* Hasty approval, no transparency

- DCGI gave Emergency Use Authorisation (EUA) to
  - SII's – Covishield
  - Bharat Biotech's – Covaxin
- While some have pointed out lack of transparency in DCGI's approval process
  - as FDA of US had a live telecast of advisory committee's examination of Pfizer's & Moderna's vaccine data before granting EUA
  - UK regulator also made assessment of vaccines by Pfizer & Astrazeneca → publicly available
- Covishield – (Restricted Use approval)
  - Safety & immunogenicity data available from phase-2/3 trials on 1600 participants
  - But no efficacy data
  - Approval was based on efficacy data from UK, as Covishield is nearly same as Oxford-Astrazeneca vaccine data.

- Full approval will be given when efficacy data from India is available

– Covaxin (Restricted Use Approval)
  - No efficacy data available here also
  - phase 3 trials ongoing

– Thus, India joined China & Russia in giving approval to Covaxin without efficacy data
  ↳ China approved Sinovac, but only for military use.
  ↳ Russia's claim of Sputnik V's 92% efficacy is based on a review of just 20 COVID-19 cases

– 9 global vaccine manufacturers
  ↳ had issued a joint pledge last Sept to not seek premature approval.
  ↳ Bharat Biotech's haste in seeking approval stands in contrast to the pledge.

– Consequences
  - Vaccines may not have public faith.
  - If there is vaccine hesitancy among the people, the companies & regulator have themselves to blame

★ Cuba develops the world's first conjugate vaccine for COVID-19

↳ Cuba's indigenously developed two vaccine against SARS-COV-2

- Soberana 2 and Abdala

↳ Both vaccine are subunit vaccines

- In soberna 2, the spike protein is chemically linked to the tetanus toxoid, making it a conjugate vaccine.

↳ About sub-unit vaccine

- It includes only parts of the virus or bacteria or sub-unit instead of entire germs, which have been selected for their ability to stimulate immune cells

↳ About conjugate vaccine

- It combines a weak antigen with strong antigen as a carrier so that immune system has a stronger immunological response to the weak antigen.
- common conjugate vaccines are Haemophilus influenza type b (Hib) and the Pneumococcal vaccine

* Plasmid DNA vaccine ZyCoV-D

- ZyCoV-D vaccine-

- World's first plasmid DNA vaccine
- Received Emergency Use Authorization in India.

- Plasmids DNA Vaccines

- A plasmid is a small, circular, double-stranded DNA molecule that is distinct from a cell's chromosomal DNA.
- Plasmids naturally exist in bacterial cells, and they also occur in some eukaryotes
- A piece of DNA encoding the antigen is inserted into a bacterial plasmid and injected into humans.
- It then stimulates the immune system to generate antibodies and T-cells immunity against the virus.

– Significance

- Plasmid DNA has huge potential
- Quickly develops vaccines with fairly generic manufacturing processes
- The specified DNA piece disintegrates after it has completed its action and thus is unable to interfere with the genetic composition of humans.
- As vaccine does not use any part of the virus they are considered relatively safer.
- The plasmid vaccines have good genetic stability and are also easy to administer.

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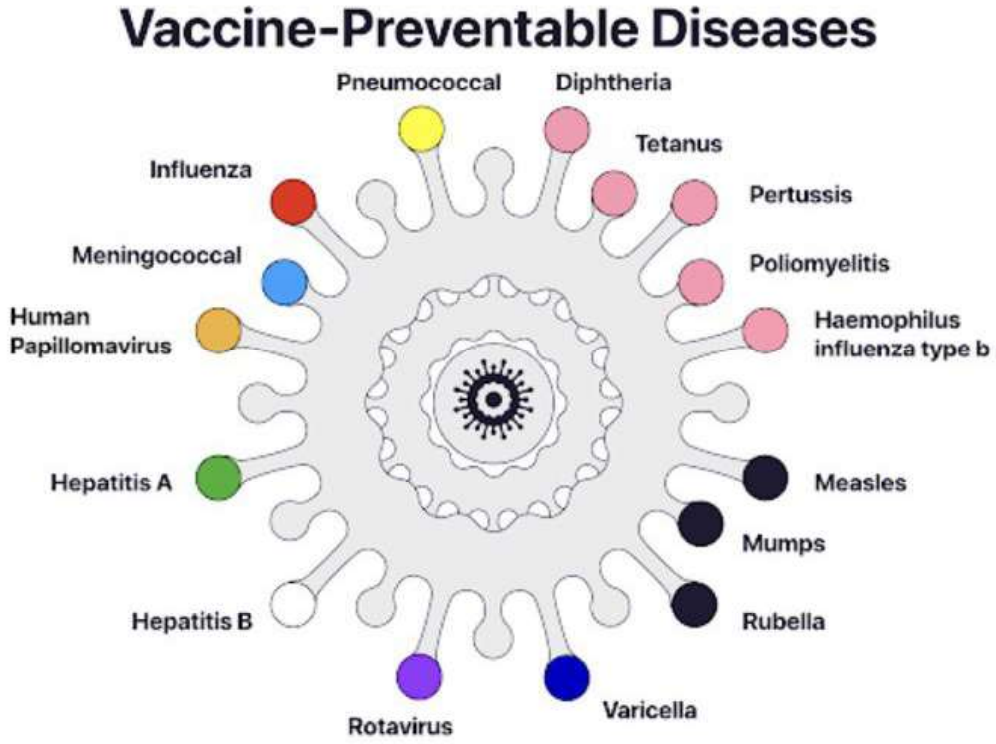
Vaccine-Preventable Diseases (VPDs)

Vaccine-preventable diseases (VPDs) are bacterial and viral infections that can be avoided using vaccinations.

- VPDs can be transmitted by a variety of means, including the air, respiratory droplets, and body contact.

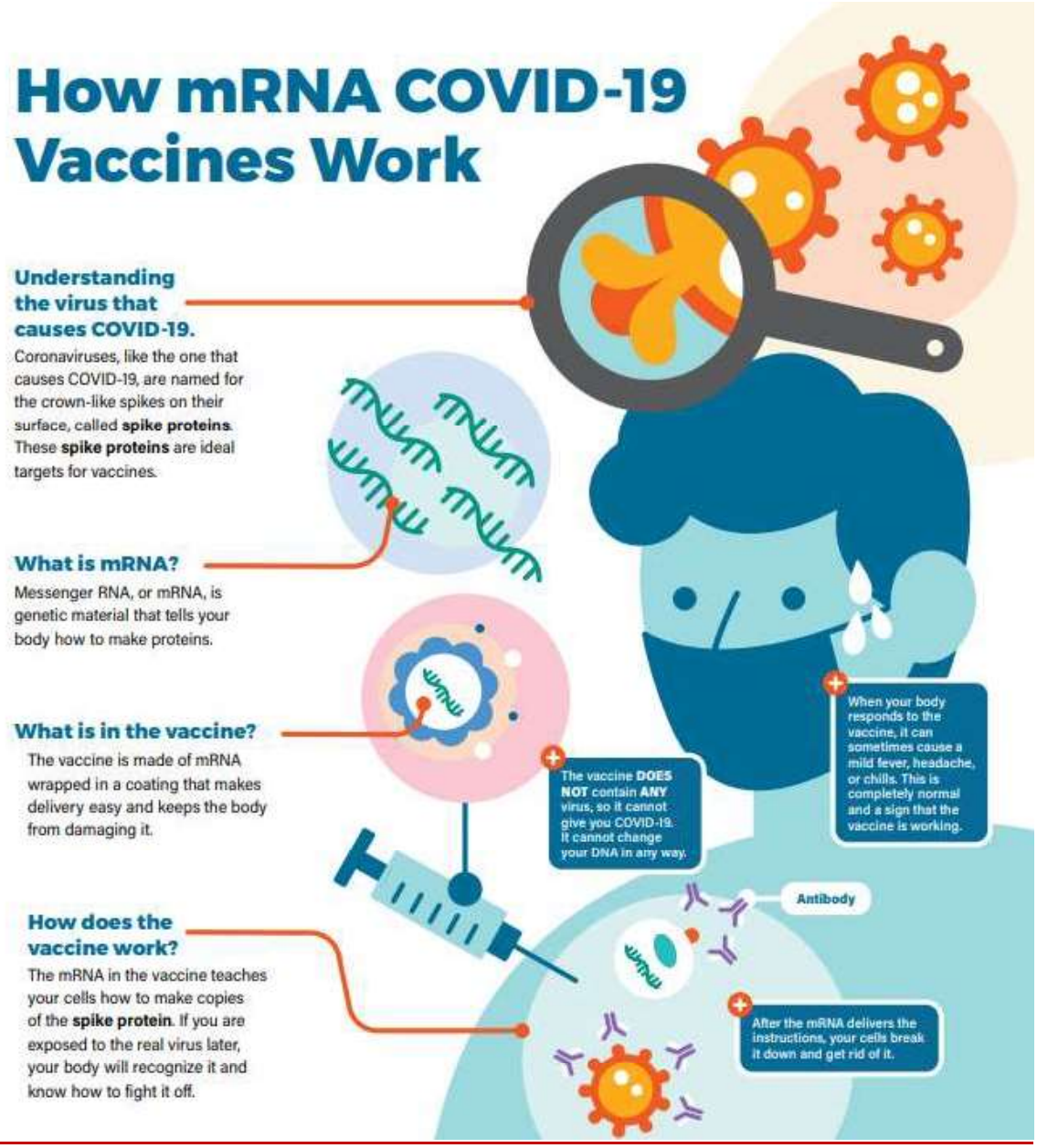


- Mission Indradhanush provides vaccination against 12 Vaccine-Preventable Diseases (VPD).
- The VPDs covered under Mission Indradhanush are
  - Diphtheria
  - Whooping Cough
  - Tetanus, Polio
  - TB
  - Hepatitis B
  - Meningitis
  - Pneumonia
  - Haemophilus Influenzae Type B infections
  - Japanese Encephalitis (JE)
  - Rotavirus Vaccine
  - Pneumococcal Conjugate Vaccine (PCV)
  - Measles-Rubella (MR).

When will India's mRNA vaccine be out?

India's first indigenously developed mRNA vaccine is expected to be released by the Pune-based Gennova Biopharmaceuticals.

About mRNA vaccine:



The Present Status of the Vaccine:

- The mRNA vaccine in India is currently in phase 2 and 3 trials to examine the immunogenicity, safety and tolerability.

Advantages:

- Evidence reveals that mRNA Vaccine shows robust immune response in the trials and enhanced protection against infections.
- As it employs only the genetic code, it is easily updated in response to the emergence of variants.

Challenges with respect to mRNA vaccines–

- Its storage mandates temperature spanning from minus 90 degree C to minus 50 degree C.
- Such stringent freezing conditions are expensive to be maintained.
- There is a wide gap between vaccine preparation and its supply due to challenges in scaling up production.

* Norms eased for foreign-made vaccines

- DCGI waived
  - ↳ requirement of conducting bridging clinical trials & testing of every batch of vaccine imported
  - ↳ Done by Central Drugs Lab, Kasauli
- Eligibility :
  - Must have approval of USFDA or European Medicines Agency or UK & Japan's regulators OR
  - Those listed in WHO's Emergency Use Listing
- Purpose :
  - ↳ Ease supply of imported vaccines
- To enhance domestic production
  - 3 PSUs to start manufacturing vaccines.
  - under Atma Nirbhar Bharat 3.0 Mission Covid Suraksha. Supported by Deptt of Biotech
    - ↳ Haffkine Biopharma, Mumbai ⇒ will produce Covaxin under Tech transfer by Bharat Biotech Ltd
    - ↳ Indian Immunologicals Ltd, Hyderabad
    - ↳ Bharat Immunologicals & Biologicals Ltd, UP

* SII too seeks indemnity from liability

- Serum Institute of India (SII)
  - ↳ manufactures Covishield (Astrazeneca)
  - ↳ also manufacturing Covovax (Jointly developed by SII & Novovax)
  - ↳ also applied to DCGI to manufacture Sputnik V (Currently manufactured by Dr Reddy's Lab)
- Foreign vaccine makers (Pfizer, Moderna)
  - ↳ demanded grant of indemnity against legal proceedings prior to roll out in India
- Now SII
  - ↳ All vaccine makers (whether Indian or foreign) should be given same protection.
  - ↳ Indemnity is being demanded against cost of compensation in event of severe side-effects.
- Till now in India
  - ↳ no vaccine maker has ever paid indemnity.
  - ↳ Neither the Govt.

* Centre orders 30 crore doses from Biological E

- Biological E Ltd, Hyderabad
  - ↳ licensed a recombinant protein based COVID19 vaccine (developed by Houston based Health Sciences University) in Aug 2020
  - ↳ GoI supported (provided grant-in-aid of over ₹100 crore)
  - ↳ partnered with THSTI, Faridabad to conduct animal & assay studies.
- Present Status
  - ↳ undergoing Phase 3 Clinical Trials
  - ↳ NEGVAC gave approval to proposal.
- Govt of India's support to the made-in India vaccine
  - ↳ Reserved 30 crore doses
  - ↳ Advance payment of ₹1500 crore
- Biological E also executed agreement
  - ↳ to manufacture J&J's COVID-19 vaccine in India
  - ↳ manufacture mRNA vaccines. Deal with Canada's Providence Therapeutics.
- J&J's Quad Vaccine Partnership
  - ↳ To make over 1 bn doses for use in Asia by 2022

* COVID-19 vaccines & the indemnity clause

- Indemnity
  - ↳ a form of contract
  - ↳ Indian laws dont have any provision for indemnity for drugs or vaccines
  - ↳ S.124 of Indian Contract Act 1872
    "one party promises to save the other from any loss caused to the latter"
  - ↳ So, GoI needs to execute an indemnity bond with the supplier.
- Consequence of such indemnity
  - ↳ If a death or lasting damage is caused due to the vaccine, any claim of compensation will be met by Govt.
  - ↳ If foreign makers are granted indemnity, then Indian ones will also demand it.
  - ↳ Thus the entire risk will be on Govt.
- Situation elsewhere
  - ↳ Pfizer is believed to have obtained such indemnity from several countries, incl. the UK ⇒ but has not made it public

- What is the Standard Practice?
  - Companies applies for approval of its drugs
  - Approvals given by national regulators on conforming with national guidelines, safety & clinical trials, etc.
  - But due to severe shortage of vaccines
    ↳ countries are not able to set conditions, instead they need to accept whatever the makers or importers are offering.
- GoI already on eased some restrictions-
  - No need for local trials if approved by regulators of US, UK, EU & Japan or listed in WHO's EUL.
  - Condition of post-approval bridging trial also waived
  - New Drugs & Clinical Trial Rules 2019
    ↳ provides for compensation by sponsor if any participant dies or suffers disability
    ↳ With conditions of trials waived off, now no risk of compensation payments.
- What if indemnity is not granted?
  ↳ Overseas manufacturers will load the risk onto the price of vaccines

* Vaccine related news

- Brazil gave approval to import Covaxin
  - ↳ earlier had denied permission to import
  - ↳ as its regulators alleged that Bharat Biotech's plant did not meet the Good Manufacturing Practices (GMP) requirements.

- SII gets DCGI's approval to produce
  - ↳ Sputnik V @ its Hadapsar facility, Pune. (By Gamaleya Research Inst., Moscow)

- US lifted restrictions on export of vaccine ingredients to Astrazeneca vaccine manufacturers worldwide, incl. SII
- Also US' vaccine 'gift'
  - ↳ may not be substantial.
  - ↳ Not more than 2-3 million doses
  - ↳ India vaccinates ~2.8 mn people per day at present.
  - ↳ Also indemnity issue may delay the vaccine gift.

What is Genome Sequencing?

How genome sequencing has changed our understanding of monkeypox virus

Over 600 genomes have been sequenced this year alone from over 35 countries

- Genomic surveillance help provide unique insights into outbreaks, track the spread of pathogens, help public health decision-making as well as for epidemiology
- Being a DNA virus, the monkeypox virus like other poxviruses was believed to have a small rate of accumulating genetic changes
- But a recent study revealed that the observed rate of genetic changes in the virus was higher – average of around 50 genetic changes
- Infections in the animal reservoirs could also enable continued transmission and accumulation of mutations before the virus jumps to humans
- One study has suggested continued evolution of the virus, including deletions, suggesting newer ways in which the virus continues to evolve with sustained human-to-human transmission

Largely ignored: Before the first case was reported in the U.K. in May this year, only 50 complete genome sequences of monkeypox isolates were deposited in public databases

- Over 95% of the recently deposited genome sequences of the virus belong to the B.1 lineage linked to the superspreader events in Europe
- The A.2 lineage of the monkeypox virus encompasses six genome sequences, including the two collected from Kerala
- The A.2 lineage amid the 2022 outbreak suggests a previously undetected and cryptic transmission of the virus in multiple countries since at least 2021

In News

Recent study revealed that the rate of genetic changes in the monkeypox virus was higher than expected

About Genome Sequencing

- Genome sequencing is the process of determining the complete DNA sequence of an organism's genome at a single time.
- Determines the characteristic of any organism
- Every organism has a unique genome sequence.

Why are so many genome sequences being isolated?

- When viruses multiply, or reproduce, there is a copying mechanism that transfers the gene information to the next generation.
- Since no copying mechanism is perfect so when the virus multiplies, there will be small changes, which are called mutations.
- These mutations accumulate over time, and after prolonged periods, are responsible for evolution into new organisms.
- Within a single reproduction, the changes are extremely minor.
    - More than 95% of the gene structure remains the same.

How do these small changes help?

- Minor changes that occur are crucial to understand the nature and behaviour of the organism.
- They could provide information about the origin, transmission, and impact of the virus on the patient.
- Could also hold clues to the differing effects the virus could have on patients with different health parameters.

Monkeypox accelerated evolution

- Monkeypox virus has a DNA genome of around 2,00,000 base pairs, roughly 06 times larger than that of SARS-CoV-2.
- This virus also evolves by the accumulation of genetic errors, or mutations, in its genome when it replicates inside a host.

- Being a DNA virus, the virus like other poxviruses was believed to have a small rate of accumulating genetic changes compared to viruses with
    - An RNA genome like SARS-CoV-2, which have a much larger rate of mutations.
- But it was observed that rate of genetic changes in the virus was higher than expected, average of around 50 genetic changes.

Findings of the study

- Several mutations have been identified in the new sequences of the monkeypox virus.
    - May have emerged due to interaction between the:
    - Virus genome and an important family of proteins coded by the human genome known as the Apolipoprotein B Editing Complex (or APOBEC3).
- These proteins offer protection against certain viral infections by editing the genome sequence of the virus while it replicates in the cell.
- Some researchers suggest that many of the genetic mutations in the monkeypox genomes from the current outbreak are relics of the effect of APOBEC3.

Recommendation

- Genomic surveillance of pathogens provides interesting insights by following a molecular approach for contact tracing and understanding the transmission of the virus across the world.

- With COVID-19 and monkeypox worldwide, there is a need to build a sustainable system for genomic surveillance in India and globally strengthen it.
- Since data suggest a sustained human-to-human transmission
    - Continuous genomic surveillance is important to understand the evolution and adaptation of the virus

Small Satellite Launch Vehicle (SSLV) launched into wrong Orbit

- ISRO has said that the satellite onboard its' maiden SSLV "are no longer usable" after the SSLV-D1 placed them in an elliptical orbit instead of a circular one.

All about SSLV

- Small-lift launch vehicle being developed by the ISRO with payload capacity to deliver:
  - 600 kg to Low Earth Orbit (LEO) (500 km)
  - 300 kg to Sun-synchronous Orbit (500 km)
- A dedicated launch pad in Sriharikota called Small Satellite Launch Complex (SSLC) will be set up.
- New spaceport, under development, near Kulasekharapatnam in TN will handle SSLV launches when complete.
- After entering the operational phase, the vehicle's production and launch operations will be done by
  - A consortium of Indian firms along with NewSpace India Limited (NSIL).
- It is a 04 stage launching vehicle.
- First 03 stages will use Hydroxyl-terminated polybutadiene (HTPB) based solid propellant, with a fourth terminal stage being a Velocity-Trimming Module (VTM).

Comparison between SSLV, PSLV

- SSLV was developed with the aim of launching small satellites commercially at drastically