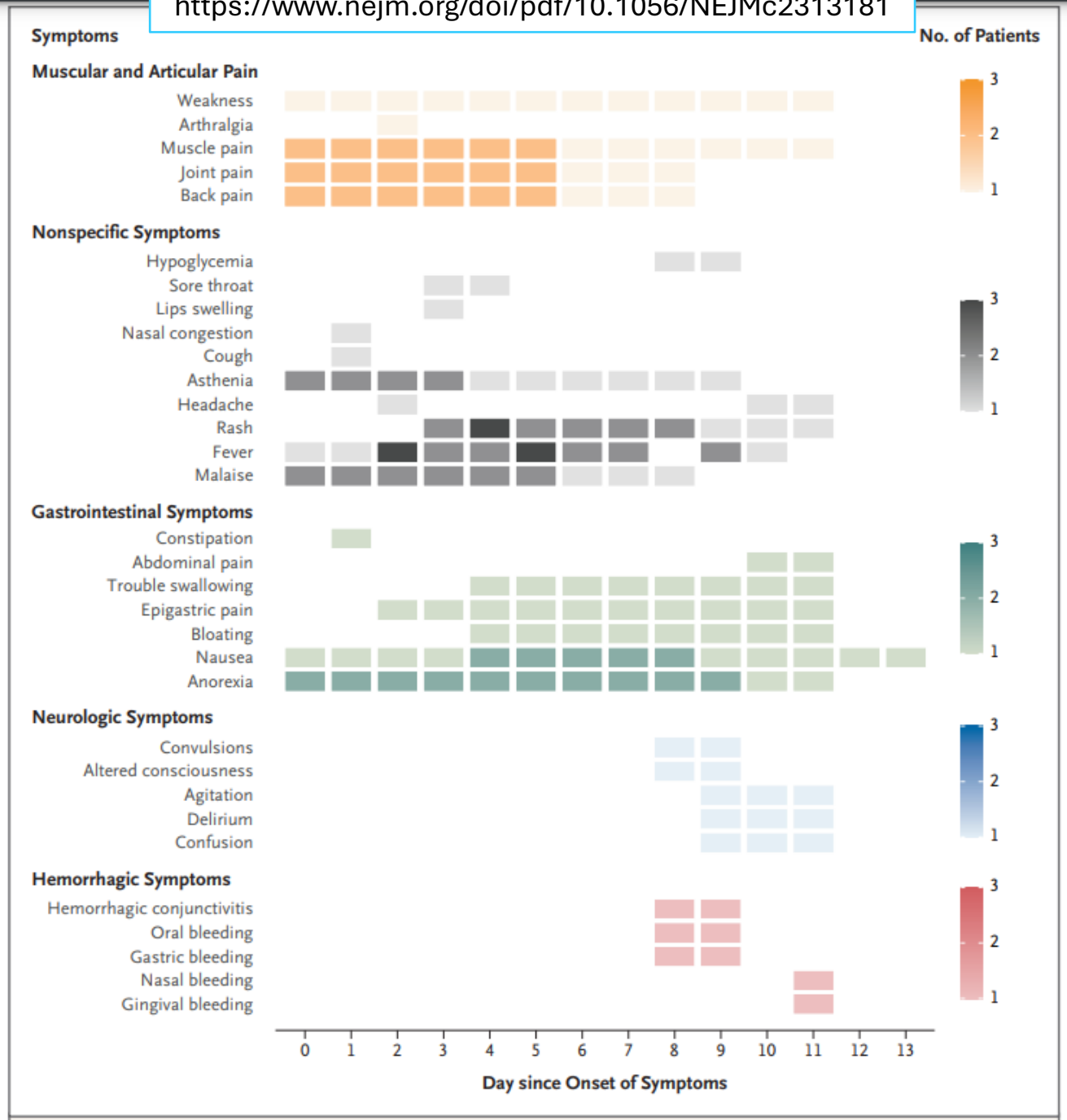


Figure 1. History of Symptoms in Five Patients with Marburg Virus Disease.

Two patients died: Patient 3, woman, 72 & Patient 5: girl, 2. Admitted 9 and 8 days after symptom onset, resply. Patient 3 had multiorgan dysfunction, primarily hemodynamic instability, and Patient 5 had encephalopathy with seizures and respiratory dysfunction. The viral RNA levels in the patients who died (Ct values at admission, 15.1 for Patient 3 and 21.6 for Patient 5) were higher than those in the patients who survived (Ct values at admission, 25.1 for Patient 1, 25.5 for Patient 2, and 27.6 for Patient 4). Both patients rapidly deteriorated to shock and death within 1 day after admission. Shortly before death, bleeding from the mouth & nares was noted in 3, and oral & gastric bleeding was noted in Patient 5.

Laissez Faire Lippenbekenntnisses ?

Prof Ira M. Longini (bio-statistician at University of Florida, Gainesville, FL, MARVAC member) says that if the Rwandan outbreak continues, the plan is to trial one vaccine as ring vaccination. The approach showed effectiveness of an Ebola vaccine in Guinea (2014–2016 West African outbreak) which involves immunizing contacts of an infected individual.

nature.com/articles/d41586-024-03218-3

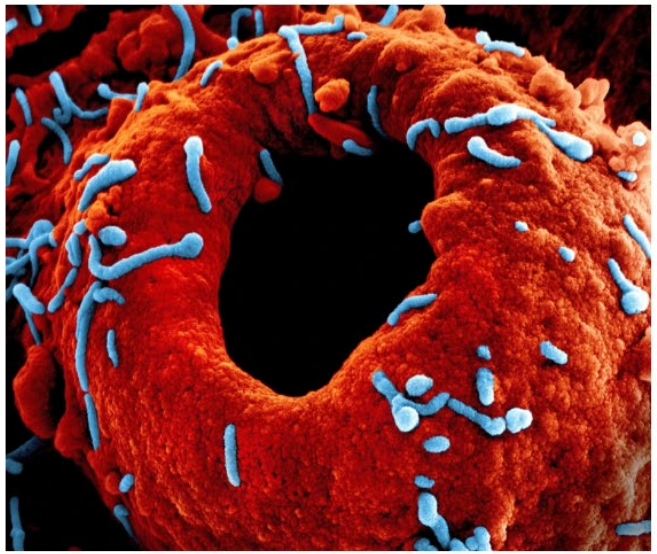
https://doi.org/10.1038/d41586-024-03275-8

NEWS | 01 October 2024

Deadly Marburg virus: scientists race to test vaccines in outbreak

There are no approved treatments for the Ebola-like haemorrhagic fever, which is spreading in Rwanda.

By Ewen Callaway



Marburg virus particles (blue) on the surface of an infected cultured cell (red). Credit: NIAID/SPL

Researchers are in a race against time to deploy vaccines and treatments against a deadly virus that has exploded in Rwanda.

The fact that clinical-trial plans are in place and that other groundwork has been laid increases the odds that Marburg vaccines and treatments will be used in Rwanda, says Nancy Sullivan, a viral immunologist at Boston University, Boston, MA. It's likely that data on Marburg vaccines and treatments will be needed from multiple outbreaks before conclusions can be drawn about their effectiveness.
"The idea now is that you just move forward and don't worry that the outbreak will end before trial enrolment is complete," Sullivan adds. "It's just a piece of the overall trial."

Nature **634**, 278 (2024)
https://doi.org/10.1038/d41586-024-03218-3

Hamer *et al* (2023) ***Safety, tolerability, immunogenicity of the chimpanzee adenovirus type 3-vectored Marburg virus (cAd3-Marburg) vaccine in healthy adults in USA: irst-in-human, phase 1, open-label, dose-escalation trial***. **Lancet.** 2023 January 28; 401(10373):294-302. doi: 10.1016/S0140-6736(22)02400-X. PMID: 36709074; PMCID: PMC10127441. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10127441/pdf/nihms-1871339.pdf

Anticipating the Next Pandemic

H. Cody Meissner, M.D., Bill G. Kapogiannis, M.D., and Daniel N. Wolfe, Ph.D.

Reflecting on a pandemic that killed nearly twice as many people in the United States as the 1918 influenza pandemic — which had been the worst infectious disease outbreak in the country's recorded history before Covid-19 — offers several lessons for pandemic preparedness and response. First, the Covid-19 pandemic led to extraordinary advances in vaccinology, resulting in the availability of safe and effective vaccines and demonstrating the ability of the medical community to rapidly address a major challenge in the face of an urgent public health need. Paradoxically, a second lesson is about the fragile state of the national and global vaccine enterprise, including issues associated with vaccine distribution and acceptance. A third lesson is that partnerships involving private, government, and academic resources were critical for facilitating the rapid development of the first generation of Covid-19 vaccines. Building on these lessons in the current interpandemic period, the Biomedical Advanced Research and Development Authority (BARDA) is seeking to support the development of a new generation of improved vaccines.

Project NextGen is a $5 billion initiative sponsored by the Department of Health and Human Services aimed at developing next-generation medical countermeasures against Covid-19.[1] This initiative will support double-blind, active-comparator, controlled phase 2b trials assessing the safety, efficacy, and immunogenicity of experimental vaccines relative to approved vaccines in ethnically and racially diverse populations. We anticipate that the vaccine platforms could be adapted to vaccines for other infectious diseases, thereby enabling a rapid response to future health security threats. These trials will address several considerations (see table).

Objectives for Next-Generation Covid-19 Vaccines.

Objective	Justification
Establishment of a correlate of protection	Reduce the need for large, expensive clinical trials to assess vaccine efficacy
Broader protection	Prevent pan-sarbecovirus transmission and infection, including for SARS-CoV-2 variants and seasonal coronaviruses
Greater duration of immunity	More effectively induce innate and adaptive immunity, with less need for booster dosing
Prevention of infection (sterilizing immunity)	Reduce the risk of transmission and asymptomatic infection
Alternative routes of administration	Permit needle-free administration, such as mucosal or transcutaneous administration
Sustainable manufacturing approaches	Promote simplicity in production; reduce costs and the need for ultrarefrigeration
Improved safety profile	Reduce the risk of local and systemic reactions
Platform plasticity	Permit scalability and rapid production; facilitate targeting of new antigens for new variants and pathogens
Increased trust and acceptance	Enhance vaccine uptake

nejm.org/doi/full/10.1056/NEJMicm2307920

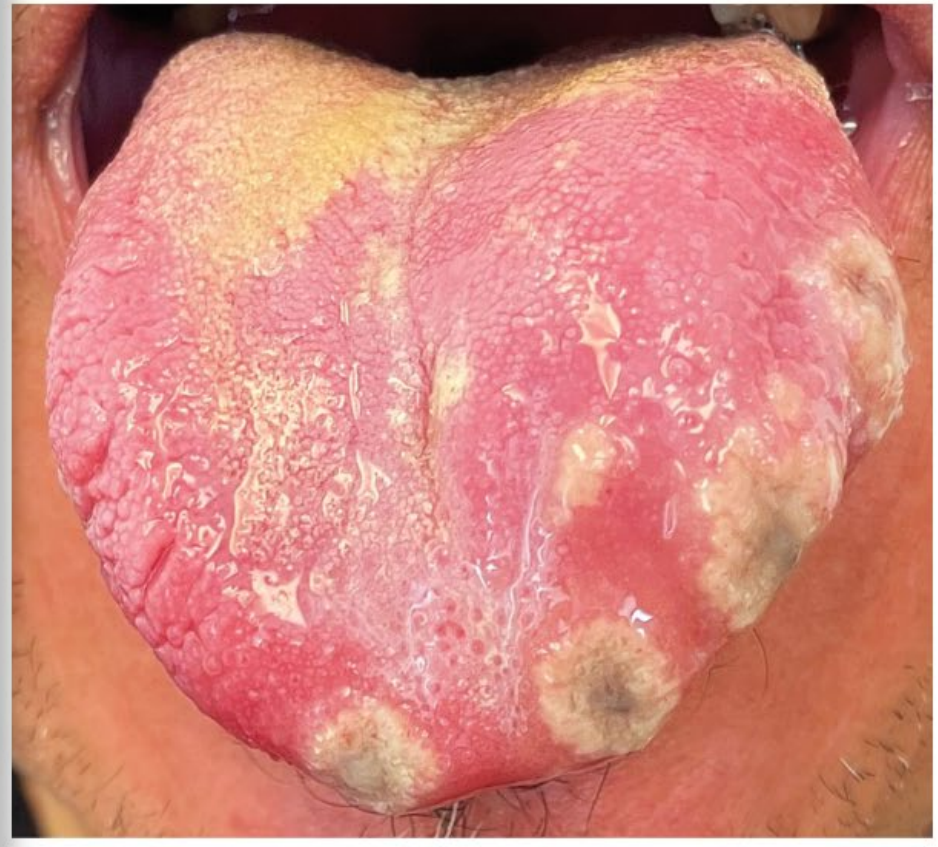
The NEW ENGLAND JOURNAL of MEDICINE

IMAGES IN CLINICAL MEDICINE

Mpox Tongue Lesions

David Dickson, M.D., Ph.D., and Angela Lai, M.D.

February 29, 2024
N Engl J Med 2024; 390:842
DOI: 10.1056/NEJMicm2307920
Metrics



A 49-year-old man with human immunodeficiency virus (HIV) infection presented to a primary care clinic with an 11-day history of painful tongue lesions and a 1-week history of sore throat and fevers. He had last been sexually active with his male partner 9 days before the onset of symptoms; his partner was asymptomatic. Five months before presentation, the patient's CD4 cell count had been 519 per microliter (reference range, 297 to 1551), and 1 month before presentation, the HIV viral load had been undetectable.

A 49-year-old man with human immunodeficiency virus (HIV) infection presented to a primary care clinic with an 11-day history of painful tongue lesions and a 1-week history of sore throat and fevers. He had last been sexually active with his male partner 9 days before the onset of symptoms; his partner was asymptomatic. Five months before presentation, the patient's CD4 cell count had been 519 per microliter (reference range, 297 to 1551), and 1 month before presentation, the HIV viral load had been undetectable. On physical examination, four ulcers with central darkening and raised borders were seen on the tip and left lateral aspect of the tongue. Tender submandibular lymphadenopathy was also present on the left side. No other lesions were seen in the mouth or throat or on the skin. Testing of a tongue lesion with a polymerase-chain-reaction assay for the virus that causes mpox (formerly known as monkeypox) was positive. A diagnosis of mpox was made. During the eruptive phase of mpox, a rash is very common, but isolated oral mucosal lesions may be the only mucocutaneous manifestation — as occurred in this case. The patient was lost to follow-up with primary care after the diagnosis was made, so no antiviral treatment was given. During a telephone appointment with a different clinic 2 weeks later, he reported feeling in his usual health.

David Dickson, M.D., Ph.D.
University of California, Los Angeles,
ddickson@mednet.ucla.edu
Angela Lai, M.D.
VA Sepulveda Ambulatory Care Center, CA

February 29, 2024

Leap Day Special

Leap of Monkey Pox

New England Journal of Medicine 2024; 390:842
DOI: 10.1056/NEJMicm2307920
https://www.nejm.org/doi/full/10.1056/NEJMicm2307920

World Health Organization

WHO Director-General declares mpox outbreak a public health emergency of international concern

14 August 2024

WHO Director-General Dr Tedros Adhanom Ghebreyesus has determined that the upsurge of mpox in the Democratic Republic of the Congo (DRC) and a growing number of countries in Africa constitutes a public health emergency of international concern (PHEIC) under the International Health Regulations (2005) (IHR).

HARVARD MEDICAL SCHOOL

News & Research

AUGUST 19, 2024

Mpox Declared Public Health Emergency of International Concern. Now What?

https://hms.harvard.edu/news/mpox-declared-public-health-emergency-international-concern-now-what
https://www.who.int/news/item/14-08-2024-who-director-general-declares-mpox-outbreak-a-public-health-emergency-of-international-concern

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE BRIEF REPORT

Neurovascular Complications of Iatrogenic *Fusarium solani* Meningitis

Nora Strong, M.D., Grant Meeks, M.D., Sunil A. Sheth, M.D., Louise McCullough, M.D., Ph.D., Julian A. Villalba, M.D., Chunfeng Tan, M.D., Ph.D., Andrew Barreto, M.D., Audrey Wanger, Ph.D., Michelle McDonald, D.O., Peter Kan, M.D., M.P.H., Hashem Shaltoni, M.D., Jose Campo Maldonado, M.D., et al.

February 8, 2024
N Engl J Med 2024; 390:522-529
DOI: 10.1056/NEJMoa2308192

9 References

Summary

A multinational outbreak of nosocomial fusarium meningitis occurred among immunocompetent patients who had undergone surgery with epidural anesthesia in Mexico. The pathogen involved had a high predilection for the brain stem and vertebrobasilar arterial system and was associated with high mortality from vessel injury. Effective treatment options remain limited; in vitro susceptibility testing of the organism suggested that it is resistant to all currently approved antifungal medications in the United States. To highlight the severe complications associated with fusarium infection acquired in this manner, we report data, clinical courses, and outcomes from 13 patients in the outbreak who presented with symptoms after a median delay of 39 days.

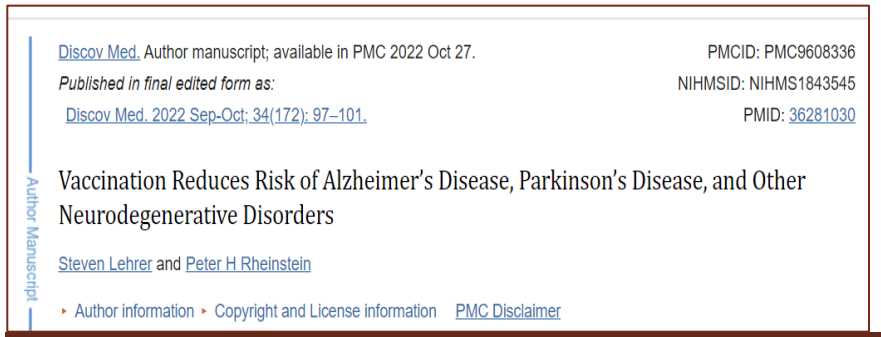
February 8, 2024
N Engl J Med 2024; 390:522-529
DOI: 10.1056/NEJMoa2308192

Table 1 | Viral infections linked to neurodegenerative diseases

Disease	Infection
Alzheimer disease	Influenza and pneumonia
	Intestinal infections
	Meningitis
	Viral encephalitis
Amyotrophic lateral sclerosis	Human papilloma virus
Generalized dementia	Influenza and pneumonia
	Viral encephalitis
Multiple sclerosis	Epstein–Barr virus
	Herpes simplex virus
	Varicella zoster virus
Parkinson disease	Hepatitis C virus
	Influenza and pneumonia
Vascular dementia	Influenza and pneumonia
	Varicella zoster virus

Levine KS, Leonard HL, Blauwendraat C, Iwaki H, Johnson N, Bandres-Ciga S, Ferrucci L, Faghri F, Singleton AB, Nalls MA. Virus exposure & neurodegenerative disease risk across national biobanks. Neuron. 2023 Apr 5;111(7):1086-1093.e2. doi: 10.1016/j.neuron.2022.12.029. Epub 2023 January 19. PMID: 36669485

Data from national biobanks offer evidence that exposure to common viral pathogens increases the risk of Alzheimer's disease and other diseases (neurodegenerative diseases).



Discov Med. Author manuscript; available in PMC 2022 Oct 27.

PMCID: PMC9608336

Published in final edited form as:

NIHMSID: NIHMS1843545

Discov Med. 2022 Sep-Oct; 34(172): 97–101.

PMID: 36281030

Vaccination Reduces Risk of Alzheimer's Disease, Parkinson's Disease, and Other Neurodegenerative Disorders

Steven Lehrer and Peter H Rheinstein

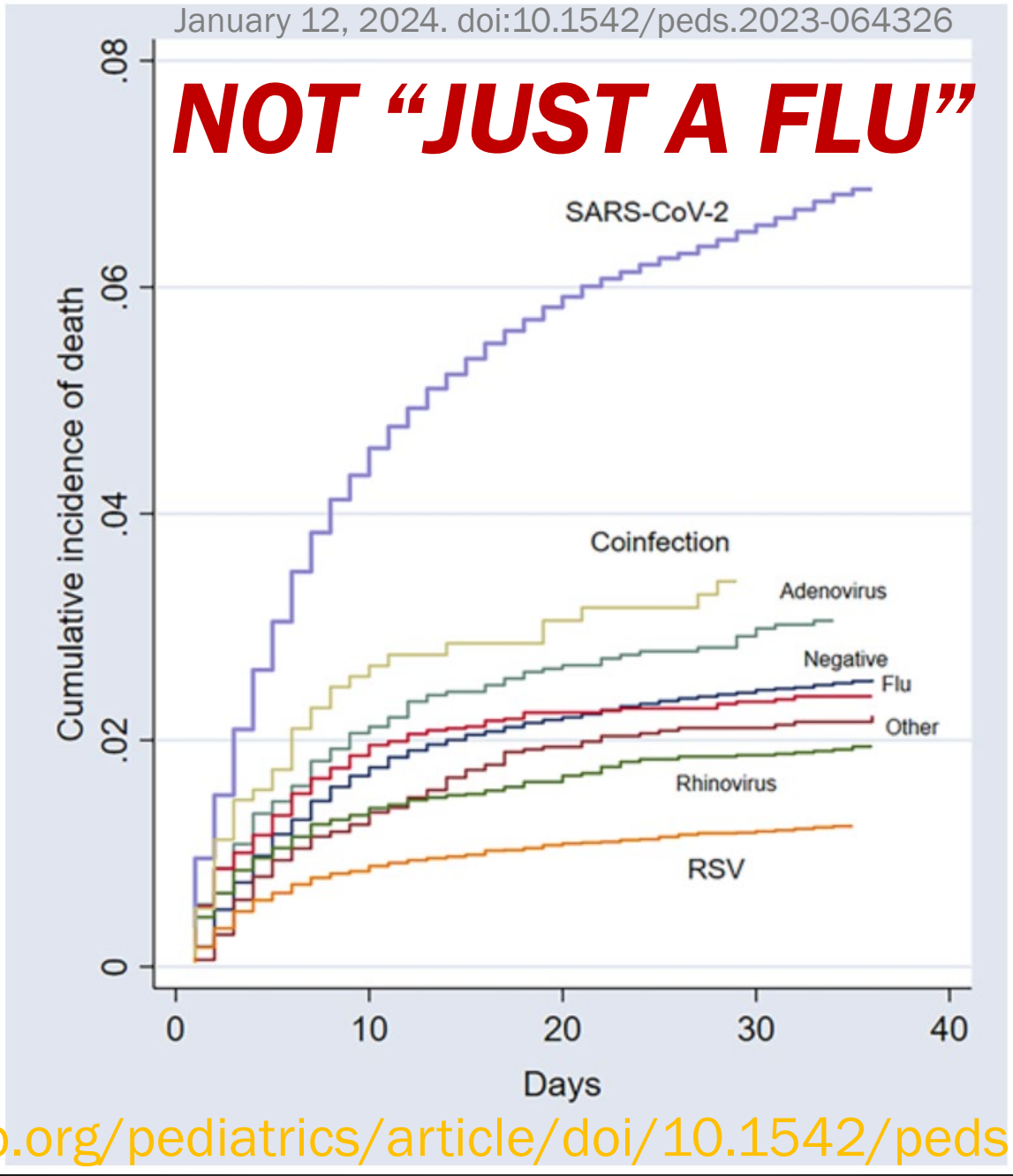
Author information ▸ Copyright and License information PMC Disclaimer

Author Manuscript

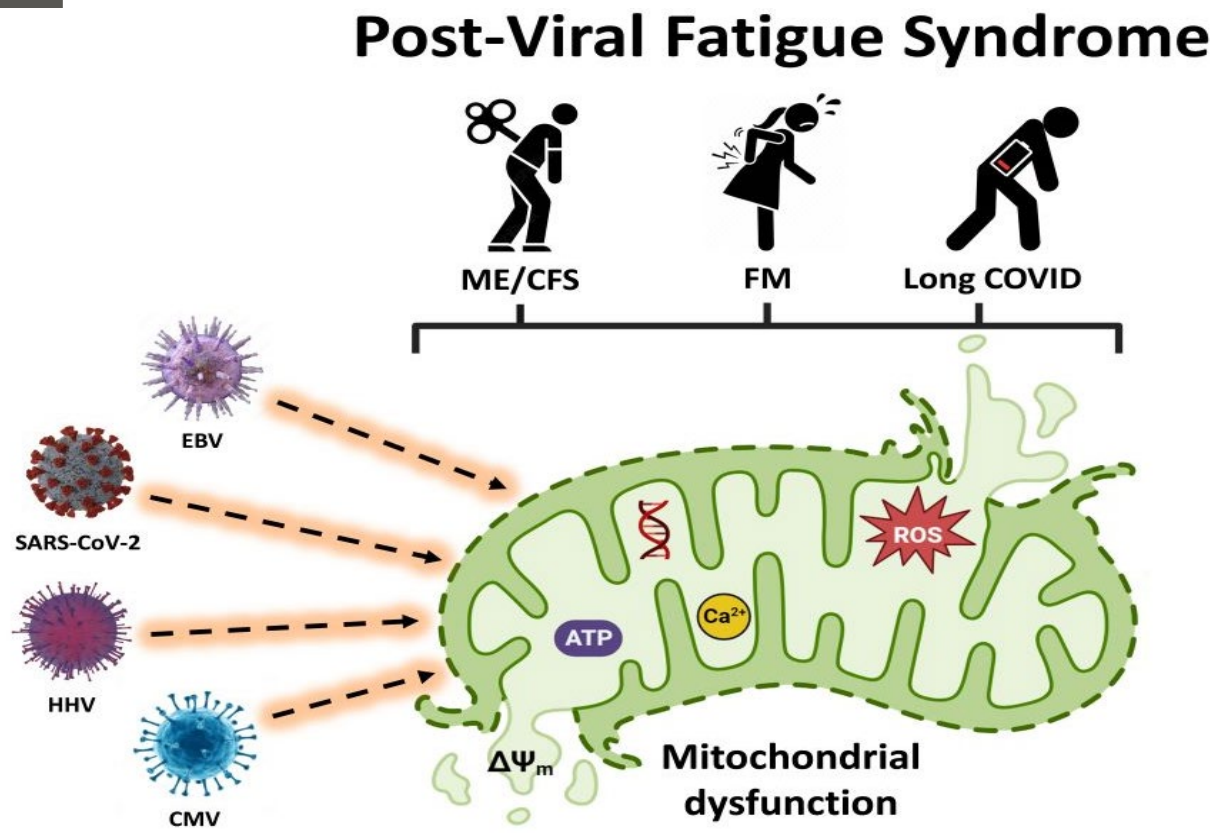
Cumulative incidence of death in children and adolescents with SARI according to viral strain.

https://doi.org/10.1542/peds.2023-064326

Understanding how severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) interacts with other respiratory viruses is key to developing public health strategies in the post-pandemic era. This study compared the outcomes of SARS-CoV-2 and other seasonal viruses in children and adolescents (total of 235,829 patients) hospitalized with severe acute respiratory infection (SARI) from February 2020 to February 2023 in Brazil. The main exposure of interest was viral etiology. The outcome was in-hospital mortality. ➔



https://publications.aap.org/pediatrics/article/doi/10.1542/peds.2023-064326/196412



Article

https://doi.org/10.1038/s41467-023-44432-3

Muscle abnormalities worsen after post-exertional malaise in long COVID

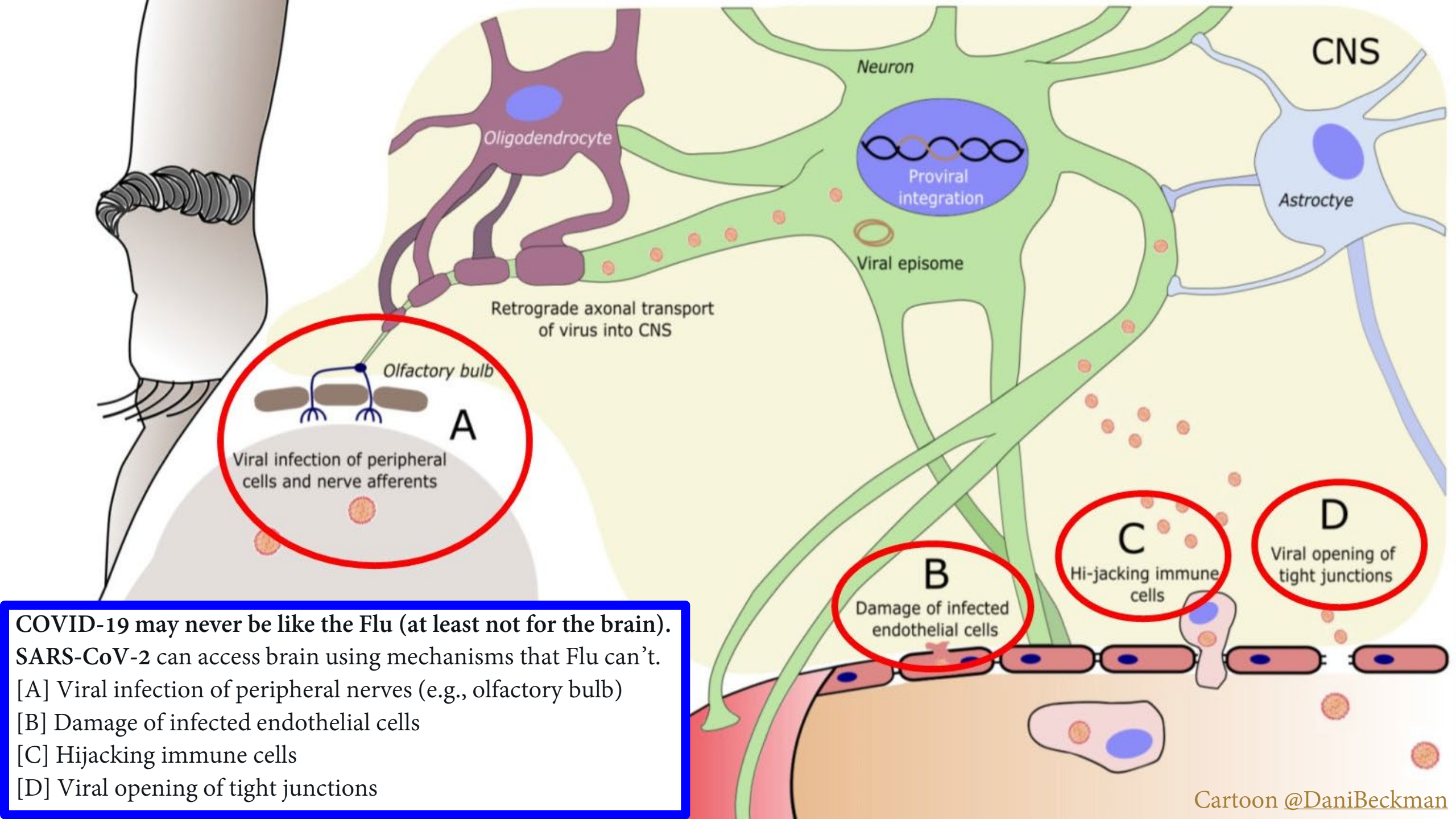
Received: 21 March 2023

Accepted: 13 December 2023

Published online: 04 January 2024

Check for updates

Brent Appelman[1,2,15], Braeden T. Charlton[3,4,15], Richie P. Goulding[3,4], Tom J. Kerkhoff[3,4,5,6], Ellen A. Breedveld[3,4], Wendy Noort[3,4], Carla Offringa[3,4], Frank W. Bloemers[4,7], Michel van Weeghel[8], Bauke V. Schomakers[8], Pedro Coelho[9,10,11], Jelle J. Posthuma[7,12], Eleonora Aronica[11], W. Joost Wiersinga[1,2,13], Michèle van Vugt[2,14,15] & Rob C. I. Wüst[3,4,15]



COVID-19 may never be like the Flu (at least not for the brain).
SARS-CoV-2 can access brain using mechanisms that Flu can't.
[A] Viral infection of peripheral nerves (e.g., olfactory bulb)
[B] Damage of infected endothelial cells
[C] Hijacking immune cells
[D] Viral opening of tight junctions

Cartoon @DaniBeckman

Greene, C., Connolly, R., Brennan, D. *et al.* **Blood–brain barrier disruption and sustained systemic inflammation in individuals with long COVID-associated cognitive impairment.** *Nat Neurosci* (2024). https://doi.org/10.1038/s41593-024-01576-9

nature neuroscience

Article

https://doi.org/10.1038/s41593-024-01576-9

Blood–brain barrier disruption and sustained systemic inflammation in individuals with long COVID-associated cognitive impairment

Received: 16 November 2022

Accepted: 9 January 2024

Published online: 22 February 2024

Check for updates

Chris Greene[1], Ruairi Connolly[2], Declan Brennan[2], Aoife Laffan[2], Eoin O'Keeffe[1], Lilia Zaporojan[2], Jeffrey O'Callaghan[1], Bennett Thomson[1], Emma Connolly[3], Ruth Argue[4], Ignacio Martin-Loeches[5], Aideen Long[6], Cliona Ni Cheallaigh[6,7], Niall Conlon[7,8], Colin P. Doherty[2,9,10] ✉ & Matthew Campbell[1,10] ✉

Vascular disruption has been implicated in coronavirus disease 2019 (COVID-19) pathogenesis and may predispose to the neurological sequelae associated with long COVID, yet it is unclear how blood–brain barrier (BBB) function is affected in these conditions. Here we show that BBB disruption is evident during acute infection and in patients with long COVID with cognitive impairment, commonly referred to as brain fog. Using dynamic contrast-enhanced magnetic resonance imaging, we show BBB disruption in patients with long COVID-associated brain fog. Transcriptomic analysis of peripheral blood mononuclear cells revealed dysregulation of the coagulation system and a dampened adaptive immune response in individuals with brain fog. Accordingly, peripheral blood mononuclear cells showed increased adhesion to human brain endothelial cells in vitro, while exposure of brain endothelial cells to serum from patients with long COVID induced expression of inflammatory markers. Together, our data suggest that sustained systemic inflammation and persistent localized BBB dysfunction is a key feature of long COVID-associated brain fog.

Post-Ebola syndrome

Two high-profile cases with this syndrome have allowed close scrutiny of its pathology raising hope that the lessons can be used to help other sufferers. Talha Khan Burki reports.

For more on the **PREVAIL study** see https://www.niaid.nih.gov/news/newsreleases/2016/Pages/CROI-PREVAIL3.aspx

Ian Crozier, an American infectious disease specialist, had been working in Uganda for 7 years when the west African Ebola epidemic took hold in Guinea, Liberia, and Sierra Leone. He joined the WHO team responding to the outbreak in Kenema, Sierra Leone. It was there that he contracted Ebola virus disease in August, 2014. "I still don't know how I was infected—there were no obvious breaches in the IPC [infection prevention and control] protocol", he recalls. Crozier was medevaced to Emory University Hospital (Atlanta, GA, USA). His conditioned worsened. He became delerious. He was intubated, hooked up to a ventilator for 2 weeks, and on dialysis for 3 weeks. For a time, it was touch and go. But in October 2014, Crozier emerged as an Ebola survivor.

Within weeks, however, there were complications. Crozier developed an aggressive sight-threatening uveitis. His left eye changed colour. "I started to suffer from significant fatigue, and pretty severe joint pain; for a while it was quite disabling—that has been a common theme in most survivors", he added. Soon afterward, he lost most of the hearing in his left ear. He is still plagued by a high-pitched ringing sound. In hospital, Crozier had suffered several strokes. But the seizure he experienced a year or so later was wholly unexpected. "It was probably related to a post-encephalitic brain scar that is epileptogenic; these days I am on seizure medication", he explained. "I have a long list of sequelae, many of them are typical of west African Ebola survivors."

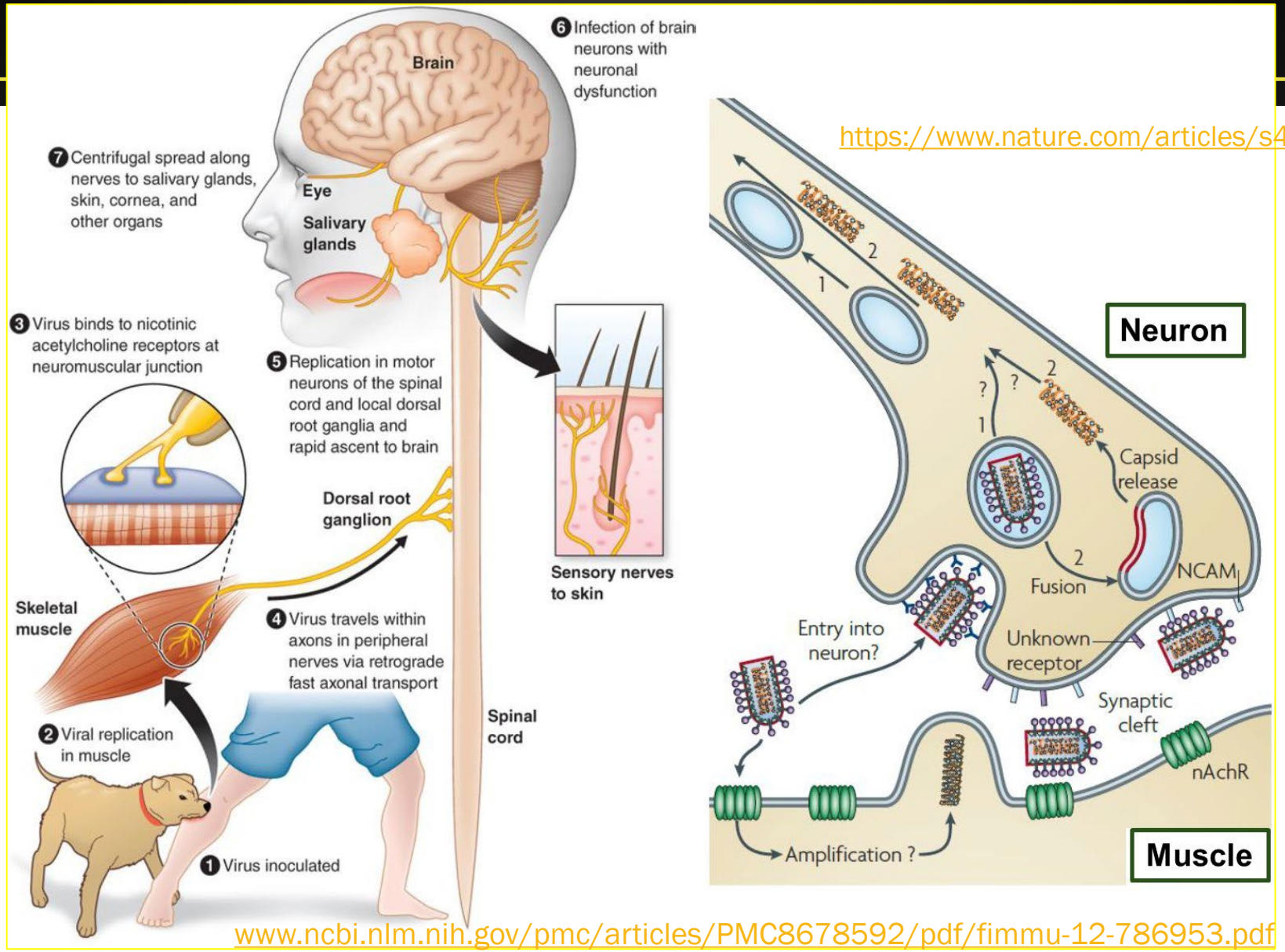
> "Of the Ebola survivors that I saw coming out of our treatment centres in Sierra Leone, everybody was suffering from something; there was not a single person who walked away unscathed"

Day by day, researchers are filling in the gaps on post-Ebola syndrome. The PREVAIL study in Liberia will track some 1500 survivors for up to 5 years, in an effort to categorise the long-term consequences of Ebola and assess the extent to which previously infected individuals remain contagious. Preliminary findings indicate that 68% of survivors suffer from neurological complications, 60% have eye problems, and 53% have musculoskeletal complications.

CAN VACCINATION AND IMMUNIZATION AGAINST EBOLA REDUCE THE RISK OF POST-EBOLA SYNDROMES?

www.thelancet.com/action/showPdf?pii=S1473-3099%2815%2900259-5

More deadly than Ebola ?



https://www.nature.com/articles/s41541-023-00615-z

LYSSAVIRUSES cause RABIES

www.ncbi.nlm.nih.gov/pmc/articles/PMC8678592/pdf/fimmu-12-786953.pdf

Lyssaviruses the world's deadliest virus? ~100% fatality rate if symptoms develop (more than Ebola)

Treating rabies costs around USD 124 billion, killing an estimated 59,000 people a year, a large proportion of whom are children.

WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

TRANSACTION COST

HEALTHCARE ECONOMICS

THE NOBEL PRIZE

Nobel Prizes & Laureates | Nomination | Alfred Nobel | News & insights | Events | Educational

Economic Sciences | Prize in Economic Sciences 1991 | Ronald H. Coase - Facts

www.nobelprize.org/prizes/economic-sciences/1991/coase/facts/

The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1991

Ronald H. Coase

Ronald H. Coase
Facts

Photo from the Nobel Foundation archive.

Ronald H. Coase
The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1991

Born: 29 December 1910, Willesden, United Kingdom

Died: 2 September 2013, Chicago, IL, USA

Affiliation at the time of the award: University of Chicago, Chicago, IL, USA

Prize motivation: "for his discovery and clarification of the significance of transaction costs and property rights for the institutional structure and functioning of the economy"

Prize share: 1/1

WHY VACCINATION IS CRITICAL ?

T C E

TRANSACTION

COST

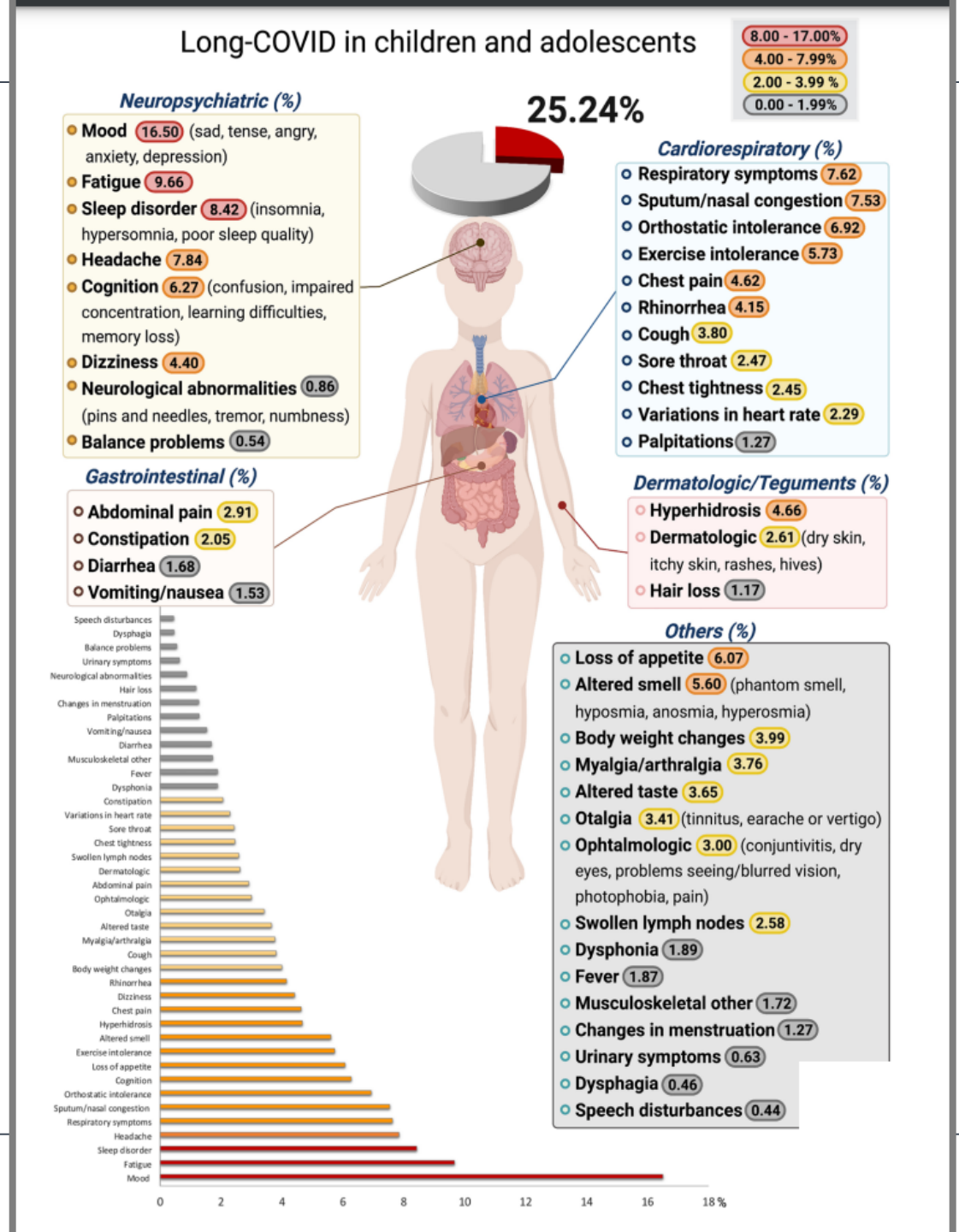
ECONOMICS

(HEALTHCARE)

ECONOMIC BURDEN OF LONG TERM HEALTHCARE

WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

VICTORY LOVES PREPARATION



Lopez-Leon S, Wegman-Ostrosky T, Ayuzo Del Valle NC, Perelman C, Sepulveda R, Rebolledo PA, Cuapio A, Villapol S. Long-COVID in children and adolescents: a systematic review and meta-analyses. Sci Rep. 2022 June 23; 12(1):9950. doi: 10.1038/s41598-022-13495-5. PMID: 35739136 www.ncbi.nlm.nih.gov/pmc/articles/PMC9226045/pdf/41598_2022_Article_13495.pdf

Meta-Analysis

Long-COVID in children and adolescents: a systematic review and meta-analyses

Sandra Lopez-Leon [1,2], Talia Wegman-Ostrosky [3], Norma Cipatli Ayuzo Del Valle [4], Carol Perelman [5], Rosalinda Sepulveda [6], Paulina A Rebolledo [7,8], Angelica Cuapio [9], Sonia Villapol [10,11]

Sci Rep. 2022 Jun 23;12(1):9950. doi: 10.1038/s41598-022-13495-5.

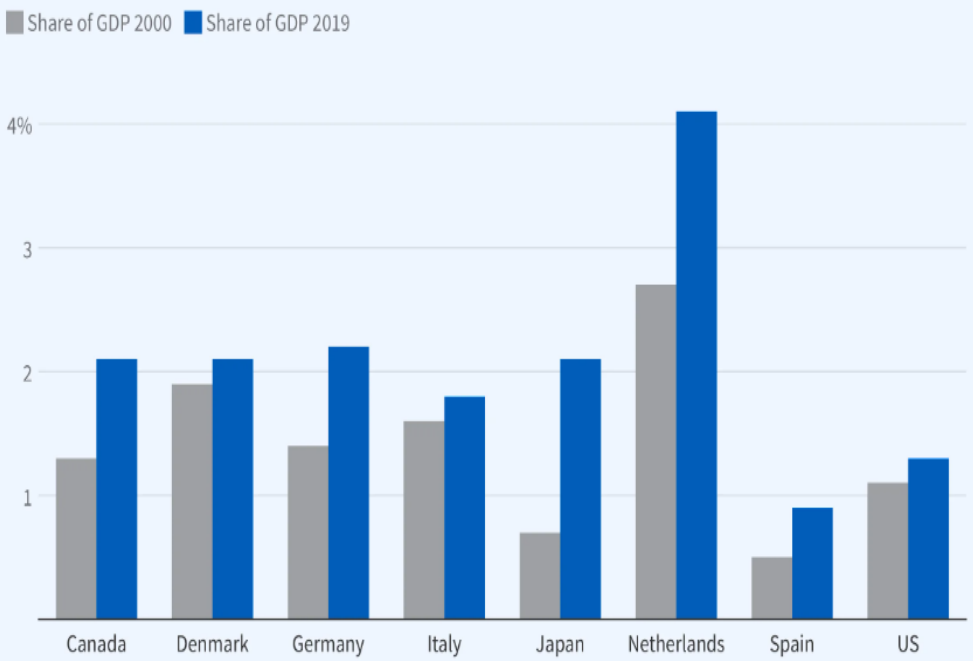
nber.org/brd/20234/long-term-care-around-world

www.nber.org/programs-projects/programs-working-groups/economics-health

Long-Term Care around the World

12/31/2023 Summary of Working Paper 31882

Share of GDP Spent on Formal Long-Term Care over Time



The reported percentages of GDP are for all formal long-term care expenditures, regardless of the age of the care recipient. Spain's estimates are for 2003 and 2019 and Italy's are for 2004 and 2019.

Source: Researchers' calculations using data on long-term services from multiple countries.

Related

RESEARCHERS

Jonathan Gruber
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Center for Aging and Health Research

ARTICLES

Tax Breaks for Employer-Sponsored Health Insurance
Social Security and Elderly Poverty
Racial Concordance and the Take-Up of Preventive Care

Increasing life expectancy and decreasing fertility rates have led to an aging population, raising fiscal concerns about demand for long-term healthcare. Additional spending due to morbidity from diseases and chronic care, when combined, could easily destabilize national and global economies. The most glaring example is that of NHS, in the UK.

https://www.bmj.com/bmj/section-pdf/724776?path=/bmj/347/7916/Observations.full.pdf

www.instituteforgovernment.org.uk/comment/how-bad-nhs-crisis

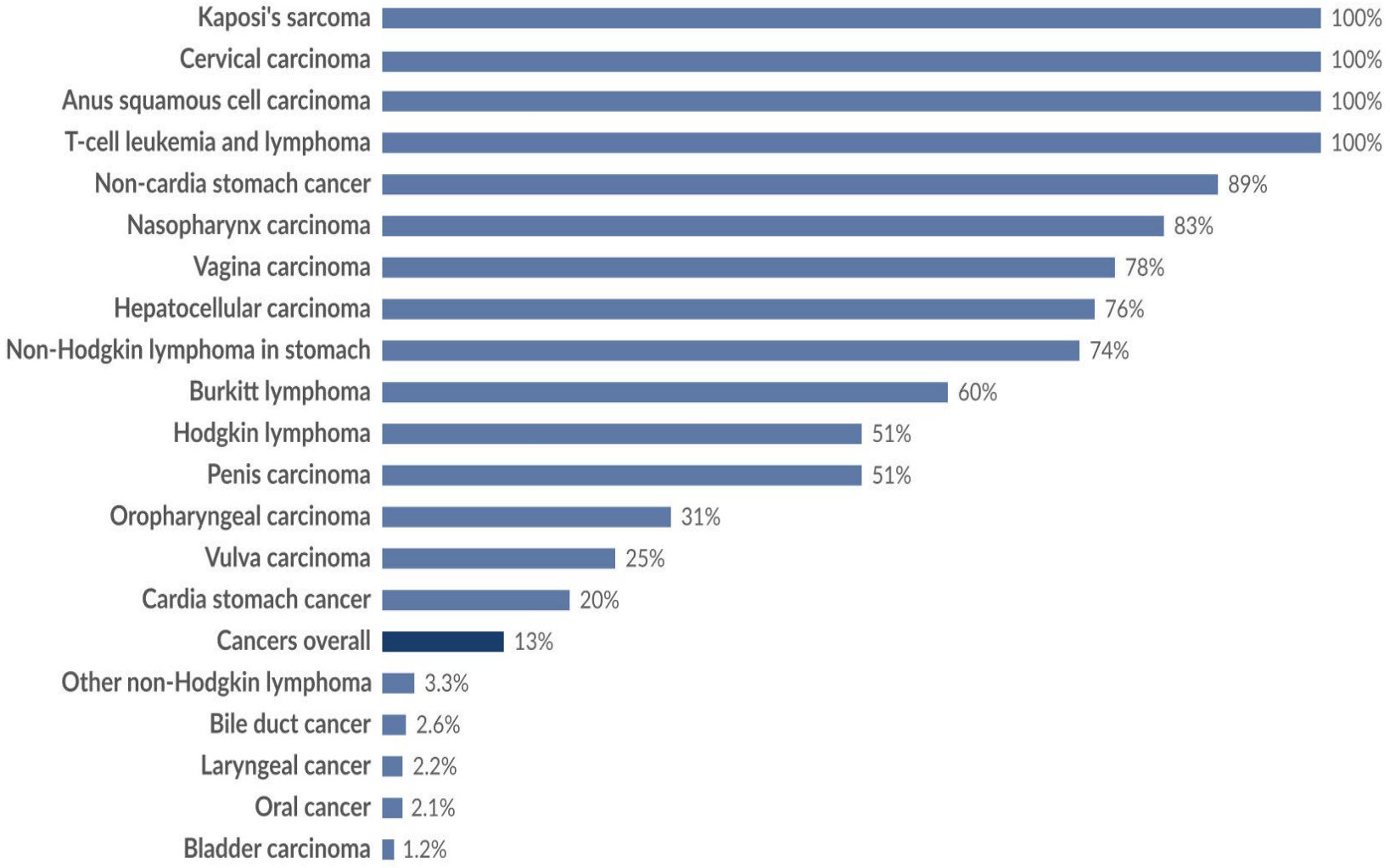
WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

INFECTION AS A "CANCER" BURDEN IN HEALTHCARE

What share of new cancers globally are caused by infections?

Our World in Data

Global estimates for the year 2020. The estimated share of new cancer cases attributed to all known cancer-causing pathogens.



Data source: International Agency for Research on Cancer (2020)

OurWorldinData.org/cancer | CC BY

Note: Non-melanoma skin cancers are excluded due to potentially incomplete records and inconsistent registry practices.

MORE THAN 90% OF THE GLOBAL ADULT POPULATION IS CHRONICALLY INFECTED BY EPSTEIN–BARR VIRUS (EBV).

HERE IS HOW EBV CONTRIBUTES TO EXACERBATING THE GLOBAL ECONOMIC BURDEN OF HEALTHCARE

MORE THAN 90% OF THE GLOBAL ADULT POPULATION IS CHRONICALLY INFECTED BY EPSTEIN–BARR VIRUS (EBV).

SIX CANCERS WITH A RELATIVELY LARGE EBV-RELATED CASE BURDEN ARE – 1. NASOPHARYNGEAL CARCINOMA (NPC), 2. GASTRIC CARCINOMA (GC), 3. HODGKIN LYMPHOMA (HL), 4. BURKITT LYMPHOMA (BL), 5. DIFFUSE LARGE B-CELL LYMPHOMA (DLBCL) & 6. EXTRANODAL NK/T-CELL LYMPHOMA, NASAL TYPE (ENKTL-NT).

> 90% OF THE GLOBAL ADULT POPULATION IS CHRONICALLY INFECTED BY EPSTEIN–BARR VIRUS

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

News

> News > Press Releases > 2022 > Epstein-Barr virus may be leading cause of multiple sclerosis

Epstein-Barr virus may be leading cause of multiple sclerosis

For immediate release: January 13, 2022

Boston, MA – Multiple sclerosis (MS), a progressive disease that affects 2.8 million people worldwide and for which there is no definitive cure, is likely caused by infection with the Epstein-Barr virus (EBV), according to a study led by Harvard T.H. Chan School of Public Health researchers.

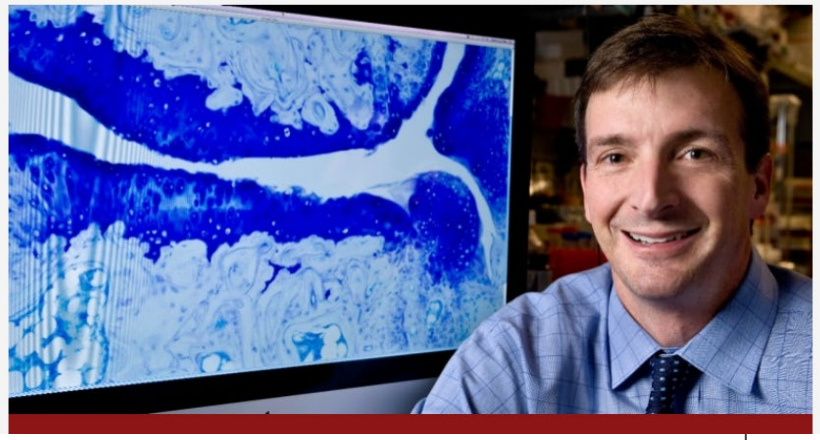
Their findings were published online in Science on January 13, 2022.

Stanford MEDICINE | News Center

Study identifies how Epstein-Barr virus triggers multiple sclerosis

A new study found that part of the Epstein-Barr virus mimics a protein made in the brain and spinal cord, leading the immune system to mistakenly attack the body's nerve cells.

January 24, 2022 - By Hadley Leggett



https://www.hsph.harvard.edu/news/press-releases/epstein-barr-virus-may-be-leading-cause-of-multiple-sclerosis/
https://med.stanford.edu/news/all-news/2022/01/epstein-barr-virus-multiple-sclerosis.html

RECENT EVIDENCE – EPSTEIN-BARR VIRUS (EBV) IMPLICATED AS A TRIGGER FOR MULTIPLE SCLEROSIS (MS)

MS Society News www.nationalmssociety.org/About-the-Society/News/New-Research-How-EBV-May-Trigger-MS

Soldan, S.S., Lieberman, P.M. **Epstein–Barr virus and multiple sclerosis**. *Nat Rev Microbiol* **21**, 51–64 (2023). https://doi.org/10.1038/s41579-022-00770-5

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Aloisi F, Giovannoni G, Salvetti M**. Epstein-Barr virus as a cause of multiple sclerosis: opportunities for prevention and therapy.** Lancet Neurol. 2023 April; 22(4):338-349 doi: 10.1016/S1474-4422(22)00471-9. Epub 2023 Feb 7. PMID: 36764322.

Bjornevik K, Münz C, Cohen JI, Ascherio A. **Epstein-Barr virus as a leading cause of multiple sclerosis: mechanisms and implications.** Nat Rev Neurol. 2023 March; 19(3):160-171 doi: 10.1038/s41582-023-00775-5. Epub 2023 Feb 9. PMID: 36759741. https://www.nature.com/articles/s41582-023-00775-5

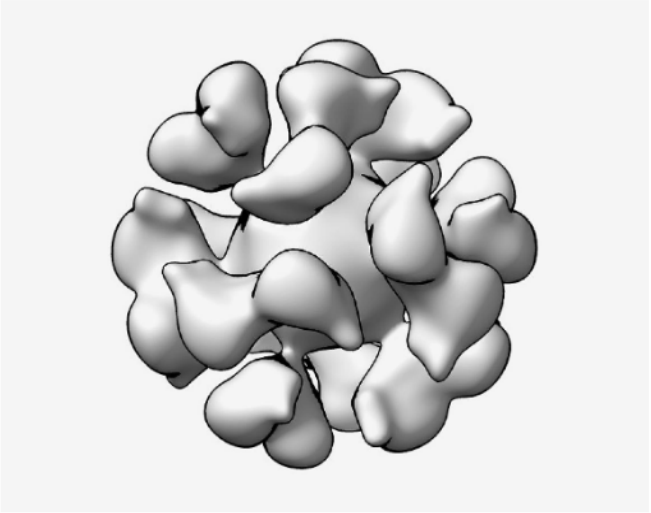
Bjornevik K**,** Cortese M, Healy BC, Kuhle J, Mina MJ, Leng Y, Elledge SJ, Niebuhr DW, Scher AI, Munger KL, Ascherio A. **Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis.** Science. 2022 January 21; 375(6578):296-301 doi: 10.1126/science.abj8222. PMID: 35025605. https://www.science.org/doi/10.1126/science.abj8222

Friday, May 6, 2022

NIH launches clinical trial of Epstein-Barr virus vaccine

www.clinicaltrials.gov/ ● Identifier NCT04645147

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has launched an early-stage clinical trial to evaluate an investigational preventative vaccine for Epstein-Barr virus (EBV). EBV is the primary cause of infectious mononucleosis and is associated with certain cancers and autoimmune diseases. The Phase 1 study, which will be conducted at the NIH Clinical Center in Bethesda, Maryland, is one of only two studies to test an investigational EBV vaccine in more than a decade.



An cryoelectron microscopic reconstruction model of the EBV gp350-ferritin nanoparticle. *Geng Meng, Purdue University*

EBV is a member of the herpes virus family and one of the most common human viruses. It is spread through bodily fluids, primarily saliva. An estimated 125,000 cases of infectious mononucleosis occur each year in the United States; roughly 10% of those persons develop fatigue lasting six months or longer. Approximately 1% of all EBV-infected individuals develop serious complications, including hepatitis, neurologic problems, or severe blood abnormalities. EBV also is associated with several malignancies, including stomach and nasopharyngeal cancers and Hodgkin and Burkitt lymphomas, as well as autoimmune diseases, such as systemic lupus erythematosus and multiple sclerosis.

"A vaccine that could prevent or reduce the severity of infection with the Epstein-Barr virus could reduce the incidence of infectious mononucleosis and might also reduce the incidence of EBV-associated malignancies and autoimmune diseases," said NIAID Director Anthony S. Fauci, M.D.

www.nih.gov/news-events/news-releases/nih-launches-clinical-trial-epstein-barr-virus-vaccine

ECONOMIC BURDEN OF LONG TERM HEALTHCARE

WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

EBV infection is chronic in 90% of the population, implicated in the etiology of at least six cancers and potentially triggers autoimmune diseases (SLE) including the debilitating affliction (morbidity) of MS (multiple sclerosis). Still wish to ask why vaccinate?

UNHEALTHY INDIVIDUALS = INEFFICIENT PERFORMANCE = DECREASED PRODUCTIVITY

THE PRODUCTIVITY PARADOX HAS BEEN DEFINED AS A PERCEIVED "DISCREPANCY BETWEEN MEASURES OF INVESTMENT IN INFORMATION TECHNOLOGY AND MEASURES OF OUTPUT AT THE NATIONAL LEVEL.“

ATTRIBUTED TO **ROBERT SOLOW**, IN REFERENCE TO HIS 1987 QUIP, "YOU CAN SEE THE COMPUTER AGE EVERYWHERE BUT IN THE PRODUCTIVITY STATISTICS."

https://en.wikipedia.org/wiki/Productivity_paradox

Health of Nations ➔ Economic Growth

Bob Solow (L), 18 September 2009, MIT
(on the right side - Shoumen Datta, MIT)

At MIT, Solow served as principal advisor to over 70 doctoral students and four of his PhD students went on to win the Nobel Prize in Economics (George Akerlof PhD '66, Peter Diamond PhD '63, William Nordhaus PhD '67, and Joseph Stiglitz PhD '67). One student who wrote an undergraduate economics thesis for Solow, (H. Robert Horvitz '68) also won the Nobel Prize but in Physiology or Medicine.
https://news.mit.edu/2023/institute-professor-emeritus-robert-solow-dies-1222
https://www.technologyreview.com/2019/12/27/131259/the-productive-career-of-robert-solow/

THE NOBEL PRIZE

Nobel Prizes & Laureates | Nomination | Alfred Nobel | News & insights | Events | Educational

Economic Sciences | Prize in Economic Sciences 1987 | Robert M. Solow - Facts

The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1987

Robert M. Solow

Robert M. Solow
Facts

Photo from the Nobel Foundation archive.

Robert M. Solow
The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1987

Born: 23 August 1924, Brooklyn, NY, USA

Died: 21 December 2023, Lexington, MA, USA

Affiliation at the time of the award: Massachusetts Institute of Technology (MIT), Cambridge, MA, USA

Prize motivation: "for his contributions to the theory of economic growth"

Prize share: 1/1

http://piketty.pse.ens.fr/files/Solow1956.pdf
www.nobelprize.org/prizes/economic-sciences/1987/solow/facts/

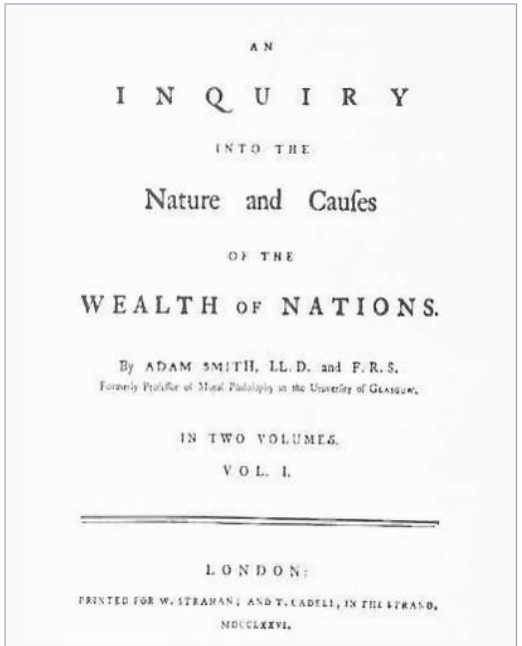
HEALTH OF NATIONS = WEALTH OF NATIONS

An Inquiry into the Nature and Causes of the Wealth of Nations, generally referred to by its shortened title ***The Wealth of Nations***, is the *magnum opus* of the Scottish economist and moral philosopher Adam Smith (1723-1790). First published in 1776, the book offers one of the world's first connected accounts of what builds nations' wealth, and has become a fundamental work in classical economics. Reflecting upon economics at the beginning of the Industrial Revolution, Smith addresses topics such as the division of labour, productivity, and free markets.[1]

History [edit]

The Wealth of Nations was published in two volumes on 9 March 1776 (with books I–III included in the first volume and books IV and V included in the second),[2] during the Scottish Enlightenment and the Scottish Agricultural Revolution.[3] It influenced several authors and economists, such as Karl Marx, as well as governments and organizations, setting the terms for economic debate and discussion for the next century and a half.[4] For example, Alexander Hamilton was influenced in part by *The Wealth of Nations* to write his *Report on Manufactures*, in which he argued against many of Smith's policies. Hamilton based much of this report on the ideas of Jean-Baptiste Colbert, and it was, in part, Colbert's ideas that Smith responded to, and criticised, with *The Wealth of Nations*.[5]

The Wealth of Nations


AN

INQUIRY

INTO THE

Nature and Cauſes

OF THE

WEALTH OF NATIONS.

By ADAM SMITH, LL.D. and F.R.S.

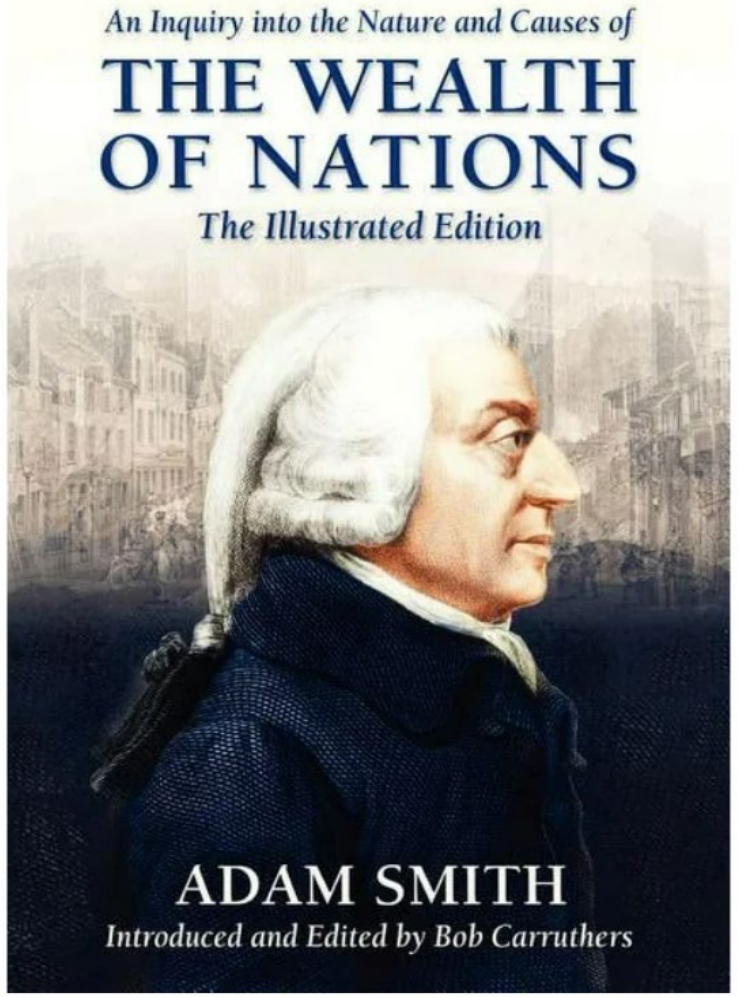
IN TWO VOLUMES.

VOL. I.

LONDON:

Title-page of the 1776 London edition

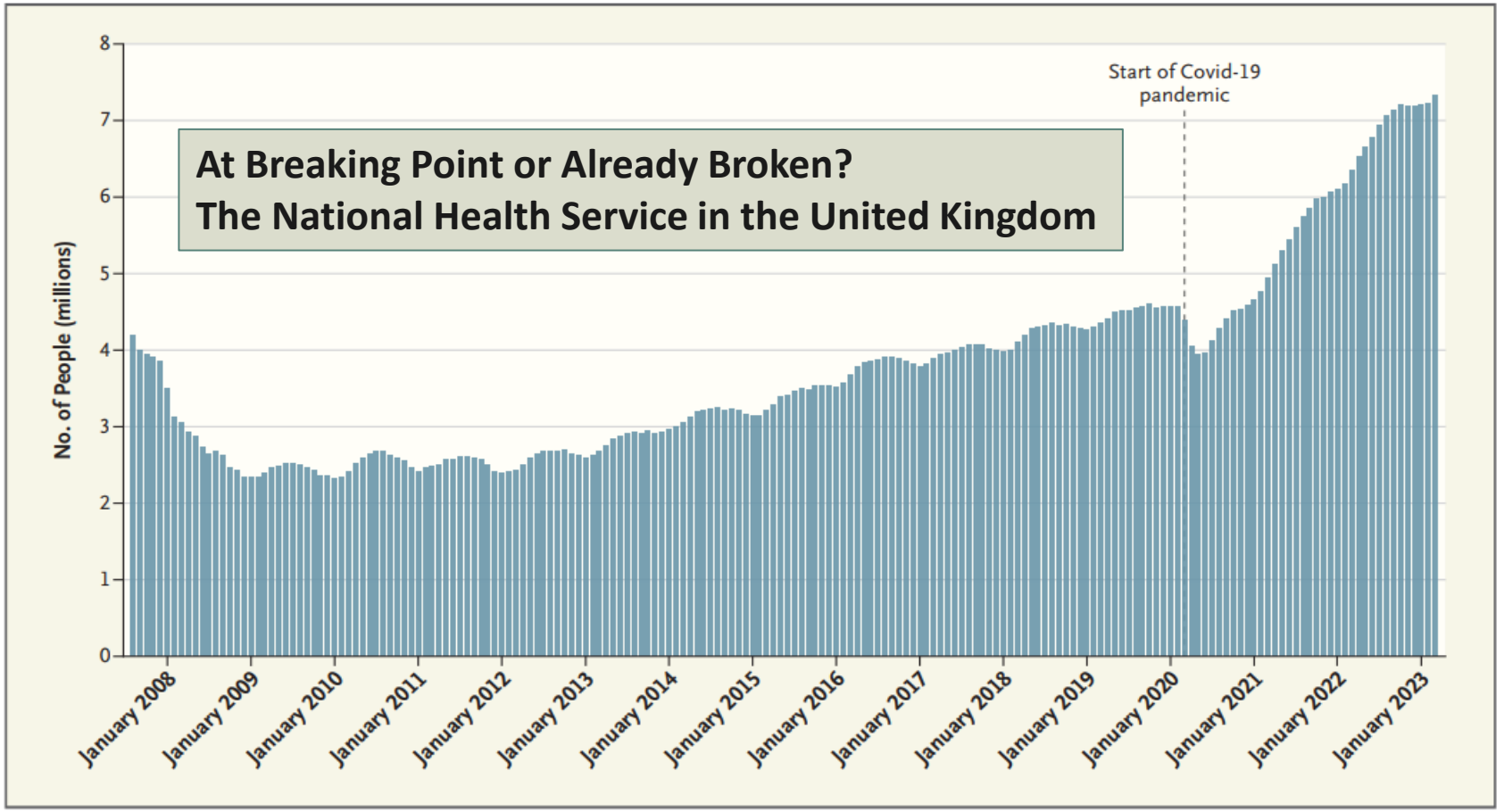
Author	Adam Smith
Country	Scotland, Kingdom of Great Britain
Language	English
Genre	Economics, Philosophy
Publisher	W. Strahan and T. Cadell, London
Publication date	9 March 1776



WHY VACCINATION / IMMUNIZATION IS SO CRITICAL

Could Plant based Oral Vaccines save people in UK?

July 13, 2023
N Engl J Med 2023; 389:100-103
DOI: 10.1056/NEJMp2301257



Number of People on National Health Service Waiting Lists for Consultant-Led Elective Care, August 2007 to March 2023.
Data are from the National Health Service (https://www.england.nhs.uk/statistics/statistical-work-areas/rtt-waiting-times/rtt-data-2022-23/).

STUPIDITY OF A NATION ??

- The Pfizer vaccine, used in most developed countries, applied for permission in India in Dec-2020. India instead asked them to do more studies in India. Pfizer withdrew its application in Feb-21. Imagine lives saved if the Indian government accepted the offer.

WHY DOCTORS OVERLOOK A USEFUL TREATMENT

Science Current Issue

What drives poor quality of care for child diarrhea? Experimental evidence from India

ZACHARY WAGNER, MANOJ MOHANAN, RUSHIL ZUTSHI, ARNAB MUKHERJI, AND NEERAJ SOOD Authors Info & Affiliations

SCIENCE · 9 Feb 2024 · Vol 383, Issue 6683 · DOI: 10.1126/science.adj9986

Editor's summary

Diarrhea is a leading cause of child mortality in India. It becomes deadly when excretions exacerbate severe dehydration and loss of electrolytes. Most health care providers in India know that oral rehydration salts (ORS) are an inexpensive, lifesaving treatment for child diarrhea, yet they are widely underused. Wagner *et al.* undertook randomized controlled trials involving standardized patients (actors trained to seek care for a child's diarrhea) who visited 2282 private health care providers in India. Trials were designed to identify three barriers driving underutilization: assuming patients lack interest in ORS, incentives to prescribe more lucrative (but inappropriate) medicines, and incentives to sell non-ORS medicines in stock when ORS are unavailable. The dominant barrier was assuming that patients were uninterested, showing that simple interventions could save many lives. — Ekeoma Uzogara

The study highlights "gap between knowing the right thing and doing the right thing."

https://www.science.org/doi/10.1126/science.adj9986
https://www.nature.com/articles/d41586-024-00351-x

Physicians often don't prescribe a cheap, lifesaving treatment for diarrhoea because they think their patients don't want it. That's the result of a large study looking at the use of oral rehydration solution in India. A survey showed that clinics, pharmacies and carers of sick children are mostly aware of the efficacy of the salty-sweet solution in preventing dehydration and reducing the risk of death in cases of diarrhoeal disease, but that it is often not prescribed. If an actor posing as the father of a sick child expressed a preference for the oral rehydration solution, they were twice as likely to get it as those who mentioned no treatment. The study highlights "the gap between knowing the right thing and doing the right thing," says health economist David Levine.

"Physicians often don't prescribe a cheap, lifesaving treatment for diarrhoea because they think their patients don't want it."

Association of profit and overtreatment

Lyu H, Xu T, Brotman D, Mayer-Blackwell B, Cooper M, Daniel M, Wick EC, Saini V, Brownlee S, Makary MA.(2017) **Overtreatment in the United States.** PLoS One. 2017 Sep 6;12(9):e0181970. doi: 10.1371/journal.pone.0181970. PMID: 28877170; PMCID: PMC5587107. www.ncbi.nlm.nih.gov/pmc/articles/PMC5587107/pdf/pone.0181970.pdf

Overtreatment in the United States

Heather Lyu[1]*, Tim Xu[2], Daniel Brotman[2], Brandan Mayer-Blackwell[2], Michol Cooper[2], Michael Daniel[2], Elizabeth C. Wick[2], Vikas Saini[3], Shannon Brownlee[3], Martin A. Makary[2,4]

1 Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, United States of America, **2** Department of Surgery and the Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States of America, **3** The Lown Institute, Boston, Massachusetts, United States of America, **4** Department of the Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America

* hlyu@partners.org

OPEN ACCESS

Citation: Lyu H, Xu T, Brotman D, Mayer-Blackwell B, Cooper M, Daniel M, et al. (2017) Overtreatment in the United States. PLoS ONE 12(9): e0181970. https://doi.org/10.1371/journal.pone.0181970

Editor: Imelda K. Moise, University of Miami, UNITED STATES

Received: March 24, 2017

Accepted: July 10, 2017

Published: September 6, 2017

Abstract

Background

Overtreatment is a cause of preventable harm and waste in health care. Little is known about clinician perspectives on the problem. In this study, physicians were surveyed on the prevalence, causes, and implications of overtreatment.

Methods

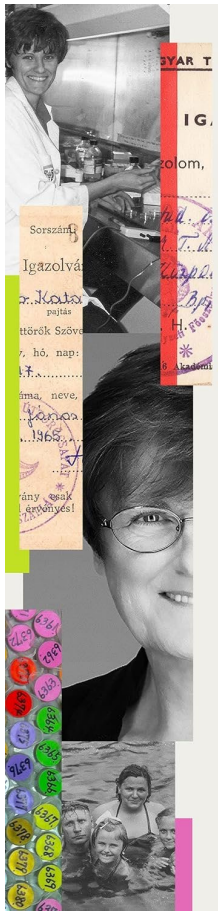
2,106 physicians from an online community composed of doctors from the American Medical Association (AMA) masterfile participated in a survey. The survey inquired about the extent of overutilization, as well as causes, solutions, and implications for health care. Main outcome measures included: percentage of unnecessary medical care, most commonly cited reasons of overtreatment, potential solutions, and responses regarding association of profit and overtreatment.

(continued from front flap)

Breaking Through isn't just the story of an extraordinary woman. It's an indictment of closed-minded thinking and a testament to one woman's commitment to laboring intensely in anonymity—knowing she might never be recognized in a culture that is driven by prestige, power, and privilege—because she believed that her work would save lives.

Katalin Karikó, PhD, is a Hungarian American biochemist who specializes in RNA-mediated mechanisms. She is an adjunct professor of neurosurgery at the University of Pennsylvania, and her research was foundational in the development of the Pfizer-BioNTech and Moderna mRNA vaccines.

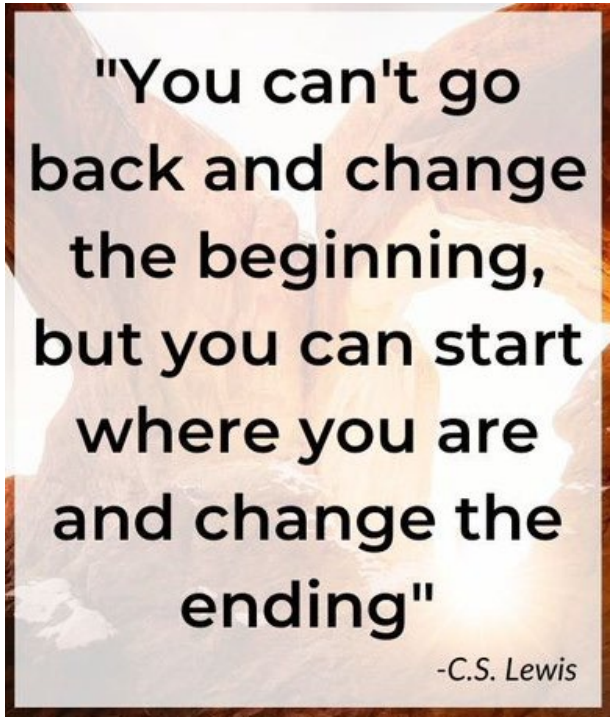
Twitter: @kkariko



Breaking Through

My Life in Science

Katalin Karikó



This is a clarion call for scientific leadership as well as other skills (financial, political, diplomatic). Paralysis due to analysis and "purified to perfection" are platitudes to be retired. Translating the patent-free (or expired) published research to pragmatic working reality requires a few students skilled in molecular biology and plant genetics, a few human volunteers and a host laboratory. Operating funds may be sourced as a consortium with tiny contributions from donors/foundations or crowd funding. The entity can also be a business if investors agree to the convergence of for-profit and not-for-profit *under one roof*. Products and services for affluent nations may be a for-profit operation (signatories[16] at The Convention on the OECD, on 14 December 1960) while the not-for-profit operation will apply to the rest of the world. The scientific credibility of this proposal assures outcome which will be catalytic to build capacity for global vaccinations, if implemented. Sourcing the recombinant antigens (vectors, plasmids) and creating transgenic plants will need help from scientists (geneticists) and other global experts.

For more than a quarter century, the destructive demonization of transgenic plants and ill-informed fanatical resistance to genetically-modified[17] crops has robbed the poor of global public goods, food, nutrition and healthcare. The cruel march of unreason[18] is a debilitating blow to our sense of the future by forcibly destroying[19] the fruits of science which could be of service to society, especially for communities under severe economic constraints. We view malicious, mis-information fueled social cataclysms as a point of inflection. We are optimistic that the tide is beginning to turn[20] from bad[21] to good[22] in the court of public opinion, both in Africa[23] and Asia[24], the geographies with the greatest need for plant-based oral vaccines.

The ability to prevent infection through low-cost self-vaccination and plant-based oral vaccines for immunization can reduce the horrendous scale of mortality and morbidity due to future infectious diseases and/or chronic diseases. Ethical globalization demands that affluent nations enable the less affluent nations to develop and implement this cottage industry of plant based vaccines, in the economic interest related to immigration, travel, commerce, and growing markets. Our collective inaction to neglect scientific proof and turn a blind eye to sourcing vaccines from transgenic plants is inhuman and unethical.

1-Page Extended Summary "POV" may be downloaded from the MIT Library https://dspace.mit.edu/handle/1721.1/145774

TEMPORARY CONCLUSION

1 ▪ S. Datta, Massachusetts Institute of Technology shoumen@mit.edu & Massachusetts General Hospital, Harvard Medical School sdatta8@mgh.harvard.edu

ACKNOWLEDGEMENTS

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Katalin Karikó, UPenn

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https://dspace.mit.edu/handle/1721.1/145774

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Shoumen Palit Austin Datta, Massachusetts General Hospital, Harvard Medical School and Department of Mechanical Engineering, Massachusetts Institute of Technology

It will be remiss of me, if I conclude here …

WHY

THIS WILL NOT WORK.

AFTER MORE THAN ONE YEAR (2022-2023) OF COMMUNICATION WITH VARIOUS DOMAINS OF SCIENTISTS AND INVESTORS,

GLOBALLY, THE OVERWHELMING SENSE IS THAT NEITHER PHILANTHROPISTS NOR VENTURE CAPITALISTS WISH TO CONSIDER

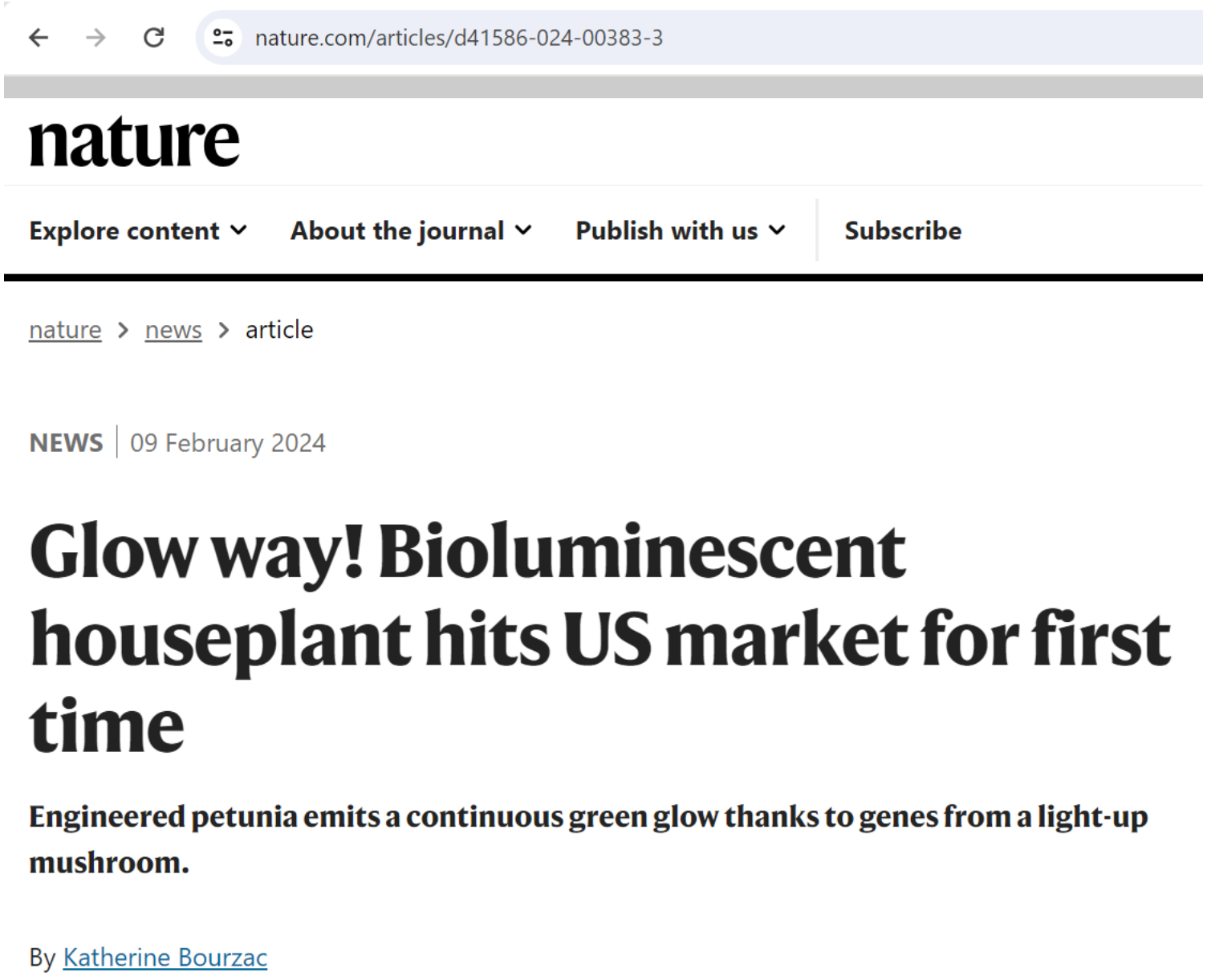
GENETICALLY ENGINEERED PLANTS AS A SOURCE OF UNPURIFIED ANTIGEN (EVEN IF IT IS PHYSIOLOGICALLY SAFE) FOR THE

PURPOSE OF VACCINATION AND IMMUNIZATION (EVEN IF IT SAVES ~7 BILLION LIVES IN NON-AFFLUENT ECONOMIC REGIONS).

WHAT ABOUT $29 FOR GENETICALLY ENGINEERED "GLOWING" PLANTS ?

YES !! THAT WORKS FOR US !!

YES !! THAT WORKS FOR US !!



https://doi.org/10.1038/d41586-024-00383-3

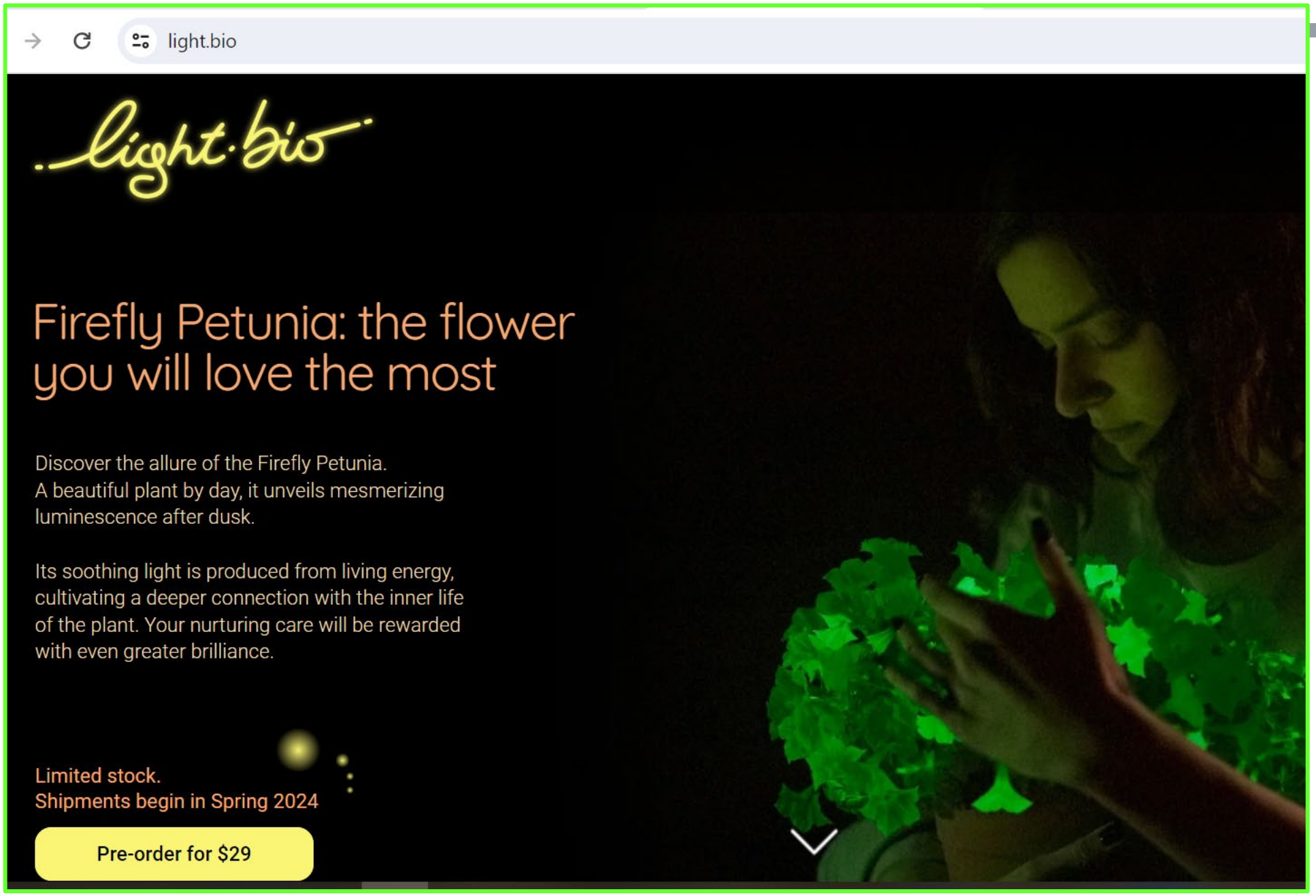
The firefly petunia glows a continuous, faint green in the dark. Credit: Light Bio

US consumers can now pre-order a genetically engineered plant for their home or garden that glows continuously. At a base cost of US$29.00, residents of the 48 contiguous states can get a petunia (*Petunia hybrida*) with flowers that look white during the day; but, in the dark, the plant glows. Biotechnology firm Light Bio in Sun Valley, Idaho, will begin shipping a batch of 50,000 firefly petunias in April.

Fast-growing parts of the plant, such as budding flowers and leaves, glow the brightest. Credit: Light Bio

Genetic engineering in a different light (USDA Approved)

Firefly petunia glows brightly due to a group of genes from the bioluminescent mushroom *Neonothopanus nambi*. The fungus feeds its light-emitting reaction with the molecule caffeic acid, which terrestrial plants also happen to make. By inserting the mushroom genes into the petunia, researchers made it possible for the plant to produce enzymes that can convert caffeic acid into the light-emitting molecule luciferin and then recycle it back into caffeic acid to enable sustained bioluminescence[2]. Keith Wood co-founded Light Bio with two of the researchers behind this work, Karen Sarkisyan, a synthetic biologist at the MRC Laboratory of Medical Sciences in London, and Ilia Yampolsky, a biomolecular chemist at the Pirogov Russian National Research Medical University in Moscow.



This “groundbreaking event” - a plant that can bioluminesce to be seen with the naked eye and sold to plant lovers, says Diego Orzáez, at the Institute of Plant Molecular and Cellular Biology in Valencia, Spain. “Being a European, I have envy that consumers in the United States can have their hands on these plants.”

GENETICALLY ENGINEERED PLANTS FOR VACCINATION

NO, IT DOES NOT WORK FOR US

CLICK TO ADD CA-CHING !! INCENTIVE

THIS SECTION IS FOR THOSE WHO MUST MAKE SOME

The Nobel Prize in Physiology or Medicine 1937

Photo from the Nobel Foundation archive.

Albert von Szent-Györgyi Nagyrápolt

Prize share: 1/1

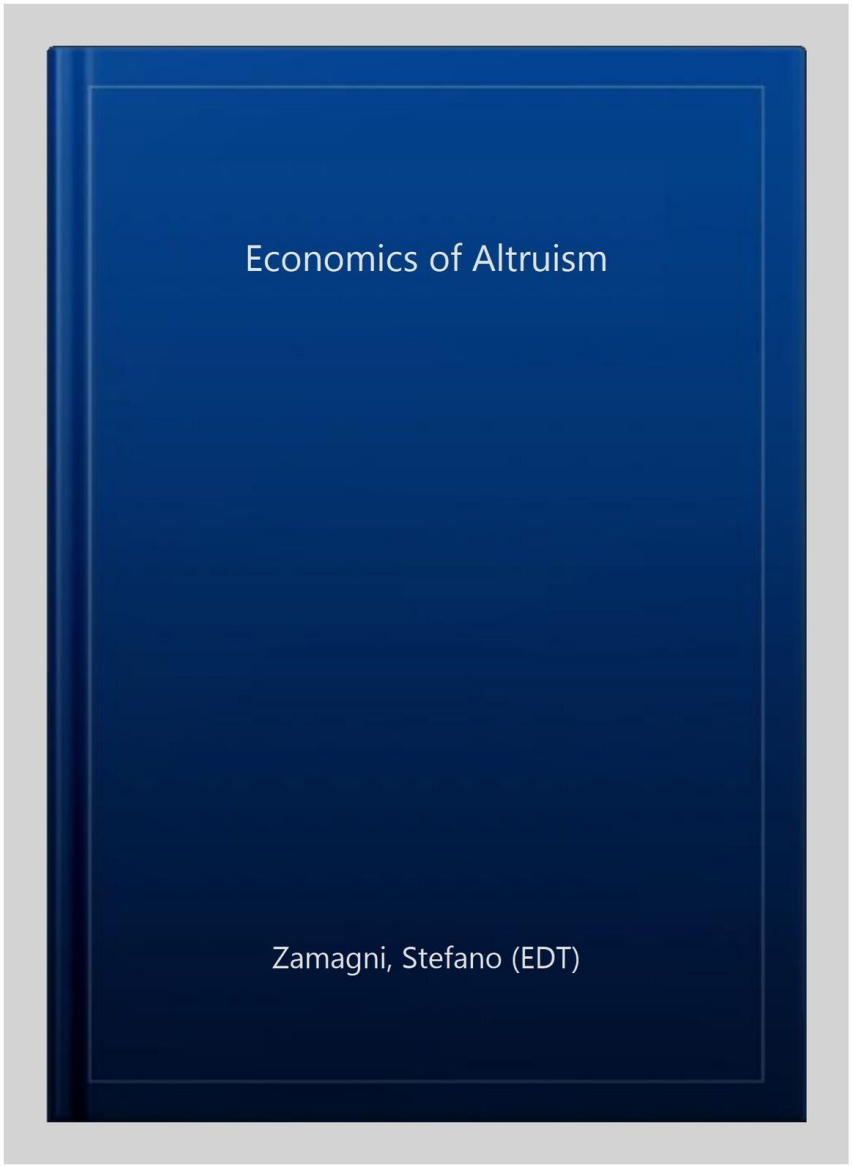
HTTPS://WWW.NOBELPRIZE.ORG/PRIZES/MEDICINE/1937/SUMMARY/

Research is four things: brains with which to think, eyes with which to see, machines with which to measure and, fourth, money.

— Albert Szent-Gyorgyi —

MONEY IS IMPORTANT

www.nber.org/system/files/working_papers/w32151/w32151.pdf



THE NOBEL PRIZE

Economic Sciences | Prize in Economic Sciences 1978 | Herbert Simon - Facts

The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1978

Herbert Simon

Herbert Simon
Facts

Photo from the Nobel Foundation archive.

Herbert A. Simon
The Sveriges Riksbank Prize in Economic Sciences in Memory of Alfred Nobel 1978

Born: 15 June 1916, Milwaukee, WI, USA

Died: 9 February 2001, Pittsburgh, PA, USA

Affiliation at the time of the award: Carnegie Mellon University, Pittsburgh, PA, USA

Prize motivation: "for his pioneering research into the decision-making process within economic organizations"

Prize share: 1/1

#786

Altruism and Economics[1]

A Summary Statement

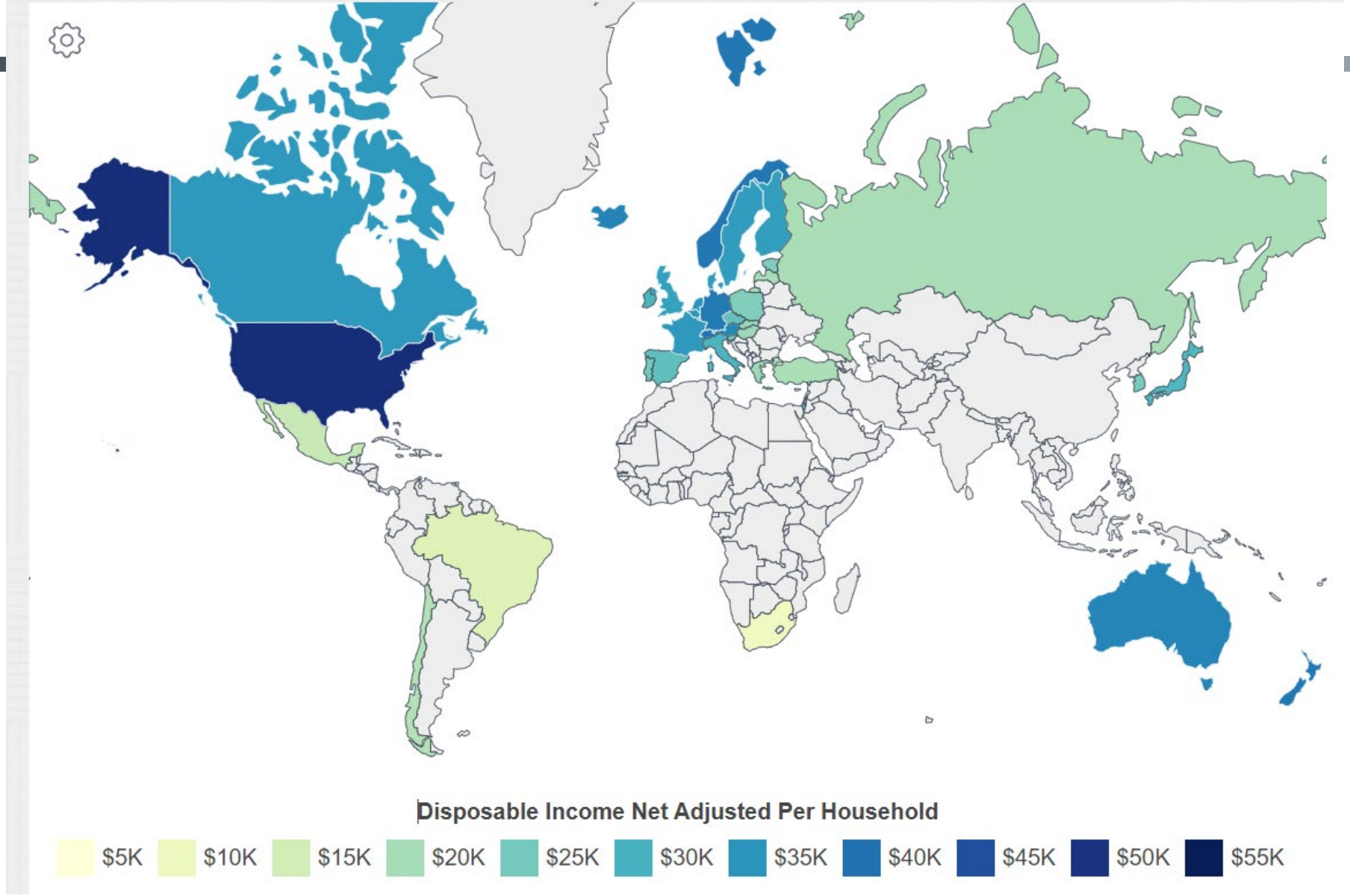
By HERBERT A. SIMON*

Altruism is an elusive concept. To pin it down, I must begin with population genetics, distinguishing altruism's technical meaning there from its everyday meanings in social and economic affairs. Then I will examine the role of altruism in the operation of the economy.

https://iiif.library.cmu.edu/file/Simon_box00069_fld05365_bdl0001_doc0001/Simon_box00069_fld05365_bdl0001_doc0001.pdf

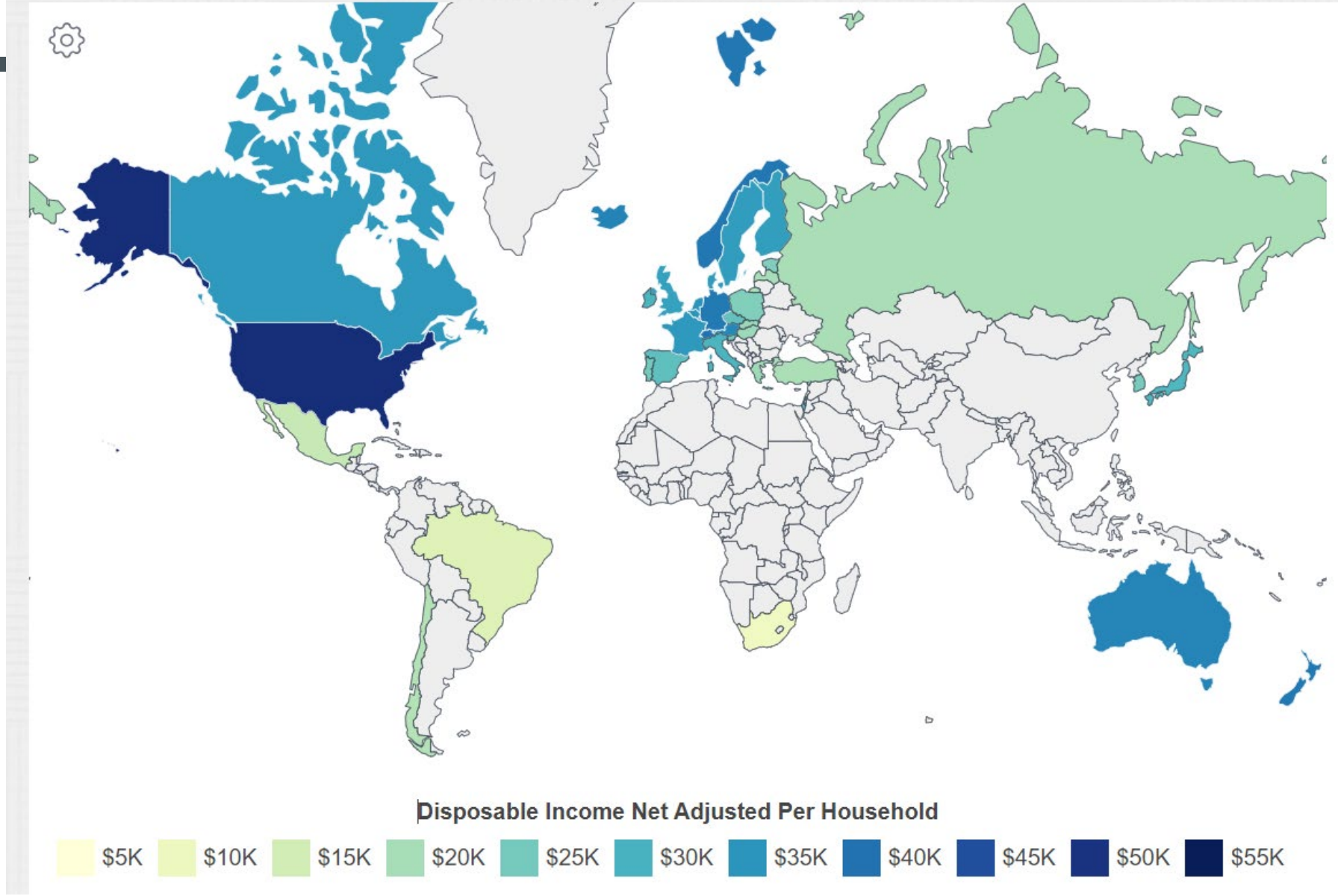
CAN WE PROFIT FROM PLANT VACCINES FOR POOR PEOPLE

YES



>80% of the global population (~7 billion people) DO NOT LIVE IN COUNTRIES WITH DISPOSABLE INCOME

https://worldpopulationreview.com/country-rankings/disposable-income-by-country



Can ~ 7 billion poor people spend US$1 per month for plant based oral vaccination ?

https://worldpopulationreview.com/country-rankings/disposable-income-by-country

Can ~7 billion poor people spend US$1 per month for plant based oral vaccination ?

CAN WE PROFIT FROM PLANT VACCINES FOR POOR PEOPLE

YES

Can ~7 billion poor people spend US$1 per month for plant based oral vaccination ?

CAN WE PROFIT FROM PLANT VACCINES FOR POOR PEOPLE

DID WE JUST SUGGEST A SOCIAL BUSINESS WITH A POTENTIAL REVENUE OF APPROX $84 BILLION PER ANNUM ?

Can ~7 billion poor people spend US$1 per month for plant based oral vaccination ?

WHAT IF OUR PROFIT FROM PLANT VACCINES IS ONLY ~ 1%

CAN THIS IDEA DEVELOP INTO A SOCIAL BUSINESS WITH A POTENTIAL PROFIT OF APPROX US$1 BILLION PER ANNUM ?

PAY A PENNY PER USE (PAPPU) – CENTRAL CONCEPT FOR SOCIAL BUSINESS PROFITABILITY

LET US PROFIT FROM SOCIAL BUSINESS FOR POOR PEOPLE

The idea is to lower the barrier to market entry for products and services by eliminating initial capital cost (for example, you get a free phone if you pay a small charge per call). The concept of PAPPU suggests charging a very small fee (penny?) each time the customer uses the product and/or the service.

PAPPU

Open Access Review

Peer-Review Record

Sensor-as-a-Service: Convergence of Sensor Analytic Point Solutions (SNAPS) and Pay-A-Penny-Per-Use (PAPPU) Paradigm as a Catalyst for Democratization of Healthcare in Underserved Communities

Diagnostics **2020**, *10*(1), 22; **https://doi.org/10.3390/diagnostics10010022**

by **Victoria Morgan** [1], **Lisseth Casso-Hartmann** [2,3], **David Bahamon-Pinzon** [4], **Kelli McCourt** [4], **Robert G. Hjort** [5], **Sahar Bahramzadeh** [6], **Irene Velez-Torres** [2,3], **Eric McLamore** [1], **Carmen Gomes** [5], **Evangelyn C. Alocilja** [7,8], **Nirajan Bhusal** [7,9,10], **Sunaina Shrestha** [10], **Nisha Pote** [10], **Ruben Kenny Briceno** [11,12,13,7], **Shoumen Palit Austin Datta** [1,14,15,16] and **Diana C. Vanegas** [3,4,*]

Reviewer 1: Anonymous

Reviewer 2: Anonymous

Diagnostics **2020**, *10*(1), 22; **https://doi.org/10.3390/diagnostics10010022**

Received: 18 December 2019 / Revised: 29 December 2019 / Accepted: 30 December 2019 / Published: 1 January 2020
(This article belongs to the Special Issue **Biosensors-Based Diagnostics**)

Round 1

Reviewer 1 Report

The manuscript is clearly written, well structured, I recommend this paper for publication in Diagnostics.

MOST (> 80% ??) OF THE WORLD'S POPULATION HAS STILL NOT RECEIVED A SINGLE DOSE OF THE COVID-19 VACCINE. THE DEATH TOLL RESULTING FROM VACCINE NATIONALISM STILL CONTINUES.

HERE (THIS PDF) ARE PROVEN OUTCOMES THAT COULD WORK FOR GLOBAL VACCINATION. WE HAVE KNOWN THESE FACTS FOR 30+ YEARS. WHAT IS PREVENTING US FROM EXECUTION?

Farlow A, Torreele E, Gray G, Ruxrungtham K, Rees H, Prasad S, Gomez C, Sall A, Magalhães J, Olliaro P, Terblanche P. **The Future of Epidemic and Pandemic Vaccines to Serve Global Public Health Needs.** Vaccines. 2023 March 17;11(3):690. doi: 10.3390/vaccines11030690 www.ncbi.nlm.nih.gov/pmc/articles/PMC10052681/pdf/vaccines-11-00690.pdf

BUT

ARE'NT WE BEING OBLIVIOUS OF NON-COMMUNICABLE DISEASES

VACCINES AND VACCINATION ARE NOT A PANACEA FOR HEALTH AND HEALTHCARE

MUSCULOSKELETAL HEALTH

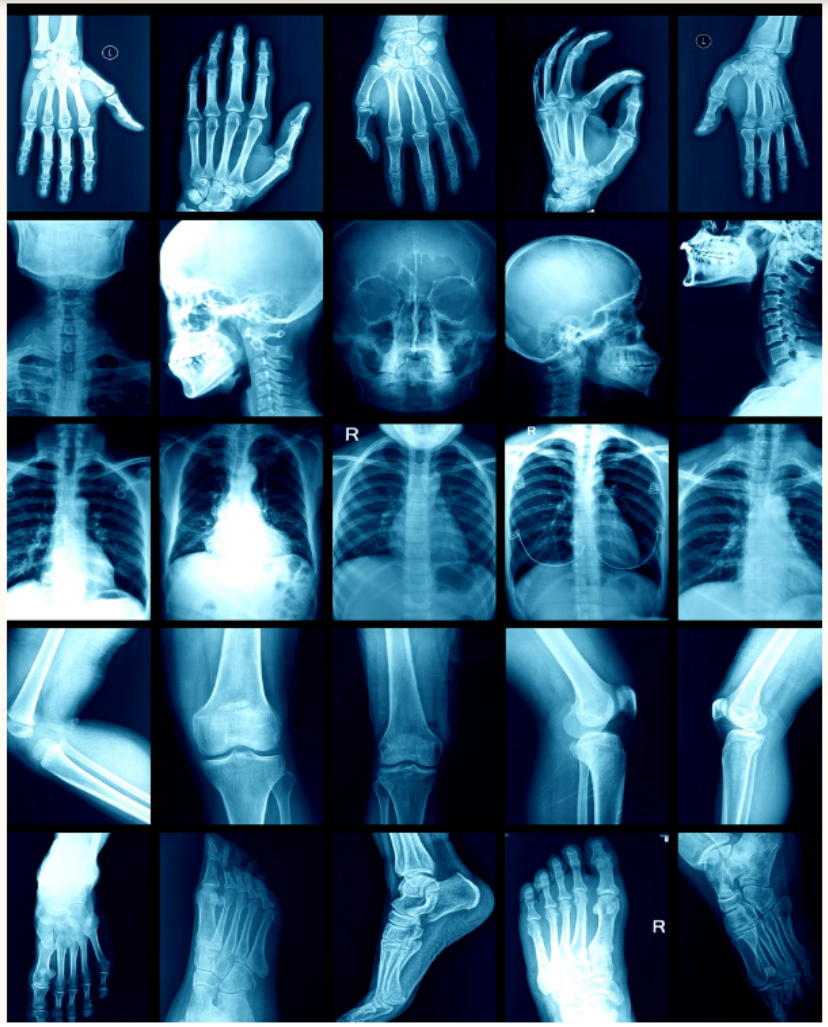
Global health morbidity has shifted in recent decades from communicable, maternal, neonatal, and nutritional (CMNN) diseases to non-communicable diseases (NCDs).[1] As death rates decline, non-fatal injuries and NCDs have become a significant concern for health systems. In addition, since 2000, the global population has increased by 1.7 billion,[2] and life expectancy has risen by 6.3 years.[3] However, the health-adjusted life expectancy, the average number of years that a person can expect to live in full health, has only increased by 4.9 years,[3,4] indicating a shift in disease burden from childhood illness and infectious disease to unhealthy adulthood. The trend of lower fertility rates, older population, and increased healthy life expectancy may present unique challenges for healthcare systems unprepared to address the shift from communicable to non-communicable diseases.[5]

Musculoskeletal disorders encompass diverse conditions affecting bones, joints, muscles, and connective tissues.[6] As a result of an aging population, musculoskeletal diseases are an emerging cause of health and financial burden in the United States,[1] where they affect more than one in three or approximately 127.4 million individuals.[7] In 2016, they were the leading driver of healthcare spending with an estimated direct cost of $380.9 billion, exceeding diabetes ($309.1 billion), cardiovascular diseases ($255.1 billion), mental disorders ($180.7 billion), cancer ($123.8 billion).[8] Despite this, research funding has predominantly focused on diseases associated with death rather than those that cause disability.[9] Despite the burden of musculoskeletal disease, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) has historically received less than 2% of the NIH budget.[15] A study in 2017 found that medical expenses from osteoarthritis were more significant than those from diabetes and similar to those from cancer, yet received 16 and 70 times less NIH funding, respectively.[16] Additionally, an NIH report in 2017 assessing research funding and disease burden included 74 disease categories. Still, it did not include major musculoskeletal diseases such as low back or neck pain,[17] despite being the leading causes of disability in the same year. The burden of trauma is often unaccounted for, despite the total cause of traumatic injuries in the U.S. estimated at $671 billion per year.[18]

www.thelancet.com/journals/lanam/article/PIIS2667-193X(23)00235-1/fulltext

The Harvard Gazette

https://news.harvard.edu/gazette/story/2024/03/despite-prevalence-arthritis-neck-and-back-pain-receive-few-research-dollars/



HEALTH

Despite prevalence, arthritis, neck and back pain receive few research dollars

Musculoskeletal diseases are the leading cause of years lived with disability

Jacqueline Mitchell | BIDMC Communications

March 8, 2024 ▪ 4 min read

Costing billions and affecting millions, musculoskeletal diseases impact more than one in three people in the U.S. and are a leading driver of healthcare spending, at an estimated cost of more than $380 billion in 2016. The numbers put the illnesses — which attack bones, joints, muscles, and connective tissues — ahead of diabetes, cardiovascular disease, and cancer, according to a new study out of Beth Israel Deaconess Medical Center.

Investigators led by Ara Nazarian at the Musculoskeletal Translational Innovation Initiative in the Carl J. Shapiro Department of Orthopaedics at BIDMC evaluated the relationship between the disease burden for 60 conditions and the federal funding assigned to research them.

Costing billions and affecting millions, musculoskeletal diseases impact a third of the U.S. and are a leading driver of healthcare spending (>$380 billion, 2016). The numbers put the illnesses - which attack bones, joints, muscles, connective tissues - ahead of diabetes, cardiovascular disease, and cancer.

https://doi.org/10.1016/j.lana.2023.100661

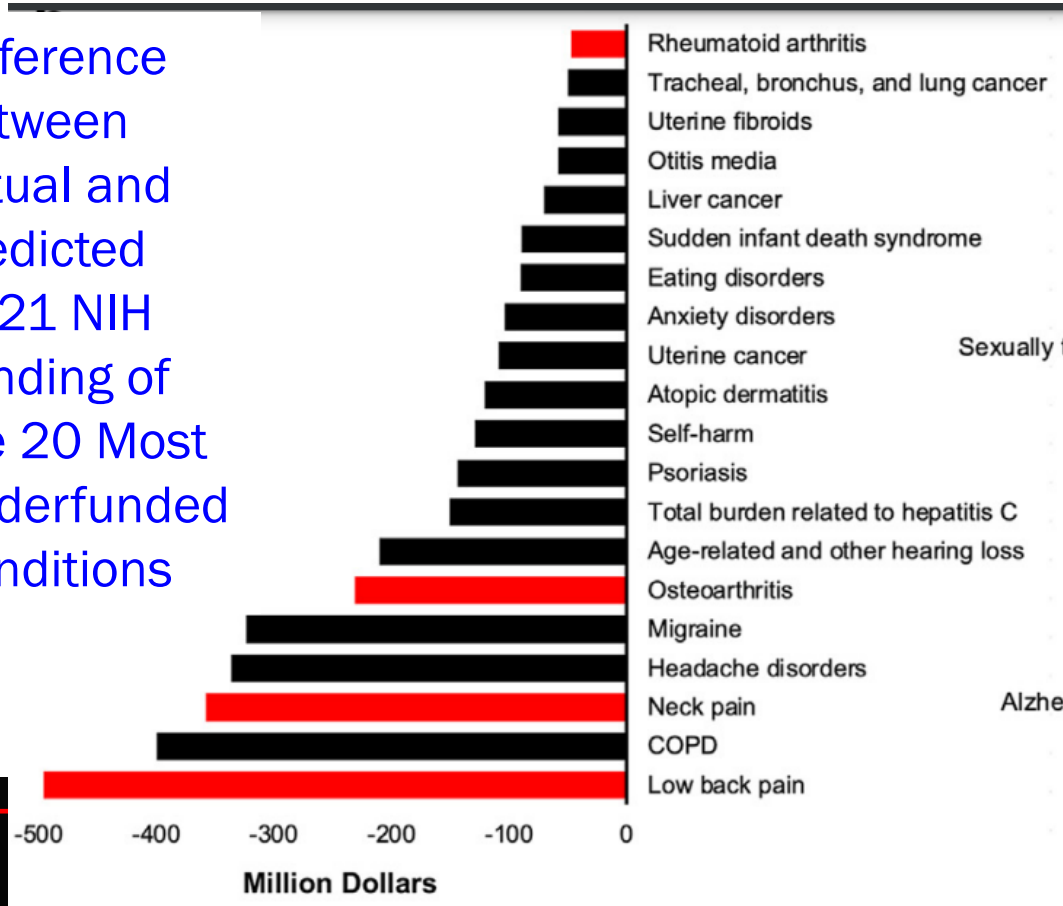
https://doi.org/10.1016/j.lana.2023.100661

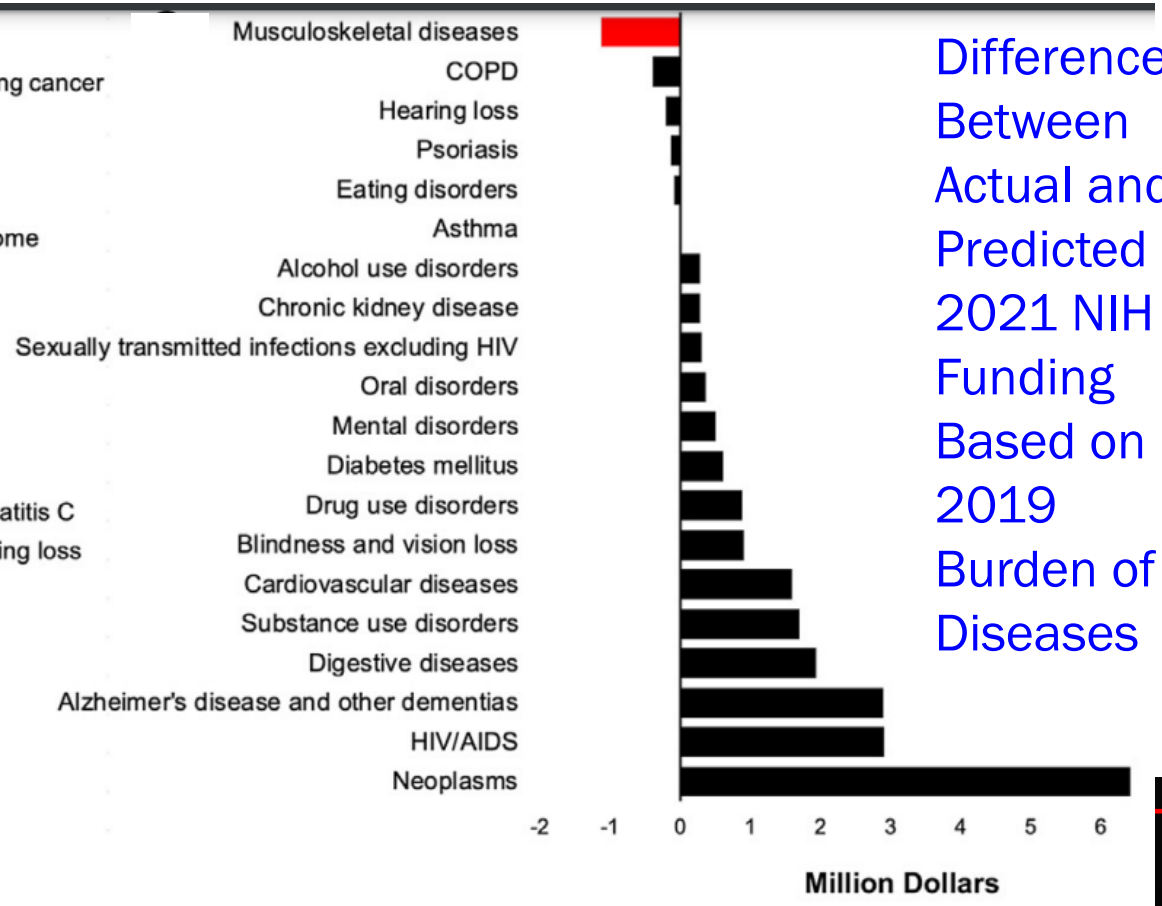
Musculoskeletal health: an ecological study assessing disease burden and research funding

Andrew T. Nguyen,[a,b] Izzuddin M. Aris,[c] Brian D. Snyder,[a,b,f] Mitchel B. Harris,[a,d] James D. Kang,[a,e] Martha Murray,[a,f] Edward K. Rodriguez,[a,b] and Ara Nazarian[a,b,g,*]

[a]Harvard Medical School, Boston, MA, USA

Difference Between Actual and Predicted 2021 NIH Funding of the 20 Most Underfunded Conditions

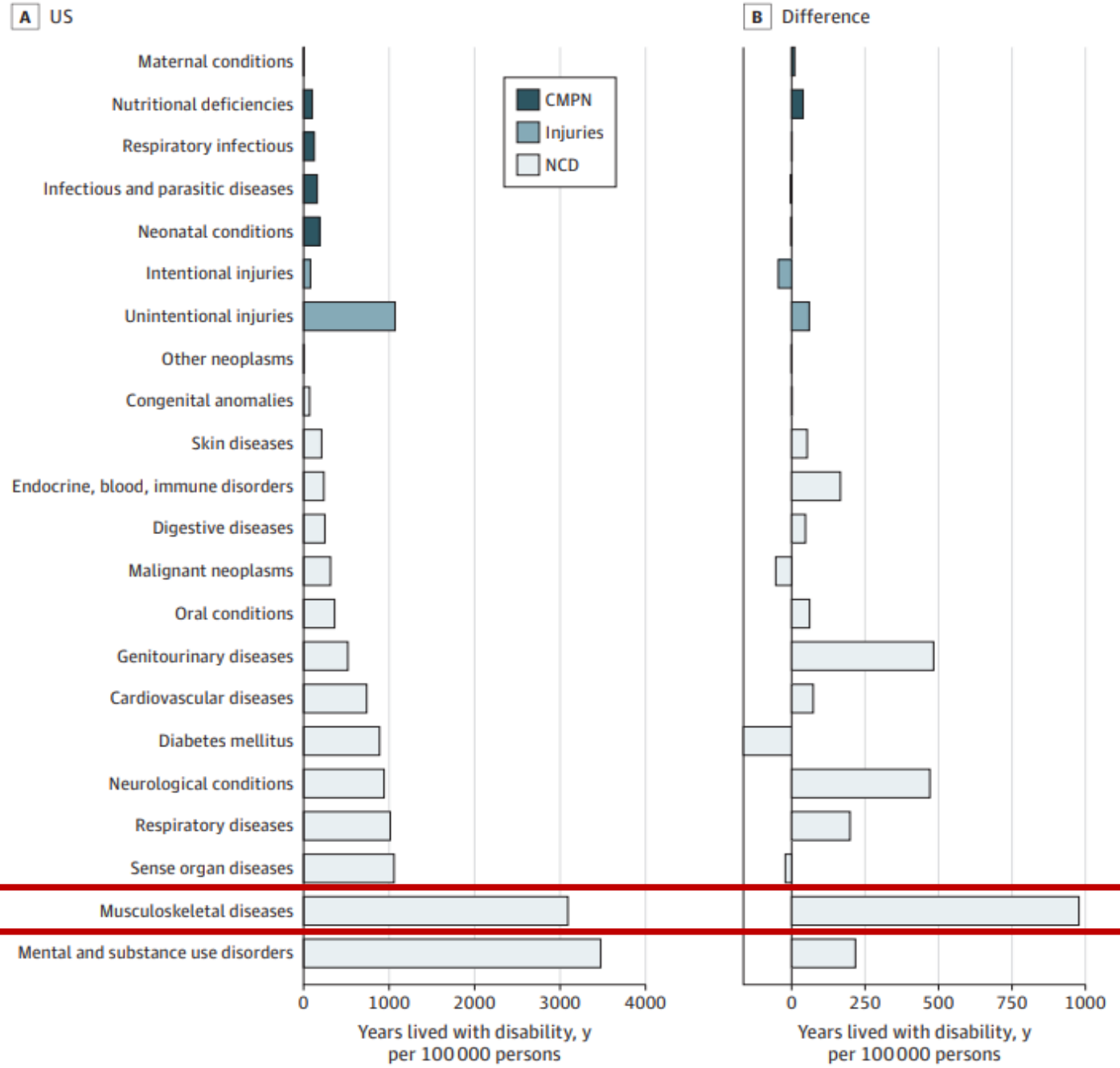




Difference Between Actual and Predicted 2021 NIH Funding Based on 2019 Burden of 20 Diseases

Garmany A, Terzic A. (2024) *Global Healthspan-Lifespan Gaps Among 183 World Health Organization Member States*. JAMA Network Open. 2024 December 2; 7(12):e2450241. doi: 10.1001/jamanetworkopen.2024.50241 PMID 39661386; PMCID PMC11635540

Figure 5. Years Lived With Disability Contributed by Disease Groups With Sex Differences in the US



NOW WE MOVE ON TO A DIFFERENT SUGGESTION WHICH WILL BE VERY DIFFICULT TO IMPLEMENT

https://dspace.mit.edu/handle/1721.1/145774

BUT NOT EXTRANEOUS

THE NEXT SUGGESTION IS UNRELATED TO THE PLANT-BASED VACCINE

SUPERVISED MOBILE MOSQUITO “BITE” STATION AS A DELIVERY MECHANISM FOR ASSISTED VACCINATION ?

THE CONVENTIONAL WISDOM

Infographic: Just one mosquito species can spread 54 viruses. Here's how genetic modification can help us conquer this disease-spreading, destructive powerhouse

Victoria Wise | Health Match | October 7, 2022

Credit: Matthew Twombly/NPR

https://geneticliteracyproject.org/2022/10/07/infographic-just-one-mosquito-species-can-spread-54-viruses-heres-how-genetic-modification-can-help-us-conquer-this-disease-spreading-destructive-powerhouse/

FLIP THE PARADIGM? THINK DIFFERENT

FROM
MOSQUITO BITE TRANSMITTING VIRUS
TO
MOSQUITO BITE DELIVERING ANTIGEN

SUPERVISED MOBILE MOSQUITO “BITE” STATIONS

Imagine boxes of genetically engineered mosquitoes (with a portfolio of antigens: Ebola, Polio, SARS, etc.).

Boxes are on a platform which is on a cycle rickshaw (peddled by a human to reach remote geographies).

Individuals go up to the platform and insert their palms in the mosquito boxes (multiple vaccinations possible).

Wait for mosquito to bite. Close trap door. Take out the hand. You have been bitten. You are now vaccinated.

“I rarely think in words at all. A thought comes, and I may try to express it in words afterwards.” (Attributed to Albert Einstein, 1916)

A malaria vaccine given by mosquito bite

A trial is looking at delivering malaria immunity through bites from mosquitoes infected with modified versions of *Plasmodium falciparum*, one of the parasites that cause the disease. The parasites are genetically engineered to stop developing around six days after they enter the body, during a crucial phase of infection where they replicate in liver cells. In the trial, almost 90% of participants exposed to the modified parasites avoided contracting the disease after being bitten by malaria-transmitting mosquitoes.

Nature | https://doi.org/10.1038/d41586-024-03817-0

Reference: *New England Journal of Medicine* paper

Lamers, O. A. C. *et al* (2024) New England Journal of Medicine **391**, 1913–1923

NEWS | 20 November 2024

This malaria vaccine is delivered by a mosquito bite

Bites from insects infected with modified malaria parasites boosted immunity and stopped people from contracting the disease.

By Helena Kudiabor

https://doi.org/10.1038/d41586-024-03817-0

https://www.nejm.org/doi/pdf/10.1056/NEJMoa2313892

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Safety and Efficacy of Immunization with a Late-Liver-Stage Attenuated Malaria Parasite

O.A.C. Lamers, B.M.D. Franke-Fayard, J.P.R. Koopman, G.V.T. Roozen, J.J. Janse, S.C. Chevalley-Maurel, F.J.A. Geurten, H.M. de Bes-Roeleveld, E. Iliopoulou, E. Colstrup, E. Wessels, G.-J. van Gemert, M. van de Vegte-Bolmer, W. Graumans, T.R. Stoter, B.G. Mordmüller, E.L. Houlder, T. Bousema, R. Murugan, M.B.B. McCall, C.J. Janse, and M. Roestenberg

ABSTRACT

BACKGROUND

Currently licensed and approved malaria subunit vaccines provide modest, short-lived protection against malaria. Immunization with live-attenuated *Plasmodium falciparum* malaria parasites is an alternative vaccination strategy that has potential to improve protection.

Lamers OAC, Franke-Fayard BMD, Koopman JPR, Roozen GVT, Janse JJ, Chevalley-Maurel SC, Geurten FJA, de Bes-Roeleveld HM, Iliopoulou E, Colstrup E, Wessels E, van Gemert GJ, van de Vegte-Bolmer M, Graumans W, Stoter TR, Mordmüller BG, Houlder EL, Bousema T, Murugan R, McCall MBB, Janse CJ, Roestenberg M. (2024) Safety and Efficacy of Immunization with a Late-Liver-Stage Attenuated Malaria Parasite. N Engl J Med. 2024 Nov 21;391(20):1913-1923. doi: 10.1056/NEJMoa2313892.

GENETICS

Gene drive mosquitoes can aid malaria elimination by retarding *Plasmodium* sporogonic development

Astrid Hoermann[1]†, Tibebu Habtewold[1]†, Prashanth Selvaraj[2], Giuseppe Del Corsano[1], Paolo Capriotti[1], Maria Grazia Inghilterra[1], Temesgen M. Kebede[1], George K. Christophides[1]*, Nikolai Windbichler[1]*

Gene drives hold promise for the genetic control of malaria vectors. The development of vector population modification strategies hinges on the availability of effector mechanisms impeding parasite development in transgenic mosquitoes. We augmented a midgut gene of the malaria mosquito *Anopheles gambiae* to secrete two exogenous antimicrobial peptides, magainin 2 and melittin. This small genetic modification, capable of efficient nonautonomous gene drive, hampers oocyst development in both *Plasmodium falciparum* and *Plasmodium berghei*. It delays the release of infectious sporozoites, while it simultaneously reduces the life span of homozygous female transgenic mosquitoes. Modeling the spread of this modification using a large-scale agent-based model of malaria epidemiology reveals that it can break the cycle of disease transmission across a range of transmission intensities.

https://www.science.org/doi/epdf/10.1126/sciadv.abo1733

Hoermann A, Habtewold T, Selvaraj P, Del Corsano G, Capriotti P, Inghilterra MG, Kebede TM, Christophides GK, Windbichler N. (2022) Gene drive mosquitoes can aid malaria elimination by retarding *Plasmodium* sporogonic development. Sci Adv. 2022 Sep 23; 8(38):eabo1733. doi: 10.1126/sciadv.abo1733. Epub 2022 Sep 21. PMID: 36129981.

Insect vectors which transmit microbes to human hosts, are, therefore, Nature's mechanism for cross-kingdom "infection". In a biomimicry approach, it may be possible to apply a "reverse" design. Could we use Nature's mechanism to "infect" people with vectors (mosquitoes) carrying antigens and virus-like particles (VLPs)? If we leave aside ethical, legal and societal issues from *pre-planned* mosquito bite, this natural biomimicry (***insects as immunization delivery platform***) may be the Holy Grail for low-cost immunization delivery for billions of people who cannot afford infrastructure costs associated with the "last mile" delivery which continues to pose insurmountable problems for vaccination programs.

Genetic engineering of viruses which infect *Anopheles*[732] and *Aedes*[733] mosquitoes are the targets for development of vectors to shuttle antigens and for creating virus-like particles for specific viruses, for example, Ebola, SARS-CoV-2, and others. Targets for genetic modification may include re-engineering tissue-specific regulation of the small interfering RNA (siRNA) pathway controlled by the double stranded (ds) RNA binding protein Loqs2[734] (and its genetic circuit) which appears to be specific to *Aedes aegypti* mosquito. Are there Loqs2 equivalents or similar pathways in other mosquitoes?

Source: Page 86 from Datta, Shoumen *et al* (2020) *Aptamers for Detection and Diagnostics (ADD): Can mobile systems process optical data from aptamer sensors to identify molecules indicating presence of SARS-CoV-2 virus? Should healthcare explore aptamers as drugs for prevention as well as its use as adjuvants with antibodies and vaccines?*

ChemRxiv Preprint server https://chemrxiv.org/engage/chemrxiv/article-details/617c108926b9c744380acf48

PDF in MIT Library https://dspace.mit.edu/handle/1721.1/128017 (Questions? shoumen@mit.edu / sdatta8@mgh.harvard.edu)

ENGINEERED MOSQUITO - A PROVEN IDEA WHICH WORKS ?

NEWS | 14 April 2023

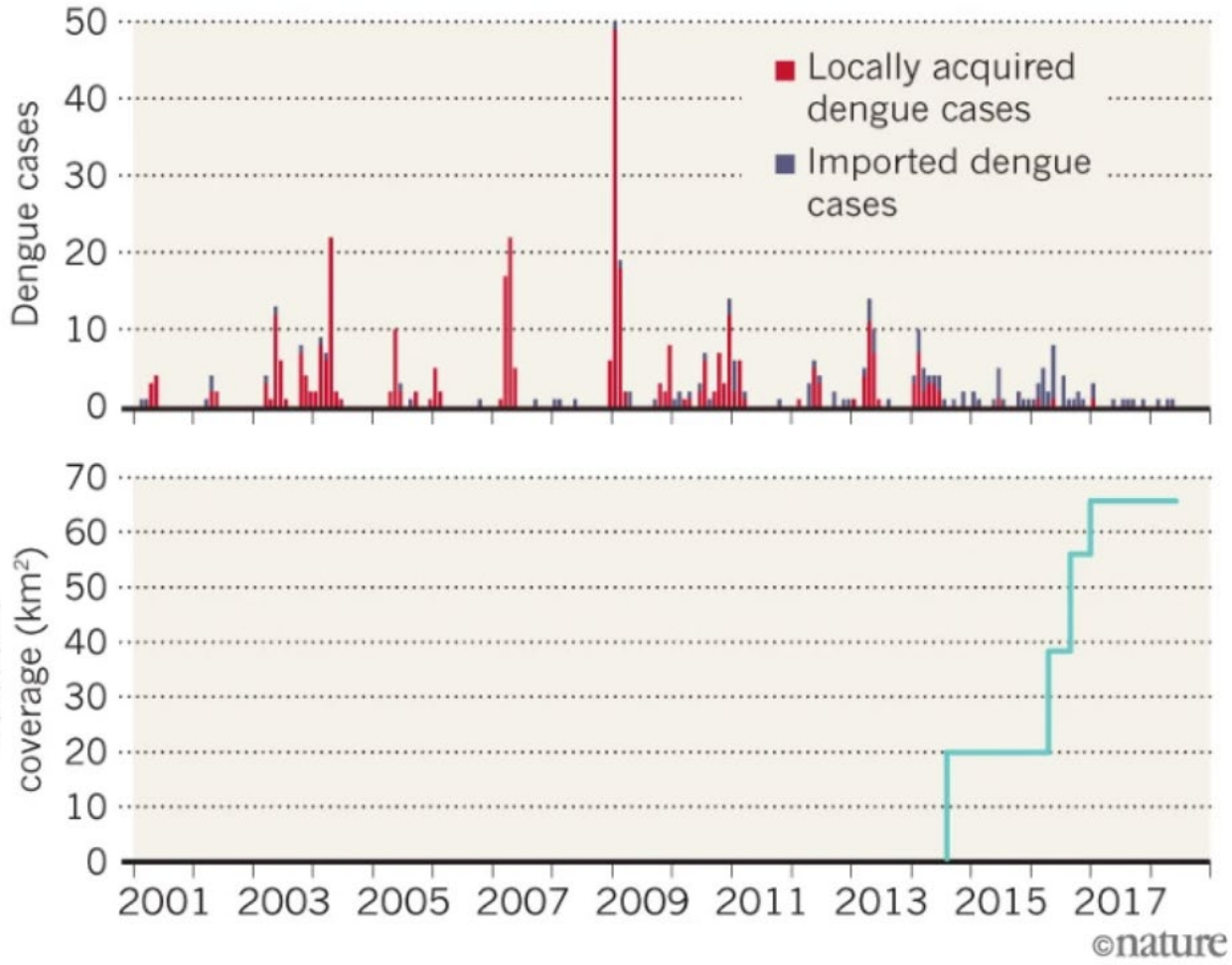
Massive mosquito factory in Brazil aims to halt dengue

Facility will produce up to five billion bacteria-infected mosquitoes per year.

"This is not a silver bullet." ▪ DOI: https://doi.org/10.1038/d41586-023-01266-9

In a series of releases starting in late 2014, 4 million mosquitoes carrying *Wolbachia* bacteria were deployed across Townsville in Australia. The graph below shows the insects taking root in the central suburb of Belgian Gardens.

After the mosquito releases, locally acquired cases of dengue plummeted.



Source: S. L. O'Neill *et al. Gates Open Res.* **2**, 36 (2018)

O'Neill SL, Ryan PA, Turley AP, Wilson G, Retzki K, Iturbe-Ormaetxe I, Dong Y, Kenny N, Paton CJ, Ritchie SA, Brown-Kenyon J, Stanford D, Wittmeier N, Jewell NP, Tanamas SK, Anders KL, Simmons CP. (2019) Scaled deployment of *Wolbachia* to protect the community from dengue and other *Aedes* transmitted arboviruses. Gates Open Res. 2019 August 13;2:36. doi: 10.12688/gatesopenres.12844.3. PMID: 30596205; PMCID: PMC6305154.

https://gatesopenresearch.s3.eu-west-1.amazonaws.com/manuscripts/13925/0023d8fa-921a-4421-8641-862269a2b36d_12844_-_scott_oneill.pdf

ENGINEERED MOSQUITO: ANOTHER PROVEN IDEA WHICH WORKS

Hawaii's birds are going extinct. Their last hope could be millions of mosquitoes

JUNE 12, 2024 · 5:00 AM ET

- Conservationists have launched an ambitious project to slow the spread by mosquitoes of avian malaria in Hawaii. They have so far released 10 million male *Aedes aegypti* mosquitoes infected with a strain of Wolbachia, a naturally occurring bacterium that disrupts mozzie reproduction. The region's birds, which have no natural immunity to avian malaria, can be killed with a single bite from an infected mosquito. The Wolbachia intervention is controversial, pricey and must be relentlessly repeated for any hope of working.

www.npr.org/2024/06/12/nx-s1-4906582/mosquito-hawaii-birds-endangered-species-extinct

“BITE” – CONTRACTILE INJECTION SYSTEM ?

Programmable protein delivery with a bacterial contractile injection system

https://doi.org/10.1038/s41586-023-05870-7

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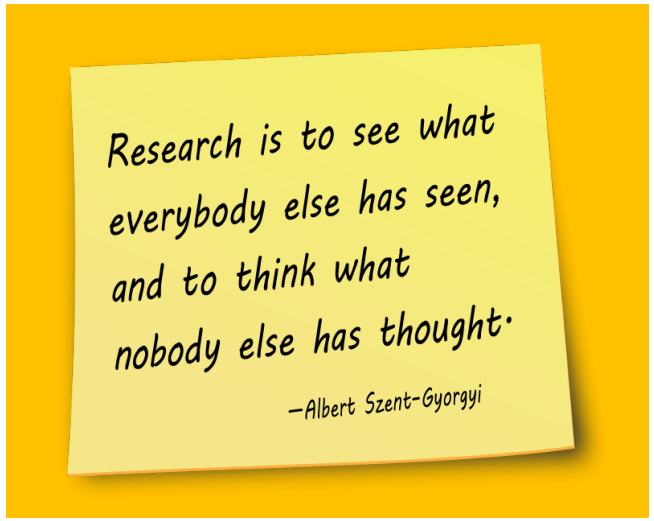
Accepted: 21 February 2023

Joseph Kreitz[1,2,3,4,5], Mirco J. Friedrich[1,2,3,4,5], Akash Guru[1,2,3,4,5], Blake Lash[1,2,3,4,5], Makoto Saito[1,2,3,4,5], Rhiannon K. Macrae[1,2,3,4,5] & Feng Zhang[1,2,3,4,5]✉

Endosymbiotic bacteria have evolved intricate delivery systems that enable these organisms to interface with host biology. One example, the extracellular contractile injection systems (eCISs), are syringe-like macromolecular complexes that inject protein payloads into eukaryotic cells by driving a spike through the cellular membrane. Photorhabdus virulence cassette (PVC)—an eCIS from the entomopathogenic bacterium Photorhabdus asymbiotica—is mediated by specific recognition of a target receptor by a distal binding element of the PVC. PVC can be reprogrammed to target organisms not natively targeted by these systems—including human cells and mice—with efficiencies approaching 100%. PVCs can load diverse protein payloads, including Cas9, base editors and toxins, and can functionally deliver them into human cells. Therefore, PVCs are programmable protein delivery devices with applications in gene therapy, cancer therapy and biocontrol.



Shoumen Palit Austin Datta, Massachusetts General Hospital, Harvard Medical School and Department of Mechanical Engineering, Massachusetts Institute of Technology

Last updated on 10/09/2023

https://web.mit.edu/search/?q=Shoumen+Datta

DEDICATION

TRACING HISTORICAL ROOTS

Rowing Mom Wins Nobel

Submitted by: Susan Francia
(October 3, 2023)

Longtime rowing mom Dr. Katalin Kariko won the Nobel Prize for Medicine, achieved during a time she sent in Photos of the Day to row2k over the years, really impressive. row2k asked Susan for a photo of the family at a rowing race, and she sent this one taken by her aunt, along with the following note.

https://www.nobelprize.org/prizes/medicine/2023/kariko/interview/

Dr. Katalin Karikó receiving call from Sweden at her home on Oct 2, 2023

@kkariko @zfrancia

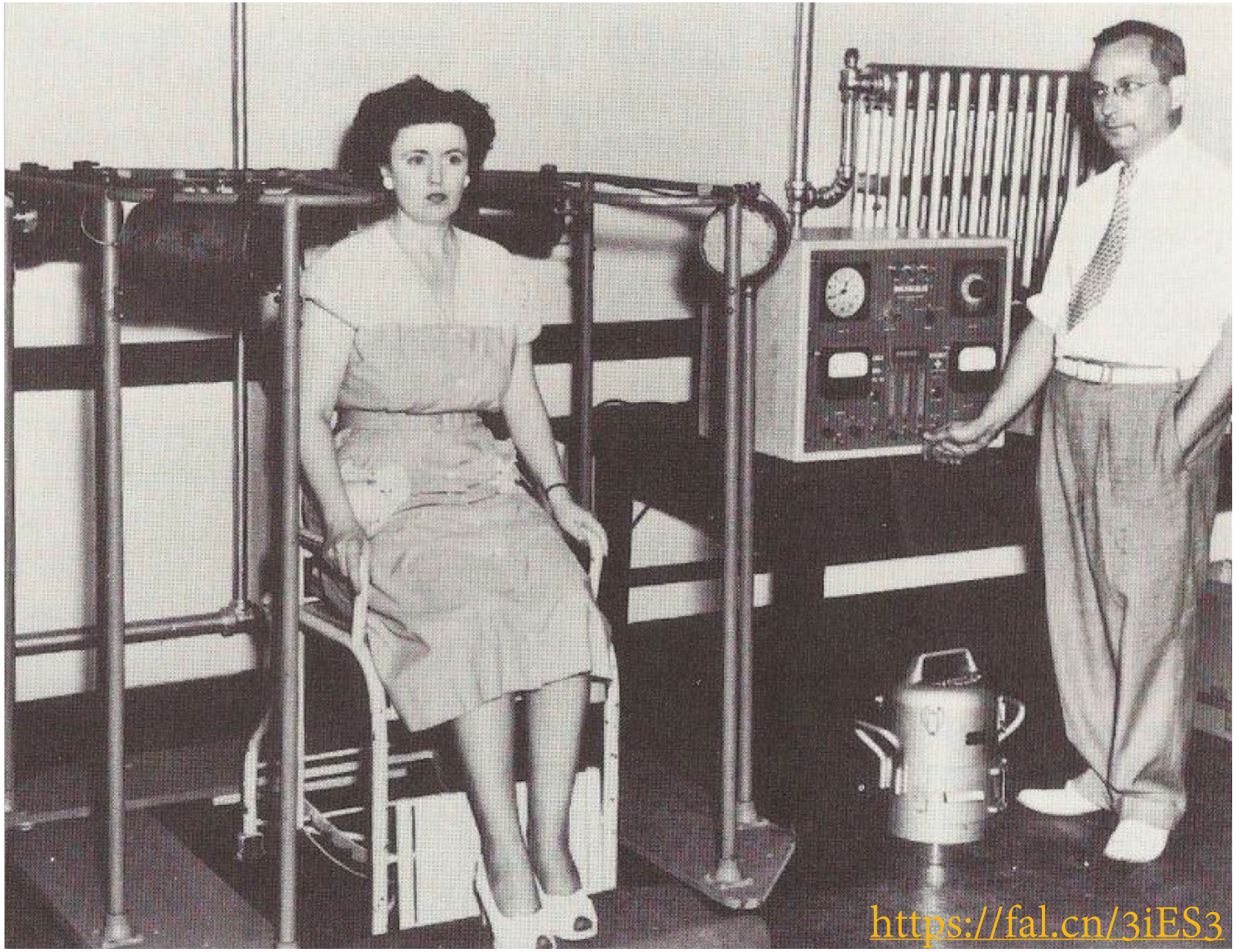
https://www.nobelprize.org/prizes/medicine/2023/summary/

The Nobel Prize in Physiology Medicine 2023

Ill. Niklas Elmehed © Nobel Prize Outreach
Katalin Karikó
Prize share: 1/2

Ill. Niklas Elmehed © Nobel Prize Outreach
Drew Weissman
Prize share: 1/2

(Basement) Bulfinch Building, Massachusetts General Hospital (MGH), 55 Fruit Street, Boston, Massachusetts 02114



https://fal.cn/3iES3

In 1937, MGH Thyroid Clinic director Saul Hertz, MD, teamed up with (MIT) Massachusetts Institute of Technology physicists to develop an early medical application of radiation. Hertz was testing his theory that iodine could deliver radiation to treat thyroid cancer, Graves' disease and goiter. The thyroid, a small gland in the neck, uses the nutrient iodine in making hormones that contribute to organ function and metabolism. When a patient drinks radioactive iodine it collects in the thyroid, destroying problem tissue without affecting neighboring organs. In this image from the 1940s, Hertz tests how much radiation his subject (colleague Doris Darby) absorbed when using radioiodine as a tracer. The radio-iodine was prepared by Glenn Seaborg at the Radiation Lab, UC Berkeley.

1989 • Thyroid Lab & Neuroendocrine Unit, Bulfinch Basement, Massachusetts General Hospital

https://www.med.upenn.edu/evpdean/jameson.html

J. Larry Jameson

Anne Klibanski

www.massgeneralbrigham.org/en/about/leadership-and-governance/anne-klibanski

1989 • (Department of Medicine) Massachusetts General Hospital, Harvard Medical School

University of Pennsylvania Almanac

A Message from Interim President J. Larry Jameson

DECEMBER 19, 2023 | **NEWS** | **PRINT**

To the Penn Community,

J. Larry Jameson

I am honored that the Board of Trustees has asked me to serve as Penn's Interim President. I accept this responsibility clear-eyed about the challenges facing our University.

Like you, I love Penn.

I have dedicated many years of my life to this amazing institution. I have been honored to serve as Executive Vice President of our health system and Dean of the Raymond and Ruth Perelman School of Medicine for more than 12 years.

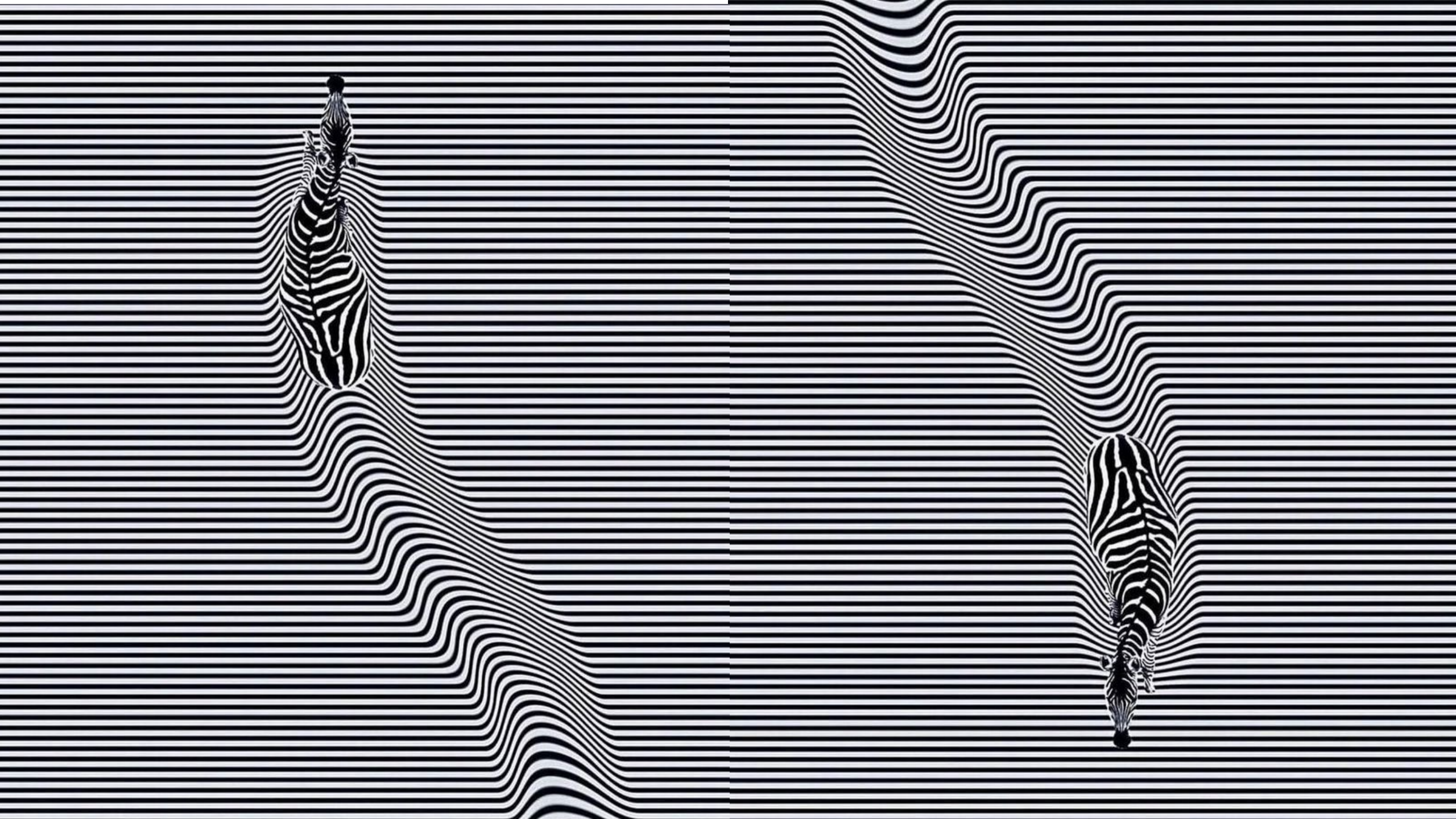
I know many of you but certainly not all. In the coming weeks and months, I look forward, with curiosity and an open mind, to learning from you and to sharing my own views with you. I am trained as a physician—healing is in my nature and skill set. I also trained as a scientist—hard-wired to ask challenging questions, pursue rigorous inquiry and debate, and ready to be proven wrong. I am a Penn parent, and I have had the pleasure of watching incredible students grow, explore their passions, and chart a path to make an impact on the world. My leadership role at Penn has exposed me to its unparalleled breadth of expertise and diversity of thought. It is humbling but invigorating to consider how I, and other leaders at Penn, can support each of you.

The last few weeks have been a profoundly painful chapter for our institution, for higher education, and for the world. I know these recent leadership transitions have been distressing and destabilizing. I feel it myself. There is pain, fear, and uncertainty in our community. I want to reiterate that every person at Penn should feel safe and be secure in the knowledge that hate has no home here. This is fundamental, but it is not enough.

wbur.org/news/2019/06/26/anne-klibanski-partners-healthcare-ceo

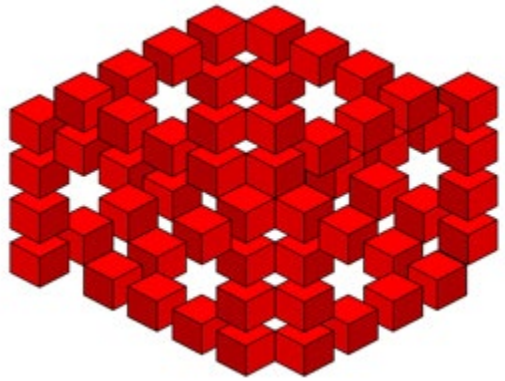
Dr. Anne Klibanski Is First Woman To Lead Partners HealthCare

June 26, 2019 | By Carey Goldberg



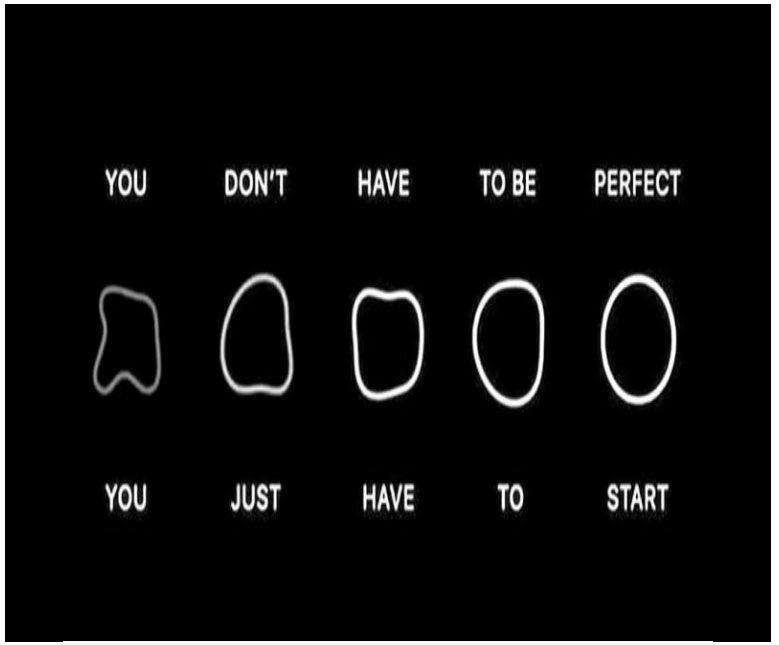
This document is "The Health of Nations – Part I"

"The Health of Nations" – Part II – is in the MIT Library https://dspace.mit.edu/handle/1721.1/152921



I HAVE CREATED NOTHING NEW

 SHOUMEN@MIT.EDU ▪ SDATTA8@MGH.HARVARD.EDU



Shoumen Palit Austin Datta

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(shoumen@mit.edu) https://autoid.mit.edu/shoumen-datta ▪ http://autoid.mit.edu/people-2

Plant-based Oral Vaccine (POV)

AMAT VICTORIA CURAM

DRAFT

TABLE OF CONTENTS PAGE(S)

RE-VIEW / RE-PRESENT / RE-DISCOVER / RE-EVALUATE / RE-SEARCH

Bio-Engineered Plant-produced Antigens, Self-Administered for Oral Vaccination: A Cottage Industry for Vaccines for Less Affluent Nations?

Shoumen Palit Austin Datta

MIT Auto-ID Labs, Department of Mechanical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, Massachusetts 02139, USA (shoumen@mit.edu)
MDPnP Lab, Cybersecurity Program and Center for Smart and Autonomous Medical Systems, Department of Anesthesiology, Massachusetts General Hospital, Mass General Brigham, Harvard Medical School, Research Building, 65 Landsdowne Street, Cambridge, Massachusetts 02139, USA (sdatta8@mgh.harvard.edu)

ABSTRACT

In this unconventional and non-systematic re-view, we re-present published results indicating that transgenic plants engineered to express (foreign) antigens show significant levels of mRNA (from viral coding region) and viral antigen (protein) in plant tissues (leaves). Oral administration of plant-produced antigens were immuno-stimulatory in humans, capable of conferring immunity from the viral infection (specific for the viral antigen bioengineered for expression in plant). Use of antigen-containing plant products for oral (or sublingual) administration does not require purification. The plant "paste" may be sufficient (?) for immunizing humans (and animals). Scientific evidence supports advocacy for oral administration of "raw" plant-based products (sublingual) without purification. Implementing this proposal may accelerate the pace of global vaccination and preventive healthcare for less affluent communities by [0] eliminating the need for purification,[1] eliminating the need for "cold" supply chain logistics, [2] eliminating the dependency on medical professionals for vaccination and [3] eliminating supply chain fulfillment dependencies by growing the antigen-producing "potted plants" in community gardens or at home, as a vaccine cottage industry. Communities may also brew the cottage industry for transgenic plants producing antigens as an entrepreneurial innovation endeavor and/or social business for vaccines. The latter, if built on pillars of ethical profitability, is expected to prioritize science as a service to society to improve access to global public goods with respect to health and healthcare.

The only thing necessary for the triumph of anti-science is for scientists to do nothing.