

World Chagas Disease Day 2023

Oswaldo Cruz, Carlos Chagas and
American Trypanosomiasis:
The long road to a medical breakthrough

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Consulate General of Brazil in Los Angeles

Think of a truly great Brazilian team...



True, but here are some players from another one



Adolpho Lutz

(1855-1940),
pioneer of tropical
medicine,
epidemiologist,
entomologist



Emílio Ribas

(1862-1925),
epidemiologist,
public health
officer



Vital Brazil

(1865-1950),
immunologist,
creator of
antivenom, anti-
spider and anti-
scorpion serums



Oswaldo Cruz

(1872-1917),
bacteriologist,
epidemiologist,
public health
officer, founder of
Fiocruz



Carlos Chagas

(1879-1934),
today's hero (along
with Cruz)

*In the last decades of the 19th C and first decades of the 20th, Brazil was home to an unprecedented number of **medical talents of the highest order**, some having studied abroad, some following developments from afar. They sparked a **revolution in public health** in Brazil, and their legacy is felt to this day.*

The 19th century: medicine transformed

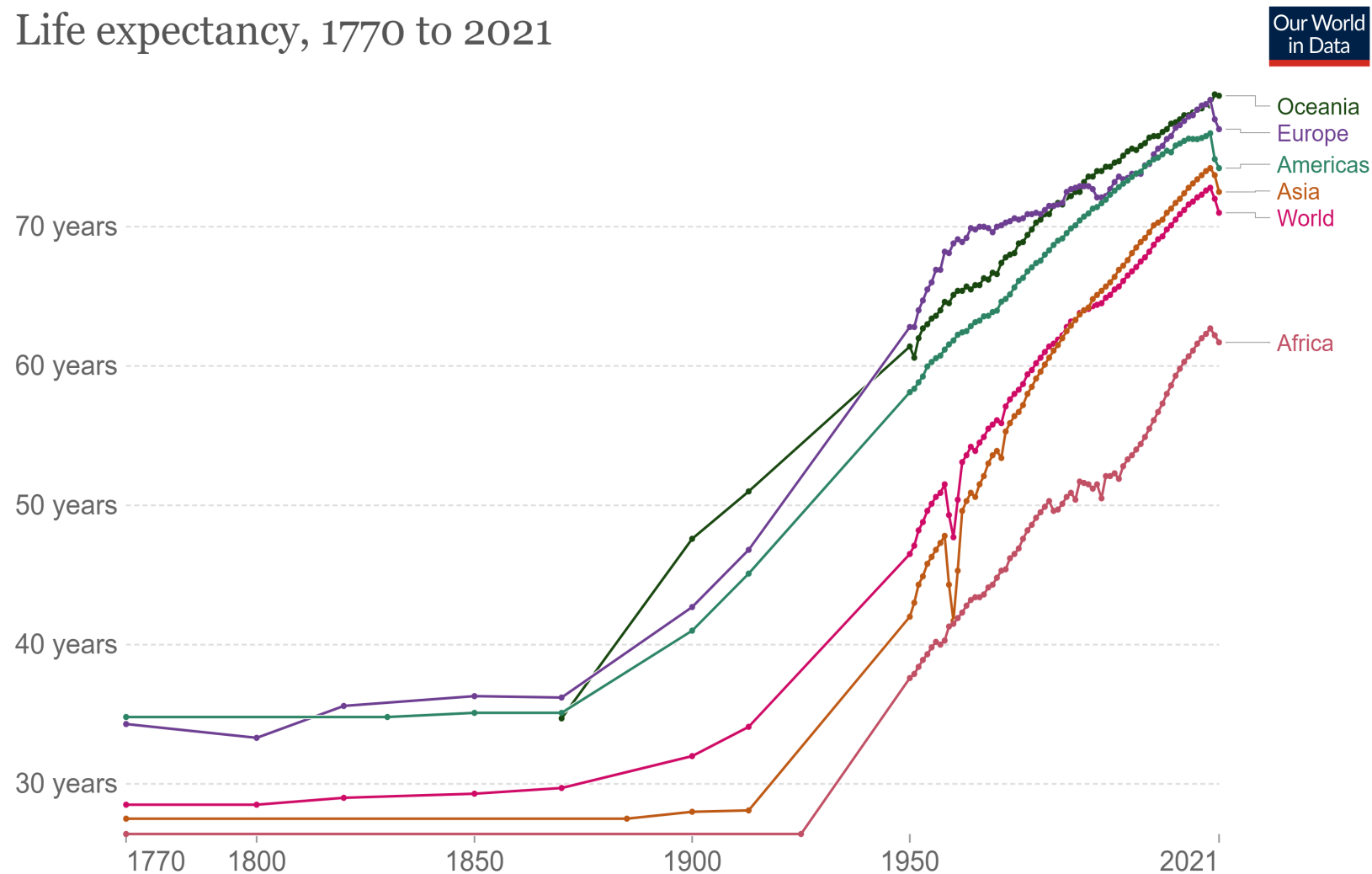
- **Jenner** defeats smallpox (1796) with vaccine (lat. *vacca*, cow)
- **Semmelweis** reduces childhood fever deaths by requiring hand sanitizing
- **Pasteur**: germ theory, pasteurization, anthrax and rabies vaccines
- **Lister**: antiseptic surgery, prophylaxis
- **Koch**: germ theory, identifies TB bacillus, microphotography
- **Microbiology** and **bacteriology** (Germany, France)
- **Mosquito-malaria theory** (Britain, Italy)
- **Institut Pasteur** founded in Paris (1887): Brazil's emperor a big donor



The impact on life expectancy

Region	1800	1850	1900
Oceania	-	-	47.6
Europe	33.3	36.3	42.7
Americas	-	35.1	41.0
Asia	-	-	28.0
Africa	-	-	
World	28.5	29.3	32.0

Life expectancy, 1770 to 2021



Source: UN WPP (2022); Zijdemann et al. (2015); Riley (2005)

Note: Shown is the 'period life expectancy'. This is the average number of years a newborn would live if age-specific mortality rates in the current year were to stay the same throughout its life.

OurWorldInData.org/life-expectancy • CC BY

Imperialism, war, and their silver lining

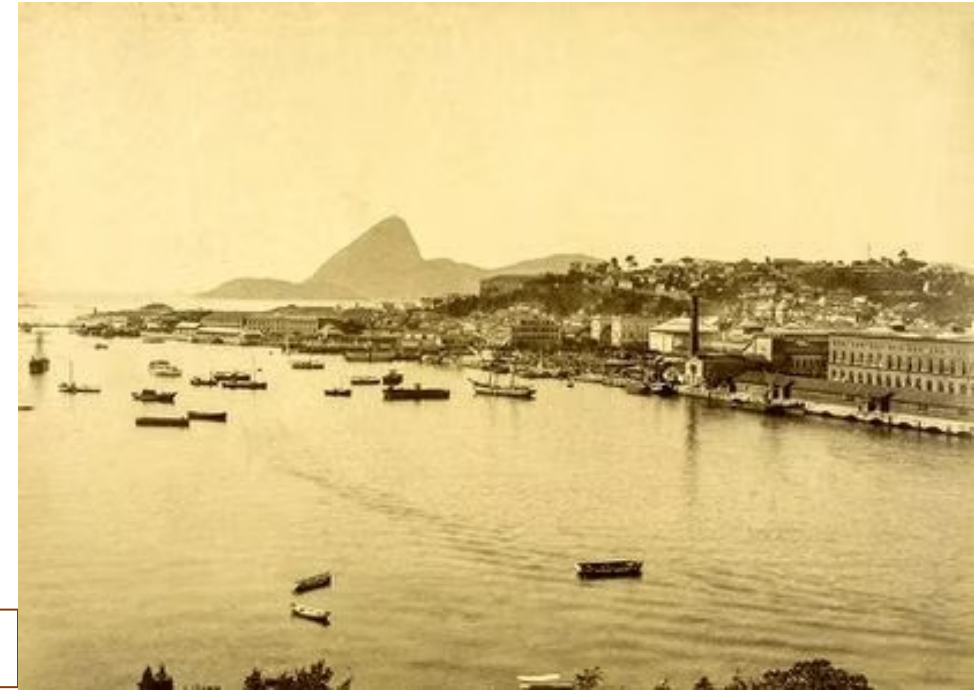
- ❖ Large parts of Africa, Asia, and Oceania come under European control
- ❖ Local diseases, incl. **African trypanosomiasis** (sleeping sickness)
- ❖ Prevent colonization, exploitation
- ❖ **Yersin** in SE Asia isolates bubonic plague bacterium, develops serum, identifies rats as carriers
- ❖ **Simond**: rat fleas transmit *Yersinia pestis* bacterium
- ❖ 1898-1900: **Tropical medicine institutes** in Liverpool, London, Hamburg
- ❖ Spanish-American War: **Walter Reed** Commission in Cuba
- ❖ Kills *Aedes aegypti* mosquitoes, disproves need for disinfection
→ **yellow fever** eliminated

Carlos Finlay, author of mosquito theory for yellow fever



Public health in 19th-century Brazil

- ✓ 1808: Portuguese royal family arrives, first two **colleges of medicine** (Salvador, Rio)
- ✓ King D. John VI lost son, two brothers to smallpox → **vaccination mandatory** for everyone, “regardless of color”
- ✓ **Yellow fever** arrives 1849-50: 4000 out of 200,000 dead in Rio
- ✓ Growth of **cities**: cholera, typhus, yellow fever, TB
- ✓ Public **sanitation insufficient**
- ✓ Even less attention to **provincial Brazil**
- ✓ **Bahian Tropicalist School** (1860-1890): focus on tropical diseases, poor population, no “*blind reproduction of European medical knowledge*”



Rio in the 19th century (Photo by Marc Ferrez)



Scenes of Rio in the 19th century, by Frenchman Jean-Baptiste Debret (l.) and Prussian Henrique Fleiuss

São Paulo, laboratory for new approaches

- **Immigrants** are needed for **coffee** production, but fear unhealthy environment
- 1891 U.S.-inspired **federalist Constitution**: public health under **states' responsibility**
- **Rodrigues Alves**, 3-time governor, loses daughter to typhus, support **public health** initiatives
- **Santos harbor** → smallpox, yellow fever (1889-1895), bubonic plague (1899)
- **Adolpho Lutz**: new diagnostic techniques, treatments, directs **Bacteriological Institute** for 15 years (now **Instituto Adolfo Lutz**)
- **Emílio Ribas**: successful strategy against epidemics, replicates Havana experiments on yellow fever, heads **Public Health Department** for 20 years
- **Vital Brazil**: antivenom, anti-scorpion, anti-spider serums, founds **Butantan Institute**
- **Oswaldo Cruz** cuts his teeth in fight against 1899 **bubonic plague** in Santos



Rodrigues Alves (1848-1919)

“It’s (also) the economy, stupid!”



Late 19th century: **coffee** represents 2/3 of Brazil's total exports, produced mainly in **São Paulo**, shipped mainly through **Santos**

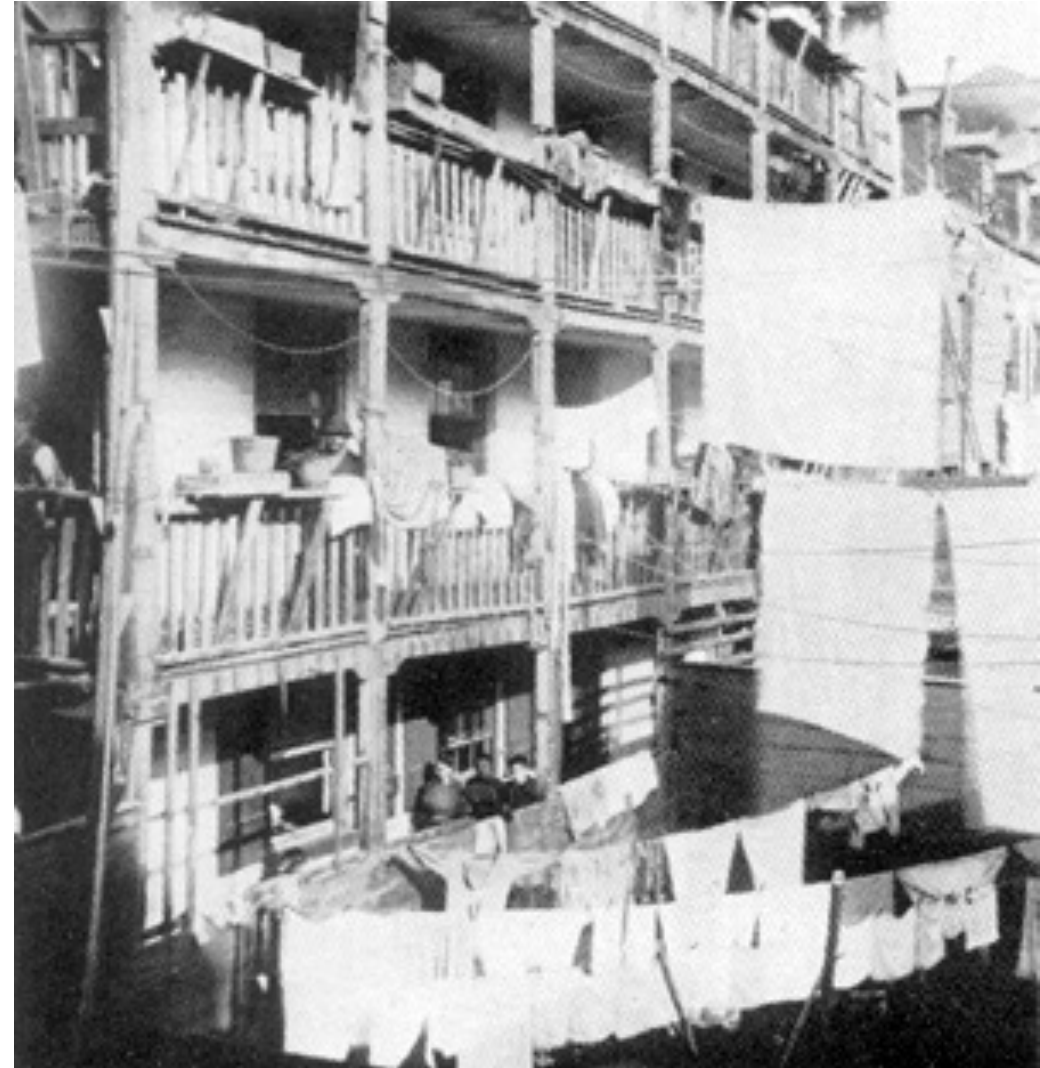
Brazil in 1900

- 3.3 mi sq miles (8.5 mi sq km)
- Population 17 million, 11 million rural (two thirds)
- Life expectancy: 33.4 years (U.S. 47.3)
- Literacy: 35%
- 1890: 6.3 million whites, 5.9 m. mixed race, 2.0 m. blacks
- Immigrants: Italy, Germany, Portugal, Spain...
- No mention of indigenous peoples
- Agricultural country: coffee, rubber, sugar



Meanwhile, in the not yet “marvelous city”...

- ✓ **Rio de Janeiro**, founded 1565, capital 1763
- ✓ **Slavery abolished** 1888, former slaves flock to capital
- ✓ Population explosion: 275,000 (1872), 811,000 (1900)
- ✓ Poor population living in **crowded tenements**
- ✓ **Bubonic plague** arrives in 1899
- ✓ **Yellow fever** since 1849
- ✓ **Smallpox** first mentioned in 1561
- ✓ Elites, government summer in Petropolis
- ✓ Travelers, immigrants **shun Brazil**



A tenement in Rio, late 19th century

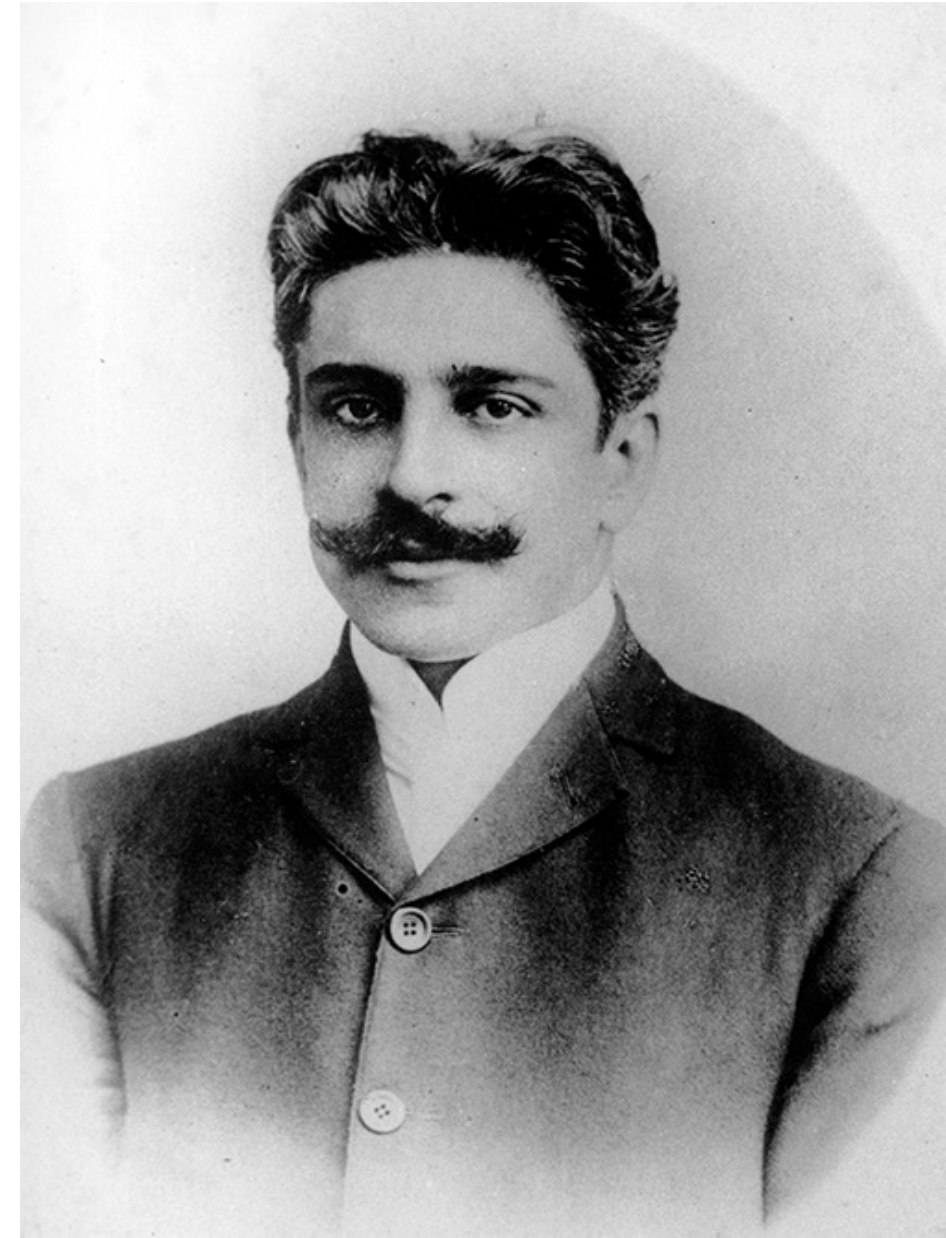


Oswaldo Cruz takes charge

- **Rodrigues Alves** President 1902-1906
- Top priorities: **sanitize and remodel Rio**, expand railroads
- Oswaldo Cruz recommended by **Émile Roux**, director of *Institut Pasteur*
- Experienced but **little known** at time of nomination
- Cruz as Director General of Public Health: *"I demand **full powers and resources**"*
- President: *"**Go ahead**. I lost a daughter and don't wish this pain to anyone"*

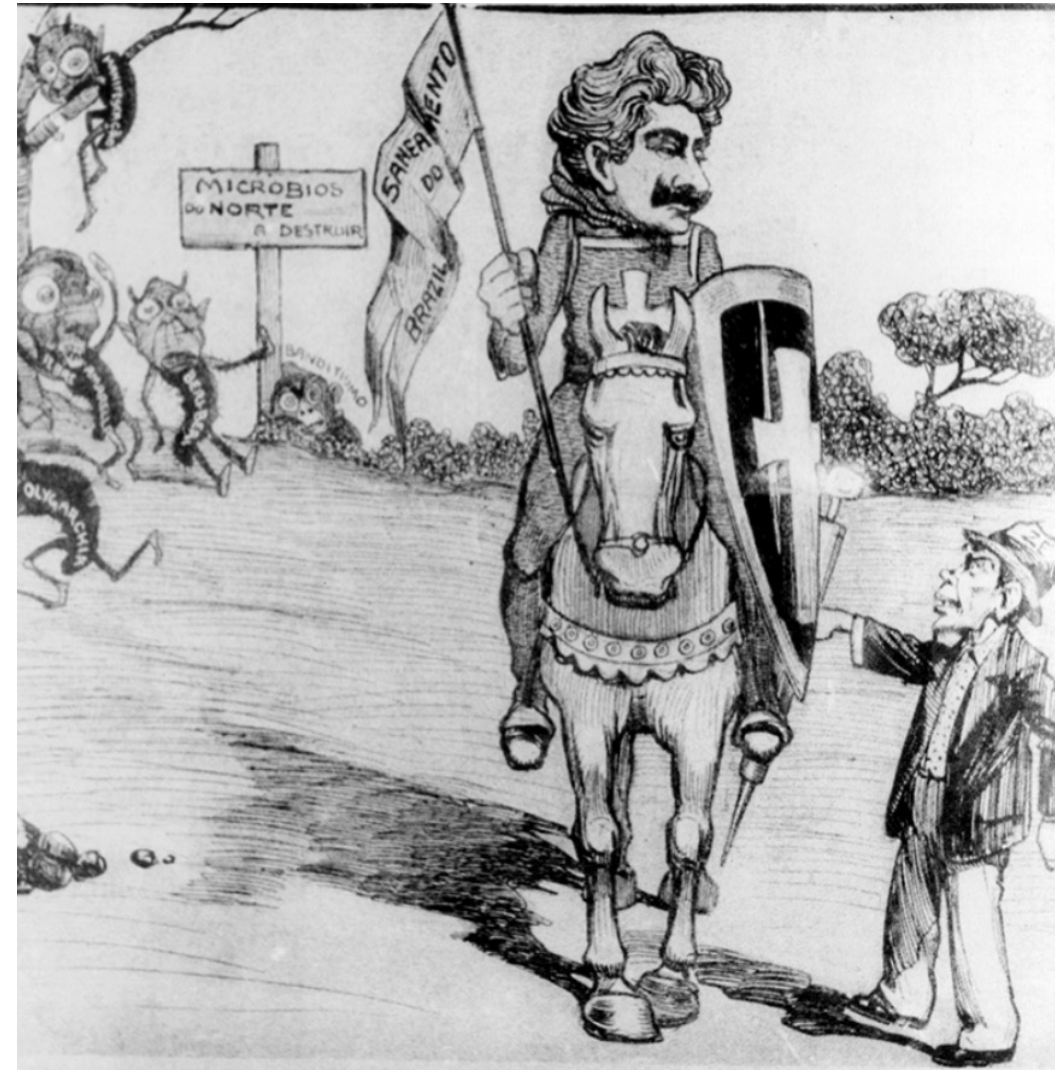
“Who is this Oswaldo Cruz, anyway?”

- Born 1872, 30 years old at time of nomination
- Enters medical school at 15, graduates at 20 with dissertation about **microbiology**
- Part of group of **Germanists**, following latest developments in German science
- Studies 1897-1899 with Roux at **Pasteur**: microbiology, serotherapy, immunology (first Brazilian there)
- 1899 in **Santos harbor**: shows that bubonic plague cannot be brought under control without **serum**
- 1900: Directs **Federal Serotherapy Institute**, created at his recommendation
- Motto: *“Thue recht und scheue niemand”* (**Do the right thing and fear no one**)
- **No compromise** with disproved theories



Oswaldo Cruz's three-pronged approach

- ❖ Cruz was fully aware of latest international medical discoveries
- ❖ **Bubonic plague** → kill/buy rats, improve sanitation, provide serum (based on Lutz, Vital Brazil in Santos in 1899)
- ❖ **Yellow fever** → eliminate larvae, stagnant waters, fumigate everywhere, NO to disinfection (follow Havana protocol)
- ❖ **Smallpox** → mandatory vaccination (inspired in successful German Empire legislation of 1874)



Banner reads: "Sanitation in Brazil"

A fourth “enemy”: public opinion

- Swindlers **breed rats** to sell to sanitary authorities
- **Truculence** (fumigation, breaking into homes, vaccination)
- Husbands/parents to allow wives and daughters to show **naked arms**?
- **Knock-it-down**: massive evictions cause anger
- **Illiterate population**: campaigns to raise awareness have little impact



A AUTHENTICIDADE DOS RATOS

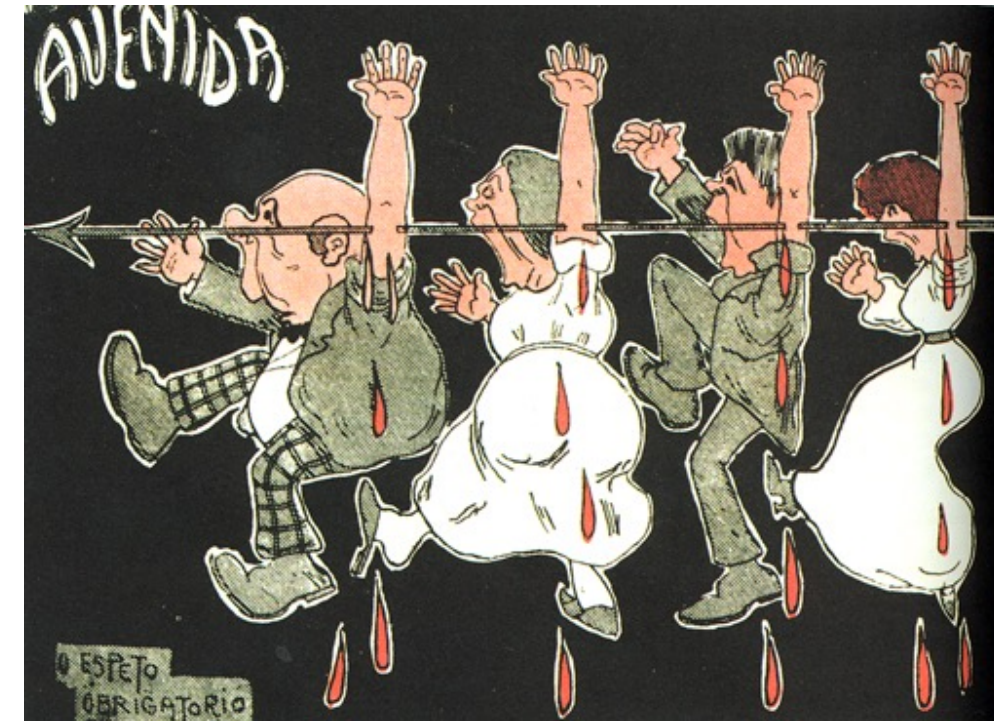


The vaccine revolt

- ❑ 1904: almost 6000 cases of smallpox
- ❑ November: **vaccination mandatory**
- ❑ Population rises in **revolt**, supported by opposition, military rebels
- ❑ Rodrigues Alves declares **state of siege**, refuses to fire Cruz
- ❑ After 10 days: c. 30 dead, 100 wounded, 1000 arrested (500 deported to Amazon)
- ❑ Obligation revoked, but **proof of vaccination** often needed
- ❑ Slow progress, full eradication only in **1970s**



Tram overturned by protesters



“Rio becomes civilized”

- ❑ Tenements demolished, downtown rebuilt
- ❑ Sanitary conditions dramatically improved
- ❑ **Yellow fever** drops from 584 cases in 1903 to 0 in 1909
- ❑ **Bubonic plague** virtually eliminated: 360 deaths in 1903, 54 in 1908, 0 in 1912
- ❑ Steady decline in **smallpox cases** (3500 deaths in 1904, 9 in 1906), but occasional outbreaks
- ❑ New epidemic in 1908 (6500 deaths) → population spontaneously **requests vaccination**
- ❑ Eventually, success of vaccination in Rio (last outbreak 1926) fosters **pro-vaccine culture** countrywide



Hausmann-inspired *Avenida Central*



Oswaldo Cruz's legacy

- **Gold medal** in 14th Congress on Hygiene and Demography (Berlin, 1907) → official and public support
- Cruz always encouraged **hands-on training** and **solid academic studies** in his staff
- Federal Serotherapy Institute renamed **Oswaldo Cruz Institute** in 1908
- Example from *Institut Pasteur*: vaccines and medicines production, scientific research, public health activities
- Inspired in **Alhambra** and Berlin synagogue
- Ensuring **independent funding**
- Fiocruz led to major improvements in **public health** since its creation
- **Covid-19 pandemic**: selected by WHO as LatAm hub for mRNA vaccine production
- WHO, 2022: Fiocruz among world's 15 largest **vaccine producers**



Dr. Nísia Trindade Lima, Brazil's Minister of Health

- Former President of **Fiocruz** (2017-2023), first woman in this position (also first to lead Ministry of Health)
- Steered Foundation successfully during Covid-19 pandemic



Dr. Jarbas Barbosa da Silva, Director of Pan-American Health Organization (PAHO)

- Specialized in public health and epidemiology at **Fiocruz's** National School of Public Health

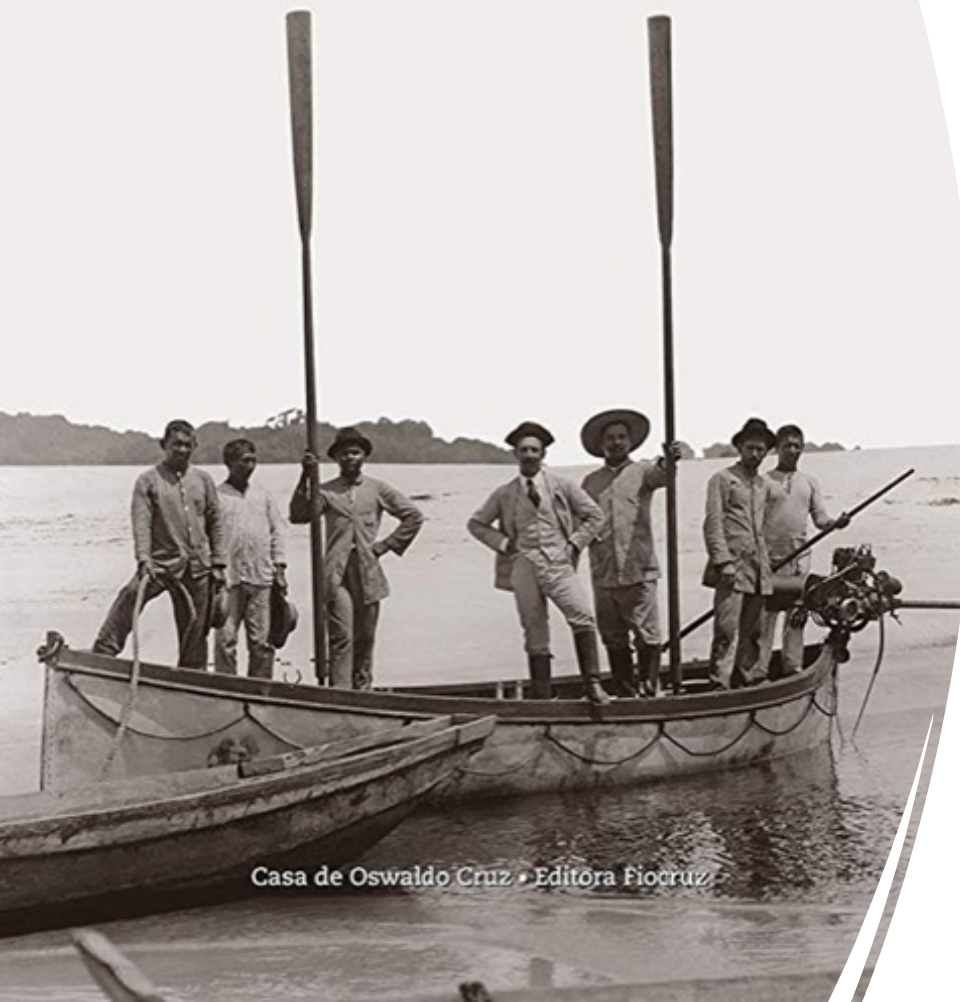


Dr. Pedro Albajar Viñas, Head of WHO's Global Chagas Disease Program

- Ph.D. in Tropical Medicine at **Fiocruz**

A ciência a caminho da roça:

imagens das expedições científicas do
Instituto Oswaldo Cruz ao interior do Brasil entre 1911 e 1913



Casa de Oswaldo Cruz • Editora Fiocruz

Beyond Rio de Janeiro

- ✓ With success in Rio, Cruz and team **expand coverage**
- ✓ 1905-06: inspect sanitary conditions in **30 Brazilian harbors**
- ✓ **State governments** and **private businesses** hire services
- ✓ 1906: first mission, to **Maranhão** (NE) against bubonic fever
- ✓ **Carlos Chagas** sent to remote areas of São Paulo and Rio, ends malaria outbreak affecting dam and aqueduct construction workers
- ✓ First antimalaria campaigns based on **recent science**
- ✓ 1907: Chagas sent to **Minas Gerais** to fight malaria outbreak preventing railroad expansion...

Carlos Chagas (1878-1934)



Young Carlos Chagas

- ✓ Born in a coffee plantation in Minas Gerais state
- ✓ 1897: flunks tests for engineering college, enrolls in **medical school**
- ✓ Learns about experimentation, tropical medicine
- ✓ For PhD dissertation about malaria, joins Federal Serotherapy Institute and is mentored by **Oswaldo Cruz**
- ✓ 1904: joins **General Directorate for Public Health**
- ✓ 1905-07: assigned sanitary missions inland to deal with **malaria outbreaks**
- ✓ Pioneering, successful contributions to fight against malaria
- ✓ These early successes seal his fate...

The *Trypanosoma cruzi*

- ❑ 1907: Cruz sends Chagas to **Lassance**, Minas Gerais to fight bout of malaria among railway workers
- ❑ Builds lab in **train wagon**, also researches animals, insects
- ❑ Finds **protozoan** in blood of marmosets: *Trypanosoma minasense*
- ❑ Railway engineer shows him insect that bites humans, often in the face → nicknamed **barber** (the “kissing bug”)
- ❑ In some of these, Chagas finds Trypanosoma-shaped **protozoan**
- ❑ Sends insects to lab in Rio → Cruz notices a lab monkey falls ill after insect bite
- ❑ Chagas realizes it is a new species of parasite, baptizes it ***Trypanosoma cruzi*** in honor of his mentor



American trypanosomiasis

- ◇ 1909: Chagas publishes about discovery in Germany
- ◇ Raises enormous interest: Europeans concerned about **African trypanosomiasis** (Sleeping sickness)
- ◇ Chagas returns to Lassance: research impact on humans
- ◇ 1909: After finding infected cat, identifies *T. cruzi* in blood of **Berenice**, a two-year-old girl
- ◇ Worldwide repercussion of discovery of **American trypanosomiasis**
- ◇ Soon baptized **Chagas Disease**
- ◇ Main attraction at Brazil's booth at **First International Hygiene Exhibition** (Dresden, 1911)

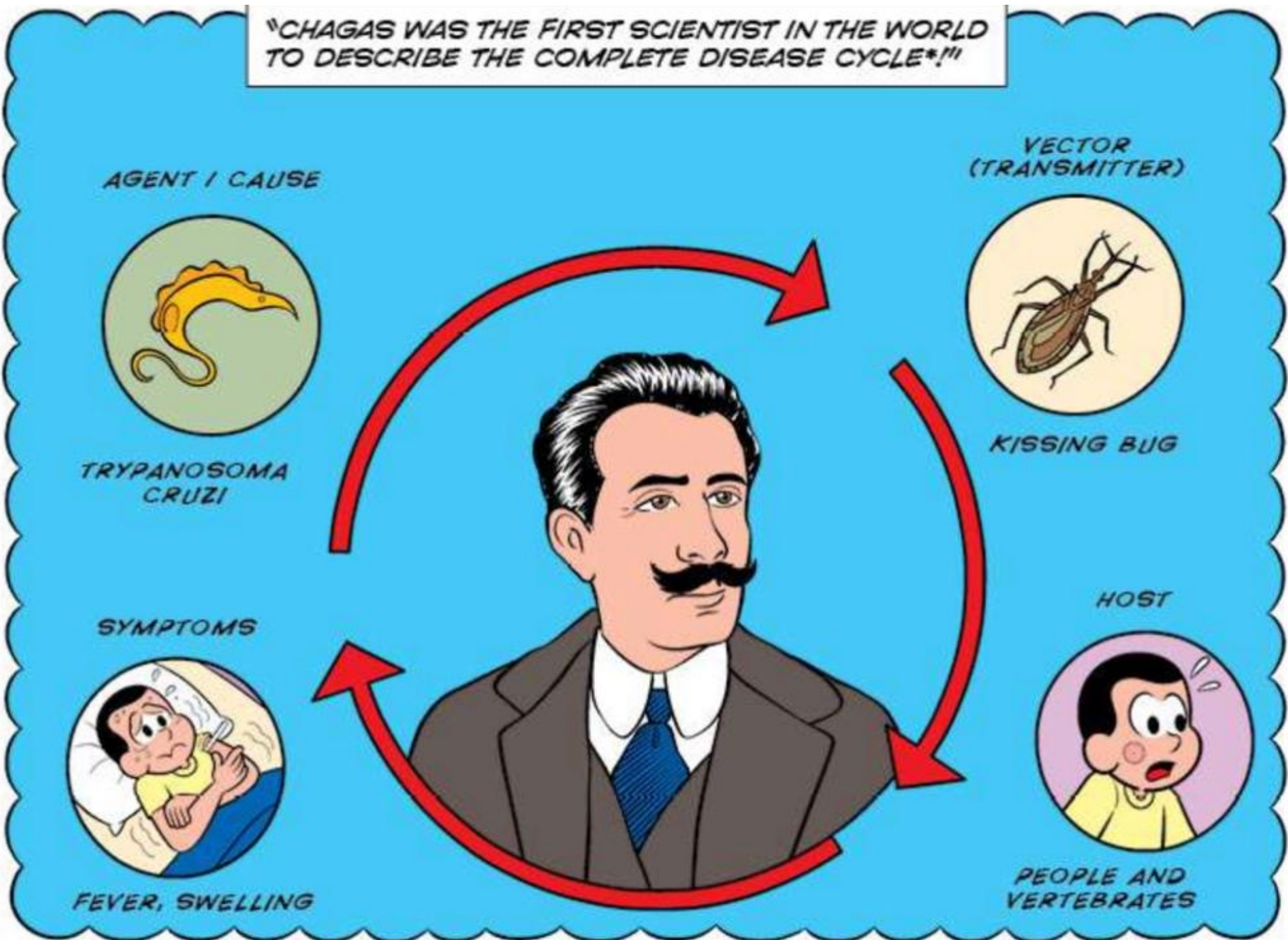


Berenice Soares de Moura with great-grandson. Monitored all her life and never developing symptoms, she died at 74.

Chagas's achievement



Instituto Maurício de Souza,
MsF, Fiocruz, DNDi



**THAT'S WHY HE WAS NOMINATED TWICE FOR THE NOBEL PRIZE IN MEDICINE, IN 1913 AND IN 1921.*

The legacy of Carlos Chagas

- Discovery of Chagas disease in Brazilian hinterland encourages **further expeditions** and research on **local infirmities**
- Oswaldo Cruz Institute extends activities **nationwide**, develops **international partnerships**
- After Cruz's death at 44 (1917), Chagas becomes **president of Institute for 17 years**, until his own death at 55 (1934)
- Mounts effective response to **Spanish flu** epidemic in Rio (1918)
- Twice nominated to **Nobel**, honored worldwide
- Wanted **Berenice** to study in Rio, but her family refused
- Continues research on Chagas, other diseases, **trains scientists**
- **Fiocruz** a **joint legacy** of Oswaldo Cruz and Carlos Chagas



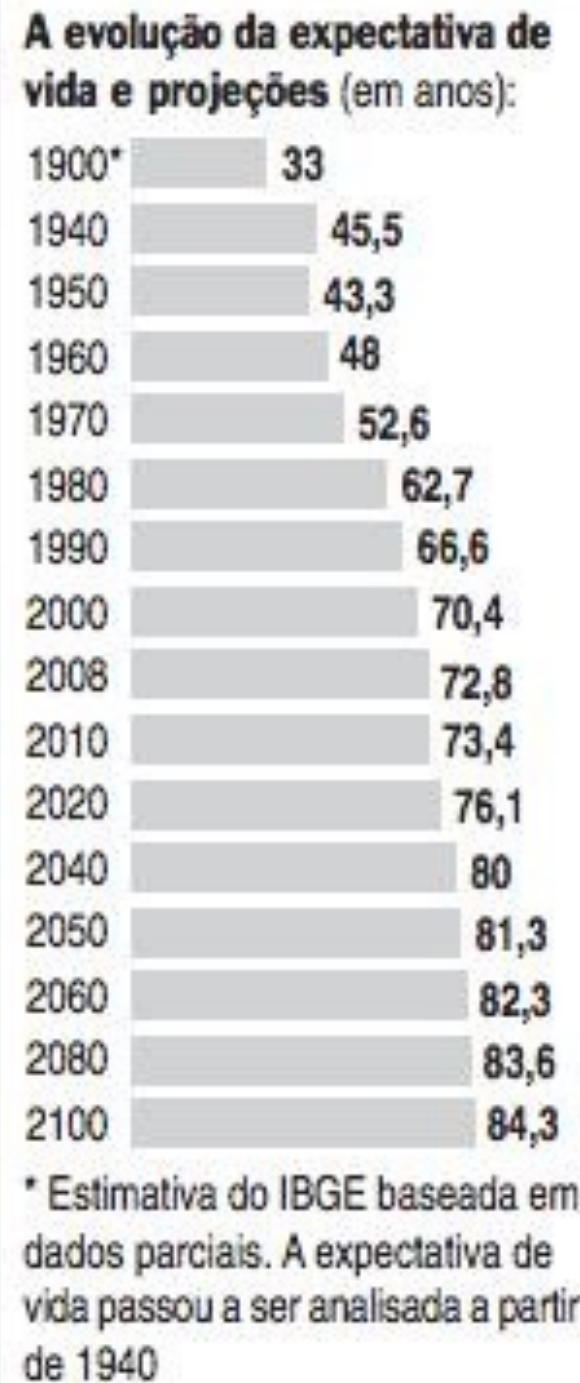
With sons Evandro (l.) and Carlos Jr., both to become acclaimed doctors



Albert Einstein's visit to Fiocruz (1925): to the right of Chagas, Adolpho Lutz

Evolution of life expectancy in Brazil

- From 1900, when serious public health efforts began nationwide, to 2020, average life expectancy in Brazil **more than doubled**
- Many factors counted, such as **migration** to the big cities, economic **growth**, and improvements in **education**
- But it is due most of all to a comprehensive and effective **public health structure**
- This is the **true legacy** of Oswaldo Cruz, Carlos Chagas, Adolpho Lutz and many, many others
- Yet much remains to be done, including about **Chagas disease**...

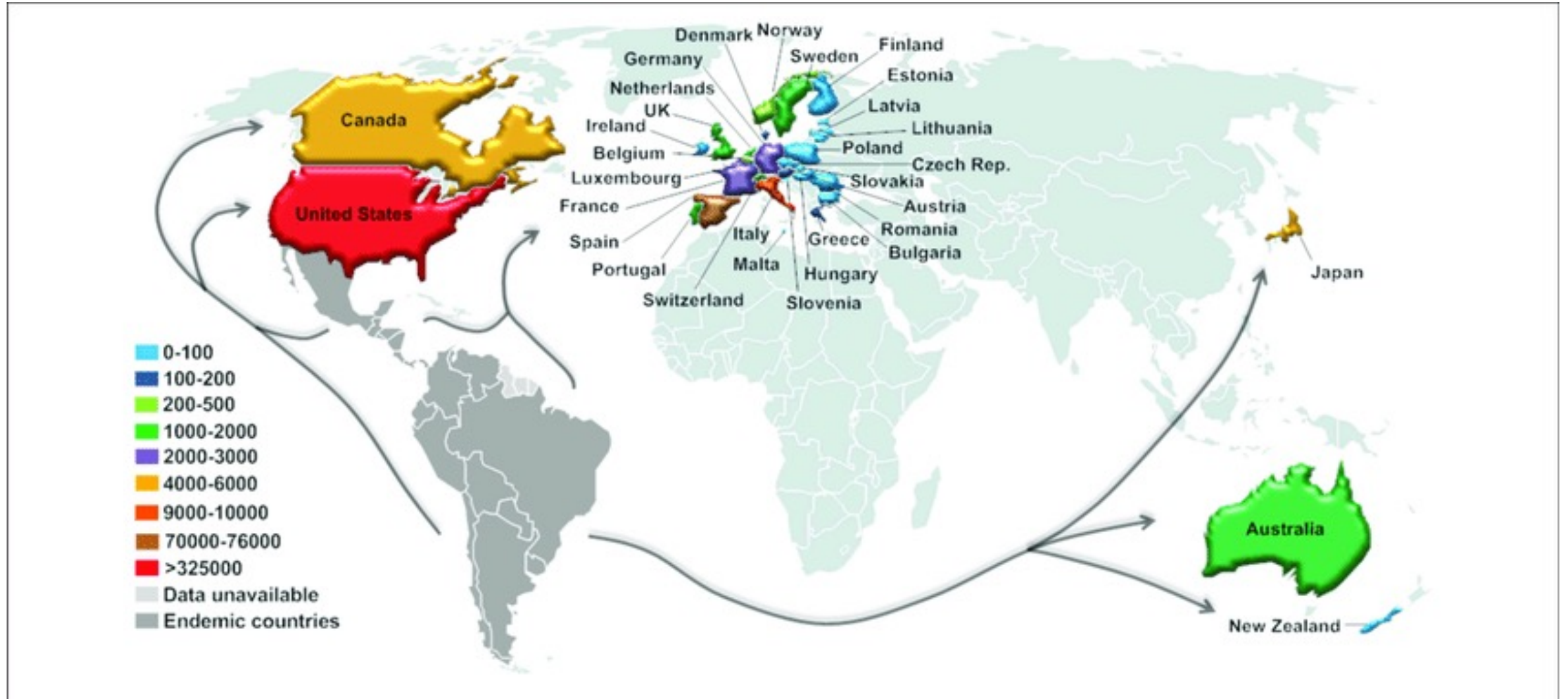


What is the impact of Chagas disease?

- Over 6 million people estimated to have Chagas in the world
- Over 75 million people at risk
- 30,000 new cases per year
- 12,000 deaths per year
- Only 30% of those infected have been diagnosed
- Endemic in 21 countries across Latin America
- Also present in North America, Europe, Japan, and Australia

Source: <https://dndi.org/diseases/chagas/facts/>

Should we still call it a neglected *tropical* disease?



Current estimated number of immigrants with *T. cruzi* infection in non-endemic countries (Source: *Chagas Disease: From Discovery to a Worldwide Health Problem* (Lidani et al, 2019))

Reasons for hope

- ❑ World Chagas Disease Day (since 2020)
- ❑ Growing number of **researchers worldwide** studying Chagas
- ❑ **New treatments** being tested
- ❑ Possible **vaccines**?
- ❑ WHO, PAHO, international **partnerships**
- ❑ Unprecedented **global collaboration**
- ❑ **Awareness-raising** initiatives

Nísia Trindade Lima, President of Fiocruz, and
Laurent Fraisse, R&D Director at DNDi,
sign partnership agreement, 2022



Thank you for your attention!*

Daniel R. Pinto

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Consulate General of Brazil in Los Angeles

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* And thank you to our outstanding partners!