Past pandemic/s and their outcome/s, Round 2

TOM BECKER, STILL LIVING IN HIS DINING ROOM 24/7, THOUGH HE WENT OUTSIDE ONCE LAST WEEK

Game plan

- Consider non-Covid pandemics and how they changed societal and individuals' behavior….and what happened in their disease histories to alter their course/s
- I have spoken in more general terms about earlier pandemics…this time I will focus on another disease and the associated epidemics/pandemic

Objectives

- Recite key features of some prior pandemics, related to risk of infection, origins, natural history
- List agent/host/environment factors and historical landmarks that influenced the prior pandemic of interest today
- Pass a quiz at the end

Widespread (deadly) epidemics that we do not seem to talk about much, although associated with significant mortality

- TB
- Diphtheria
- Mosquito-borne diseases (numerous)
- Tick-borne illnesses
- Syphilis
- Cholera, especially during periods of increased international trade
- Small pox

Statue of Balto in New York's Central Park (Credit: Getty Images)


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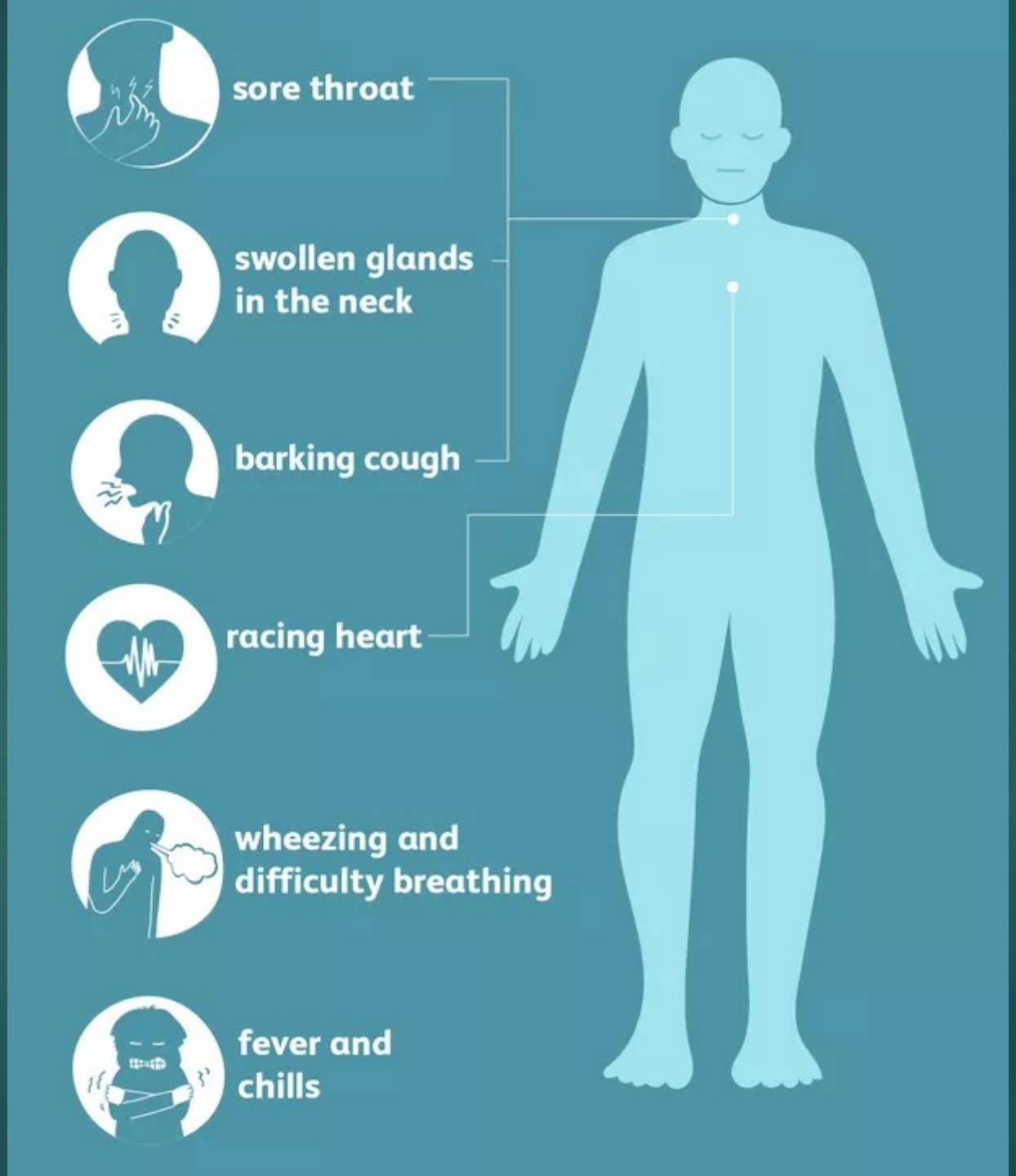

sore throat
swollen glands in the neck
barking cough
racing heart
wheezing and difficulty breathing
fever and chills

History

- Probably existed for 2000 years (from ancient descriptions), but most epidemics did not begin until the 1700's
- Named by French physician, based on Greek word 'diphthera', for leather
- In US, called 'throat distemper' and other unusual names
- In the English colonies (now US), the disease moved rapidly from north to south in 1735, stripping the region of its children

Background

- A bacterial disease in which clinical manifestations result from the action of an exotoxin
- The toxin is a protein with molecular weight of 62,000. A and B fragments
- Fragment A is responsible for toxicity and exerts its action by interfering with protein synthesis
- Fragment B is necessary for binding to surface receptors and for penetration into cells
- Toxin exerts its effects on distant tissues and organs
- Both toxigenic and non-toxigenic strains may be isolated during outbreaks

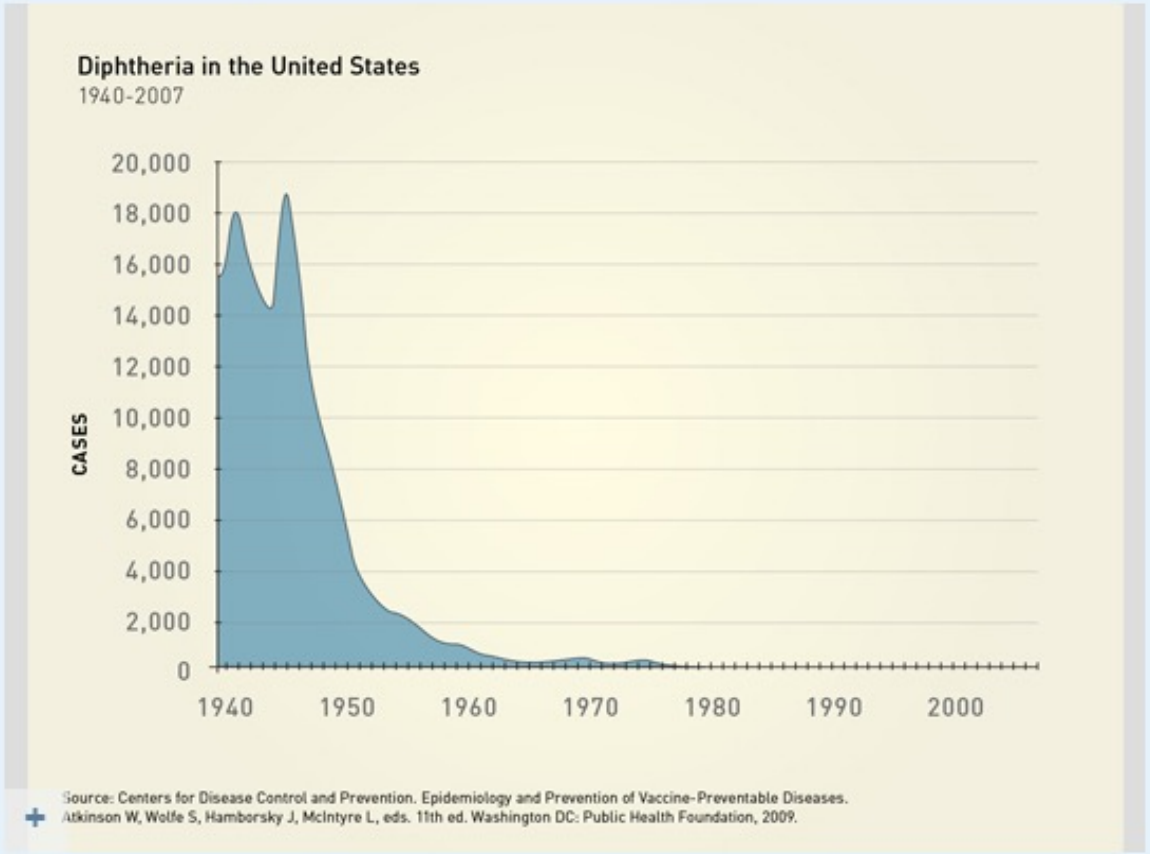
- Formaldehyde and heat causes the toxin to lose its binding and enzymatic activity, but it remains immunogenic
- The toxin is converted into a toxoid, which is used to immunize against diphtheria
- Diphtheria is acquired thru personal contact, primarily droplet spread
- Tissues affected: tonsils, pharynx, larynx, nose, skin
- Inapparent infections far outnumber clinical cases
- Antibodies to the toxin (called antitoxin) are primarily IgG
- Vaccine-induced antibodies are identical to naturally occurring infection

- Children acquire a high level of diphtheria immunity as a result of childhood immunization
- Antibodies decline in late childhood and in many of the more recent outbreaks, adolescents and adults were mainly affected
- National/international approaches to vaccination…particularly booster doses, vary widely

Notable victim families/victim fatalities

- Queen Victoria's daughter and grand daughter
- Pablo Picasso sister
- WEB DuBois son
- Drs. Abraham Jacobi and Mary Putnam's son
- President Cleveland's daughter, Baby Ruth

U.S. Diphtheria Cases



Caption: Diphtheria Cases in the U.S., 1940-2007

Description: Over almost 70 years, diphtheria cases in the United States have decreased from almost 20,000 cases per year to almost none. Immunization for diphtheria has greatly reduced the spread of a disease which once was called "the plague among children."

Creator: Centers for Disease Control and Prevention

Names for Diphtheria

Caption: Diphtheria and scarlet fever were sometimes difficult to distinguish. The illnesses were known by a variety of names in the American colonies.

Timeline Category: Diphtheria

Diseases & Vaccines

Diphtheria timeline

- 1659 first recorded outbreak in Massachusetts. Historic accounts describe some type of 'throat infection' in tribal people as well as colonists (hard to know what that infection really was)
- 1735 New Hampshire outbreak, very high fatality: case
- 1856 SF Bay area outbreak, '..few children recovered'
- 1883 Krebs identified the pathogen, later named Corynebacterium diphteriae
- 1884 Koch's postulates fulfilled
- 1890 Kitasato described methods for creating an antitoxin for humans by inoculating animals and harvesting antibody-rich serum from their blood

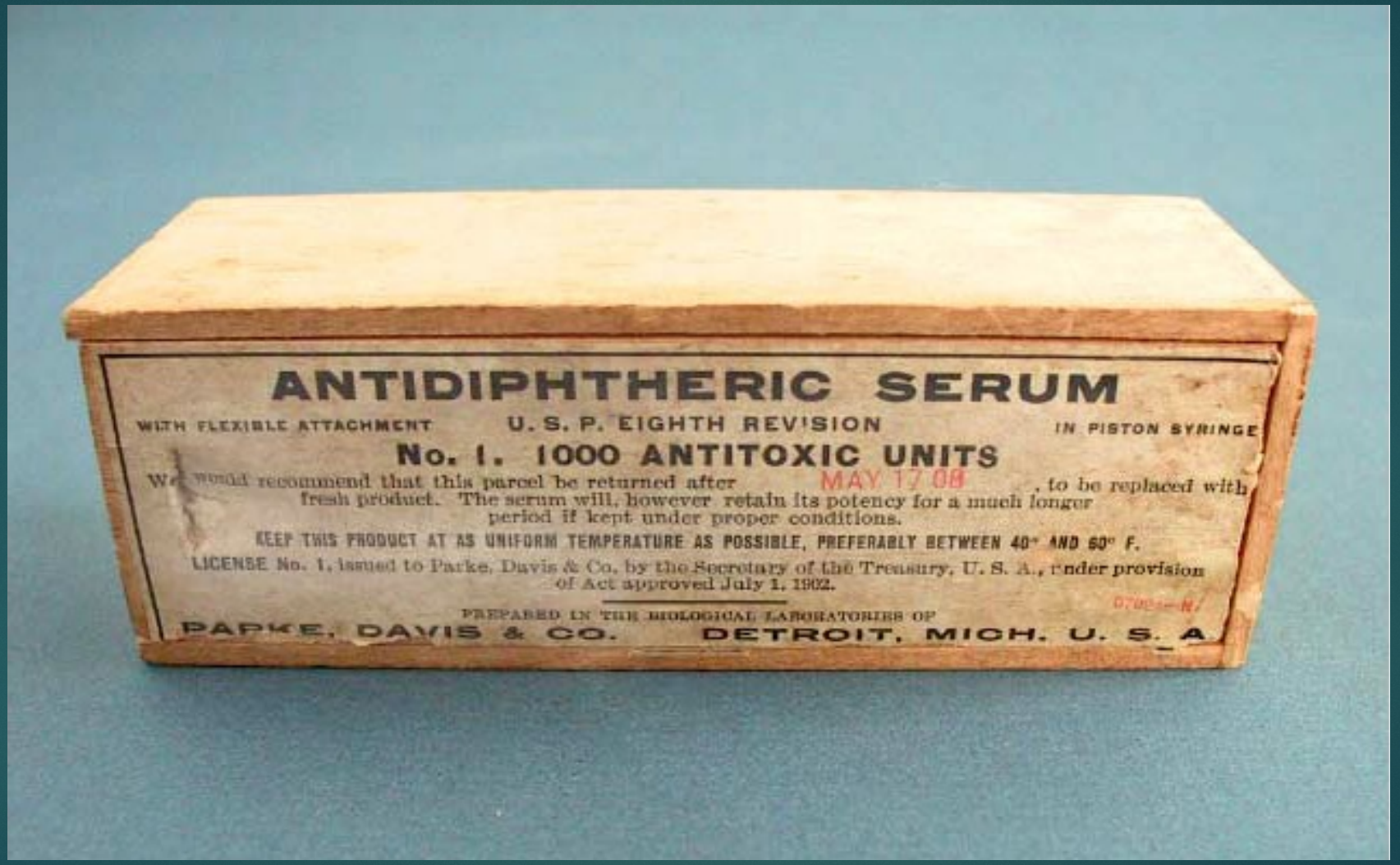
- 1894 small human experiments in clinical settings
- 1913 earliest vaccine, a mixure of toxin and antitoxin
- 1922 successful large scale trial of toxin-antitoxin vaccination in kids
- 1925 Nome, AK outbreak that led to famous dog-sled delivery of vials of treatment
- 1943 Vaccine campaigns in US, in Europe WW2 interrupted efforts with estimated 50,000 deaths
- 1948 DTP three-in-one vaccine
- 1974 WHO expands global vaccine efforts, dropping case counts by 90% over 20 years
- 1997 CDC recommends DTaP vaccine for first three doses in infants
- 2011 no cases in US for 8 years in a row

- April 15, 2022 TB gets his long overdue Td booster, his vaccine schedule having been interrupted by Covid pandemic

1. Die Gewinnung des Diphtherieserums aus Pferdeblut im Behringwerk zu Marburg

Nach der Natur gezeichnet von Fritz Gehrke

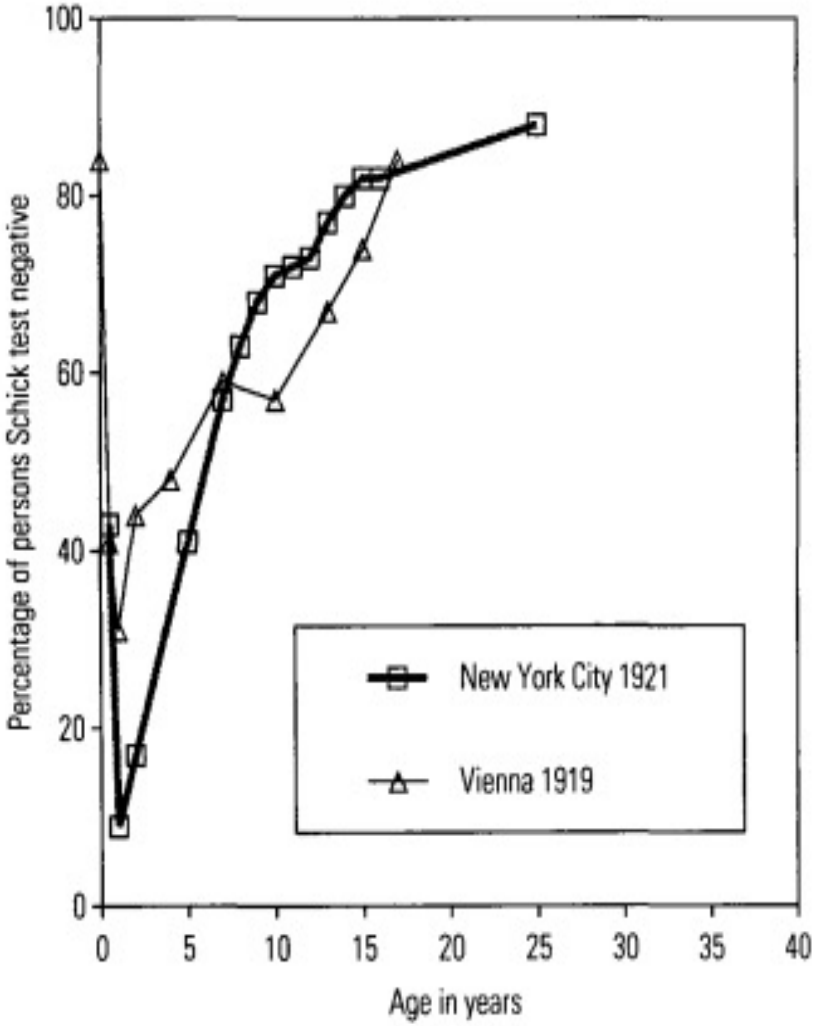
Einspritzung des Diphtheriegiftes unter die Haut. — Blutentnahme aus einer Halsader

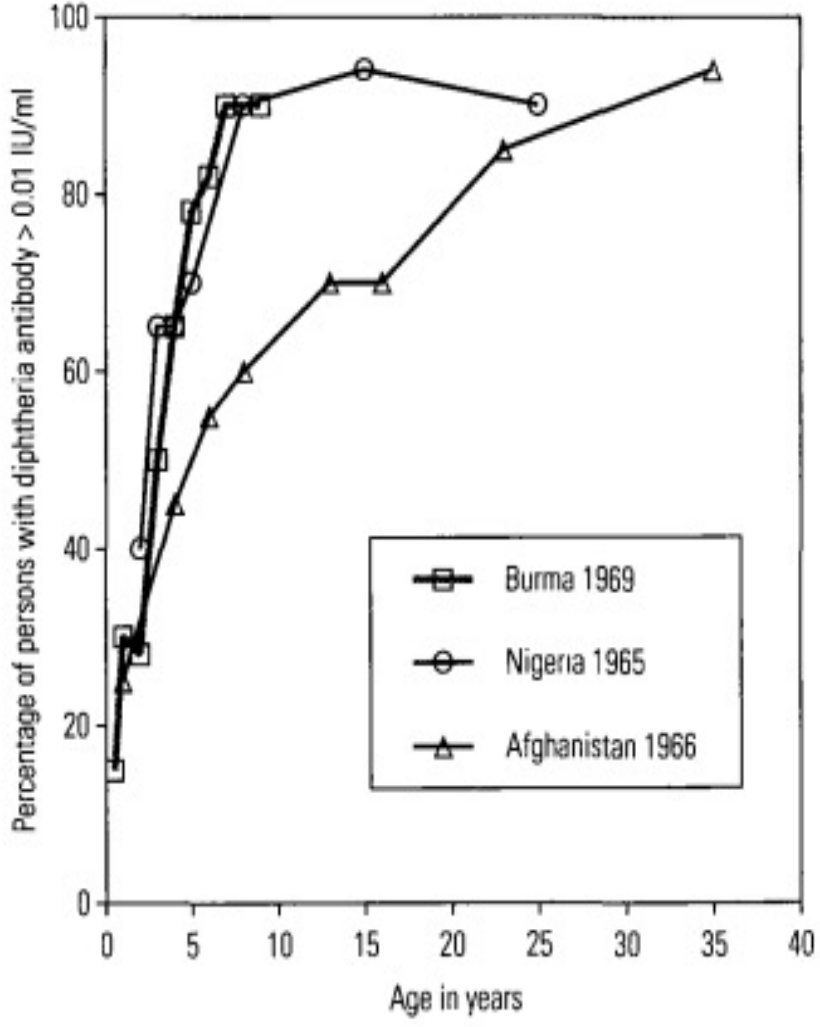

ANTIDIPHTHERIC SERUM
WITH FLEXIBLE ATTACHMENT
U. S. P. EIGHTH REVISION
IN PISTON SYRINGE
No. 1. 1000 ANTITOXIC UNITS
We would recommend that this parcel be returned after MAY 17 08 , to be replaced with fresh product. The serum will, however retain its potency for a much longer period if kept under proper conditions.
KEEP THIS PRODUCT AT AS UNIFORM TEMPERATURE AS POSSIBLE, PREFERABLY BETWEEN 40° AND 60° F.
LICENSE No. 1, issued to Parke, Davis & Co. by the Secretary of the Treasury, U. S. A., under provision of Act approved July 1, 1902.
PREPARED IN THE BIOLOGICAL LABORATORIES OF
PARKE, DAVIS & CO. DETROIT, MICH. U. S. A

Interesting factoids

- Antitoxin only provided protection for two weeks
- A sick person with diphtheria could get it again, soon after recovery, until vaccine came along
- Antitoxin still produced by horses! (efforts underway to change that)
- Long term effects among survivors: cardiac, neurologic effects
- Trach procedures were last-ditch efforts to preserve airway…rarely worked
- Some advances made with intubation, although all the instruments were metal and did not bend like now.

Figure 1. Natural diphtheria immunity in the pre-vaccine era in industrialized countries, 1919 to 1921, and in developing countries, 1965 to 1969. (Zingher 1923 for New York City; Stransky & Felix 1949 for Vienna; Kriz et al. 1980 for Burma, Nigeria and Afghanistan)





Modern case counts

- 8800 cases worldwide in 2017—mostly Yemen, Nigeria, Venezuela, Bangladesh
- Most cases in war-torn areas
- Standard treatment, little changed for 100 years, in short supply in these locations

Prevention considerations (what CDC recommends in the US)

- Primary early childhood regimen (DTaP at months 2, 4, 6, 15, and then between 4 and 6 years)
- Adolescents should receive a single dose of Tdap at age 11 or 12
- Pregnant people should get a dose of Tdap during every pregnancy during early part of 3rd trimester
- Adults who have never received Tdap should get a dose
- Adults should receive a booster dose of Tdap or Td every 10 years, or after 5 years in case of a severe or dirty wound or burn

- Not all countries follow these recommendations

Diphtheria and Covid parallels

- Supply chain disruptions, including treatment supply
- No treatments or prevention strategies available until the infection was widespread around the planet
- Progress in science surrounding this infection was measured in huge leaps (with toxoid and then vaccine later)
- Resistance to vaccine uptake could have far-reaching consequences
- High proportion of people with less severe or asymptomatic infections—they are contagious

Some key take-home messages about diphtheria

- Diphtheria has been a ‘bad actor’, at least in past centuries
- Like plague, covid, small pox, and others, few diseases have affected the course of humankind as much as this one has done
- This disease crossed economic and social barriers and took a heavy toll on rich and poor, primarily children
- Easily prevented with varying vaccine/toxoid preparations
- Currently estimated fatality:case of 1:20 persons infected
- Cutaneous form of disease is less severe than the upper respiratory form

Take home messages more broadly (they are very similar to the last presentation on plague)

- The planet has experienced diverse pandemics in recent human history, and we made it through each of them at the species level
- Scientific observation and experimentation have helped humans to conquer many of these pandemics
- Prior to germ theory, these events must have been particularly terrifying since most theories of cause of widespread death were not borne out
- Human genetic diversity related to immune response has likely come to the rescue in the past to help the species survive, along with environmental changes and recent public health measures

Quotable quotes

- "As science and medicine move forward, vaccines and treatments allow parents, and clinicians, to care for children without dreading some of the most terrifying infections of the past. Remembering these success stories can help us maintain a feeling of awe, gratitude, and willingness to do our part"

- Smithsonian magazine, Oct 2021

Quiz

- What year was diphtheria eradicated from the planet?
- What is the sometimes severe reaction to diphtheria toxid called?
- True or false: diphtheria was and is still primarily a disease of lower income people worldwide
- True or false: like Covid, diphtheria was/is spread primarily through droplets
- True or false: tribal people in North America appeared to have natural immunity to diphtheria as observed over centuries of contact

References

- Great courses, Introduction to Infectious Diseases.
- Morens and Fauci. Emerging pandemic diseases: How we got to Covid-19. Cell, 2020.08.021
- Berke LS. The plague among children: how we fought diphtheria. Smithsonian, Oct 2021.
- WHO. Diphtheria. Immunological basis for Immunization. Module 2. WHO Press, 2001.
- CWRU Library of Medicine, special exhibit on diphtheria (on line)

- A vast literature on diphtheria is available…an infection well-studied for many decades