Recommendations for Athletes to Vaccinate against SARS-CoV-2

Empfehlungen für Sportler zur Impfung gegen SARS-CoV-2

Summary

- After prioritization of populations with risk factors for severe courses of Covid-19 ("Corona") and occupational groups with a high number of close contacts with patients and other human beings, from now onward (performance-oriented) athletes will be considered for vaccination.
- Recommendations for vaccinations in this target group can be different from the ones for the general population in some aspects. However, there are only very few scientifically valid findings that may guide vaccinating medical doctors.
- This article summarizes available evidence and formulates recommendations for vaccinations in (high-performance) athletes.

General Considerations about Vaccination of Athletes

Vaccination recommendations for the general population (e.g., those from STIKO) cannot be simply transferred to athletes, particularly not to high-performance athletes, because the balance between vaccination risks and immunity effects is partly different. Local or systemic side effects may impair the eligibility for training and competition whereas such constraints would not necessarily result for other (occupation al) activities. On the other hand side, the protection resulting from a vaccination is potentially more valuable for athletes because their exposition to infectious agents who are preventable by vaccination it typically larger due to close body contacts and frequent travelling. After weighing advantages and disadvantages of vaccinations for athletes, recent publications tend to set the indication for vaccinations rather generously (6, 14). As an example, this is true for influenza and hepatitis A which are regularly only recommended for certain target groups or situations. However, the authors clearly state that available scientific studies about questions in the context of vaccinating (high-performance) athletes are rare. Besides the general consideration whether to get vaccinated or not, a second aspect for athletes is if and under which circumstances their resulting immunity might be impaired. Such scepticism stems from older findings which insinuate a temporarily reduced immunocompetence after acute exercise (so called "open window"; 9, 10) or even a long-term detriment ("J-shaped curve"; 8). However, meanwhile it is concluded that accumulated knowledge is not sufficient to postulate a transient or chronically impaired immunity from repeated strenuous training and competition in athletes (2). In this regard, changes being observed during the "open window" rather belong to the unspecific immune response that is not centrally involved in the development of the immunological memory. In addition, there are no concrete findings indicating an impaired vaccination response in competitive athletes. The few studies that have addressed the topic seem to support a regular or even above average immune response in (high-performance) athletes (3, 7, 11). Even negative effects from a training session immediately preceding vaccination have not been found (13).
Side effects were not more frequent than in control subjects and never so pronounced that training sessions had to be cancelled (7, 13). A limitation is that all recent studies were conducted using dead vaccines (influenza, hepatitis B).

It can be carefully derived from existing evidence that indications for vaccinations in performance-oriented athletes should be set rather liberally and that relevant vaccination-dependent impairments of the ongoing training process are not to be expected. High-performance training neither challenges the immunological success of vaccination nor does it lead to an overproportionate likelihood of side effects.

Currently, no scientific studies are available about vaccination against SARS-CoV-2 in athletes. One of the obvious reasons for this fact is the low priority that is assigned to young and healthy athletes in many countries with regard to urgency of their vaccination. Therefore, derivations can only be made from SARS-CoV-2 vaccinations in other populations or - with some reservation - from studies in athletes using other vaccines. An aggravating circumstance is that 2 of 4 vaccines that have been approved in the European Union are mRNA-based (Comirnaty from BionTech-Pfizer and Covid-19 Vaccine Moderna from Moderna) and, thus, do represent a new vaccination concept. Similarly, for vector-based vaccines like the other two ones being approved (Vaxzevria from AstraZeneca, Covid-19 Vaccine Janssen from Johnson & Johnson) the available evidence is not satisfactory because only few vaccines have been developed of that type so far.

When vaccination is carried out according to the administrative approval (Comirnaty twice within 3-6 weeks, Covid-19 Vaccine Moderna twice within 4-6 weeks, Vaxzevria twice within 9-12 weeks; Covid-19 Vaccine Janssen as a single shot) for both mRNA vaccines as well as for Vaxzevria a similar efficacy can be expected for the avoidance of severe courses of Covid-19. Efficacy is a bit lower for Covid-19 Vaccine Janssen presumably due to the fact that an approval was already targeted after only one injection. A summary about vaccine properties can be found in figure 1.

In their respective approval studies, vaccines were either tested against sodium chloride or against another vaccine (1, 5, 12, 15). As with all vaccinations, local side effects were recorded (local pain at injection site, reddening, swelling). Additionally, systemic side effects like fatigue, fever, chilling or headache and myalgias occurred. A comparison between such results is not valid because vaccines were not tested against each other in a single study. It appeared that side effects were stronger after the second injection with Comirnaty whereas this was the other way round for Vaxzevria.

Different profiles of side effects can be derived from reports to the Paul-Ehrlich-Institut: Whilst the mRNA vaccine from BioNTech mainly elicited local pain, headache and particularly fatigue, after application of the AstraZeneca vaccine fever and chilling dominated. The Moderna vaccine most frequently led to rashes and itching. Data about Johnson & Johnson’s vaccine do not exist in this database because it has not been applied in Germany so far. Very rare side effects were brought up by the media over the last few months. Data from the Paul-Ehrlich-Institut show that allergic reactions to the vaccines are in the frequency range of 1:100,000 vaccinations with slightly higher values for Comirnaty. Thrombocytopenias (reduction of the blood platelets) and thromboses were recorded for all vaccines but more frequently for Vaxzevria from AstraZeneca.

Based on the risk profile for side effects of all available vaccines it makes sense not to plan any important training sessions, journeys or even competitions for 2 days afterwards. Also, to make sure that professional medical care can be provided after allergic reactions, vaccinees should remain at the vaccination center (or general practitioner) for about 30 minutes. Intake of non-steroidal anti-inflammatory drugs (“pain killers”) is possible when complaints become too severe. A prophylactic use is not recommended. The preferred substance is paracetamol which should not be taken earlier than 6 hours after vaccination because otherwise there is a danger or lower vaccination titers (4).

In athletes who have endured a symptomatic SARS-CoV-2 infection only a single-shot vaccination (all vaccines possible) is recommended not earlier than 6 months later. The reason for such postponement is that after a symptomatic infection immunity develops for at least 6 months which means that an earlier vaccination would not lead to any relevant advantage. In addition, there exist anecdotal reports that side effects might be larger after a vaccination too early after initial infection. However, no systematic studies are available about that question. A further reason for the 6 months recommendation is an existing shortage of vaccines. From a population perspective, it is more important to offer the first vaccination to a person that has not yet developed any immunity.

When a SARS-CoV-2 infection remained symptom-free and there are no other clinical indicators for a likely existing immunity (e. g. antibody titers or low Ct values in the initial positive PCR test) a complete vaccination after 3-6 months can be considered. Such a consideration may take other individual circumstances like competition schedules into account. Main criterion should be whether the slightly increased likelihood for side effects is more important or safety from future contagions. In this situation, the one-shot vaccination from Johnson & Johnson might be a pragmatic choice.

Vaccination schedules may vary from the ones of the approval studies, particularly for Vaxzevria. In Germany, this vaccine is currently not recommended for persons below 60 years of age. When a first shot has already been made with this vaccine, the second one can be carried out with the same vaccine but changing to another one is possible, too. Under the given circumstances, the most likely second vaccine will be Comirnaty. Data from animal studies suggest that vaccination success will not be impaired by such a switch. Of course, no statements about side effects are possible based on these investigations. Due to logistical problems in many vaccination centres, a choice between vaccines will not be possible for the second shot.

Summary of Recommendations for the Vaccination of Athletes against SARS-CoV-2

- The Covid-19 pandemic induced health risks and restrictions of individual freedom and of opportunities for athletic training and competition which gives a general indication to vaccinate athletes - in particular high-performance athletes - against SARS-CoV-2. In cases of intolerance or specific contraindications against certain vaccines, there are existing alternatives.
- Although scientific evidence is sparse, at least an equivalent efficacy to the general population can be expected for SARS-CoV-2 vaccinations in athletes.
- All currently available SARS-CoV-2 vaccines lead to side effects more frequently than more established vaccines against other infectious agents and in particular dead vaccines. This has to be taken into account and, thus, vaccinations should not be
Recommendations for Athletes to Vaccinate against SARS-CoV-2

| Manufacturer (Trade name) | Recommended age by manufacturer | Dosing and Schedule (i. m. injection) | Vaccine efficacy |
|---------------------------|---------------------------------|--------------------------------------|-----------------|
| BioNTech/Pfizer (Comirnaty) mRNA-based | 15 y, application for approval: 12 y | Covid-19 vaccine + 3-5 weeks + Covid-19 vaccine + 7 days | Up to 95% |
| Moderna (COVID-19 Vaccine) mRNA-based | 18 y | Covid-19 vaccine + 4-6 weeks + Covid-19 vaccine + 14 days | Up to 95% |
| AstraZeneca (Vaxzevria) Vector-based | 18 y, STIKO recommended: 60 y | Covid-19 vaccine + 12 weeks + Covid-19 vaccine + 15 days | Up to 80% |
| Johnson&Johnson (COVID-19 Vaccine Janssen) Vector-based | 18 y | + | Up to 70% |

Figure 1
Summary of relevant properties of currently available SARS-CoV-2 vaccines, modified after Paul-Ehrlich-Institut (https://www.pei.de/DE/arzneimittel/impfstoffe/covid-19/covid-19-node.html).

placed immediately prior to important competitions or training sessions. According to first reports, Vaxzevria leads to side effects more frequently after the first injection whereas the mRNA vaccines tend to do this after the booster injection.

- In cases of an endured Covid-19 disease, a single booster injection should be applied after 6 months. When the infection was asymptomatic, the decision about vaccination procedures should be based on all available clinical information and possibly on competition schedules. In such cases, a "de novo" (complete) vaccination may be considered.

- Under the current circumstances, there is no choice of the vaccine for each individual athlete. In principle, all vaccines can be utilized. The available vaccines have different efficacy, side effects and temporal profiles of their effects. Particularly the efficacy against virus variants cannot be assessed at this moment because new ones are steadily arising (e. g. from India). An advantage of vaccines from BionTech, Moderna and AstraZeneca is its better protective effect whereas the Johnson & Johnson vaccine owns the simplest vaccination schedule and potentially a shorter overall duration of side effects given that only one injection is needed.

- Covid-19 Vaccine Janssen should be considered when it is necessary to quickly produce immune protection, e. g. shortly before an important competition. Another reason could be the collision of a second injection with inevitable other requirements, e. g. an absence due to a longer lasting event.

- It can be expected that the pandemic will last for many months or even years and that new virus mutations occur. Therefore, it has to be taken into account that booster vaccinations with slightly altered vaccines will be necessary - similar to influenza.

Conflict of Interest
The authors have no conflict of interest.
Empfehlungen für Sportler zur Impfung gegen SARS-CoV-2

(1) BADEN LR, EL SAHLY HM, ESSINK B, KOTLOFF K, FREY S, NOVAK R, DIEMERT D, SPECTOR SA, ROUPHAEL N, GREECH CB, MCSGETTIGAN J, KRIETAN S, SEGALL N, SOLIS J, BROZS A, FIERRO C, SCHWARTZ H, NEUZIL K, COREY L, GILBERT P, JANES H, FOLLMANN D, MAROVICH M, MASCOLA J, POLAKOWSKI L, LEDGERWOOD J, GRAHAM BS, BENNETT H, PAJON K, NIGHTLY C, LEAV B, DENG W, ZHOU H, PAN S, IVARSSON M, MILLER J, ZAK T, COVE STUDY GROUP. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021; 384: 403-416. doi:10.1056/NEJMoa2035389

(2) CAMPBELL JP, TURNER JE. Debunking the Myth of exercise-induced Immune suppression: Redefining the impact of exercise on immunological health across the lifespan. Front Immunol. 2018; 9: 648. doi:10.3389/fimmu.2018.00648

(3) CÔTÉ TR, SIVERTSON D, MORAN JM, LINDEGREN ML, DYER DM. Evaluation of a two-dose measles, mumps, and rubella vaccination schedule in a cohort of college athletes. Public Health Rep. 1993; 108: 431-435.

(4) ETMINAN M, LODHI M, GANJIZADEH-ZAVAREH S. Should Antipyretics Be Used to Relieve Acute Adverse Events Related to Coronavirus Disease 2019 Vaccines? Chest. 2021; 20012-3692(21)00254-3. doi:10.1016/j.chest.2021.01.080

(5) FOLEGATTI PM, EWER KJ, ALEY PK, ANGUS B, BECKER S, BELLAMY D, BIBI S, BITTAYE M, BIBI S, BRUNNER M, DOLD C, FAUST SN, FINN A, FLAXMAN AL, HALLIS B, HEATH P, JENKIN D, LAZARUS R, MARINSON R, MINASSIAN AM, POLLOCK KM, RAMASAMY M, ROBINSON H, SNAPDE LB, TANNER T, VOITZER M, GREEN C, DOUGLAS AD, HILL AVS, LAMBE T, GILBERT SC, POLLARD AJ, OXFORD COVID VACCINE TRIAL GROUP. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. Lancet. 2020; 396: 467-478. doi:10.1016/S0140-6736(20)31604-4

(6) GÄRTNER B, MEYER T. Vaccination in elite athletes. Sports Med. 2014; 44: 1361-1376. doi:10.1007/s40279-014-0217-3

(7) LEDO A, SCHUB D, ZILLER C, ENDERS M, STENGERT T, GÄRTNER BC, SCHMIDT T, MEYER T, SESTER M. Elite athletes on regular training show more pronounced induction of vaccine-specific T-cells and antibodies after tetravalent influenza vaccination than controls. Brain Behav Immun. 2020; 83: 135-145. doi:10.1016/j.bbi.2019.09.024

(8) NIEMAN DC. Exercise, infection, and immunity. Int J Sports Med. 1994; 15: S131-S141. doi:10.1055/s-2007-1021128

(9) PEDERSSON BK, BRUNNAS AJO. How physical exercise influences the establishment of infections. Sports Med. 1995; 19: 393-400. doi:10.2165/00007256-199519060-00003

(10) PYNE DB, GLEESON MJ. Effects of intensive exercise training on immunity in athletes. Int J Sports Med. 1998; 19: S183-S194. doi:10.1055/s-2007-971991

(11) ROSIC I, MALICEVIC S, MEDIC S, VLASICH C. Immune response by athletes to hepatitis B vaccination. Vaccine. 2008; 26: 3190-3191. doi:10.1016/j.vaccine.2008.03.051

(12) SADDOF J, GRAY G, VANDEBOSCH A, CAÑEDAS Y, SHUKAREV G, GRINSZEITEN B, GOEPFERT PA, TRUERS C, FENNEMA H, SPIESSENS B, OFFERGELK K, SCHEGER T, TAYLOR KL, ROBB ML, TREANOR J, BAROUCH DH, STOOGARD J, RYSER MF, MAROVICH MA, NEUZIL KM, COREY L, CAUVENBERGS H, TANNER T, HARDY K, RUIZ-GUÑAZO J, LE GARS M, SCHUITEMAKER H, VAN HOOF J, STRUYF F, DOUGUINH M; ENSEMBLE STUDY GROUP. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. N Engl J Med. In press. doi:10.1056/NEJMoa2101544

(13) STENGERT T, LEDO A, ZILLER C, SCHUB D, SCHMIDT T, ENDERS M, GÄRTNER BC, SESTER M, MEYER T. Timing of vaccination after training: immune response and side effects in athletes. Med Sci Sports Exerc. 2020; 52: 1603-1609. doi:10.1249/MSS.0000000000002278

(14) TAFURI S, SINESI D, GALLONE MS. Vaccinations among athletes: evidence and recommendations. Exp Rev Vacc. 2017; 16: 867-869. doi:10.1080/14760584.2017.1358092

(15) VOITZER M, CLEMENS SAC, MADIH SA, WECKX LK, FOLEGATTI PM, ALEY PK, ANGUS B, BAILLIE VL, BARNABAS SL, BHRAT DE, BIBI S, BRINER C, CICCONI P, COLLINS AM, ET AL.; OXFORD COVID VACCINE TRIAL GROUP. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021; 397: 99-111. doi:10.1016/S0140-6736(20)32661-1