Imam Reza General Hospital Newsletter
Tabriz University of Medical Sciences

In this issue we read:

Covid-19 New Findings

Prof. Soodabeh Davaran

Development of New Generation Vaccines with Nanotechnology Approach

After the entering of the Covid-19 pandemic in the third year of the outbreak, and the successful impact of vaccination on controlling the disease, much research is being done to develop next-generation vaccines to prevent diseases caused by a variety of microorganisms. There are currently four types of vaccines used against the SARS-CoV-2 virus including vaccines made from attenuated or killed viruses (first generation), vaccines consisting of a protein subunit (second generation), and RNA or DNA (third generation) vaccines. First and second generation vaccines have characteristics with low immunogenicity and inability to stimulate strong and long-term immune responses. Therefore, in order to achieve modern and effective vaccines, innovative devices

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Happy Nowruz
Wishing a healthy and free-Corona life in New Year

Prof. Behzad Baradaran

Different Variants of SARS-CoV-2 and the Effectiveness of Developed Vaccines Against them

With the introduction and prevalence of the newer mutated variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), concerns are being raised about the effectiveness of existing vaccines and the immunity of the vaccinated people provided by developed vaccines. First of all, we should know that virus mutation is a completely normal phenomenon in the world of viruses. All viruses mutate over time, meaning that their genetic code changes, and the SARS-CoV-2 virus are no exception. The mutated viruses are called the strains or variants. Contrary to what may seem at first, such mutations are not a completely harmful phenomenon and many viral mutations can weaken it because if the virus becomes more and more dangerous and lethal, it will eventually disappear itself by destroying all of its hosts. Hence, the virus moves in the direction of weakening itself to be able to guarantee its life. The SARS-CoV-2 genome is about 30,000 nucleotides, and in each mutation, a number of these nucleotides change and the SARS-CoV-2 has undergone thousands of mutations since

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Mojtaba Mohammadzadeh

Director-In-Charge's Message
Assistant Professor of Intensive Care Medicine
Dean of Imam Reza Generel Hospital

The Effect of Covid-19 Vaccines on Reducing Corona Mortality

Vaccines can prevent serious illness, ICU admission, and death. Depending on the type of vaccine, underlying diseases and genetics of individuals, non-therapeutic control measures and the severity of their observance, including wearing masks, distance observation, travel prevention, etc. can also be effective. Fortunately, vaccination in our country has significantly reduced the hospitalization and death rate. More than 95 percent of patients who have died of coronary heart disease in recent months in the country either did not receive the vaccine or received only one dose of the vaccine. The role of reduced traffic, both within and between countries, is an effective way to reduce Covid-19 mortality. Furthermore, this method is effective against the possible occurrence of Covid-19 due to seasonal changes. The results of the vaccination analysis of one study showed that the vaccination efficiency in terms of protection against mortality is 72%, which reduces the number of deaths for the B.1.1.7 variant versus other variants (70 % and 78%, respectively).

The editorial boards of the Imam Reza General Hospital Newsletter kindly appreciate the efforts of Dr. Masood Faghihdinevari (former Director-In-Charge) during his headship of the center.

Hassan Soleimanpour

Editorial
Editor in Cheif
Professor of Intensive Care Medicine
Deputy of Education and Research

Third Generation University; Dream to Reality

Undoubtedly, university as one of the most important parts of the modern world and representation of the most important achievements of the new era has a long history. The two Iranian universities of Rabe Rashidi, Tabriz, Iran (founded in the 13th century), Jundishapur of Ahvaz, Khuzestan, Iran (founded in the 3rd century, AD) and the University of Bologna (Italy, founded in 1088, AD), the oldest university in Europe, evidence of this claim. The evolution of universities in terms of structure and mission can be divided into three generations. The first generation university (education-oriented) was formed in the late nineteenth century, the second generation university (research-oriented) was formed at the beginning of the twentieth century, which played an important role in science and research, and the third generation university was formed in the second half of the century following the World War II that is known as a leading, innovator, technology-based and entrepreneur-based university. It is worth saying that Rabe Rashidi University with four complexes: Dar Al-Shifa (hospital and pharmacy), Dar Al-Siyadeh (coin mint, guest house, bathhouse, and orphanage), Dar Al-Ebadeh (mosque, school, library, and monastery) and Dar Al-Sanaye (textile factories, paper mills and industrial workshops) is a scientific-industrial city which had presented a successful model of a third-generation entrepreneurial university. In this university, lessons had been taught in three living languages of the world. Unfortunately, regarding the characteristics of third-generation universities, it has shown that there is no, currently, an Iranian university which we can call a complete third-generation university. Total independence from

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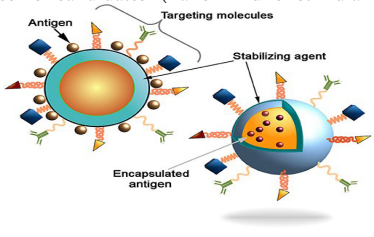
(Soodabeh Davaran, cont.)

and delivery systems are needed to increase the immunization of vaccines. The use of nanotechnology in vaccination and the integration of nanotechnology with immunology provide a promising opportunity to address these limitations. Nanotechnology-based formulations have several benefits for developing new generation vaccines. Third-generation vaccines are made from nucleic acid, the genetic material for RNA or DNA, which works by giving cells instructions for making antigens. The mRNA vaccines carry the genetic information of the virus spike protein. When this genetic material enters human cells, it uses the protein factories of our cells to make antigens. In mRNA vaccines, which have been developed by Pfizer / BioNTech or Moderna, mRNA is encapsulated in a specially designed lipid nanoparticles which is enable to enter the cells of the human body by injection of a vaccine. Suitable carriers are needed to improve the efficacy of such nucleic acid vaccines. These carriers must protect their cargo from premature proteolytic degradation, facilitate antigen uptake and processing by antigen-presenting cells, control the release of antigen or gene that produces it, and must be safe for human use. Nanocarriers consisting of lipids, proteins, metals or polymers have been used to achieve some of these requirements. The advantages of such vaccines are that they are easy to make and inexpensive. Because antigens are produced within living cells in large quantities, the immune response must be strong. There are different mechanisms for delivering vaccines by nanocarriers to specific locations. Vaccine antigens can be encapsulated inside nanocarriers or decorated on their surface. Encapsulation within nanoparticles (NPs) can protect the antigen against premature degradation of the protease and cause continuous release, while adsorption facilitates their interaction with similar surface receptors such as APCs. As a result, compared to unconjugated antigens, they produce innate, humoral, cellular, as well as strong mucosal immune responses. The size, shape and surface chemistry of nanocarriers are important factors that determine their potential to activate immune responses. Furthermore, nanoparticles can deliver immune stimuli such as genes to specific locations as well as to deep tissues that nucleic acids alone may not be able to reach. In addition, nanoparticles have also been used as adjuvants to enhance the immunogenicity of vaccine candidates (nanoimmune stimulants).



Nano-immunostimulants are nanoscale vaccine particles (20 to 100 nm) that can improve vaccine performance in vivo. Different types of nanoparticles such as gold, magnetic iron oxide, carbon-based nanoparticles, dendrimers, polymers, lipid-based and liposomes have the ability to induce cytokine and antibody responses. Experiences of vaccination against Covid-19 pandemic have shown that the combination of nanotechnology and immunology in the development of third generation vaccines will be a promising approach in preventing and controlling viral diseases and prevent-

(Hassan Soleimanpour, cont)

government budgets, professional management, and teaching and research in English are the most important differences between our current universities and third-generation universities. Education and research in third-generation universities are defined in the context of innovation and entrepreneurship. Concepts such as accelerator, growth center and science and technology park are the concepts that the world's major universities created over the past 30 years to change the second-generation to the third-generation university. The researches in these universities meet the needs of society, industry and business. Teaching and education programs are based on the needs of the labour market, and the student's curriculum should be designed in a way to prepare them for innovation and wealth creation. It is noteworthy that all researches even basic researche of basic sciences is implemented and applied practically. Among the global ranking of the best business universities, indicators such as the average income, and the employment rate of graduates (the percentage of employment of graduates during the three months after graduation) are considered. It is worth reviewing the performance of three successful universities in this field:[1]

1- Harvard University:
Harvard University is located in Cambridge, Massachusetts, USA and is considered to be the oldest institution of higher education in the country. Harvard's teaching method is based on case studies, and students can study in two disciplines at the same time. Harvard graduates are recognized as the best and most qualified MBA specialists in the world and students have a great job offers even during their studies. University Mission Statement: We raise leaders who change the world, Average primary students' income after graduation: is $ 131,600, Percentage of employment up to 3 months after graduation: is 91%.
2. Massachusetts Institute of Technology (MIT),
Sloan College:
MIT is a research and private university located in Cambridge, Massachusetts, USA. Sloan College was founded in 1914 as a sub-department of Statistics and Economics, and today, after a hundred years, it is undoubtedly one of the best business universities in the world. University Mission Statement: To raise innovative and principled leaders who lead the world in a better direction, Average primary Students' Income after graduation: $ 126,300, Percentage of employment up to 3 months after graduation: is 94%
3- University of Pennsylvania, Wharton College:
The university is located in Philadelphia, Pennsylvania, USA. Wharton College is the first American business school, founded in 1881 and currently has the world's largest financial and economic database. University Mission Statement: Knowledge for action, Average elementary students' income after graduation: is $ 127,300, Percentage of employment up to 3 months after graduation: 95%
In order to prevent the accumulation of dissertations and academic research in libraries, Iran country's universities are changing from first and second generation universities to third ones, as well as, to maintain and promote the material and spiritual assets of our country. It seems that the progress to create the third generation universities will be hopefully created. In the end, it should be mentioned that Imam Reza General Hospital, Deputy of Education and Research, Innovation Office, Tabriz, support the technological ideas of the professors, students and staff of the center. We hope that with strong determination in entrepreneurship and technology areas, investing in innovation and commercialization of the ideas in universities, will generate more wealth and entrepreneurship.

(Behzad Baradaran cont.)

its detection in late 2019. The first identified strain originates from the city of Wuhan in China. After that, several SARS-CoV-2 mutations have been reported, and most mutated variants of coronavirus have no difference in prevalence or mortality rate when compared to the original strain, but some of them have many increased potential risks. The structure of SARS-Co-2 spike protein is crucial, and most of the mutations are associated with this spike protein, a vital target for several developed vaccines. Companies around the world have developed vaccines based on spike protein, which have been proven effective in generating neutralizing antibodies. According to the World Health Organization (WHO), most of these changes did not affect the characteristics of the virus, and many mutated viruses have disappeared over time. But sometimes the mutation increases the ability of the virus to survive or escape from the immune system or multiply. Despite this idea, it is too early to conclude about SARS-CoV-2 that it will soon weaken and disappear, as some scientists at the beginning of the coronavirus disease 2019 (COVID-19) epidemic thought would last only a few months. It seems that the mutations will weaken the SARS-CoV-2 strains, but this has not happened so far, and at least three species are more dangerous compared to the primary virus or other variants of concern: Alpha (B.1.1.7), Beta (B.1.351), and Delta (B.1.617.2), which were first identified in the UK, South Africa, and India respectively. The most important SARS-CoV-2 strains are now called with Latin letters from alpha to omicron. The WHO has described some species as "worrying" because they pose a greater risk to public health, because the virus is more contagious, or causes more serious illness, or because vaccines are less effective. The Alpha strain spreads faster and easier than the Wuhan type and is potentially 30% more deadly. The Beta strain appears to be less responsive to vaccines and antibody treatments than other strains. The concern of world vaccine researchers is that the South African type will return their efforts to zero. The Delta strain has caused wider and more intense epidemics than the other three strains and is therefore now the focus of much attention. Delta is 60% more contagious than Alpha, while Alpha itself was 50% more contagious than the primary SARS-CoV-2. In addition to these variants of concern, the SARS-CoV-2 Gamma variant (P.1) has an outbreak in several countries especially in Brazil. In addition to this, Omicron (B.1.1.529) has recently been added to the list of SARS-CoV-2 variants of concern, and has an outbreak, particularly in South Africa, and has increased risk of reinfection. Altogether, mutations in the virus raise concerns that may lead to the worsened disease, or cause mild-to-substantial loss of vaccine efficacy and make the efforts ineffective.
Vaccination is currently the most efficient way against the virus, however, the effectiveness of vaccines has been questioned due to recurrent mutations in the virus genome. All vaccines seem to be safe and efficient mechanisms to control severe COVID-19, hospitalization, and death against all strains, but the quality of evidence differs depending on the received vaccines. It is crucial to comprehend how coronavirus acquires mutated to develop efficient vaccines, providing sustained defense and neutralizing broad mutant variants. Fortunately, studies show that current vaccines are still effective in the control of new strains of the COVID-19. Their efficacy needs to study for emerging SARS-CoV-2 variants. However, the effectiveness of these vaccines on new strains is less than the original strains of Corona,

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(Behzad Baradaran, Cont)

especially after a single injection. Increasing evidence about the SARS-CoV-2 mutants and a detailed description of the efficacy of COVID-19 vaccine candidates against them may help to design the most efficient vaccine to combat the COVID-19 To date, more than one hundred vaccines have been developed with different platforms including protein subunit; RNA; inactivated virus; and viral vector. The mechanism of action, advantages, and potential limitations of them have been evaluated in phase III clinical trials, according to the WHO reports. However, the emergence of variants of the SARS-CoV-2 may threaten the global impact of mass vaccinations. The impacts of the variants of concern on the COVID-19 vaccines are being extensively studied. Here, we discussed mutants of SARS-CoV-2 and the vaccine's efficacy against them. Regardless of the variants of SARS-CoV-2, our most important weapon at the moment is a mask, keeping a distance, proper ventilation indoors, and continuous strengthening of the immune system to be more immune to this unprecedented global health crisis.

Dr. Ommoleila Molavi

COVID-19 Prophylactic Vaccines

The world has been troubled with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since the beginning of 2020. Despite the pandemic precaution measures around the world, up until now, more than 6 million lives have been lost due to this infection. The antiviral and anti-inflammatory therapeutic approaches available for this infection, have limited efficacy in most cases and they are only considered as supportive medications. Thus the prevention in reducing the transmission of SARS-CoV-2 virus was the best hope for public health until WHO approved a number of vaccines developed for SARS-CoV-2 infection in 2021. An effective vaccination against this infection, could activate the innate and adaptive immune responses and provide a protection against severe forms of coronavirus disease 2019 (COVID-19) disease. In spring 2020, the race for the development of an effective and safe vaccine began and by 2022, more than dozens of COVID-19 vaccines were approved for emergency use by WHO. Five major platforms including inactivated, viral vector-based, mRNA, protein-based, and attenuated vaccines have been used to develop COVID-19 vaccines. Among the approved COVID-19 vaccines, mRNA vaccines (Pfizer-BioNTech and Moderna) and viral vector based vaccines (AstraZeneca) have shown superior efficacy in protection against COVID-19 infection. Inactivated COVID-19 vaccines (Sinopharm, Sinovac, Barakat, and Covaxin) were also among the earliest vaccines approved for COVID-19 and they were found to be effective in induction of immunity against COVID-19. Late in 2021, COVID-19 recombinant subunit vaccines included with SARS-CoV-2 spike protein were introduced to the world and approved by WHO for emergency use. Novavax (USA), Soberana (PastoCovac, Iran), COVIFENZ (Canada), and SpikoGen (Iran) are the leading subunit vaccines which are included with viral recombinant spike protein plus new generation adjuvants. Subunit recombinant vaccine have a potential to become the most effective COVID-19 vaccines with the best safely profile in mankind. Therefore, most of the studies in the area of COVID-19 vaccines have been focused on the development of recombinant subunit vaccines for this infectious disease. While all of the developed COVID-19 vaccines have been shown to be effective at preventing the symptomatic COVID-19 infection caused by the different variants of SARS-CoV-2, some of the vaccine are found to have higher efficacy than others in induction of immunity in the vaccinated people. The differences in the efficacy of COVID-19 vaccine in induction of immunity is mainly due to the way, each vaccine activate immune responses against SARS-CoV-2 virus. As viruses are intracellular pathogens, both humoral (antibody) and cell mediated immune responses are needed to get activated and work together to combat the virus. Anti-virus antibodies neutralize the invading virus and prevent its binding to the cells and resulting cell infection. Cytotoxic T cells of cell mediated immunity are needed to destroy viral infected cells thereby preventing the infection of neighboring cells and tissues. Thus a COVID-19 vaccine which strongly activate both antibody and cell-mediated immune responses, is expected to induce better protection against the viral infection. Our immune system need two main signals to get activated against an infectious agent and induce immunity. The first signal comes from a non-self-antigen which is mostly a structural protein in the infectious agent. Among the four structural proteins of SARS-CoV-2, spike protein is the leading mediator of virus entry into human cells and the main determinant factor of virus virulence, therefore spike protein has been used as an antigen in COVID-19 vaccines. The second type of signals required for the induction of adaptive immune responses are called danger signals which are some molecular pattern found in invading pathogens, known as pathogen associated molecular patterns (PAMP). Danger signals function as adjuvant and the selection of the appropriate types of adjuvant significantly impact the magnitude of adaptive immune responses and its efficacy in combating the infectious agents. Non-self-antigen included in COVID-19 vaccines is the full length spike protein or some epitopes of this protein. These protein/peptide-based antigens are included in the COVID-19 vaccines in the forms of either ready to use antigens or mRNA or DNA coding sequences of the selected protein/peptide. In DNA and mRNA vaccines, antigen is made intracellularly by body's own cells and DNA/RNA molecules function as adjuvants, thus they can strongly induce both antibody and cell mediated immune responses. Based on the extensive clinical studies, both mRNA and DNA vaccines are very effective at preventing symptomatic COVID-19 illness. In inactivated and subunit vaccines, viral antigen is included in vaccines along with an adjuvant. Since the antigen of these vaccines are considered exogenous proteins for antigen presenting cells of innate immunity, antibody responses will be the major type of immunity induced by these vaccines, unless a particular adjuvant capable of inducing cell mediated immunity is included in these vaccines. Saponin-based matrix-M in Novavax, TLR7/8 ligand in Covaxin, tetanus toxoid in Soberana, and TLR9 ligand in SpikoGen are examples of the new generation adjuvants which are capable of inducting cell-mediated immune responses. Based on the findings of the published and in progress studies, all of the above mentioned subunit vaccines show over 70% efficacy at preventing the symptomatic COVID-19 disease caused by the original and emerging new SARS-CoV-2 variants. All types of COVID-19 vaccines have been reported to have an acceptable short-term safety profile. Mild to moderate and self-limited short adverse effects have been reported for the COVID-19 vaccines approved for emergency uses. The most common side effects of COVID-19 vaccines include fever, fatigue, headache, muscle pain, chills, diarrhea, and pain at the injection side. Nevertheless, uncommon or long-term adverse effects of COVID-19 vaccines are mostly unknown and require extended post-authorization study to detect. Among the vaccine platforms, inactivated and subunit vaccines have a long history of administration for preventing infectious diseases and they have well-known short-term and long-term safety profile. An important example of widely used subunit vaccine is recombinant influenza vaccines which is given worldwide to millions of people at high risk of developing flu-related complications. Therefore, it is expected that the most widely used COVID-19 vaccines of future will be recombinant COVID-19 vaccines and they will be mostly used in individuals at increased risk of severe illness from contracting this infection.

Dr. Saeid Safiri

Cardiac Complications Following mRNA COVID-19 Vaccines: A Systematic Review of Case Reports and Case Series

Published in Reviews in Medical Virology

Since the beginning of the coronavirus disease 2019 (COVID-19) pandemic, different platforms have been utilized to develop safe and effective vaccines. COVID-19 mRNA vaccines, like mRNA-1273 and BNT1626b2, trigger innate immunity, cytotoxic and helper T cells, and in particular B-cell responses. There have been several local and systemic adverse events associated with mRNA COVID-19 vaccines, which are mostly non-serious. However, there are several complications affecting the cardiovascular systems like pericarditis, myocarditis and myocardial infarction, which can be life-threatening. To our knowledge, there is no large-scale observational study or systematic review to specifically focus on cardiac complications following COVID-19 mRNA vaccines. Furthermore, most of the conducted papers are case reports and case series reporting these adverse events or studies only presenting the frequency of them. Therefore, we conducted a systematic review of case reports and case series to identify the clinical profile, investigations, and management of reported cardiac complications following COVID-19 mRNA vaccination. We systematically searched PubMed, Scopus, Web of Science, and Google Scholar, as well as the medRxiv preprint server, with terms including: 'SARS-CoV-2', 'COVID-19', 'messenger RNA vaccine', 'mRNA-1273 vaccine', 'BNT162 vaccine', 'myocarditis', 'pericarditis', 'stroke' and 'myocardial ischemia' up to 25 September 2021. Studies were excluded if they were not case reports or case series, or reported cases from non-mRNA vaccines. Case reports and case series that investigated the potential cardiac complications associated with mRNA COVID-19 vaccines were included. The JBI checklist was used to assess quality. Data synthesis was conducted using a qualitative methodology called narrative synthesis. Sixty-nine studies, including 43 case reports and 26 case series, were included. Myocarditis/myopericarditis and pericarditis were the most common adverse events among the 243 reported cardiac complications, following COVID-19 mRNA vaccination. Males with a median age of 21 years had the highest frequency of myocarditis. Almost three quarters (74.4%) of cases with myocarditis had received the BNT162b2 vaccine and 87.7% had received the second dose of the vaccine. Chest pain (96.1%) and fever (38.2%) were the most common presentations, followed by headache (18.8%), myalgia (18.8%), fatigue (15.5%), chills (12.6%) and shortness of breath (10.1%). CK-MB, troponin, and NT-proBNP were elevated in 100%, 99.5% and 78.3% of subjects, respectively. ST-segment abnormality was the most common electrocardiogram (ECG) feature. Cardiac magnetic resonance imaging, which is the gold-standard approach for diagnosing myocarditis, was abnormal in all patients diagnosed with myocarditis. Among anti-inflammatory pharmacological options, non-steroidal anti-inflammatory drugs, mainly ibuprofen and aspirin, were prescribed for 48% of the patients, followed by colchicine (22.5%), steroids (14.1%) and intravenous immunoglobulin (IVIg) (11.5%). Furthermore, 10.1% of the patients needed beta-blockers, 5.9% of them needed ACE inhibitors, and 2.2% needed diuretics for managing possible heart failure. Apart from inflammatory conditions, some rare cases of Takotsubo cardiomyopathy, myocardial infarction, myocardial infarction with non-obstructive coronary arteries (MINOCA), and isolated tachycardia were also reported following immunization with COVID-19 mRNA vaccines. We acknowledge that only reviewing case reports and case series studies is one potential limitation of our study. We found that myocarditis/myopericarditis was the most commonly reported event which presented as chest pain with a rise in cardiac biomarkers, while MINOCA and isolated tachycardia are the least common. Chest pain should be considered an alarming symptom, especially in those who had received a second dose of the BNT162b2 vaccine in the last 3 days. For diagnosis, CK-MB and troponin levels are better biomarkers to confirm myocarditis than ECG, CRP, ESR, and NT-proBNP. Large-scale observational studies and systematic reviews on those studies are highly recommended. Moreover, subgroup analysis needs to be conducted, based on behavioral risk factors (e.g., alcohol consumption and smoking), comorbidities, and prior history of SARS- CoV-2 infection.

Dr. Vahdat Poortahmasebi
Different Variants of Covid-19 Virus

Since the outbreak of the new coronavirus until today, we have seen mutations in it that have challenged the immune system and the vaccination and control of the virus. Alpha species (B.1.1.7) was first identified in the fall of 2020 in the UK. This type of mutation is located at the receptor (RBD) junction of the Spike protein at position 501, where the amino acid asparagine (N) is replaced by tyrosine (Y). This type also has several other mutations as follows: Deletion 69/70: Occurs spontaneously many times and possibly changes the structure of the Spike protein. P681H: Near the F1 S1/S2 clearance site, a highly diverse site for coronaviruses. This mutation has also appeared several times on its own. this type of coronavirus spreads more easily and faster than other types and is potentially 30% more deadly than the original version. Research shows that people who become infected with the coronavirus have the main symptoms, including cough, fatigue, muscle aches, sore throat, and fever. Symptoms such as loss of taste or smell are less common in patients with the mutated type. The B.1.351 (or Beta) variant was first discovered in South Africa. The beta has nine spike mutations and D614G, including a cluster of mutations (e.g., R246I and 242–244del) in the NTD, three mutations (K417N, N501Y, and E484K) in the RBD, and one mutation (A701V) near the furin cleavage site. Mutations in S protein characterize this variant: E484K may be involved in the structural modification of the end of the spike, which may escape antibody neutralization or vaccination against the S protein, and K417N and N501Y mutations may be involved in enhancing the binding of the spike to ACE2. Compared with the prototype virus, the beta variant is less likely to be neutralized by the convalescent plasma of patients infected with the previous variant and the serum of the vaccine. In Brazil, a species called P.1(Gama) emerged. This species was first discovered in late January 2021 in the United States. type P.1 has 17 unique mutations, including three that are associated with S protein binding (K417T, E484K, N501Y). There is evidence that some mutations in type P.1 may affect the ability of antibodies to detect and neutralize the virus. N501Y and K417T may be involved in enhancing transmission, while E484K may be related to a slight improvement in receptor-binding affinity and immune escape. This variant is 1.4–2.2 times more infectious than the original strain. There is a specific mutation called D614G enabling faster transmission than non-mutant viruses and increasing the incidence of COVID-19. Patients with Delta (B.1.617.2) mutation often have cold symptoms such as headache, sore throat, and runny nose. Loss of sense of smell and taste is less common in this mutation. Not everyone has symptoms such as shortness of breath, fever, and persistent cough. Also affects children. B.1.617 was first identified and recorded in India in October 2021, and in just a few weeks, the variant of the coronavirus has become the main species throughout India, followed by forty other countries, including the United States and Singapore. In early November 2021, Omicron (B.1.1.529) was discovered in Botswana. People who have been fully vaccinated against the coronavirus have reported nausea, fever, sore throat, and headaches following an Omicron mutation. They also suffered from sore throats and headaches. The difference between omicron and other variants is in the severity of its pathogenicity. One possible difference is that Omicron may be less likely than earlier variants to cause a loss of taste and smell. Research suggests that 48 percent of patients with the original SARS-CoV-2 strain reported the loss of smell and 41 percent reported loss of taste. It's unclear, though, whether these differences are because of Omicron or some other factor, like vaccination status. The Omicron has more than 50 mutations, of which the spike protein has 26–35 amino acids different from the original SARS-CoV-2 virus or the Delta, some of which are associated with humoral immune escape potential and greater transmissibility. Omicron has a significant growth advantage over Delta, leading to rapid spread with higher incidence levels. The disease so far has been mild compared to the Delta. Mutations that make a virus more deadly may not give the virus an opportunity to spread efficiently. However, as we have seen with delta and omicron, more infections from a faster-spreading variant will lead to more hospitalizations and deaths. The mutation is part of being a virus. Viruses mutate to adapt to their surroundings and more effectively move from host to host. Mutations can cause viruses to better evade our immune systems, treatments, and vaccines. The future of these mutations is unpredictable, but vaccination and the passage of time so far indicate that the virus is weakening, but the virus is taking unexpected steps.

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