



Hypersensitivity reactions to fillers in combination with COVID-19 vaccinations

The Dutch reporting and expertise centre for adverse effects of medical implants (*Meldpunt en Expertisecentrum Bijwerkingen Implantaten*, MEBI) would like to alert healthcare professionals, people who have or are considering fillers, and the manufacturers of fillers, to hypersensitivity reactions to fillers that can sometimes occur in combination with a COVID-19 vaccination. These hypersensitivity reactions should not deter individuals from getting vaccinations, because they usually last only a short time (a few days) and are easily treatable. This was confirmed by the Netherlands Pharmacovigilance Centre Lareb in its earlier article on the subject.¹ In this alert, MEBI outlines the information available, examined from the point of view of the fillers.

In January 2022, Lareb published an article on hypersensitivity reactions to fillers after a COVID-19 vaccination in the *Pharmaceutisch Weekblad*.¹ Lareb had received 28 reports about reactions of this nature, in combination with three of the four COVID-19 vaccines used in the Netherlands (Pfizer/BioNTech, AstraZeneca and Moderna). Previously, Lareb had published information about hypersensitivity reactions to fillers after vaccination with the AstraZeneca vaccine on its website.²

All filler-related reports that Lareb has received to date were forwarded to MEBI because they involved besides a medicine (vaccine), also an implant (filler). A further examination of the reports – the number of which has since increased to 32 – has confirmed what Lareb reported in its previous publication ([Frequently asked questions about coronavirus vaccines \(lareb.nl\)](https://www.lareb.nl))³:

'Hypersensitivity reactions may occur after injecting fillers. These may include swelling, redness, pain or itching in the area where the filler was injected. Individuals may also experience lumps under the skin, infections or changes in skin pigmentation. A COVID-19 vaccine may cause a delayed hypersensitivity reaction to fillers. This may happen within a day to a few months of vaccination. These reactions can also occur after infections, such as a COVID-19 infection. To date, hypersensitivity reactions to fillers are only known in individuals who have had the AstraZeneca, Pfizer/BioNTech or Moderna vaccines and in individuals who had an influenza vaccine.'

Reports to MEBI

MEBI has received 32 reports about reactions to fillers after a COVID-19 vaccination (see Table 1). Out of these, 10 reports were about reactions to hyaluronic acid fillers (a temporary filler), one report on a silicone oil filler and one on an acrylic acid filler (both permanent fillers). One of the reports related to two different types of filler. In respect of 21 fillers for which reports were received, it was unclear which type of filler had been used. The individuals who submitted the reports had been vaccinated with the Pfizer/BioNTech, Moderna or AstraZeneca vaccines.

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The adverse effects occurred at different points in time, but in most cases (n=18) after the first vaccination. Nine of the reports involved a reaction that occurred after a second vaccination and four reports on a reaction after a booster vaccination with a different vaccine. According to one report, a reaction had occurred both after the second vaccination and after the booster vaccination. The time between the vaccination and the occurrence of the adverse effect varied between 15 minutes and three months. In one report, the reaction occurred after a filler had been injected into a vaccinated individual. This happened a number of hours after the injection of the filler (four days after the COVID-19 vaccination).

According to information in the reports in question, reactions occurring in combination with a vaccination can occur shortly or a long time after a filler has been injected. In 10 of the reports, it was indicated that the reactions occurred within two months after the injection of the filler. In 11 reports, this happened between two months and one year after injection of the filler and in five reports after one to approximately two years. One report indicated that the adverse effects had happened after 12 years and another after 26 years (the permanent fillers). In five reports, it was not known when the fillers had been injected.

Table 1 Reports to MEBI of hypersensitivity reactions to fillers in combination with COVID-19 vaccinations

Type of filler	Number of reports of a reaction after the first or second vaccination with the same vaccine	Number of reports of a reaction after a booster vaccination with another vaccine	Number of reports of a reaction after injection of a filler	Indicated time duration between the vaccination and the adverse effect	Indicated time duration between the injection of a filler and the adverse effect
Hyaluronic acid filler	7*	3*	1	Hours up to three months	Hours up to two years
Silicone oil filler	-	1	-	Two weeks	26 years
Acrylic acid filler	1	-	-	16 days	12 years
Unknown	20	1	-	15 minutes to 1 month	13 days to 2 years

* According to one report, a reaction happened after the second vaccination and again after the booster vaccination, so this report has been included in the table twice. Another report was about two different fillers; this report has also been included in the table twice. The total number of reports in the table would therefore seem to be 34, but is actually 32.

Literature

An increasing number of publications is available about individuals experiencing reactions to previously injected fillers after a COVID-19 vaccination with the vaccines indicated in the Dutch reports (AstraZeneca, Pfizer/BioNTech and Moderna).^{4,5,6,7} They paint the same picture as the reports described above.

Local reactions to previously injected fillers after influenza or shingles vaccinations have also been reported.⁸ It is not known exactly why a reaction may occur after a vaccination. The publications hint at a delayed inflammatory reaction.^{4,5,6,7} The vaccination stimulates the immune system, which subsequently reacts to the foreign material: the filler.⁹

The occurrence of this reaction is triggered by the activation of the immune system.

There are also publications about hypersensitivity reactions to fillers after COVID-19 infections⁵, which also activate the immune system.

Instructions for use

The Summary of Product Characteristics (SmPC) for both Moderna and Pfizer/BioNTech (and the insert for the latter vaccine) mentions reactions in combination with fillers. If they have not already done this, manufacturers of fillers should take such reactions into consideration in their risk management and in the instructions for use of the products. This information should also be included in the information provided to people before a filler is injected. Last year, the Dutch Association of Cosmetic Medicine (*Nederlandse Vereniging Cosmetische Geneeskunde*, NVCG) advised its members not to inject fillers in the two weeks before their clients get COVID-19 vaccinations or in the two weeks after these vaccinations.

MEBI operates a voluntary reporting system for suspected adverse effects of implants. The frequency of occurrence of an adverse effect cannot be derived from the number of reports received because of their voluntary nature. As such, the number of reports does not provide any information about the probability of the occurrence of an adverse effect, nor does it identify a causal relationship. The objective of a reporting system like MEBI is to identify signals of possible problems with implants as soon as possible. Based on this, research questions can be formulated, which could for example require large-scale (epidemiological) studies. This kind of research does not fall within MEBI's remit. MEBI website: www.meldpuntbijwerkingenimplantaten.nl

References

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3. [Veelgestelde vragen coronavaccins \(lareb.nl\)](#)
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