

STANDARD DEVIATIONS:

Greetings,

Today is history class.

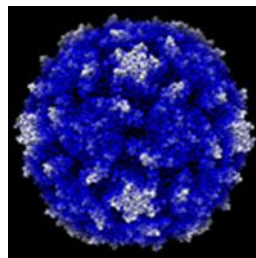
As the world watches the spread of COVID-19 and the SARS-CoV2 virus, one question keeps coming up, “**How soon will a vaccine be available?**” So, it’s imperative that we recognize the risks, consequences and tribulations that vaccines bring to the table. **Polio** gives us a picture of the difficulties vaccine development and deployment entail; and there are some interesting similarities to the current pandemic that beg observation.

Vaccines have been around a while. Evidence exists that the Chinese employed smallpox inoculation (or variolation, as such use of smallpox material was called) as early as 1000 CE. It was practiced in Africa and Turkey as well, before it spread to Europe and the Americas.

Edward Jenner is noted for his successful 1796 use of cowpox material to create immunity to smallpox. His method underwent medical and technological changes over the next **200 years**, and eventually resulted in the eradication of smallpox.

Louis Pasteur’s 1885 rabies vaccine was the next to make an impact on human disease. And then, with the advent of bacteriology, developments rapidly followed. Antitoxins and vaccines against diphtheria, tetanus, anthrax, cholera, plague, typhoid, tuberculosis, and more were developed through the 1930s.

Now, Polio has been around for a long, long time. The transmission of this virus during ancient times was suggested in studies on Egyptian mummies, which showed a shortening of a lower limb in a child. In 1789, in the second edition of *A Treatise on Diseases of Children*, Michael Underwood described the disease as “debility of the lower extremities in children”.



{Poliovirus}

Poliovirus (PV), an enterovirus belonging to the *Picornaviridae* family is the etiological agent of poliomyelitis, an acute paralytic disease. This disease results from lower motor neuron damage and is characterized by asymmetric persisting weakness (flaccid paralysis).



On Saturday, June 17, **1916**, an official announcement of the existence of an epidemic polio infection was made in Brooklyn, New York. That year, there were over 27,000 cases and more than 6,000 deaths due to polio in the United States, with over 2,000 deaths in New York City alone. If you look at those numbers with “2020” vision (and population), we’d be discussing 100,000 cases, 20,000 deaths, and 7,000 deaths in NYC alone. Sound familiar?

There is **no cure** for polio. Polio is most **infectious** between 7 and 10 days **before and after the appearance of symptoms**, but person-to-person transmission is possible as long as the virus remains in the patient. Flaccid paralysis causes diaphragmatic **respiratory failure that requires mechanical ventilation**. Sound familiar?



{Will the iron lung make a comeback?}

Polio epidemics kept occurring in the early 20th century. Franklin D. Roosevelt’s diagnosis in 1921 (age 39) led to the creation of the March of Dimes™ and mass awareness and fear of polio. National and global recognition became the impetus for vaccine research. The American public, and the world, were desperate for a cure. Sound Familiar?

In **1935**, when vaccine research was expanding, Maurice Brodie, MD prepared a killed poliovirus vaccine, testing it on chimpanzees, on himself, and finally on children. He enrolled about 11,000 individuals (in both control and vaccine groups) in his trial.

Meanwhile, John Kolmer, MD, in Philadelphia developed an attenuated poliovirus vaccine, which he tested in about 10,000 children.

The tests proved a **disaster**. Several subjects died of polio, and many were paralyzed, made ill, or suffered allergic reactions to the vaccines.



It took another two decades for the research to really bear fruit and even then controversy and disaster were part of the story. Two paths had emerged with the early work; killed vs live-attenuated virus.

Hilary Koprowski at Lederle Laboratories conducted the first human trial of his **attenuated oral poliovirus vaccine** at a New York State facility for intellectually disabled children and children with epilepsy in 1948. **Jonas Salk** championed rapid deployment of a **killed-virus vaccine injection** and tested on resident children in institutions for the physically and intellectually disabled in 1952. A manufacturing debacle, in 1955, by Cutter Laboratories (CA) resulted in 11 deaths from the vaccine and hundreds paralyzed. Though the cause of the disaster was never proven, it is likely that certain production resulted in a failure to completely kill the Type 1 poliovirus in the vaccine. Vaccine production stopped. Reforms in production were mandated.

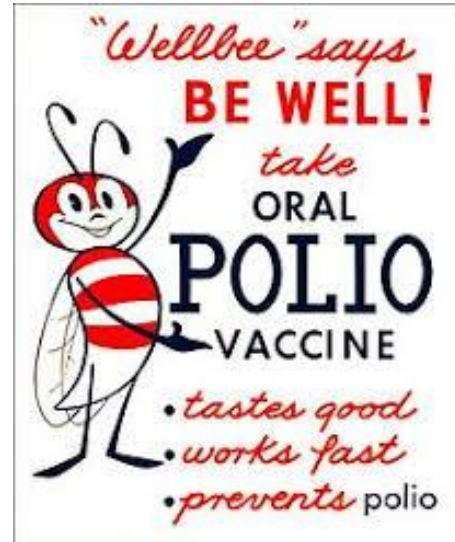


{Rapid use of injected vaccine leads to trouble in 1955}

Albert Sabin, who was also working up the attenuated live strain for the **oral vaccine**, objected to the practices of human trials without consent and animal models, and eventually brought his product to the Soviet Union in 1959 and the world shortly afterwards (1960).

The oral polio vaccine has proven safe and led to the near eradication of polio around the world, and **still there are issues.**





{Oral vaccine administered on sugar cubes}

Mutant strains of circulating vaccine derived polio virus (type 2), cVDPV, have emerged and present a new challenge to eradication. In 2016, transmission of type 2 cVDPVs was detected in 12 countries in Africa and also in China. Type 1 cVDPVs were identified in Indonesia, Myanmar, and Papua New Guinea, and type 3 cVDPVs were identified in Somalia.

Our outcry for immediate treatment of COVID-19 bears an eerie resemblance to the polio panic and suspect protocols of the last century. Vaccine research is certainly more sophisticated at this time but our need for a vaccine must be weighed against the importance of safety and efficacy in its fabrication and distribution.

I've said it before, and I'll say it again. "There's right and there's right away."

In the race for a SARS-CoV2 vaccine (**and this applies in the laboratory**), safety must supersede our need for speed.

Have a great week and be safe,

Bryan

