



## COVID-19 Vaccine-Associated Adverse Effects; Benefits Outweigh the Risks?

### COVID-19 Aşısına Bağlı Yan Etkiler; Faydalar Risklerden Ağır Basıyor Mu?

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#### Öz

COVID-19 vaccines are vaccines produced with the latest technology in a very short time to get rid of this disease. These vaccines have been produced and used in millions around the world. Although some simple local side effects have been reported during and immediately after the administration of the vaccine, long-term side effects affecting various organs have recently been begun to be reported, especially with the use of mRNA vaccines. This minireview discusses the issues related to these simple and less common side effects.

**Anahtar Kelimeler** COVID-19, SARS-CoV-2, side effect, vaccine

#### Abstract

COVID-19 aşılı, bu salgını kontrol altına almak için çok kısa sürede, son teknolojiyle üretilen aşılardır. Bu aşılarda dünya çapında milyonlarca üretilip kullanılmaktadır. Aşının uygulanması sırasında ve hemen sonrasında bazı hafif lokal yan etkiler bildirilse de, son zamanlarda özellikle mRNA aşılılarının kullanılmaya başlanmasıyla birlikte çeşitli organları etkileyen uzun vadeli yan etkiler de bildirilmeye başlanmıştır. Bu derlemede, hafif ve daha nadir olan yan etkilerle ilgili konular tartışılmaktadır.

**Keywords** COVID-19, SARS-CoV-2, yan etki, aşı,

## INTRODUCTION

The SARS-CoV-2 outbreak was declared a pandemic by the World Health Organization (WHO) on March 11, 2020, and a public health emergency of international concern (PHEIC) in late January 2020.<sup>1</sup> It has caused a lot of morbidity and mortality. Since the beginning of the pandemic, studies have been carried out for effective vaccines and disease-specific antiviral treatments to minimize the harmful effects of the disease.<sup>2</sup>

Vaccines have a significant place in preventing infectious diseases. The way to make it easier to control the epidemic is to ensure that the susceptible population becomes immune by vaccinating them. While vaccination protects individuals against the disease, if administered to a sufficient number of people, it also provides adequate 'herd immunity' to reduce the spread of the virus, morbidity, and mortality worldwide.<sup>3</sup>

In recent years, increasing anti-vaccination movement and vaccine hesitancy with the influence of social media has led to the re-increase of many infectious diseases such as measles.<sup>4</sup> According to the World Health Organization (WHO) statement in 2019, one of the top 10 health threats in the world is anti-vaccination movement.<sup>5</sup> Unfortunately, anti-vaccination movement and vaccine hesitancy towards COVID-19 vaccines is quite common.

COVID-19 vaccines may effectively contain the devastating social and economic impacts of this new virus (SARS-CoV-2) and alleviate the severity of this epidemic. Herd immunity provides an indirect protection against an infectious disease that occurs when a population is immune through vaccination or previous infection.<sup>6</sup>

### Types of vaccines developed for COVID-19

There are vaccines developed against SARS-CoV-2 using different principles. These are complete virion vaccines (live attenuated, inactivated), nucleic acid-based DNA and mRNA vaccines, viral vector vaccines (replicative and

nonreplicative), recombinant protein/protein subunit and virus-like particle (VLP)] vaccines.<sup>7</sup>

Some of the vaccine types developed for COVID-19 are listed in the Table 1.<sup>8</sup>

**Table 1.** Some of the types of vaccines developed for COVID-19

Manufacturer	Vaccine name	Vaccine type
Pfizer-Biontech	BNT162b2/ COMIRNATY Tozinameran (INN)	RNA based vaccine/ BNT162b2(3 LNP-mRNAs )
AstraZeneca +University of Oxford	AZD1222	Viral vector/ ChAdOx1-S-(AZD1222)
Janssen/Johnson & Johnson	Ad26.COV2.S	Viral vector/Ad26.COV2.S
Moderna+National Institute of Allergy and Infectious Diseases (NIAID)	mRNA -1273	RNA-based vaccine/mRNA-1273
Sinovac Research and Development Co., Ltd. (CoronaVac)	COVID-19 Vaccine (Vero Cell), Inactivated / CoronavacTM	Inactivated SARS-CoV-2 vaccine
Sinopharm+China National Biotec group Co. + Wuhan Institute of Biological Products	SARS-CoV-2 Vaccine (Vero Cell), Inactivated (InCoV )	Inactivated SARS-CoV-2 vaccine
Novavax	NVX-CoV2373/ Covovax	Protein subunit / SARS-CoV-2 rS / Matrix M1-Adjuvant
IMBCAMS, China	SARS-CoV-2 Vaccine, Inactivated (Vero Cell)	Inactivated SARS-CoV-2 vaccine
Erciyes University Hakan Çetinsaya Good Clinical Practice and Research Centre and Erciyes University Vaccine Research, Development and Application Centre (ERAGEM)	ERUCoV-VAC (Turkovac)	Inactivated SARS-CoV-2 vaccine

### Expected (Common) Side Effects of Vaccines

Sinovac vaccine is a vaccine containing an inactivated virus and has been produced using the same methods that have been used to produce vaccines for decades. BioN-

Tech, on the other hand, is made using m-RNA, a newer technology. Both vaccines are particularly effective at preventing severe infections and death.<sup>9</sup>

Sinovac vaccine is a vaccine containing inactivated virus. Inactivated vaccines are produced by growing SARS-CoV-2 in cell culture and chemically inactivating the virus. The inactivated virus is often combined with an adjuvant such as aluminum to enhance the immune response. The Coronavac vaccine produced by Sinovac and Turkovac vaccine was also prepared with this method.<sup>10,11</sup>

No severe side effects have been found in clinical studies and current vaccine applications for both BioNTech® and Sinovac® used in our country and other vaccines used in various countries worldwide. Turkovac vaccine, which received emergency use authorization (EUA) by the Turkish Medicines and Medical Devices Agency in December 2021, was also used in our country. The side effects seen in the Turkovac vaccine were similar to other inactive vaccine studies.<sup>11</sup> Side effects that occur after vaccination are mostly mild. After vaccination, complaints such as redness, swelling, and pain may appear on the arm where the vaccine was applied.<sup>12-14</sup> Side effects such as headache, feeling tired, fever, pain in the arm where the vaccine is used, redness in the area where the vaccine is applied, muscle and joint pain, chills, nausea, and diarrhea are the most common side effects of COVID-19 vaccines.<sup>14-16</sup>

Side effects such as severe hypersensitivity reactions are rare and usually occur shortly after vaccine administration. Therefore, vaccines should be administered in settings where immediate allergic responses can be appropriately managed. The mRNA vaccines, Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273) contain polyethylene glycol. The vector vaccine Janssen/Johnson & Johnson (Ad26.COV2.S) contains polysorbate.<sup>17</sup> Allergy to these substances in individuals constitutes a contraindication for vaccination.

### Rare Side Effects of Vaccines

The Pfizer/BioNTech (BNT162b2) vaccine is an mRNA-based vaccine. Myocarditis and pericarditis have been reported more frequently than expected in male adolescents and young adults who received the Pfizer/BioNTech (BNT162b2) and Moderna (mRNA-1273) vaccines.<sup>18,19</sup> Signs of myocarditis usually appear within the first week after administration of the vaccine and, more commonly, after the second dose. Considering the low rates of myocarditis and pericarditis developing after mRNA vaccines, its mild clinical course, and its rapid and good response to medical treatment, it is obvious that it can be preferred to the devastating consequences of COVID-19.<sup>20-21</sup> The second dose can be postponed if the side effect occurs after the first dose. If the risk of COVID-19 is high, these people can be given a second dose of vaccine after the myocarditis episode resolves. Myocarditis should be suspected when palpitations, chest pain, and shortness of breath develop in adolescents after administration of the mRNA vaccine.<sup>22</sup> Meanwhile, it should not be forgotten that SARS-CoV-2 infection simultaneously with the vaccine can also cause myocarditis.<sup>18</sup>

A potential relationship between Adenovirus vector vaccines e.g. AstraZeneca and Janssen/Johnson & Johnson and Guillain-Barre syndrome (GBS) is being investigated.<sup>23</sup> Despite this possible side effect, the US Food and Drug Administration (FDA), US Centers for Disease Control and Prevention (CDC), and European Medicines Agency (EMA) confirm that the benefits of these vaccines outweigh their risks.<sup>24</sup> Cases of GBS have also been reported during SARS-CoV-2 infection; for individuals with a previous history of GBS, vaccines other than adenovirus vector vaccines should be preferred.<sup>25</sup>

Since thrombosis with thrombocytopenia can be seen at very low rates after the administration of Adenovirus vector vaccines such as AstraZeneca and Janssen/Johnson & Johnson mRNA vaccines [BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines] or other vaccines

(such as CoronaVac) are preferred if possible. However, if access to these vaccines is not possible, the AstraZeneca or Janssen vaccine can also be administered according to the benefit-risk analysis.<sup>26</sup>

### **Relation between COVID-19**

#### **Vaccination and Autoimmune Diseases**

Some studies have shown that human papillomavirus, hepatitis B, and influenza vaccines may trigger the onset or exacerbation of autoimmune diseases through molecular mimicry that causes autoimmunity.<sup>27-29</sup>

Studies show that new-onset autoimmune symptoms, including thrombosis with thrombocytopenia after vaccine administration, myocarditis, chronic spontaneous / idiopathic urticaria, autoimmune liver diseases, GBS, and IgA nephropathy might be associated with COVID-19 vaccines.<sup>30,31</sup> Possible mechanisms by which COVID-19 vaccines cause autoimmune manifestations include molecular mimicry, production of specific autoantibodies, and the role of particular vaccine adjuvants. Further studies are needed to elucidate the underlying biological mechanisms and determine precise causality.<sup>30</sup>

### **CONCLUSION**

In conclusion, even when all side effects are considered, vaccine effectiveness prevents rare problems. The benefits of COVID-19 vaccines in preventing disease and related deaths far outweigh any possible adverse effects. Studies show that approved vaccines against COVID-19 have a primary role in controlling hospitalizations and deaths. To create herd immunity, most of the population must be vaccinated. Negative effects on the functioning of social life can be minimized through vaccination. Concerns about rare side effects following COVID-19 immunization should not diminish overall confidence in the value of vaccination.

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### **Authorship Contributions**

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### **Conflict of Interest**

The authors declare that they have no conflict of interest.

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