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Viruses | Vaccines

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"Breaking the Normal"

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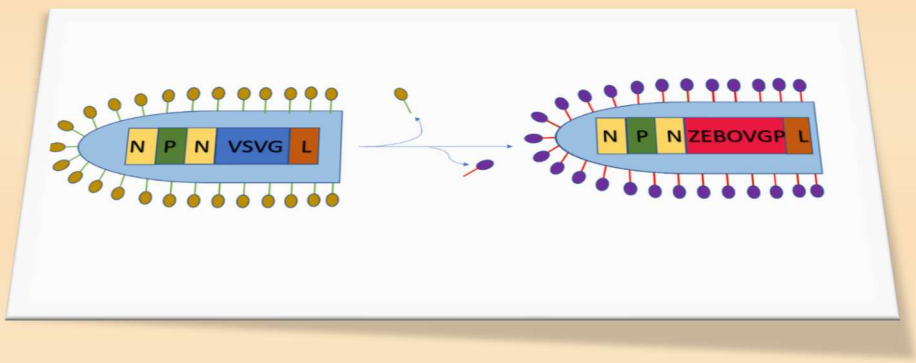
Before SARS-CoV-2 forced us into the new 'normal' rhythm, the African countries were struck with outbreaks of the Ebola virus that belonged to the family Filoviridae. The transmission vector of which is the fruit bat. The outbreaks soon culminated in an epidemic in West Africa (2013-2016) and the death count surpassed 11,000. A cure or a preventive measure was the need of the hour.

The vaccine:

Relief came in the form of the vaccine Rvsv-Zebov, released by Merck under the brand name Ervebo. Rvsv-Zebov is targeted against the Zaire species of the virus. It is a viral vector-based vaccine.



Viral vector-based vaccines involve a virus acting as a vehicle that carries the genetic code for the antigen against which immunity is desired. These antigens when made in the body, trigger a strong immune response brought on by the T cells and the antibodies produced by the B cells. The genes necessary for the replication of the virus vector are removed hence, making it quite harmless. This is the mechanism behind the working of this vaccine.

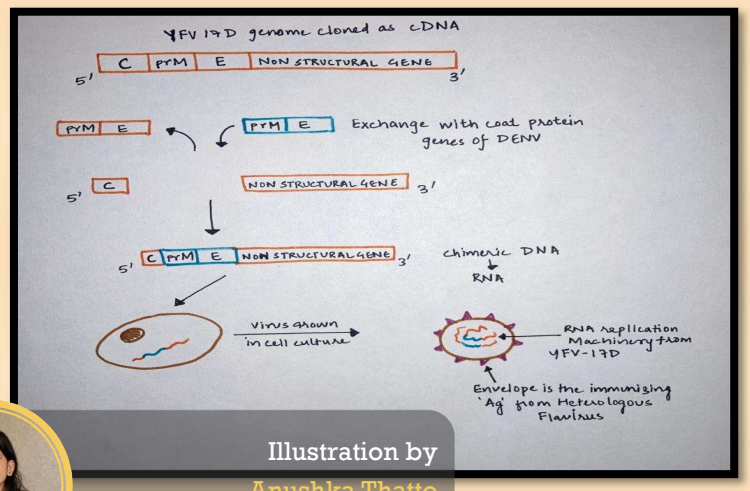
The Ebola virus has single stranded RNA that codes for seven proteins: Nucleoprotein (NP), Virion protein (VP) 35, VP40, VP30, VP24, Glycoprotein (GP), RNA dependant RNA polymerase. The glycoprotein is the only protein expressed on the surface of the virus, thereby initiating immune response. Thus, this is the antigen associated with the vaccine. The viral vector used in the Ebola vaccine is *Indiana vesiculovirus* or *Vesicular stomatitis Indiana virus* (VSV), of the family *Rhabdoviridae.* The gene for the glycoprotein of VSV is replaced with that of the Ebola virus. The production of glycoprotein elicits an immune response. A very novel technique indeed!

Even though there were side effects the vaccine like headache, fatigue, fever, muscle pain, nausea etc, the benefits far surpass the slight discomfort.

Et tu, *Aedes?*

Dengvaxia – Revolution in fight against Dengue

When we say Dengue, what comes into our mind is a deadly disease that takes many lives every year. Dengue is a viral disease caused by Arbo Virus and transmitted by *Aedes* mosquitoes. In India itself the disease has a mortality rate of 4.2%. To be honest, it's interesting to note that the COVID-19 Pandemic seems to have a lower mortality rate as compared to Dengue i.e., around 1.5% in India specifically. That makes the development of a vaccine 'a must' in this case.



'Dengvaxia,' developed by Sanofi Pasteur and approved in 2015, has proved to be our savior in the fight against Dengue with approximately 76% effectiveness. Dengvaxia, scientifically, also known as CYD-TDV stands for Chimeric Yellow Fever Virus - DENV-Tetravalent Dengue Virus. CYD-TDV is basically a live recombinant, tetravalent, chimeric vaccine that provides protection against all four stereotypes of DENV (Dengue Virus) and hence, the name TDV i.e., Tetravalent Dengue Virus.

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The part ‘CYD’ comes from the fact that the vaccine is constructed from Chimeric Yellow Fever Viral Backbone of strain 17D. In addition to this, DENV and YFV belong to same virus family of Flavivirus which makes the task of construction easier as both would depict similar behaviour as well as course of action.
The vaccine consists of prM (Para-myosin) and E (Envelope small membrane protein) genes of DENV which are inserted into the YFV17D-cDNA backbone which is then transcribed to RNA and later RNA transfection leads to development of an envelope around the cell in culture which works as an antigen for receptors for the formation of antibodies i.e., activation of immune system. At the same time, RNA machinery of YFV17D is used for replication.

Moving on to the trials conducted, the vaccine is injected in a three-dose series, in a period of 0-6-12 months. Most of these trials were conducted in endemic areas like the Southeast Asian and Latin American countries. The trials were conducted with the aim to inspect immunogenicity and safety of CYD-TDV. It was also observed that people aged between 15-45 were able to tolerate the vaccination and suffered only from mild headache and pain at the site of injection.

The results, found to be pretty promising the vaccine was declared to be capable of providing partial protection against the disease.

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Get a clue, Fight the Flu!

It was during the spring of 2009 when the Influenza virus spread from pigs to humans. This spread of the virus infected around 500 million people. This virus was special in the sense that it contained a unique combination of influenza genes. At that time this virus, which is now casually referred to as ‘The Flu’ lead to a Pandemic. This Influenza virus, also known as H1N1 virus was a mixture of North American swine virus and Eurasian swine virus.

It’s M.O. includes human respiratory infection and its symptoms are cough, fever, sore throat, weakness, chills, headache.

After intensive research by scientists, two types of Vaccines for Swine flu were made available:

One is in the form of injection and other type is a nasal spray. Let us have a look at them in detail.

1) Injectable form

Trivalent inactivated vaccine (TIV) is widely used. It has 3 seasonal influenza viral strains.
This vaccine can have formulations of inactivated virus (were first the virus is grown in hen’s egg then inactivated, broken down, purified and then used in the vaccine), detergent-split (where detergent dissociates the lipid envelope of virus and exposes its elements), or subunit form.

TIV induces antibodies which will target epitopes belonging to the pathogen. It contains 15 micrograms of Haemagglutinin per strain. This vaccine is delivered in form of intramuscular injection, and is of low cost. Younger children are given 2 doses.

2) Nasal spray

The second type of vaccine is the nasal spray influenza vaccine, also known as – Live attenuated influenza vaccine (LAIV). It is made from weakened or killed influenza virus. These killed virus particles are made to adapt to grow in the temperature of nasal passage. LAIV induces humoral and cell mediated immunity. This is delivered intranasally.

LAIV is administered to children belonging to the age group of 6 months to 8 years. These children similar to TIV, are given 2 doses.

It is recommended that the adults including pregnant women, those who are above 49 years of age, or those having weak immune system due to any disease, etc should not be given the influenza vaccines, as there is a chance that the body will not be able to contest against the virus even if it is weakened.

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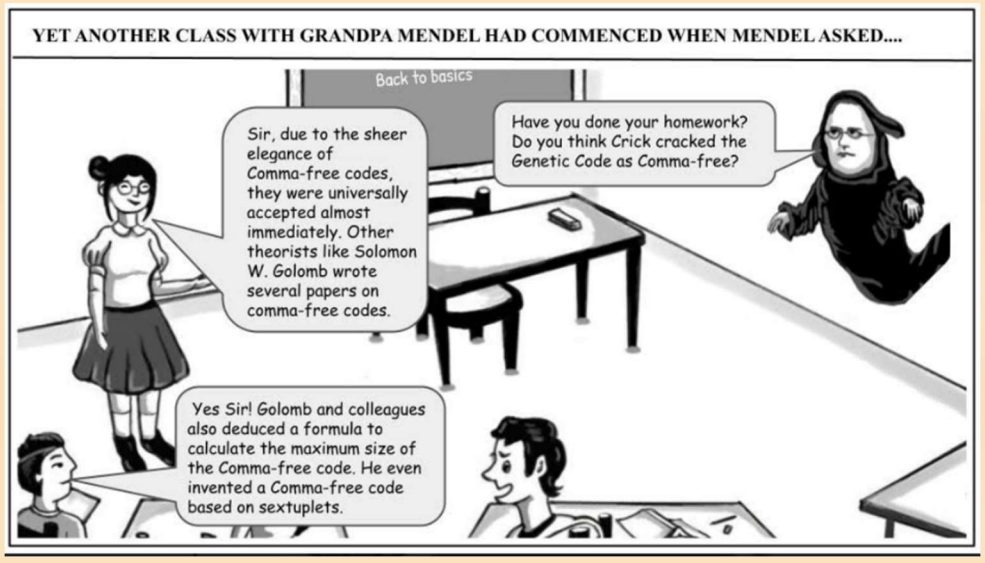
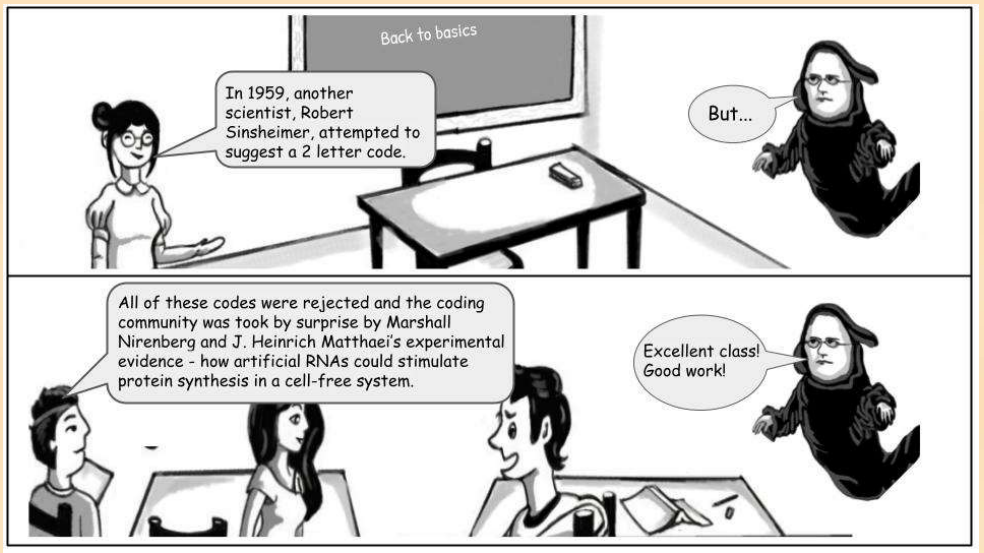
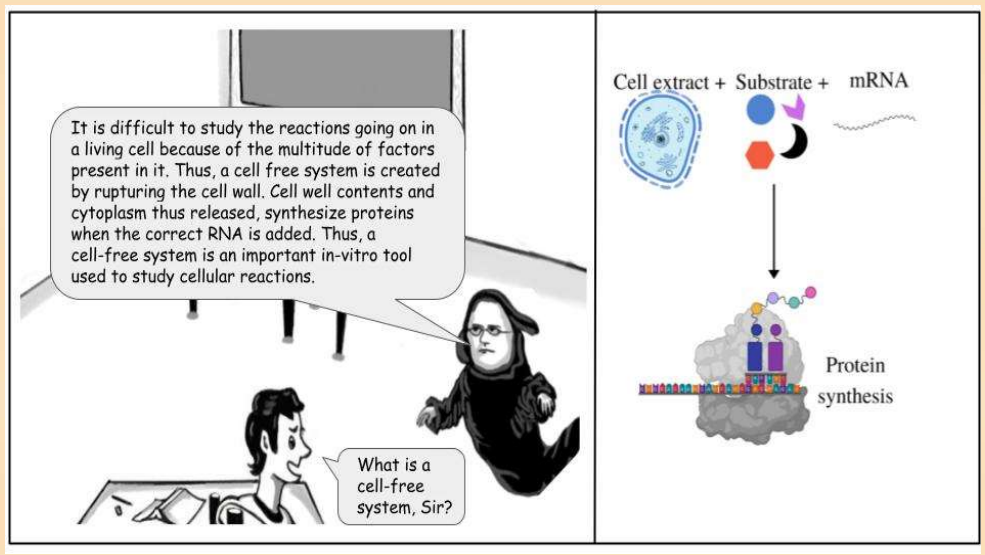
Back to Basics with Friendly Grandpa Ghost Mendel!

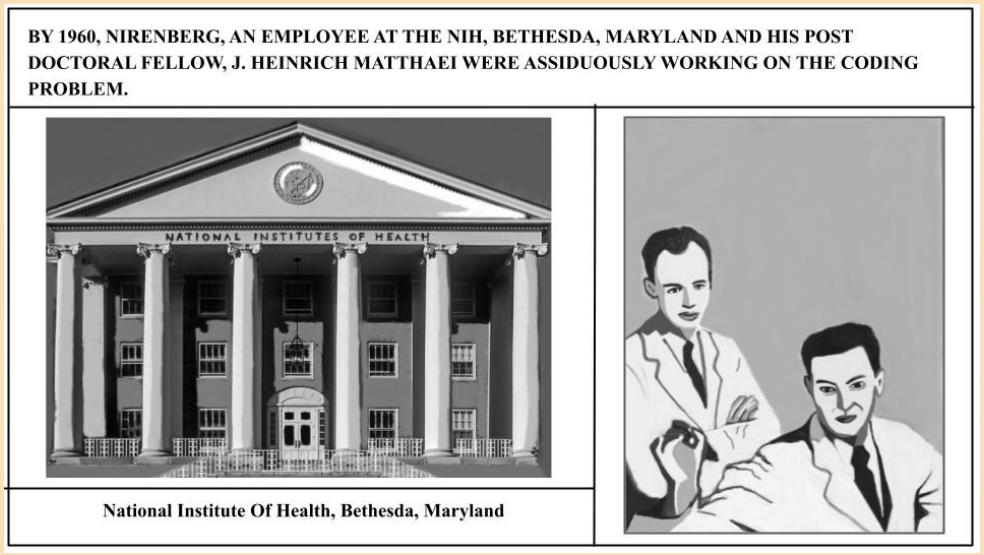
You know the legendary Gregor Mendel. You might not know the legends in the race to find messengers of life! Come, discover the story with Mendel himself, and see where the journey takes you!

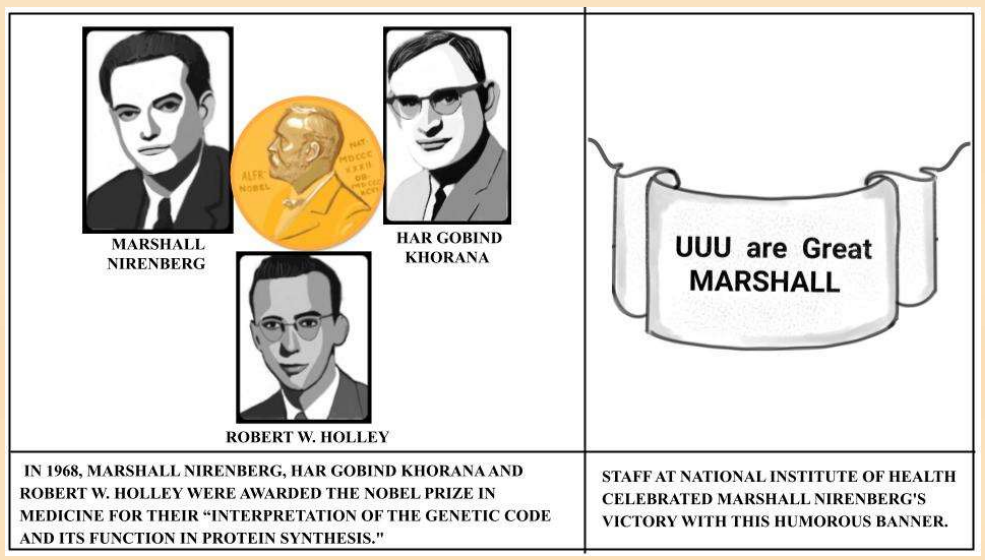
(Note: Read Left to Right)

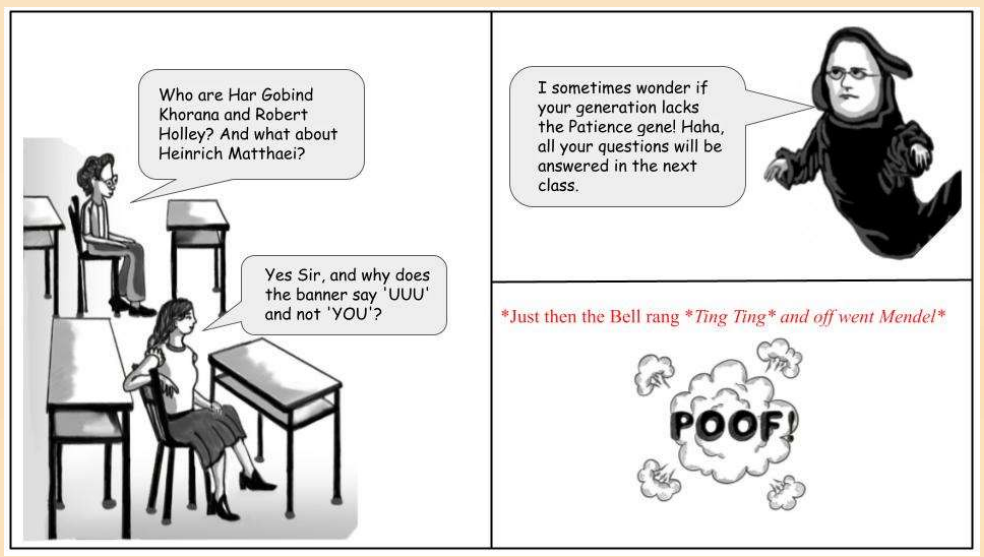












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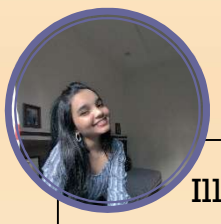

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No Tears?

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According to WHO, Rotavirus is the most common cause of gastroenteritis leading to severe diarrhoea in infants and children throughout the world. Every year rotavirus causes more than 500,000 deaths worldwide among infants and children, with 90% of these deaths occurring in Africa and Asia alone. A serious complication of rotavirus is severe dehydration which is the leading cause of rotavirus-related deaths.

Improving sanitation and increasing use of oral rehydration solution is important to keep diarrheal diseases in check but this has limited benefits in preventing rotavirus infection. Vaccination is considered to be the best way to reduce the load of fatal rotavirus. WHO has prequalified four vaccines as safe and not associated them with adverse vaccine reactions like intussusception, a condition where the intestine telescopes into itself.

- **Rotarix** - Produced by GlaxoSmithKline Biologicals, Rotarix is a live vaccine containing the attenuated monovalent G1, P[8] human rotavirus strain, and is recommended to be orally administered in 2 doses to infants at ages of 2 and 4 months.
- **RotaTeq™** - Produced by Merck & Co. Inc., contains five reassortant rotaviruses developed from human and bovine parent rotavirus strains that express the human rotavirus outer capsid proteins of five common circulating strains (G1, G2, G3, G4, and P[8]. It is recommended that three doses of this vaccine are administered orally to infants at ages 2, 4, and 6 months.
- **Rotavac™**- Produced by Bharat Biotech International Limited India, Rotavac® is a monovalent, naturally occurring bovine-human reassortant containing live rotavirus 116E strain prepared in Vero cells. It is administered as a 3-dose regimen, 4 weeks apart, beginning at 6 weeks of age and should not be administered to children older than 8 months of age.
- **RotaSiil™**- Produced in Serum Institute of India, RotaSiil™ is a Live Attenuated Bovine - Human Rotavirus Reassortant with G1, G2, G3, G4 and G9 grown on Vero cells. It should be administered as a 3-dose regimen, 4 weeks apart, beginning at 6 weeks of age.

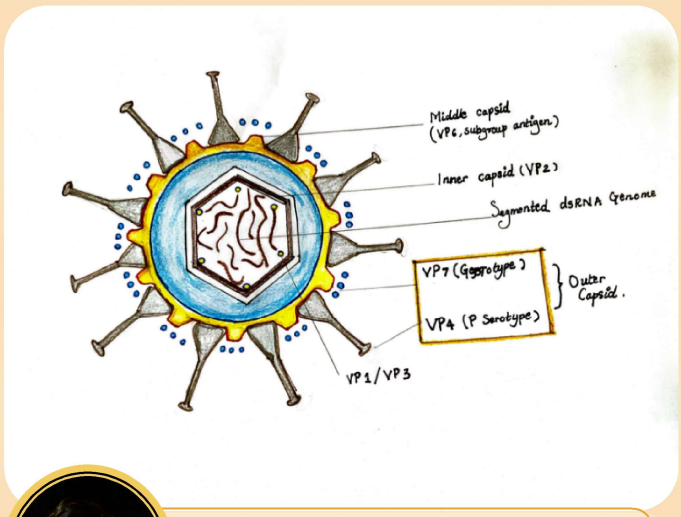

Illustration by:
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Studies have proven that Rotavirus vaccines can prevent 74% of rotavirus infections, 96% of hospitalizations from rotavirus and 98% of severe infections. These safe and effective vaccines provide the best hope of reducing the toll of acute rotavirus gastroenteritis in both developed and developing countries.

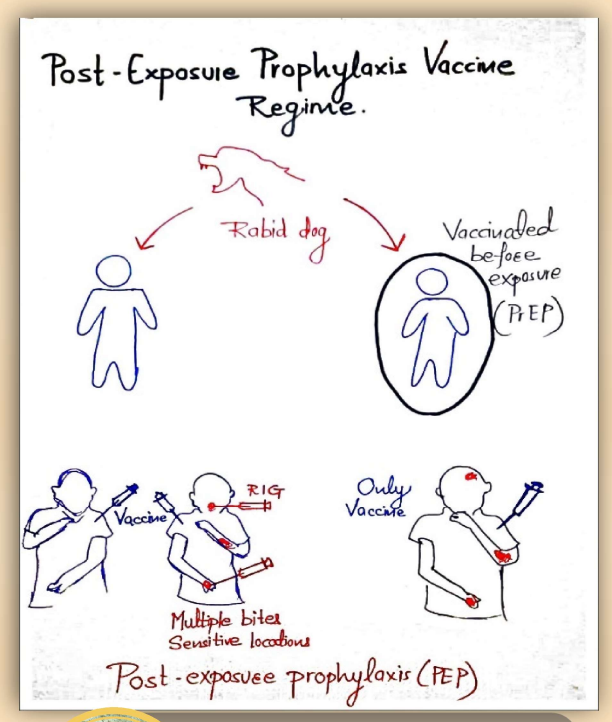
Roll up your sleeves!

People have been scared of rabies for thousands of years, many times depicting their fear in drawings and carvings of menacing dogs. However, rabies is scary for more reasons than just a painful bite. I say this because, once the virus is inside us, it not only destroys our body, but damages our mind and it can do so very soon or lay dormant for years before fatally attacking.

So how exactly do we go from getting a dog bite to having a complete behavioural change leading up to death? The virus that causes rabies spreads through saliva, so the most common way to contract rabies is through an animal bite, most likely from a dog, bat, raccoon, skunk or fox. There have been a few, rare cases of transmission through infected organ donors and even rarer instance of a lab accident, but for the most part it comes down to a bite from a rabid animal.

Before rabies vaccine, a bite from a rabid dog was a death sentence. But on July 6, 1885, Louis Pasteur changed history by vaccinating the first human against the deadly virus. That day, a little boy was rushed to Pasteur after being bitten by a rabid dog. Even though Pasteur was not a doctor and had never successfully tested his vaccine on humans, he gave the boy 13 injections containing a weakened rabies virus. Due to the fact that he was inoculated before the symptoms appeared, the disease never developed and the boy survived. The rabies virus belongs to the genus *Lyssavirus* (a negative stranded RNA virus, with a distinct ‘bullet’ shape). “Lyssa” means rage, really! So that kind of tells you what this group of viruses is capable of. The virus causes a very quick and painful death by making its way into your brain. It is a neurotropic virus, which means that it has an affinity for nerve tissue and selectively localises there.

When the virus gets injected into the skin or the muscle, it is not going to replicate extensively, however it doesn’t even necessitate so, all it needs to do is replicate enough that it can travel to the neuromuscular junction wherein it can go from the muscle cells into the central nervous system. Usually this is the point where the immune system would kick in, recognise its dangerous intruder and destroy it. Having said that, the immune system doesn’t see it. This is thought to be due to the reason that the virus replicates slowly in the muscle tissue; slow enough to not cause any alarm. This gives the virus a chance to reach the nervous system, where it hitches a ride up to the brain and slips through the blood brain barrier.



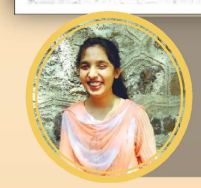


Illustration by
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As the virus replicates in the brain, it starts to mess with the brain cellular proteins, causing neural dysfunction. This is where certain symptoms of rabies start to manifest and you get the indication that the infection has been set in. But a bite from a rabid animal doesn't always mean certain death. People who have been exposed to the rabies virus can get a series of shots that can boost the immune system and fight against the virus, you just need to get it before it reaches the brain.

There are a number of rabies vaccines available that are both safe and effective. There are currently 6-7 listed brands of rabies vaccine in India, the most commonly used are: Berirab-P, Equirab, Erig, Hrig, Rabipur and Verorab. The vaccine works by inducing your body to produce its own protection (antibodies) against the rabies virus. Rabies vaccine is used in two ways. The vaccine is given to people who have been exposed to an animal that is known, or thought, to have rabies. This regime is called post exposure prophylaxis. Rabies vaccine may also be given ahead of time to people who have a high risk of getting infected with rabies virus. This is called pre-exposure prophylaxis.

People who have been exposed to rabies without previous vaccination, post-exposure prophylaxis should include administration of both human rabies immune globulin (HRIG) and rabies vaccine, on the day of rabies exposure to prevent the progressive, invariably fatal disease. Then, three more shots of only the vaccine are administered on days 3, 7 and 14.

People receiving pre-exposure vaccination should only receive the rabies vaccine. They receive three doses of vaccine. The second should be given seven days after the first dose, and the third dose should be administered 21 to 28 days after the first dose.
So surviving rabies is all about timing and the location where you get bit. People who work with rabies in laboratory settings and animal control and wildlife officers are just a few of the people who should consider rabies pre-exposure vaccinations. Although preexposure vaccination does not eliminate the need for additional therapy after a rabies exposure, it simplifies management by eliminating the need for rabies immune globulin and decreasing the number of doses of vaccine needed.

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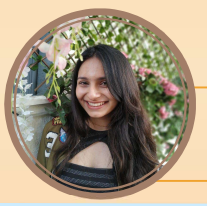

And Sifa Lalani
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Story of the Pneumococcal Vaccine

Article and Illustration by
Akanksha Mahajan
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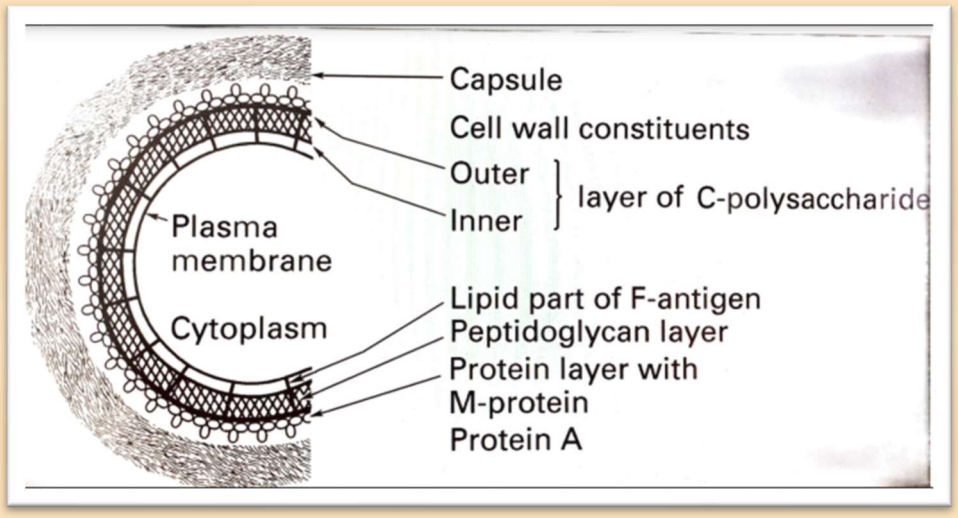
Streptococcus pneumoniae is a Gram-positive, spherical bacteria and a facultative anaerobic member of the genus Streptococcus. This bacterium asymptomatically colonises the upper respiratory tract. It has been reaffirmed by studies that a high colonisation rate is a risk factor for developing an infection. Pneumococcal infections are acquired through aspiration of droplets, leading to pneumonia with or without bacteraemia (presence of bacteria in the blood). Different vaccines have been developed to reduce or eliminate the burden of the infections caused by S. pneumoniae. Currently, two types of vaccines are in use:

- The unconjugated 23-valent polysaccharide vaccine (PPSV)
- The 10- or 13-valent conjugated polysaccharide vaccine (PCV).

Both the vaccine types have been proven to stimulate the production of long-lasting antibodies in not only healthy humans but immunocompromised adults as well; conjugate vaccines have an 'oomph' factor and have demonstrated some additional benefits. Benefits of polysaccharide conjugate vaccine over traditional polysaccharide vaccine include the fact that conjugate vaccines stimulate the production of antibodies in infants and toddlers, and not only healthy adults. It has been experimentally proven that the conjugate vaccines stimulate the mucosal immunity resulting in decreased colonization, as well as providing herd immunity and priming the patient immunologically for an enhanced host response as opposed to traditionally polysaccharide vaccines which are incapable of doing so. This activity helps us describe the mode of action of pneumococcal vaccines.



Potential protein antigens for pneumococcal vaccines are:

Pneumococcal Surface Protein A

Pneumococcal surface protein A (PspA) is an antibody-accessible surface protein attached non-covalently via binding to choline residues in lipoteichoic acid and cell wall teichoic acid on the pneumococcal surface. PspA has been found on all clinical isolates and is necessary for pneumococcal virulence. It aids pneumococcus in escaping complement-dependent immune phagocytosis, both by inhibiting the deposition of complement on the surface of the bacterium and by inhibiting the killing of pneumococcus by the innate immune molecule 'lactoferrin'.

Pneumolysin

Another potential protein vaccine antigen is pneumolysin, a thiol-activated toxin expressed by almost all clinical isolates of pneumococci. Pneumolysin interferes with neutrophil function during the immune response and inhibits proliferation and antibody-production by immune cells and toxicity to alveolar epithelial cells. Due to its wide array of effects on both pulmonary tract cells and immune cells, the protein is too toxic to be used in human vaccines in its native form. Inclusion of this antigen along with PspA has shown to be protective against pneumococcal infection, suggesting again that a protein-based vaccine with multiple antigen targets may be an effective path for the production of future vaccines.

PCV13

PCV 13 actively immunises against the invasive disease caused by S. pneumoniae capsular serotypes.

PPSV 23 - PPSV 23 contains 23 capsular polysaccharides types of S. pneumoniae that represent at least 85% to 90% of pneumococcal disease isolates in the United States. Pneumococcal conjugate vaccine (PCV13 or Prevnar13) includes purified capsular polysaccharide of 13 serotypes of Streptococcus pneumoniae conjugated to a nontoxic variant of diphtheria toxin known as CRM197.

Pneumococcal Polysaccharide Vaccine

Pneumococcal polysaccharide vaccine (PPSV23 or Pneumovax23) includes purified preparations of pneumococcal capsular polysaccharide. PPSV23 contains polysaccharide antigen from 23 types of pneumococcal bacteria.

Pneumonia is one of the most common—though dangerous—disease going around in populations today. It's curable, however remains a source of extreme discomfort for those suffering from it. The advent of pneumococcal vaccines was to battle this disease and has proved to provide excellent and efficient protection against this disease. Development is one thing that will never halt in science and as such search for improvements in this vaccine continues in labs worldwide.

The Merry Game-te Corner

Created by Divya Bhardwaj
S. Y. BSc. Biotechnology

Code Decode

Fill in the blanks and unjumble the highlighted letters to decode the word of this issue.

I. The famous rebuttal for the Polio vaccine: _ _ _ _ _ _

II. The vaccine that immunizes against S. *pneumoniae* capsular stereotype: _ _ _ _ _

III. Rotavirus is the most common cause of: _ _ _ _ _ _ _ _ _ _ _ _ _

IV. Injectable form of swine flu vaccine: _ _ _

Word of the Issue

_ _ _ _ _ _ _

Heredity Hunt

Find the words listed in the word search below:

Let the Hunt Begin!

Find Us:

ROTAVIRUS ZAIRE

HRIG PNEUMONIA

POPPER NASAL

PIGS SALK

PPSV INFANT

A	S	U	A	D	Z	J	S	A	N	V	S	C	K	E
D	F	J	F	G	C	B	T	N	A	F	N	I	I	U
S	I	O	I	G	P	P	C	H	S	E	R	G	L	U
G	P	R	D	Y	I	E	O	A	I	D	I	Y	A	H
U	H	W	O	H	R	Y	C	P	N	S	J	G	I	P
O	A	E	R	T	V	O	B	T	P	A	F	E	N	S
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R	O	L	U	I	S	V	U	R	A	G	R	N	M	T
K	L	A	H	T	S	C	I	E	N	N	Y	W	U	H
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E	R	N	S	W	U	F	T	A	L	S	T	O	P	H
N	D	H	Q	T	R	D	H	Z	I	A	G	E	W	G

Gags by Gregor

Q. Why did the knife have a genetic disease?

A. It was in Bread.

Extirpating the Formidable: Poliomyelitis

No More Worries About Polio Again

Article by
Divyanshi Motwani
S. Y. BSc. Biotechnology

One of the most dreaded diseases since the 19th century, poliomyelitis, has come to an end! However, what exactly was the history of this disease, it causative viral strains and what went behind the development of its vaccine; these topics will be addressed in this article.

Polio became an epidemic in the US by the late 19th century and has spread throughout the world ever since, which led to the discovery of it's contagious nature by Ivar Wickman after a series of polio epidemics in Sweden.

In 1908, Landsteiner and Popper, after filtering spinal cord fluid from a person who died of polio, concluded that the causative pathogen for poliomyelitis was an infectious particle smaller than a bacterium i.e., a virus.

Two years later, in 1910, Simon Flexner from Rockefeller Institute for Medical Research, NY proved that vaccine for polio can be developed, he did so by showing presence of "germicidal substances" or "neutralizing antibodies to polio" in the blood of monkeys that survived polio.

After many more incidences of polio epidemics, Burnet and Macnamara in the year 1931, proposed the presence of more than one strain of the polio virus. This incidence took place 20 years before Bodian and Morgan actually proved the presence of three strains of polio virus.

Though, with the proposal of Burnet and Macnamara, the circumstances now called for a vaccine effective against all types of strains.

In 1936, Olitsky and Sabin were able to grow the polio virus in the human embryonic brain tissue, this however was not considered a practical approach to develop vaccines. Later on, in 1941, it was discovered that the virus entered the body via the mouth, then into the digestive system and then spread throughout the body; this discovery gave a hope for development of a vaccine that could fight against the virus before it became fatal.

Lederle Koprowski, tested his attenuated type II vaccine on himself and his assistant in the ear 1948, after testing it on chimpanzees.

The year of 1949 brought a breakthrough where Enders, Weller and Robbins grew the polio virus in human embryonic skin and muscle tissue. This discovery landed the three, a Noble Prize in Physiology in 1954. Later on, in 1949, Bodian and Morgan confirmed the three strains of polio virus.

Jonas Salk in 1951 created a method to cultivate polio virus in monkey kidney tissue, and subsequently, in 1952, Salk conducted the first vaccine test.
Through many trials and rebuttals such as the Cutter Incident (1955), Sabin developed the Oral Polio Vaccine and tested the same on around 10 million people. The vaccine provided protection against type I strain and was licensed. Later, the controversies with Salk's vaccine caused its discontinuity in the US.

The Salk's vaccine, nevertheless had one benefit over Sabin's that it did not cause the reversion of killed forms of virus. This benefit led to welcoming Salk's vaccine in the field again in the year 2000.

Thereafter, trivalent vaccines came into use and the number of polio cases around the globe started to decrease significantly. The cases of wild type II strain have not been reported since 1999 and since bivalent vaccine against type I and III started being used.

Today, the risk of polio virus infecting our bodies has decreased too almost null. So, this was the journey of how poliomyelitis, once an epidemic has now become a rare disease and this proves the proficiency of science and research in medical sector.

How did you find it? Any feedback? Suggestions?

We would love to know what you thought of this issue of Genophilic, any suggestions are most welcome.

As we have expanded our horizons, our next issue will be on the topic "Innovations in Medical Biotechnology"- diagnostics, devices, therapeutics

We would appreciate your contributions on said topic.

Contact us on: editor.genophilic@gmail.com

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Breaking the Normal

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Et tu, *Aedes?*

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Get a clue, Fight the Flu!

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