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EDITORIAL

Covid-19 Vaccine. Time for Waiting is Over !

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COVID 19 pandemic is the defining global health crisis of this time and greatest challenge we have faced since World war II. Since its emergence in Asia in 2019, the virus has spread to every content except Antarctica. Cases were raising daily in America, Europe and Africa. Countries are racing to slow the spread of the disease by testing, treating patients, carrying out contact tracing, limiting travel, quarantining citizens and cancelling large gathering such as sporting events, concerts and schools.

But COVID 19 is much more than a health crisis. By stressing every people of the countries, it has the potential to create devastating social, economic and political crisis that will leave deep scars. Every people are losing jobs and income with no way of knowing when normality will return. The International Organization estimates that 24 million jobs could be lost.

After coronavirus was isolated in December 2019 its genetic sequence was published on 11 January 2020 triggering an urgent international response to prepare for an outbreak and hasten development of a preventive COVID 19 vaccine. Since early 2020, vaccine development has been expedited via unprecedented collaboration in the multinational pharmaceuticals industry and between government. The urgency to create a vaccine for COVID 19, led to compressed schedules that shortened the standard vaccine development timeline.

Three vaccine front runners are those developed by Pfizer/BioNTech, Moderna and Oxford/ AstraZeneca. Pfizer and Moderna have both developed mRNA vaccine- a new approach that is incredibly quick to design where they inject tiny fragments of viral genetic code into the body, this has been approved by UK, Europe and US.

Oxford vaccine is subtly different as it uses a harmless virus to carry the same genetic material into the body. This has been approved in the UK and Europe. It is the easiest of the three to use as it can be stored in a fridge, rather than needing very cold temperature.

New approach to vaccines

mRNA vaccines are a new type of vaccine to protect against infectious diseases. As in January 2021, nine different technology platforms are under research to create an effective vaccine against COVID 19. Platforms being developed in 2020 involves- Nucleic acid technology, non replicating viral Vectors, Peptides, Recombinant proteins, Live attenuated viruses, and Inactivated viruses. Currently, four main types of COVID 19 vaccine that are being used. Below is a description of how each type of vaccine prompts our bodies to recognize and protect us from the virus that causes COVID 19. Non of these vaccines can give rise to COVID 19.

mRNA vaccines contains genetic code from the virus that causing COVID- 19 and gives body cells instructions to make a harmless protein which is unique to the virus. After body cells make copies of the protein, they destroy the genetic material from the vaccine as body recognize that the protein should not be there. They build T-lymphocyte and B-lymphocytes that will remember how to fight against the virus that causes COVID-19 if infected in future.

Protein subunit Vaccines include harmless pieces of the virus that cause COVID-19 instead of the entire germ. After vaccination immune system recognizes that this proteins do not belongs to the

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body, so they begins to build T- lymphocytes and antibodies. If we are ever infected in future memory cell will recognize and fight against the virus.

Vector vaccines contain a weakened version of a live virus other than the virus causes COVID- 19. That different virus has genetic material from the virus causes COVID-19 which is inserted by genetic engineering (this is called vector virus).Once the vector virus is inside our body cell, the genetic material gives cells instructions to make a protein that is unique to the virus that causes COVID 19. Using these instructions our cells make copies of the protein. This prompts our bodies to build T lymphocytes and B lymphocyte that will remember how to fight COVID- 19 virus if we are infected in the future.

Inactivated virus Vaccine consist of virus particles that have been grown in culture and then are killed using a method such as heat or formaldehyde to lose disease producing capacity while still stimulating an immune response.

After vaccination it typically takes a few weeks for the body to produce T lymphocyte and B lymphocyte. Therefore it is possible that a person could be infected with the virus that causes COVID- 19 just before or after vaccination and the get sick because the vaccine did not have enough time to provide protection.

Vaccines are safe except minor symptoms after vaccination such as fever which are thought to be associated with the process of building immunity. But very rarely there is evidence of blood clotting specially in cerebral sinus venous thrombosis(CSVT) may occur in vector based vaccination,

Some expert continue to work of this very rare side effect associated with AstraZeneca vaccine. The vector vaccine COVID-19 appears to be associated with autoimmune thrombosis that mimics heparin-induced thrombocytopenia (HIT). The United Kingdom, European Union, and Scandinavian countries have reported rare cases of cerebral sinus vein thrombosis (CSVT) and thrombocytopenia in patients who received the vector based COVID-19 vaccine. The majority of affected patients are women under the age of 55 years, and CSVT seems to occur 4 to 20 days after vaccination. The likely mechanism is antibodies that induce massive platelet activation, reducing the platelet count and causing thrombosis.[1,2] This phenomenon mimics heparin-induced thrombocytopenia (HIT) yet it does not require heparin as a trigger. It has been named vaccine-induced prothrombotic immune thrombocytopenia (VIPIT). The incidence of VIPIT appears to be between 1 in 125,000 and 1 in 1 million.[3]

Clinically Patients with VIPIT may present with CSVT, or with other arterial or venous clots. Some symptoms make it more likely that a patient has VIPIT: persistent and severe headache, focal neurological symptoms, seizures, or blurred or double vision; shortness of breath or chest pain suggesting pulmonary embolism or acute coronary syndrome; abdominal pain suggesting portal vein thrombosis; or limb swelling, redness, pallor, or coldness suggesting deep vein thrombosis or acute limb ischemia. VIPIT seems to occur between 4 to 20 days post-vaccination. Symptoms in this time frame should raise the clinical suspicion of VIPIT.

For diagnosis clinicians should ask patients about their COVID-19 vaccine history and should draw a complete blood count (CBC). VIPIT is more likely if symptoms of blood clotting fall in the 4-to-20-day time frame AND the platelet count is < 150 x 109/ L.[3] Patients with suspected VIPIT should go on to have a D-dimer level and a blood film drawn. They should also have diagnostic imaging to investigate for blood clots based on clinical suspicion. Other than clinical suspicion and blood count the confirmatory diagnosis of VIPIT is made by testing for heparin-induced thrombocytopenia (HIT). This testing should be done even if the patient has had no previous exposure to heparin. HIT testing involves two steps: identification of antibodies against the complex of platelet factor4 and heparin; and confirmatory functional testing of the antibodies' ability to activate platelets.[4]

The Presumptive and confirmed VIPIT should be treated similarly to HIT. Until VIPIT has been ruled out, anticoagulation with heparin (both unfractionated heparin and low molecular weight heparins) and Platelet transfusions should not be given.[4]

Alternative anticoagulants that are safe to use in HIT are likely safe to use in VIPIT include direct thrombin inhibitors and anti-Xa inhibitors (e.g., rivaroxaban, apixaban, edoxaban). If the patient

has severe renal impairment that makes direct oral anticoagulants unsafe, advice from a hematologist should be sought to guide the use of parenteral anticoagulants that are safe to use in HIT.

In patients with confirmed VIPIT and severe or life-threatening blood clots (e.g., CSVT, splanchnic vein thrombosis), it is important to dampen the prothrombotic response with intravenous immunoglobulin (IVIG). Administration of high dose IVIG (1 g/kg of body weight daily for two days) is appropriate and can be guided by the consulting hematologist.[5]

Controversy /Confusion

Commonly asked questions:

-*Whether the existing vaccine will be effective against the new variant of covid-19 virus?*

-Can some body receive different type of vaccine in two doses of Covid-19 vaccine ?

-After Covid-19 infection how long should wait to receive the first dose or second dose?

The COVID-19 vaccines are expected to provide at least some protection against new virus variants and are effective at preventing serious illness and death. That's because these vaccines create a broad immune response, and any virus changes or mutations should not make vaccines completely ineffective. Thus vaccines protect us from these new variants and this is something that is kept in mind when vaccines are being manufactured. If any of these vaccines become less effective against one or more variants, it will be possible to change the composition of the vaccines to protect against these variants. Data continues to be collected and analysed on new variants of the COVID-19 virus.[6]

Till the time it is very confused that a single person can take two different type of vaccine in first and second dose and is not recommended. Some scientists says that there is no reason to believe that giving two dose of different production will boost a persons' immune response beyond what can be achieved by giving same. They also said there may be some adverse effect and truly they do not favor to mismatch with previously received vector vaccine specially Astra Zeneca vaccine. NACI(National advisory committee on immunization) do not preferred AstraZeneca as they are associated with VIPIT.

In this regard COVID-19 Heterologous Prime boost study or ComCOV study is going on in UK. The early massage from the senior officer of the study, they do not see any safety problem or additional danger in mismatched vaccine. This is because different vaccine administration as a part of two dose regimen do not directly interact with each other because the vaccine particles are swiftly cleared by the immune system within days of immunization. There is no remaining vaccine mRNA or viral vector around when given a second dose.

Canadian health officials are now reviewing the research on mismatched vaccine for COVID-19, though their current guideline is AstraZeneca to AstraZeneca for two shots. Very recently Christine Elliott, Ontarios' Health Minister declared that person who received the AstraZeneca vaccine may receive a different vaccine for their second dose.

Fritz, microbiologist and immunologist, professor at McGill university said it better to take mismatched vaccine than to wait too long time for second dose. He also urgue that we give immunization to infant with several different types of vaccine over a period of one month and year without safety concern. He also mention that mismatched vaccine regimen was approved for Ebola last year

Time between two shots was initially 4 months thinking about availability of vaccine and lack of study. Now Pfizer vaccine scheduled 21 day between two dose and Moderna scheduled 28 days between two dose. If some body suffered from COVID-19 he or she should wait 4 weeks to receive the covid-19 vaccination. If someone get infected after 1st dose he can take the second dose after 10 days of recovery from symptoms. Patients suffering from severe disease of COVID- 19 treated by Convalacent plasma or monoclonal antibody, they should wait for 90 days to receive the vaccination.

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