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REVIEW ARTICLE **OPEN ACCESS**

Effective Utilization of Immunotherapy in Treatment of Coronavirus

P.P. Deshmukh*[1], H. L. Tare[2], N. S. Deshmukh[2], S. R. Chaudhari[3]
1. Trimurti Shikshan Prasarak Mandal's Trimurti Institute of Pharmacy, Jalgaon, M.S., India.
2. Amrutvahini Sheti and Shikshan Vikas Sanstha's Amrutvahini College of Pharmacy, Sangamner, Savitribai Phule Pune University, M.S., India.
3. KJ's Educational Institute's Trinity College of Pharmacy, Pune, M.S., India.
Email- harshaltare51@gmail.com

ABSTRACT
The novel coronavirus (2019-n Cov) is an emerging pathogen that was first described in late December 2019 and causes severe respiratory infections in human. Since the outbreak of COVID-19, international attention has raised to develop treatment and control option such as types of Immunotherapies. Coronavirus causes Respiratory infection including pneumonia, cold, sneezing, and coughing while in the animal it causes diarrhoea and upper respiratory diseases. Coronavirus transmitted human to human or human to animal via airborne droplets. The Immunotherapy is an effective method for fighting against similar viral infection such as SARS- Cov and MERS- Cov. These methods include several types of vaccines, monoclonal antibody candidates, etc. The effective of IVIg would be better if the immune IgG antibiotics who have recovered from COVID-19 in the same city. These immune IgG antibiotics will be a specific immune response in newly infected patients. This systematic review article was designed to evaluate the existing evidence and experience related to Immunotherapy for 2019 – n Cov.
Keywords:- *COVID-19, Immunotherapy, Monoclonal antibody, vaccine, IVIg- Immunotherapy.*

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INTRODUCTION

History and Origin

The first case of coronavirus was notified as cold in 1960. According to the Canadian study 2001, approximately 500 patients were identified as a flu-like system. 17-18 case of them were confirmed as infected with coronavirus strain by a polymerase chain reaction. Corona was treated as a simple non-fatal virus until 2002. In 2003, various reports published with the proofs of spreading the corona to many countries such as the United States of America, Hong Kong, Singapore, Thailand, Vietnam and in Taiwan. Several cases of severe acute respiratory syndrome caused by corona and they are mortally more than 1000 patients were reported in 2003. This was the black year for the microbiologist. When microbiologist was started focus to understand the pathogenesis of disease and discovered as coronavirus. But till total 8096 patients were confirmed as infected with coronavirus, so in 2004, world health organization and centres for disease control and prevention declarable as "State emergency". Another study report of Hong Kong has confirmed 50 patients of severe acute respiratory syndrome while 30 of coronavirus infected. In 2012, Saudi Arabian reported patients and death. COVID-19 was first identified and isolated from pneumonia patient belong to Wuhan, China. [1]

A coronavirus is a group of related viruses that causes disease in mammals and birds. In humans, coronavirus causes respiratory tract infections that can range from mild to lethal. Until recently, most people will never have heard of coronavirus but, the disease causes in humans and animals have been recognized for over 50 years. [1]

Coronavirus was first identified by a group of virologists (J D Almeida, DM Berry, C H Cunningham, D Hamre, M S Hofstad, L Mallucci, K Mclntosh and DAJ Tyrrell), who relayed their finding in 1968 to the journal Nature , which published a brief annotation. [2]

Coronavirus (COVID-19) are positive sense, single-stranded RNA virus. Family of the virus is Coronaviridae (subfamily – coronavirinae) that infect a wide host range to produce disease ranging from the common cold to severe/fatal illnesses. The novel virus was initially named "2019-n Cov" which was changed to "SARS-Cov 2" by the coronavirus study group (CSG) of the international committee on taxonomy of virus (ICTV), since it was found to the sister virus of severe acute respiratory syndrome coronavirus (SARS –Cov). The ongoing coronavirus threat that emerged in China has rapidly spread to other countries and has been declared as a Global Health Emergency by the World Health Organization (WHO). [2]

As both SARS – Cov and SARS – Cov 2 (2019-n Cov) have the same receptor for virus entry, potential biotherapeutics to prevent SARS entry could be extrapolated to block the virus attachment or entry, monoclonal antibodies are preferred due to their specificity, purity, low risk of blood-borne pathogen contamination and safety compared to serum therapy and intravenous immunoglobulins preparation. [2]

Four Human coronaviruses produce symptoms that are generally mild:-

- Human coronavirus OC43 (HCov-OC43), beta-Cov
- Human coronavirus HKU (HCov-HKU1), beta-Cov
- Human coronavirus 229E (HCov-229E), alpha-Cov
- Human coronavirus NL63 (Hcov-NL63), alpha-Cov

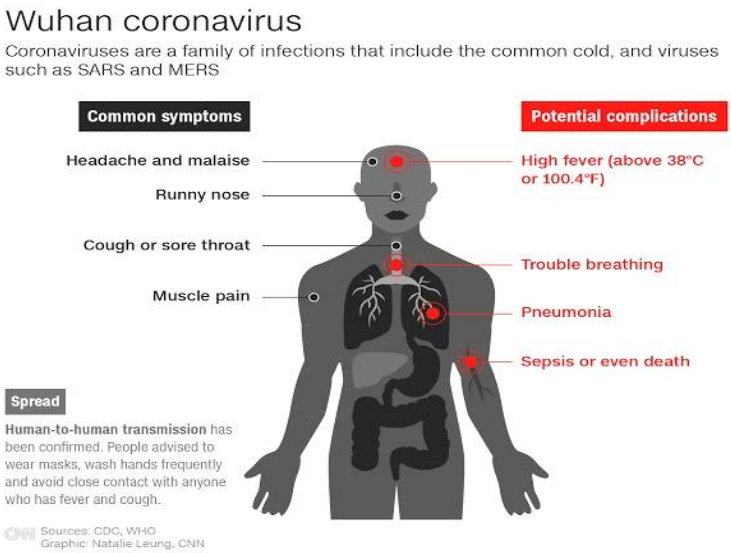

Fig 1:- Covid 19 Symptoms and Potential Complications [3]

Three Human coronaviruses produces symptoms that are potentially severe:-

- The Middle East respiratory syndrome-related coronavirus (MERS-Cov), beta-Cov
- Severe acute respiratory syndrome coronavirus (SARS-Cov), beta-Cov
- Severe acute respiratory syndrome (SARS-Cov2) beta-Cov

Characteristics of human coronavirus strains MERS-Cov, SARS-Cov, SARS-Cov2 and related disease:-

Class	MERS-Cov	SARS-Cov	SARS-Cov-2
Diseases	MERS	SARS	COVID-19
Outbreak	2012, 2015, 2018	2002-2004	2019-2020 pandemic

Epidemiology:-

Date of first identified case	June 2012	November 2002	December 2019
Location of first identified case	Jeddah, Saudi, Arabia	Shunde, China	Wuhan, China
Age average	56	44	56
Sex ratio (M:F)	3.3:1	0.8:1	1.6:1
Confirmed cases	2494	8096	2,416,135
Deaths	858	774	165,939
Case fatality rate	37%	9.2%	6.9%

Symptoms :-

Fever	98%	99-100%	87.9%
Dry cough	47%	29.75%	67.7%
Dyspnoea	72%	40-42%	18.6%
Diarrhoea	26%	20-25%	3.7%
Sore throat	21%	13-25%	13.9%
Ventilation use	24.5%	14-20%	14.1%

Note:-

- Based on data from Hong Kong
- Data as of 20 April 2020

Virus classification:-

Sr. No	Unranked	Virus
1)	Realm	Riboviria
2)	Phylum	Incertae sedis
3)	Order	Nidovirales
4)	Family	Coronaviridae
5)	Subfamily	Orthocoronavirina

IMMUNOTHERAPY

Immunotherapy or biological therapy is the treatment of disease by activating or suppressing the immune system. Immunotherapies designed to elicit or amplify an immune response are classified as activation Immunotherapies. [4]

Immunomodulators :-

Immunomodulators are the active agent of Immunotherapy. They are a diverse array of recombinant, synthetic and natural preparation.

Sr.No	Class	Example agent
1)	Interleukins	IL-2, IL-7, IL-12
2)	Cytokines	Interferons, G-CSF
3)	Chemokines	CCL3, CCL26, CXCL2
4)	Immunomodulatory imide drug	Thalidomide and it's analogue (lenalidomide, apremilast
5)	Other	Cytosine phosphate guanosine

Immune enhancement therapy

Autologous Immune enhancement therapy uses a person's own peripheral blood-derived natural killer cells, cytotoxic T lymphocyte epithelial cells and other relevant immune cells are expanded *in vitro* and then reinfused.

Suppression Immunotherapies:-

Immune suppression dampens abnormal immune response in autoimmune disease or reduces a normal immune response to prevent the rejection of transplanted organs or cells.

- **Immunosuppressive drugs:-** Immunosuppressive drugs help manage organ transplantation and autoimmune diseases. The immune response depends on lymphocyte proliferation cytostatic drug is immunosuppressive.
- **Immune tolerance:-** The body naturally does not launch an immune system attack on its tissues. Immune tolerance therapy seeks to reset the immune system so that the body stops mistakenly attacking its organs or cells in autoimmune disease or accepts foreign tissue in organ transplantation.

Innate Immune response:-

The innate immune response is one of the two main immunity strategies found in vertebrates (the other beings the adaptive immune system). The innate immune system is an older evolutionary defences strategy. Relatively speaking and it's the dominant immune system response found in plants, fungi, insects and primitive multicellular organism. [4].

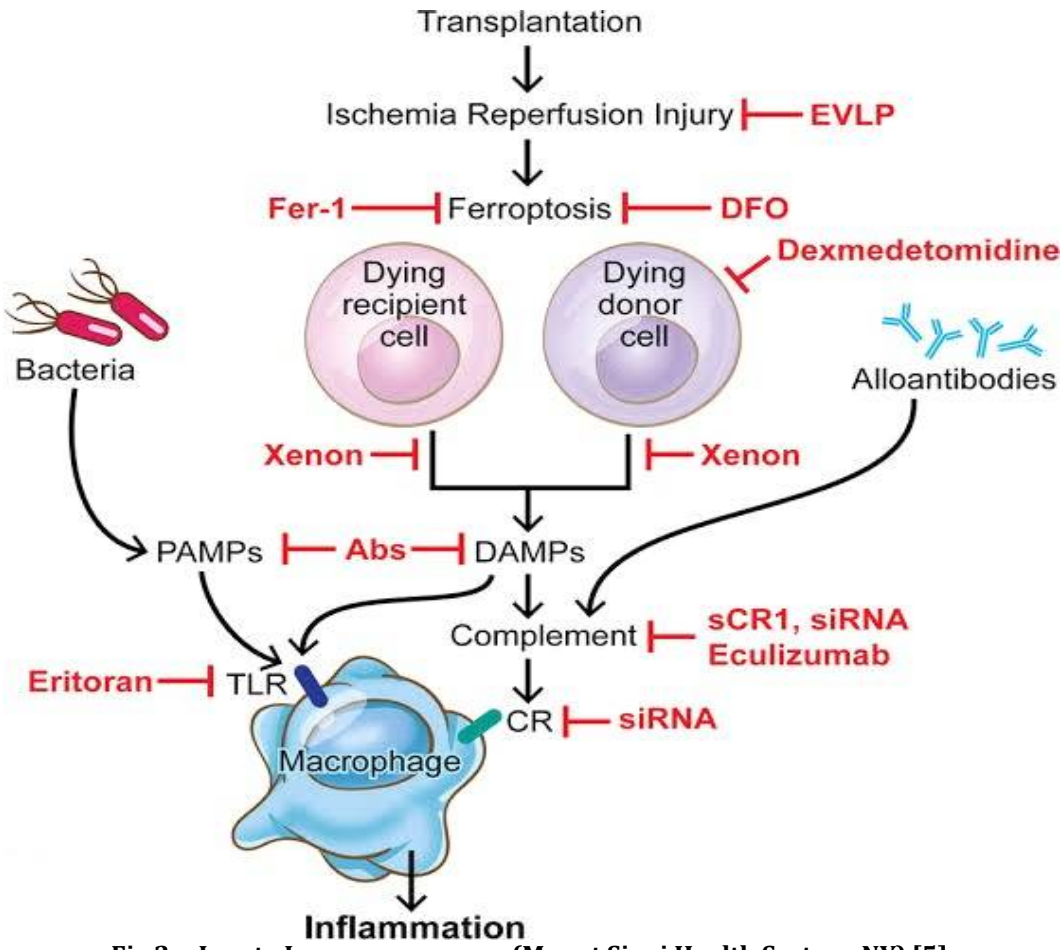

Fig 2 :- Innate Immune response (Mount Sinai Health System, NY) [5]

- **Pathogen recognition receptor:**- The host innate immune system detects viral infections by using pattern recognition receptor (PRRs) to recognize pathogen-associated patterns (PAMPs). At present, the known PRRs mainly include toll-like receptor (TLR), RIG-like, receptor (RLR), NoD- like receptor (NLR), C-type lectin-like receptor (CLmin), and free-molecule receptor in the cytoplasm, such as cGAS, IFI16, STING, DAI, and so on.
- **Toll-like receptor:-** PAMPs recognize by toll-like receptor (TLRs) include lipids, lipoproteins, protein and nucleic acid of the bacterial, viral, parasites and fungal origins. The recognition of PAMPs by TLRs also occurs in cell membranes, endosomes, lysosomes and endocytolysosomes and other location in cells. Different TLRs can include different biological response via subsequent activation of varied adapter proteins, such as MyD88, TIRAP, TRIP and TRAM but varied adapter proteins all share the Toll/Interleukin-1 receptor (TIR) structure. [6]
- **RIG-I-like receptor:-** RIG-I-like receptor (RLRs), including the H family members RIG-I (DDx58), MDAS (IFSH) , and LGP2, primarily recognize nucleic acids of RNA viruses. They have a DExD/H-box. RNA helicase structure and a C-terminal structure (CTD), while RIG-I and MDA5 have an N-terminal caspase recruitment structure (CARD), to interact with the downstream adapter MAVS.
- **Nucleotide-binding and oligomerization domain-like receptors:-** Nucleotide-binding and oligomerization domain (NOD) – like receptor (NLRS) are a class of patterns recognition receptor, which are recognized components of pathogen and contains a conserved NOD structure NLR receptor family members are divided into their subclasses according to their function. The first NLC subclasses form complexes with a variety of protein and these complexes are defined as inflammasome that contains at least eight NLR protein, including NLRP1, NLRP3, NLRP6, NLRP4, NLRC5W and AY2. The second subclass is essential to reproductive and embryo regeneration. The third subclass is comprised of regulatory NLRS. These NLRs are positive or negative conditions inflammatory signalling cascade pathways.[7]
- **C-type lectin-like receptor:-** C-type lectin-like receptor (CLRs) are a large family of soluble, transmembrane pattern recognition receptor with more than 1000 members, which are widely expressed in myeloid cells. Due to its motif structure in the intracellular region with multiple

signalling pathways, the CLR receptor has a wide range of functions including cell adhesion, induction of endocytosis, phage, tissue repair, platelet activation and natural immune response.

- **Cytoplasmic DNA receptor:-** Exogenous microbial DNAs are recognized by host DNA receptors. In addition to TLRg in the family, cytoplasmic DNA receptor (CDR) can recognize DNA CpG island. More than 10 CDRS distributed in the cytoplasm have been identified, including AIM2-like receptor (ALRs), DNA dependent activator of IFN-regulators factors (DAI), interference stimulator of interferons gene (STING).
- **Type I interferons:-** When a virus invaded the host, PRRs initially recognize the viral nucleic acid, collect the specific signal adapter protein, activate IRF3 and IRF7 before being translocated to the nucleus and promote the synthesis of type I interferons (IFNs). Type I IFNs subsequently activate the downstream JAK-STAT signal pathway, promote the expression of IFM stimulated genes (ISGS). [8]
- **Dendritic cells :-** Dendritic cells (DCs) play a key role in innate immune and adaptive immune response. As the strongest antigen-presenting cells in the organism, they effectively stimulate the activation of T-lymphocyte and beta-lymphocyte, thus combining innate and adaptive immunity.
- **Defensins:-** Defensins are a family of endogenous antibiotics peptide molecules, which widely exists in human, animals and plants, are important for the host's innate defense system. Defensins have broad-spectrum antimicrobial activities. *In vitro* inhibition experiments shows that Defensins have a killing effect on bacteria, fungi, Mycoplasma, chlamydia, spirochetes, tumour cells and viruses. [9]

Adaptive immune response:-

The adaptive immune system also referred to as the acquired immune system, is a subsystem of the immune system that is composed of the specialized pathogen by preventing that eliminate pathogen by preventing their growth. The acquired immune system is one of the two main immunity strategies found in vertebrates (the other beings the innate immune system). [10]

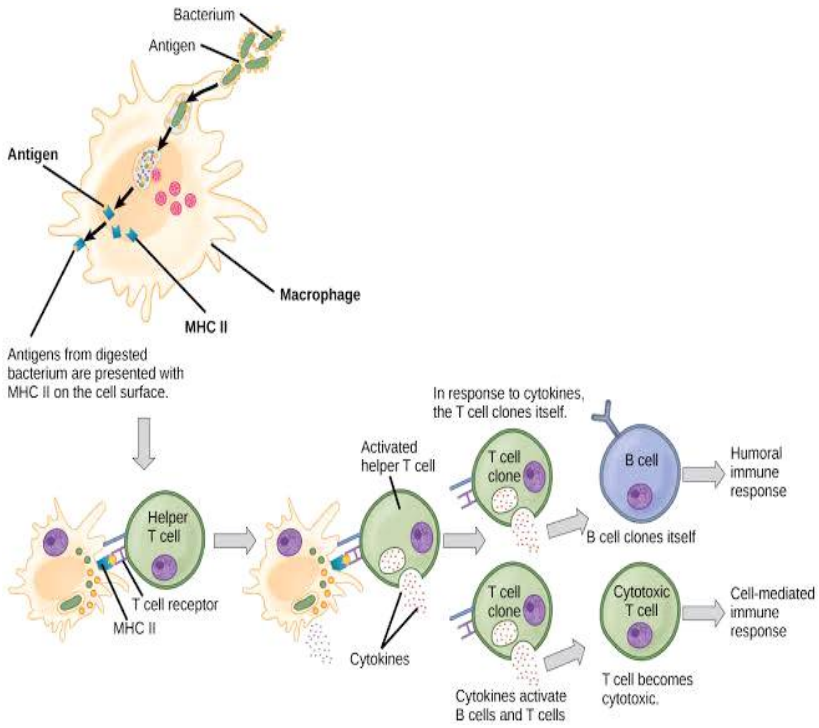

Fig 3 :- Adaptive immune system (Mount Sinai Health System) [10]

- **Immune response of T cells:-** MERS-Cov and SARS-COV are beta-coronavirus that can cause fatal lower respiratory tract infections and extrapulmonary manifestation T-cells, CD4+ T cells and CD8+ T cells particularly play a significant antiviral role by balancing the combat against pathogen and the risk of developing autoimmunity or overwhelming inflammation, CD4+ T cells promote the production or virus-specific antibodies by activating T-cells are cytotoxic and kill viral infected cells. CD8+ T-cells account for about 80% of total infiltrative inflammatory cells in the pulmonary interstitial in SARS-COV infected patients and play a vital role in clearing CoVs in infected cells and including immune injury. In addition by comparing T-cells deficient BALB/C mice (transducer by ad5-hdp4) with control and B-cell-deficient mice, some researchers determined that T-cells could survive in the infected lungs and destroy the infected cells.

- **Humoral immune response:-** B-cells subsets with phenotypes characteristic of naive, non-isotype switched, memory cells and antibody. Secreting cells accumulated in CoVs. The antigen stimulation of MERS-COV infections was clarified by using the specific 9-mer peptide "CYSSLIDY", which located at position 437 to 445 within the region of the s-glycoprotein. The sequence has the highest B cells antigenicity plot and can form the greatest number of computerized stimulation report shows that humoral immunity is essential to control the patient who has survived MERS-COV infections have been described including MCA1, CDC-C2, CSC-C5, CDC-A2, CDC-A10, MERS-GD27 and MERS-GD33. [11]
- **Antibody response to coronaviruses infections:-** The antibody response *in vivo* is a dynamic and complex mixture of monoclonal antibodies (MAbs), which work together to target different antigenic domains on the envelope glycoprotein of the virus. It is important to determine whether the antibodies are powerful in the adaptive immune response to MERS-COV infections. Research from all over the world has described more than 20 kind of monoclonal antibodies, most of which are human or humanized antibodies. The virus uses its spike proteins as an adhesion factor to facilitate host entry through a special receptor called dipeptidyl peptidase-4 (DPP4).

MODE OF SPREADING

People can get the infection through close contact with a person who has symptoms from the virus including cough and sneezing. Generally, coronavirus was spread via airborne zoonotic droplets. Virus was replicated in ciliated epithelium that caused cellular damage and infection at the infected site. According to a study published in 2019 angiotensin-converting enzymes 2 (ACE.2), a membranes exopeptidase in the receptor used by coronavirus in the entry to human cells virus transmission routes were represented. [12]

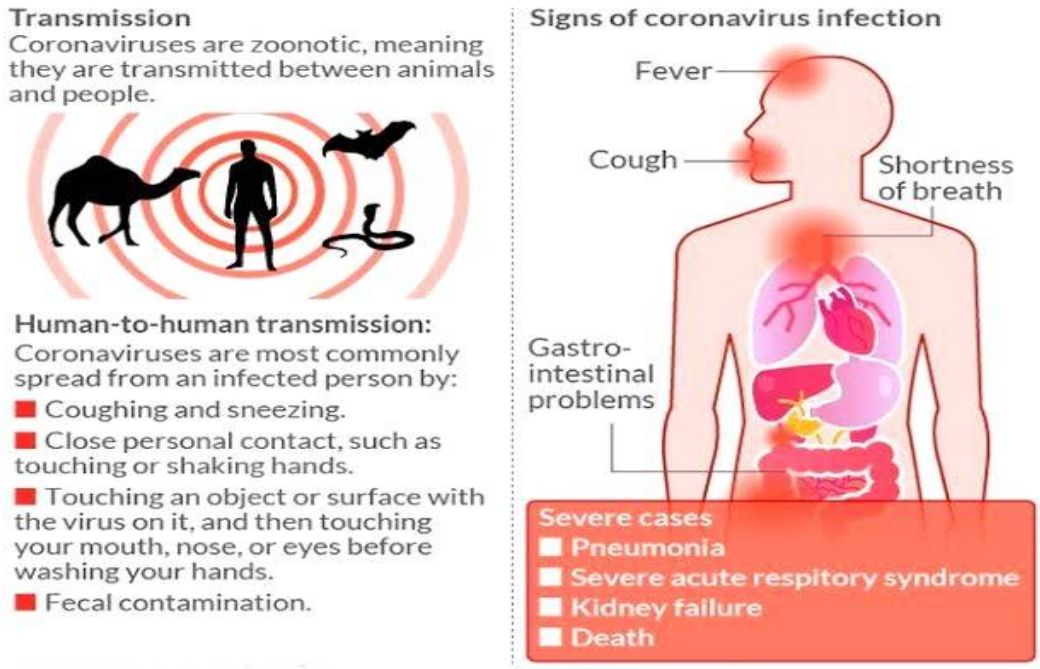

Fig 4 :- Mode of spreading (WHO, CDC, Images)

Vaccine:-

Vaccine is a biological preparation that provides active acquired immunity to a particular infection disease. A vaccine typically contains an agent that resembles a diseases-causes microorganisms and is often made from weakened or killed forms of the microbe, it's toxic, or one of it's surface protein. [13]

Type of vaccines :-

- Live-attenuation vaccine
- Inactivated vaccine
- Subunit, recommended, polysaccharide and conjugated vaccine
- Toxoid vaccine

Vaccines are a clever fake-out. They make the body thinks infected. So, it stimulates this immune response. For instance, the measles vaccines trick the body into thinking it has measles.

Multiple strategies are adopted in the development of CoVs vaccine; most of this target the surface-exposed as the major induce S-proteins based strategy have been attempted for developing Cov vaccine, e.g, use of full-length S protein or S1receptor-binding domain (RBD) and expression in virus-like particle (VLP), (DNA) or viral vectors. Recombinant adenovirus-based vaccine expressing MERS-Cov S protein induce systemically. IgG, secretory IgA and lungs residents memory T-cells response, when administered intranasal into BALB/, (mice and provided long-lasting neutralization immunity to MERS spike pseudotyped virus, thereby suggesting that the vaccine may confer protection against MERS-Cov.

The immune response to these vaccine candidates was evaluated in BALB/C mice for a cellular and humoral immune response which showed that RV-based vaccine stimulated significantly higher level of cellular immunity and earlier antibody response in comparison to the GEM particle vector.

About LEAPS :-

The ligand antigen Epitope presentation system (LEAPS) platform technology has demonstrated in several animal models the ability to design antigen-specific Immunotherapies peptide that preferentially directs the immune response to a cellular (e.g, T-cells), humoral (antibody) or mixed response and are also capable of enhancing importance T-regulatory (Treg) response.

Therefore, the LEAPS technology provides the opportunity to develop Immunotherapeutic products for disease for which disease-associated antigenic peptide (s) sequence have already been identification disease (e.g, RA), allergic asthma and allergy, select CNS disease (e.g, Alzheimer's) and the COVID-19 virus. [14].

Supplements:-

An Important Note:- No supplements will cure or prevent disease.

With the 2019 coronavirus COVID-19 pandemic, it's especially important to understand that no supplements, diet or other lifestyles modification other than physical distancing and proper hygiene practices can protect you from COVID-19.

Your immune system consists of a complex collection of cells, process and chemicals that constantly defend your body against invading pathogen, including viruses, toxins. [15].

Fig 5 :- Supplements

Here are 12 supplements that are known for their immune-boosting potential.

- **Vitamin D :-** Vitamin D is a fat-soluble nutrient essential to the health and functioning of your immune system. Vitamin D enhance the pathogen fighting effect of monocytes and macrophages white blood cells that are an important part of your immune defence and decreases inflammation which helps promote an immune response. The major natural source of the vitamin is a synthesis of cholecalciferol in the lower layers of skin epidermis through a chemical reaction that is dependent on sun exposure specifically UVB radiation skin, synthesis is biologically inactive.
- **Zinc :-** Zinc is a mineral that's commonly added to supplements and other healthcare products like lozenges that are meant to boost your immune system. This is because zinc is essential for immune system functions. Zinc is needed for immune cell development and communications and plays an important role in the inflammatory response. A deficiency in this nutrient significance affects your immune system ability to function properly resulting in an increased risk of infection and disease, including pneumonia.
- **Medicinal Mushrooms:-** Medicinal Mushrooms have been used since ancient times to prevent and treat infections and disease. Many types of medicinal mushrooms has been studied for their immune-boosting potentials. Some research specific type of medicinal mushrooms may reduce symptoms of certain conditions, including asthma and lungs infections. Many other medicinal mushrooms have been studied for their beneficial effect on immune health as well. Medicinal Mushrooms products can be found in the form of tincture, teas and supplements.

- **Astragalus:-** Astragalus is a herb commonly used in the Traditional Chinese Medicine (TCM). Animal research suggests that it's exact to significantly improve immune-related response.
- **Selenium:-** The selenium is a mineral that's essential for immune health. Animal research demonstrated that selenium supplements may enhance anti-viral defense against influence strains, including H1N1.
- **Garlic:-** Garlic has powerful anti-inflammatory and anti-viral properties. It has been shown to enhance immune health by stimulating protective white blood cells like NK cells and macrophages. Currently, garlic is used as a dietary supplement for many purposes including high blood cholesterol, high blood pressure and the common cold as well as in attempts to prevent cancer and other diseases.
- **Andrographis :-** This herb contains andrographolide, a terpenoids compound found to have an antiviral effect against respiratory diseases causing viruses, including enteroviruses D68 and influenza A.
- **Liquorice:-** Licorice contains many substances, including glycyrrhizin that may help protect against viral infection. According to test-tube research, glycyrrhizin exhibits antiviral activity against severe acute respiratory syndrome-related coronavirus (SARS-COV).
- **B complex vitamins:-** B vitamins, including B12 and B6, are important for healthy immune response. Yet many adults are deficient in them, which may negatively affect immune health.
- **Curcumin:-** Curcumin is the main active compound in turmeric. It has powerful anti-inflammatory properties and animals studies indicated that it may help improve immune function and is a very strong anti-oxidant.
- **Echinacea:-** Echinacea is a genus of plant in the daisy family. Certain species have been shown to improve immune health and may have an antiviral effect against severe respiratory viruses, including syncytial virus and retroviruses.
- **Propolis:-** Propolis is a resin-like material produced by honeybees for use as a sealant in hives. Though it has an impressive immune-enhancing effect and may have antiviral properties as well more human research is needed. [16]

Vitamin C

Vitamin C is an essential nutrient with several roles in your body, It's a potent antioxidant, meaning it can neutralize unstable compound in your body called free radicals and help prevent or reverse cellular damage caused by these compound.

While physician and Researchers are studying the effect of high dose intravenous (IV) vitamin C on the new coronavirus, no supplements, including vitamin c, can prevent or treat COVID-19.

- **How does it affect immunity? :-** Vitamin C affects your immune health in several ways. Its antioxidant activity can decrease inflammation functions vitamin c also keep your skin healthy by boosting collagen production, helping the skin severe as a function barrier to keep the harmful compound from entering your body.

  The vitamin also boosts the activity of phagocytes, immune cells that can " swallow " harmful bacteria and other particles.
- **Here are some common forms of Vitamin C:-**
- Ascorbic Acid
- Buffered Vitamin C
- Vitamin C with bioflavonoids
- Topical Vitamin C

An article published in the Chinese Journal of infection disease the Shanghai medical Association endorsed the use of high dose vitamin C as a treatment for hospitalized people with COVID-19.

Does that are magnitudes higher than the DV are recommended to be given through IV to improve lung functions, which may help keep a patient off of mechanical ventilation or life support. [17]

The best food for boosting your immune system

The immune system consists of organs, cells, tissue and protein. Together, these carry out a bodily process that fights off pathogens, which are the viruses, bacteria and foreign bodies that causes infection or disease.

When the immune system comes into contact with a pathogen, it triggers an immune response. The immune system systems release antibodies, which attach to the antigen on the pathogen and kill them.

In a corporation, specific food into the diet may strengthen a person's immune response, read on to discover 14 foods that boost the immune system.

- **Blueberries:-** Blueberries contain a type of flavonoids called anthocyanin, which had antioxidant properties that can help boost a person's immune system. A 2016 study noted that respiratory tract's immune defense system.

Researchers found that people who ate foods rich in flavonoids were less likely to get upper respiratory tract infections or common cold than those who did not.

- **Dark chocolate:-** Dark chocolate contains an antioxidant called theobromine, which may help to boost the immune system by protecting the body's cells from free radicals. Free radicals are molecules that the body produce when it breaks down food or comes into contact with pollutants free radicals can damage the body's cells and may contribute to disease.
  Despite its potentials benefit, dark chocolate is high in calories and saturated fat, so it is important to eat in moderation.
- **Turmeric:-** Turmeric is a yellow spice that many people use in cooking. It is also present in some alternative medicine. Consuming turmeric this due to the qualities of Curcumin a compound in turmeric.
- **Oily fish:-** Salmon, tuna, pilchards and other oily fish are a rich source of omega-3-fatty acids. According to a 2014 report, long-term intake of omega-3-fatty acids may reduce the risk of rheumatoid arthritis (RA).
  RA is a chronic autoimmune condition that occurs when the immune system mistakenly attacks a healthy part of the body.
- **Broccoli:-** Broccoli is another source of vitamin c. It also contains potent antioxidants such as sulforaphane for these reasons, it is a good choice of vegetables to eat regularly to support immune system health.
- **Sweet potatoes:-** Sweet potatoes are rich in beta carotene, a type of antioxidant the gives the skin of the potatoes it's organs colour. It helps to make skin healthy and may even provide some protection against skin damage from ultraviolet (UV) rays.
- **Spinach:-** Spinach may boost the immune system, as it contains many essential nutrients and antioxidant including:-
  - Flavonoids
  - Carotenoids
  - Vitamin C
  - Vitamin E
  - Vitamin C & E can help support the immune system.
- Ginger**:-** People use ginger in a variety of dishes and dessert, as well as in teas. According to a review, ginger has anti-inflammatory and antioxidant properties and is likely to offer health benefits. However more research or not it can effectively prevent illnesses.
- **Green tea:-** Green tea contains only a small amount of caffeine, so people can enjoy it as an alternative to black tea or coffee. Drinking it may also strengthen the immune system. As with blueberries, green tea contains flavonoids which may reduce the risk of a cold.
- **Kefir:-** Kefir is a fermented drink that contains the live culture of bacteria that are beneficial for Health. Initial research suggests that drinking kefir may boost the immune system. According to a 2017 Review, various studies have shown the required consumption of kefir can help with :-
  - Fighting bacteria
  - Reducing inflammation
  - Increasing antioxidant activity
- **Sunflower seeds:-** Sunflowers seeds can make a tasty addition to salad or breakfast bowls. They are a rich source of vitamin E, an antioxidant. In the same way as other antioxidants, vitamin E important immune function. It does this by fighting off free radicals which can damage cells.
- **Almond :-** Almond is another excellent source of vitamin E. They also contain manganese, magnesium and fibres. A small handful or a quarter of a cup of almond is a healthful snack that may benefit the immune system.
- **Organs or Kiwi fruit:-** Orange and kiwi are an excellent source of vitamin c, which is the vitamin that many people, turn to when they feel a cold developing. While scientists are still not sure exactly how it helps vitamin c may reduce the duration of commons cold symptoms and improve the function of the human immune system.
- **Red bell pepper:-** For people trying to avoid the sugar in fruits, red bell pepper are excellent alternative sources of vitamin C. Stir-frying and roasting both preserved the pepper better than steaming or boiling, according to study on the cooking method. [17]

CORONAVIRUS, PRECAUTIONS AND STRENGTHENING THE IMMUNE SYSTEM

Before this recent outbreak of the Wuhan Coronavirus. Likely, most people had never heard of this strain of virus even though other forms have caused a significant outbreak in the past.

A coronavirus is a group of viruses that causes disease in human and other mammals, birds, bats and reptiles. When human is infected most forms of the virus causes mild respiratory infections bud as we have seen with the infection coronavirus in rare cases coronavirus infections can be lethal.
As of now, no vaccine has been for mutated for the novel coronavirus. In light of this fact, prevention appears to be the best cure available so far with coronavirus threatening to run riot in India here how you can keep yourself safe from the scourge.

Fig 6 :– Wearing a Mask as a Preventive Measure to Keep Coronavirus Away

Here is the measure you need to take to keep the virus at bay:-

- Avoid close contact with a person who is sick. Maintain at least yourself feet distance who is coughing or sneezing.
- Avoid touching your eyes, nose and mouth.
- Stay home when you are sick.
- Cover your cough or sneeze with a tissue other dispose of the tissue safely.
- Clean and disinfect frequently touched object and surface using a regular household cleaning spray or wipe.
- Wearing a mask it's not necessary unless you are taking care of an infected person. The centre for disease control (CDC) does recommend that only infected person wear a mask to prevent the spread of the virus.
- Wash your hand often with soap and water for at least 20 seconds, especially after going to the bathroom, before eating food and after blowing your nose, coughing or sneezing.
- If soap and water are not readily available, use an alcohol-based hand sanitizer with at least 60% alcohol always wash hand with soap and water when hands are visibly dirty.
- If you have fever, cough and difficulty to breathing, seek medical attention immediately.
- Keep in mind the travel advisory set out by the Ministry of Health and welfare. [17,18]

CONCLUSION

As is evident from this systematic review, Immunotherapies are an efficient therapeutic option intervention against COVID-19 and the main method in this regard such as using immunoglobulins and plasma therapy are expected to improve clinical outcome in COVID-19 infected patients.

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