

Anti-Covid vaccination; is it time for booster shots?

Press release from the French National Academy of Medicine

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While a complete vaccination coverage against Covid-19 has not yet reached 60% in France, the administration of a booster dose is being considered for populations who were thought as priorities at the start of the national vaccination campaign: residents of EHPAD (establishment for dependent elderly people) and USLD (long term care unit), people over 80 years old living at home, people suffering from co-morbidities or immunocompromised).

This provision should not be confused with the administration of a third dose of vaccine recommended since June 18, [1] and already practiced in immunocompromised people or those suffering from some cancers [1] to compensate for a deficiency in the immune system. The purpose of a booster dose is to reinforce vaccine protection in subjects whose humoral immune response, as assessed by the titer of neutralizing antibodies, has become weak or even undetectable after a few months. The decline in antibody levels is observed in all vaccinated individuals, but is more rapid over 65 years or in cases of co-morbidity [2].

There are still a number of uncertainties about the booster shots related to the lack of knowledge of the immune correlates of protection against Covid-19 and SARS-CoV-2 infection. In addition to the humoral response active in neutralizing the virus and its main variants, there is a post-vaccination cellular immunity (CD4 and CD8 lymphocytes) with a cytotoxic expression and cytokine production, the effect of which on viral transmission and on the pathophysiology of infection is still poorly defined.

Few data are currently available to demonstrate the need to generalize a vaccination booster after the first 2 doses of vaccine. A vaccinated subject retains an immune memory that protects him/her for a minimum of 6 to 8 months against severe forms of Covid-19. If the principle of a booster is justified in the elderly or vulnerable, the modalities of this booster should be supported by clinical studies to determine, depending on the nature of the vaccine, the interval to be respected after the second dose of vaccine and the threshold age for this prescription.

It may be necessary to offer the booster to people over 65 years of age or with co-morbidities. The potential benefit of heterologous immunization [1], either with a vaccine already on the market or with a vaccine currently in phase 3 development, should also be assessed. Additional data on the nature, kinetics, persistence of antibodies and cellular responses in the elderly are needed to optimize the vaccination schedule according to individual risk factors.

The introduction of booster shots in the Covid-19 vaccination schedule is a new communication issue. It should not raise concerns about the efficacy of vaccines against SARS-CoV-2, including the Delta variant [4]. It should not deflect (et non discard) the vaccination campaign from its main objective of achieving herd immunity as quickly as possible. Finally, it should not detract from the duty to assist poor countries and the necessary sharing of vaccine stocks under the Covax program.

Given the still insufficient vaccination coverage in France and the need to maintain immunity in the most vulnerable people, **the French National Academy of Medicine recommends**

- not to err on the side of priority and to favor the completeness of collective immunity;
- to associate the vaccination booster for populations over 65 years and suffering from co-morbidities with a catch-up vaccination program for these same people who have not yet been vaccinated for the first time;
- to complete studies on the kinetics of post-vaccination antibodies in the different age groups and with regard to the new variants in order to determine the ideal time for a booster injection;
- to study the efficacy and safety of homologous or heterologous boosters by testing new generation vaccines
- to ensure that a booster program will not compromise vaccine solidarity efforts with resource-limited countries and the poorest and most marginalized populations.

1- Pinti M et al. Aging of the immune system: focus on inflammation and vaccination. *Eur.j.Immunol.* 2016, 46: 2286-2DGS-URGENT N°2021-61, 18 juin 2021.

2-DGS-URGENT N°2021-61, 18 juin 2021

3- He Q et al. Heterologous prime-boost: breaking the protective immune response bottleneck of COVID-19 vaccine candidates. *Emerg Microbes Infect.* 2021 ; 10(1) : 629-37.

4- Urbanowicz RA et al. Two doses of the SARS-CoV-2 BNT162b2 vaccine enhances antibody responses to variants in individuals with prior SARS-CoV-2 infection. *Science Translational Medicine* 10 Aug 2021: eabj0847.