Allergy to the COVID-19 vaccines

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It has been a little over a year that the COVID-19 pandemic struck this world, but with the arrival of the COVID-19 vaccines, we are now entering a phase where we can begin to envision the light at the end of the tunnel. The goal of most health officials and governments now is herd immunity so that we can prevent disease and achieve full revival of social gathering, communal activities, traveling, tourism and economic growth. Unfortunately, vaccine hesitancy remains rampant. As of April 2021, 12% and 2% of people in Hong Kong and Japan have received the vaccines, respectively, while Singapore ranks first in Asia but only at 23%.[1] These disappointing numbers are likely due to public's safety concerns regarding the vaccines. Recently, post-vaccine severe thrombotic events related to the AZD1222 by Oxford/AstraZeneca have been observed and heavily covered by the press, and this adverse effect has certainly raised doubts in many people's minds on whether the COVID-19 vaccines might be more harmful than good. Some governments have gone as far as suspending or canceling their orders of the AZD1222, a move that is unlikely to boost the public's confidence in the COVID-19 vaccines.

While the CoronaVac (Sinovac, China) containing the whole virus and the mRNA BNT162B2 (Pfizer-BioNTech) injections are ongoing in Hong Kong, so is the debate on their associated risks of allergic reactions and anaphylaxis, particularly for BNT162B2.[2] Although no anaphylaxis was observed in the clinical trials, preliminary post-marketing surveillance reported an incidence of 1 in 100,000 anaphylaxis for BNT162B2, which is 10 fold higher than other traditional vaccines.[2] The pathophysiology underlying these immediate reactions is not yet fully clear but is thought to be due to either IgE-mediated mechanisms, direct stimulation of mast cells or basophils and/or complement activation.[2,3] Since the mRNA component is a novel vaccinology technology, its implication in these reactions remains under scrutiny, but the excipient, polyethylene glycol, has been the most highly suspected culprit due to its known cause as a drug allergen.[2,3] Laxatives with PEG as its main ingredient have led to reproducible allergic reactions in some patients.[2] The precise details of PEG allergy, especially in terms of the different molecular weights, is complex, and this topic is comprehensively covered by Mr. Brian T.C. Lam and Mr. Andrew W.T. Li in the Allied Health Professionals section of this same issue.

In terms of testing for allergies to drugs and vaccines, of course the obvious, usual and traditional diagnostic method comes to mind: **skin testing**. Although a recent case series explored the non-irritating concentrations for BNT162B2 skin testing, one must remember that skin testing for many drugs and essentially all vaccines are not yet standardized or validated.[2,4-6] This is particularly important for novel drugs and vaccines, in which we have little data or experience in terms of the predictive values of the skin tests and which concentrations to use.[2,4-6] In the current setting that herd immunity is the goal, we must be careful about false positive test results and recommending that patients avoid the COVID-19 vaccines based on them. On the other hand, we must do our part to uphold the public's confidence that we maintain safety of administering these vaccines by avoiding false negative skin test results that lead to severe anaphylaxis when the injection is subsequently given. Our community of allergists must strive to conduct more research studies to improve our understanding, diagnostic and management approach for patients with suspected COVID-19 vaccine allergy so that our entire society can gain more confidence in our role in helping as many people receive immune protection from this deadly virus as possible.

Another approach to consider would be the gold-standard diagnostic test: **provocative testing** (Tables I and II).[2,4,6] A recent study found that out of 8 patients who had immediate reactions to the COVID-19 vaccine, 7 tested negative and received the vaccine subsequently without further issues.[7] One patient who was skin tested positive has yet to receive the vaccine again. Given that over 85% of the participants with suspected COVID-19 vaccine allergy from that study tolerated the vaccine, and no confirmed anaphylactic deaths have resulted from the hundreds of millions of COVID-19 vaccines given across the world to date, graded challenge to the same or an alternate vaccine is certainly a viable consideration for patients who seek our consultation.[4,6] A discussion to reach an informed decision by the patient and caretakers in balancing the benefits of the vaccine versus potential reactions will be key. No matter the choice, we should keep in mind that, whenever possible, it is our duty to identify the

responsible allergen whenever we can, especially in cases that an excipient is the suspected culprit, so that he patient will be advised to avoid all drugs that contain this excipient.[6]

References

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Table I. Recommended dosing for graded challenge to the common 0.5 mL of many vaccines[4,6]

Steps	Volume (mL)	Dilution
1	0.05	1:10
2	0.05	Full strength
3	0.1	Full strength
4	0.15	Full strength
5	0.2	Full strength

*Must be performed under direct medical supervision prepared with emergency medications and equipment to promptly treat an anaphylactic reaction should it occur. Inject incrementally, in alternating arms, with 15-minutes in between. Observe for at least 30 minutes afterwards.

Table II. Proportional increments for the 0.3 mL BNT162B2 COVID-19 vaccine

Steps	Volume (mL)	Dilution
1	0.03	1:10
2	0.03	Full strength
3	0.06	Full strength
4	0.09	Full strength
5	0.12	Full strength