

# **Review Article**

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# The corona returns to israel-this thime with the indian triple mutant 2delta

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## **Background**

The biggest threat: "Not only in Israel-the" Delta" variant worries the world [1-5] report. 'Delta' variant evolves to form 'Delta Plus', is there a cause to worry? Covid-19 The 'delta' variant of COVID-19-a version first detected in India- has evolved to form the 'delta plus' or AY.1 variant. Scientists say it has acquired a mutation associated with escaping immunity, but there is no cause for concern yet.

# **Corona Spread**

Israel Prime Minister Benett to enter special debate.

### **Expected**

The obligation to wear masks in closed spaces will soon restored. Concerns in the health system following the increase in morbidity in recent days. Prime Minister Bennett and Health Minister Horowitz expected to hold a particular discussion in which new measures will be decided. Corona projector Prof. Nachman Ash: "The increase in morbidity is a direct result of people violating the isolation" [6].

People tha receuive the 2 portion of the Pfiser vaccine have also been infected with the Indian variant: is the effectiveness of the corona vaccine declining?. The delta strain of the corona virus, 180 cases of which have been detected in Israel so far, is more contagious - but it is not at all certain that it causes a more serious disease . 1 in 3 newly verified coronation test sites returned to activity And the question is why is this happening, and does this mean that the vaccine is no longer as effective as we thought? Experts answer N12 questions.

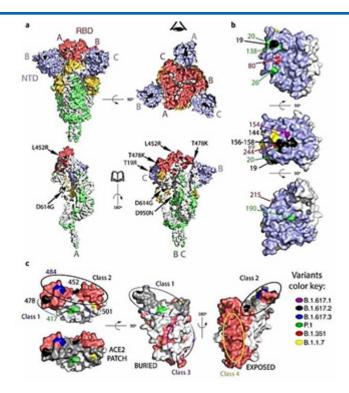
The effectiveness of the vaccine is excellent, but we know that in the face of this specific variant, the effectiveness is slightly reduced, "says Dr. Arnon Shachar, a member of the epidemiology team and the medical director of the corona at Maccabi". Obviously in terms of symptomatic infection, the Indian strain also poses a

risk of vaccinating vaccinated adults. The higher the morbidity, the more vaccinated we will see. The main emphasis now should be on reducing the gap of the unvaccinated population On a mask". Will we have to get vaccinated again to increase vaccine effectiveness?

One of the proposals currently being considered around the world is to give an "impulse dose" of the vaccine to increase its effectiveness - but in the medical world there is controversy as to whether this is indeed necessary. "In my opinion, it is too early to reach such a conclusion," explained Prof. Rahav. "We have no research data to suggest that this is necessary. The outbreaks have been discovered through extensive tests and in-depth epidemiological investigations".

With the progress of the 2019 Coronavir epidemic (COVID-19), several new versions of SARS-CoV-2 have appeared worldwide. Because of the acquisition of multiple spike mutations, many of these variations have gained evolutionary benefits, including increased infectious and venomous infections and the ability to escape host immune responses. In October 2020, the SARS-CoV-2 lineage in India, known as B.1.617, grew exponentially in COVID-19 cases across the country. The lineage is further divided into three subgroups: B.1.617.1, B.1.617.2 and B.1.617.3; Of these, variant B.1.617.2 was defined as a Variant of Concern (VOC) due to significantly increased infectivity. However, there is not enough information on the sensitivity of this lineage to host humoral immunity [7].

A team of scientists from France recently conducted a study to assess the susceptibility of B.1.617 version of acute acute respiratory syndrome to coronavirus 2 (SARS-CoV-2) to neutralize antibodymediated. The findings show that compared to other circulating versions, the B.1.617 version is resistant to therapeutic monoclonal antibodies and natural antibodies to infection or vaccination [8].

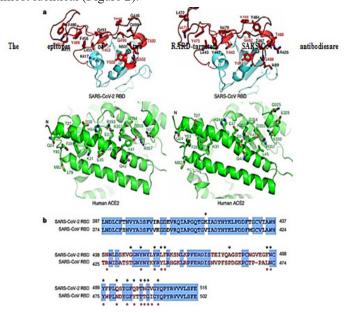


**Figure 1:** Mapping Mapping in B1.617.2 and other versions that take care of the spike surface.

In figure 1A, the Spike protein trimmer (PDB: 6XR8, corresponding to a closed spike chopper with all three RBDs in the "down" conformation) is shown with its colored surface by areas: NTD blue, RBD red, residual S1 yellow and S2 green. Interfaces between protomers were left white to help visualize the boundaries of protomers. The three polypeptide chains in the trimmer were arbitrarily defined as A, B, and C, and marked to detect NTD (blue) and RBD (red) in the same protomer. Surface patches corresponding to the mutation residues in version B.617.2 are painted black. The top panels display two orthogonal views. The lower panels display the edges with subunit A in the same direction as the upper pane, and subunits B and C rotate 180 degrees to display the trim interface (areas buried in the trimmer remain white). The eye symbol in the upper right pane is used to indicate the point of view of the lower right pane, after removing the A-chain to display internal surfaces. The mutations in B.617.2 are tagged in the bottom pane. B) Details on the surface of NTD, with mutations that appeared in the indicated versions. third. RBD is displayed in three orthogonal views. The left panel is viewed down the surface that binds ACE2, with the surface buried in a compound with ACE2 on top of the gray on the bottom panel (labeled "ACE2 Repair"). The mutations on the versions are marked. The middle panel shows the RBD surface buried in the closed barbed trim. The right panel shows its exposed surface. Note that the mutations in the RBD cluster surround ACE2 repair. Panels were prepared using the PyMOL molecular graphics system, version 2.1 Schrödinger, LLC.

# Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor

As of December 2019 it has spread rapidly across the country and to other countries Worldwide 1-3. Here, to better understand the initial stage of infection in At the atomic level, we determined the crystal structure of the domain that requires a receptor (RBD) of the SARS-CoV-2 spike protein is bound to the ACE2 cell receptor. The total The ACE2 union mode of the SARS-CoV-2 RBD is almost identical (Figure 2).



**Figure 2:** SARS-CoV-2-RBD-ACE2 and SARS-CoVRBD-ACE2 interfaces. A)Containing residues are shown as sticks at the SARS-CoV-2-RBD-ACE2 and SARS-CoVRBD- ACE2 interfaces. positions in both RBDs that are involved in ACE2 binding are indicated by red lebels.B) Sequense allignment of the SARS-CoV-2 and SARS-CoVRBDs.contacting residues in the SARS-CoV-2-RBD are indicated by black dots; contacting residues in the SARS-CoVRBD are indicated by red dots.

The biggest threat": Not only in Israel-the "Delta" variant worries the world. The United States as well as countries in Europe and Israel are facing the outbreak of the Indian variant, which has been defined as more contagious than its predecessors. Experts predict that the strain is likely to cause a spike in mortality, and return in winter as well [9].

News agencies 23/06/2021 06:00 2 min Read Only Israel is currently facing another outbreak of corona, much of which is due to the Indian variant. However, worldwide, the variant, which has already been given the name "Delta", is making waves and threatening to cause a new and more severe outbreak of the virus. According to data from around the world, the "Delta" has already spread widely in the UK, and is now threatening to re-spread in the US as well, when in fact it replaces the "Alpha" variant. Experts even estimate that the current strain is 40% faster". This is the most

contagious version of all the versions we've seen," Dr. Peter Hutz, an American expert on infectious diseases, told CNN. "We've seen what happened in the UK, where it's spread all over the country, so I'm afraid it's going to happen in the US as well", Hotz said.

One of America's leading experts on infectious diseases, Dr. Anthony Pauchi, commented on the Indian variant, saying". The delta version of the corona virus, first found in India, is the biggest threat to the US effort to eradicate the corona within its borders. The 'Delta' version is transmitted more easily than the original version of the corona and becomes the dominant version in the world of the disease".

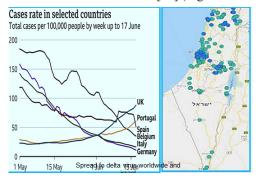
In addition, infectious disease studies suggest that variants such as Delta may return to our lives in the future. The latest research model has suggested that it is possible that the current strain may return in the fall and winter period and cause a jump in mortality.

The variant was first discovered in India about a year ago, from there it penetrated to Portugal and led to a spike in morbidity in Lisbon within weeks. Scientists in Germany, where the spread of the variant is relatively limited, expect its eruption in the coming months. In Italy, too, the number of patients is being doubled.

Bee Cure Laser-Does It Really Help? What about the vaccinated?. Dr. Ashish K. Ja, Dean of Brown University of Medicine, argued about the vaccinated population:"If you are fully vaccinated, there is nothing to worry about". This is based on a recent study showing that the Pfizer vaccine was 88% effective in protection. Because of the symptoms of "Delta". However, the study found that only one dose of the vaccine was effective at only 33 percent.

"Vaccines are expected to respond well to the virus, at this point," Peter Hutz said. "However, the protection offered by one dose is quite low, so a person who is not vaccinated is at high risk".

While "Delta" is more contagious than its predecessors, there is a belief that vaccinated people will not start hard. The spike in morbidity in the UK was sharp though, but the death toll remained stable and did not continue to soar. On the other hand, it has been argued that the variant may "elude" the antibodies produced in the body, or even reduce its effectiveness [10] (Figure 3 and Figure 4).



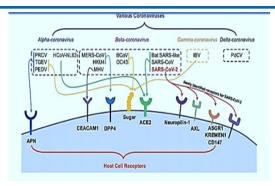
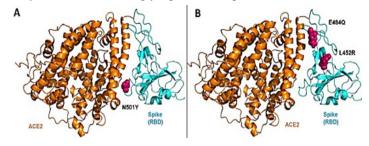


Figure 3: Different coronaviruses use a variety of receptors for viral attachment and entry. In the upper panel, various coronaviruses from four major genera, alpha, beta, gamma, and delta-coronavirus, are in the dashed line boxes. In the lower panel, distinct receptors on the surface of host cell mediates the viral entry of the specific coronavirus. Coronaviruses: PRCV porcin respiratory coronavirus, TGEV porcine transmissible gastroenteritis coronavirus, PEDV porcine epidemic diarrhea coronavirus, MERS-CoV Middle East respiratory syndrome coronavirus, MHV mouse hepatitis coronavirus, BCoVbovine coronavirus, IBV avian infectious bronchitis coronavirus, PdCVporcinedelta-coronavirus. Hostcellreceptors: APNaminopeptidaseN, ACAM1carcinoembryonic antigen related cell adhesion molecule 1, DPP4 dipeptidyl peptidase 4, ACE2 angiotensin-converting enzyme2, ASGPR asialoglycoprotein receptor.



**Figure 4:** The structure of the Receptor Binding Domain (RBD) of SARS-CoV-2 Spike protein complexed with human Angiotensin Converting Enzyme 2 (hACE2) receptor. A) The sphere shape residues in hot pink colour show N501Y mutation in Spike protein of SARS-CoV-2. B) The Double mutation at L452R and E484Q in Spike protein.

Possible link between higher transmissibility of B.1.617 and B.1.1.7 variants of SARS-CoV-2 and increased structural stability of its spike protein and hACE2 affinity[11]. The Severe Acute syndrome corona Virus 2 (SARS-CoV-2) outbreak in December 2019 has caused a global pandemic. The rapid mutation rate in the virus has causeworldwide and is being attributed to the false negativity in RT-PCR tests, which also might lead to inefficacy of the available drugs. It has also increased the chances of reinfe/Outbreak of severe acute coronavirus 2 (SARS-CoV-2) in December 2019 occurred Caused a global epidemic. The rapid rate of mutation in the virus has caused alarming situations Worldwide and attributed to false negativity in RT-PCR tests, which may also Lead to the ineffectiveness of existing drugs. It also increased the chances of re-infection Immune escape. We performed molecular dynamic simulations of three different ones Spike-ACE2 complexes,

i.e. Wildtype (WT), version B.1.1.7 (Spike N501Y mutation) and Version B.1.617 (L452R, E484Q Spike Mutation) and compared their dynamics, binding energy And molecular interactions. Our result shows that a mutation caused an increase in Binding energy between the spike and hACE2. In the case of version B.1.617, the mutations In L452R and E484Q increased the stability and interactions between the chain in the spike protein, Which may alter the ability of human antibodies to interact with this spike variable. Additionally, We found that version B.1.1.7 increased the interaction of hydrogen with HACE2 LYS353 And affinity is more binding than WT. The present study provides the biophysical basis for understanding the molecular mechanism and rationale behind the tumor transmission and infection of the mutations compared to SARS-CoV-2 wild-type. 219 people were found to be verified in Corona last week - about half of them children. Data from the Ministry of Health reveal that a third of all those infected are vaccinated, which probably led to the low number of patients in critical condition. Despite the increase in infection, Prof. Hezi Levy says that now Restoration of restrictions: "Highly recommend - the vaccine is safe". Ministry of Health: We will tighten enforcement at Ben Gurion Airport for flying to high-risk countries.

Israeli health Ministry Director General Prof. Hezi Levy said last night. Despite the increase in the number of verified people in Corona in recent days, "There is no intention to return to restrictions on the public and now the recommendation is to vaccinate young people". The world and also compared to the periods when closure was announced. In the past week, an average of 26,000 tests were conducted daily, of which only 0.1% came out positive on average very far from the numbers we knew in the past.

In the past week 219 people are infected with the virus, 111 of them under the age of 16. That means half of the last infected are children. It is usually an asymptomatic disease. Earlier we reported that about 70% of all those verified were infected with the Indian strain.

According to the Ministry of Health, a third of all those infected, and were vaccinated. This is not to say that the vaccine is completely ineffective against the Indian strain because infection does not necessarily mean a disease with symptoms. The vaccine is also measured by how well it prevents serious illness. In this figure, our situation is still good-only 3 new patients are in a difficult situation.

The director general of the Ministry of Health, Prof. Hezi Levy, said last night that "we are happy that the disease that is now breaking out, both among the vaccinated and among the unvaccinated, is a milddisease and for the most part also not symptomatic." Because all these patients, even with a few symptoms, are a source of infection.

Prof. Levy also noted that so far we have vaccinated about 21-20,000 boys between the ages of 12 and 16. According to him, following the increase in morbidity in the Ministry of Health, vaccinations for youth are now being expanded, and now the recommendation is to get vaccinated". I appeal to people and highly recommend - the vaccine is safe", said the director general of the Ministry of Health. "We are after 2 and a half million vaccinated in

the US and 21 thousand here there are no side effects".

The Ministry of Health announced that within a few days, strict enforcement will begin, and fines in the amount of thousands of shekels will be imposed on those who fly to the banned countries. This is due to the increase in those infected with the corona virus and the high number of flights of thousands of Israelis to countries that are considered at maximum risk of disease.

Under current regulations, flying is prohibited to six countries at maximum risk: Argentina, Brazil, South Africa, India, Mexico and Russia. But the Israelis continued to fly to these countries, and every day full flights departed without real enforcement. It turned out that despite the ban, thousands of Israelis have flown in recent weeks to countries with very high morbidity, and then returned to Israel without any factor following them.

Health Minister Nitzan Horowitz has announced that he is working to close this loophole and tighten enforcement. "It turned out that the ban on flying to these countries, set by the previous government, did not include effective enforcement mechanisms," the health minister explained. He said it was a calculated risk-taking. Said Prof. Levy. "Here too we had a calculated risk, we returned to routine. We now recommend and teach that all medical institutions in doctor-patient contact be with masks. We do not currently intend to return to the restrictions [12].

India is currently in the midst of a deadly surge of COVID-19 cases, which has severely overwhelmed the healthcare infrastructure. More than 250,000 daily cases have been reported since 17th April 2021 and more than 300,000 cases since 21st April 2021. Experts suggest that the spike may be due to a new mutant, termed the 'triple mutant,' another variant of the 'double mutant,' which was the first lineage identified in India.

Genome sequences of the SARS-CoV-2 virus analyzed from cases in India showed that the viral strain predominant in cases from the state of Maharashtra since early this year contained two mutations-L452R and E484K. This variant was named B.1.617 and was classified as a 'variant of concern.' The E484 mutation is linked to higher infection rates and is also found in COVID-19 variants from Brazil and South Africa.

### **Triple Mutant**

While mutations are common as the virus navigates its way through multiple infections, some mutations can result in higher infectivity and lethality. Latest reports show a new variant in cases from West Bengal, a state in the eastern region of India.

This 'triple mutant'-B.1.618 is suspected of having evolved from the double mutant and could be highly transmissible and likely to evade the immune response. It is characterized by the deletion of two amino acids in the spike protein and also contains the E484K and D618G mutations. This triple mutant has been detected in other states such as Maharashtra, Delhi, and Chattisgarh too.

"There are many unknowns for this lineage at this moment, including its capability to cause reinfections as well as vaccine breakthrough infections. Additional experimental data is also

required to assess the efficacy of vaccines against this variant," Dr. Vinod Scaria, a scientist at the CSIR-Institute of Genomics and Integrative Biology, New Delhi, wrote on Twitter.

As of April 23, 2021, the triple mutant was detected in 8% of the samples sequenced by INSACOG (Indian SARS-CoV-2 Genomic Consortia), as compared to 29% of samples that contain the double mutant. To make matters complicated, the percentage of viral strains sequenced from infected people is neither consistent nor adequate to estimate the prevalence of mutations accurately. This is due to the rapid increase in the number of cases and inadequate healthcare infrastructure to sequence each sample.

Currently, the variants are being investigated for their infection rates and susceptibility to approved COVID-19 vaccines. Preliminary results suggest that vaccines can protect against the double mutant. Scientists believe that most vaccines should reduce the severity of infection, irrespective of the variant.

Speaking to Business Insider, Dr. Paul Tambyah, a Professor of Medicine at the National University of Singapore, said, "there is good data suggesting that the immune system, not just antibodies, can respond to multiple different mutants".

The World Health Organization has called on the countries of the world to increase the rate of immunization and has sought to speed up vaccination campaigns. The organization also asked countries with a high percentage of vaccinated people to donate the vaccines to third- world countries that do not have a hand in it and have difficulty purchasing the expensive vaccine doses. The organization's health experts believe that the new strain is causing more severe symptoms, but they are asking for more time to investigate the issue. And yet, no vaccine-resistant strain has been discovered so far and causes a much more serious disease than that of the original virus discovered about a year and a half ago in China [13].

### New 'Triple Mutant' Deepens COVID-19 Crisis in India

The corona on the way back? The Indian strain or by its official name "Delta," raises concern among health professionals worldwide. Although it is estimated that Pfizer's vaccine as well as that of some of the other companies is resistant to it, its potency significantly exceeds that of other strains. The World Health Organization warned tonight (Monday through Tuesday) that "Delta" is expected to be the deadliest of all.

The head of the organization's emergency program, Dr. Mike Ryan, warned that the Indian strain would lead to widespread mortality for at-risk patients including those who had not yet been vaccinated. 90 countries are 60% more contagious than the British strain, which is more contagious than the original Corona strain. The organization added that it is responsible for at least 10% of all new cases.

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mutant, termed the 'triple mutant,' another variant of the 'double mutant,' which was the first lineage identified in India.

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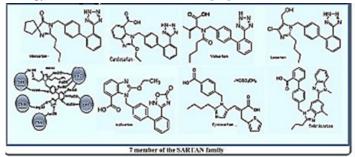


Figure 5: Antihypertensive drugs, the SARTANS.

University of Minnesota Launches COVID-19 Clinical Trials of Blood Pressure Drug Losartan. One family of antihypertensive drugs, the SARTANS\*(LOSARTAN for example) is kbown to block the ACE2 receptors in the body. Kellllyy Gllyynn, Mediia Rellattiions Coorrdinattorr, APRIIL 20, 2020, Supported by Minnesota Partnership for Biotechnology and Medical Genomics and COVID-19 Therapeutics Accelerator Funding

Miinneapoliis, MN,Aprriill 20, 2020, Uniiverrsiitty off Miinnesotta Mediicall School, researchers have begun enrrolling patientts iin newly launched cliinical trrials iinvolving a blood presure medication, losartan, as a potenttial treatment for those recently, diagnosed witth COVID-19. Both studies are multisite trials, one for patients requiring hospitalization and the other for diagnosed patients who do not require a hospital stay. The first evaluates whether the angiotensin IIII receptor blocker (ARB) losartan can prevent lung injury in those hospitalized witth COVID-19 pneumonia, while the secondevaluates if the drrug can prreventt hospitalizations. The trial ''s co-principal investigators are Christopher Tignanelli, MD, assistant professor in the Medical School''s Department of Surgery, Division of Critical Care/Acute Care Surgery, and Michael Puskarich, MD, associate proffessor in the Department of Emerrgency Medicine at the University and

emergency physician at Henepin.

### **Healthcare HCMC**

1.5 million doses will be thrown away? The battle for the youth vaccine and the effects of the Pike News. In the shadow of the increase in the number of people infected and the sweeping recommendation to vaccinate young people, only 10% of 15-12 year olds went to get vaccinated • In an attempt to speed up the vaccination rate: If they had recommended vaccination first - we would reach 70% vaccinated.

### **Translation results**

On Monday, the Ministry of Health issued an official and sweeping recommendation to vaccinate all youth aged 15-12, but the number of vaccinated in this age group remains very low and stands at only 10%. In an effort to persuade teens and their parents to get vaccinated, HMOs will launch digital campaigns and recruit celebrities. Senior source: If they had recommended vaccination as early as 3 weeks ago -

we would have reached the target of 80-70 percent vaccinated. Those who do not get vaccinated this month will have to wait for delivery in September. Despite the enforcement efforts at Ben Gurion Airport, it is estimated that without significant vaccination of adolescents aged 15-12 it will not be possible to suppress the spread of the Indian variant.

Influencers will also be recruited for campaigns to encourage immunization and text messages will be sent to parents every two to three days until they take their children to be vaccinated, and doctors will also be recruited for the effort and call parents in an attempt to convince them themselves.

### Is there a risk of myocarditis in children?

It is indeed a complication that can happen from a vaccine, we have tested it in the country and we estimate that there is a connection between the two things. Fortunately, the prevalence is relatively low, we found it in a ratio of one to 6,000, and abroad it is even rarer. In most cases it is a mild disease that passes, so the risk is not great. The risk of this complication. We learned from US vaccinators that the data are less common than ours.

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