"Forewarned is forearmed":

Anecdotal examples of some post-COVID-19 vaccine adverse effects

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It has been more than one year since Covid-19 was first identified. The disease has become more manageable now than when it burst upon a world, which was unprepared for it and so spread like wildfire. Since it is a new disease caused by a new virus, there is also no immunity against the virus. Allowing herd immunity to develop naturally was not a viable option as it would add to the considerable high morbidity and mortality. Hence it was imperative to have a vaccine ready for use, at the earliest. Many vaccines - Pfizer-BioNTech, AstraZeneca-Oxford, Moderna, Johnson & Johnson, Sputnik V, Sinopharm – have been granted emergency use authorisation in various countries in view of the public health emergency.

India too rolled out its Covid-19 vaccination drive on 16th January this year, with two vaccines, Covishield and the indigenously developed Covaxin. Till date, more than 14 crore vaccine doses have been administered across the country. India has also approved its third Covid-19 vaccine, Sputnik V, developed by Russia.

A Covid-19 vaccine has been one of the most or perhaps the most awaited event in recent times. However, reports of post-vaccine adverse effects have generated a fair amount of vaccine hesitancy.

Adverse events with vaccines are inevitable. And, like any other vaccine, Covid-19 vaccines too can cause side effects. Most are mild or moderate and may resolve spontaneously.

The benefits of vaccines far outweigh the risks; hence, as physicians, we should encourage people to take the vaccine. Vaccines are beneficial; they reduce the risk of infection and also protect from developing serious disease.

But, it is also important to be aware of the possible adverse effects because most post-vaccine complications are manageable and preventable (Table 1). Evaluate the risks in every individual. In the high risk individuals, give the vaccine by doing appropriate risk reduction and under observation with proper informed consent. This way, adverse events can be anticipated and prevented.

Table 1: Type of adverse reactions with Covid-19 vaccines

Allergy reactions			
Type 1 Immediate	IgE mediated	First 30 minutes	Anaphylaxis, treatment is adrenaline
Type 1 delayed	Non IgE mediated, complement mediated	After 6 hours	Urticaria, rash, treatment involves montelukast and H1 blocker
Type IV delayed cell mediated hypersensitivity reaction	Cell mediated	After 48 hours up to a week	On the injecting arm, local or distant, symptomatic treatment
Non allergy reactions			
Exaggerated Th1 response	Day 2-4	Immuno-inflammation anywhere in the body, skin, eyes, heart, blood, liver	Treatment is mefenamic acid, colchicine or short course of steroids
Exaggerated Th17 response	Day 4-14	Thrombo-inflammation, venous thrombosis, splanchnic or cavernous sinus thrombosis or pulmonary. Features are high d-dimer and low platelet count.	Treatment is aspirin or non-heparin oral anticoagulants or artemisinin
		Or temporary activation of underlying Th 17 diseases, like psoriasis, Crohn's disease, ulcerative colitis, eczema, auto-immune thyroiditis	Treatment is supportive and symptomatic
Autonomic Overlay Short lived			
Bradycardia	Vagal stimulation	Symptomatic	
Postural hypotension	Autonomic dysfunction	Symptomatic	
Post meal hypotension	Autonomic dysfunction	Symptomatic	
Inappropriate tachycardia	Autonomic dysfunction	Symptomatic	
Accelerated hypertension	Sympathetic overactivity	First 48 hours after vaccine	
Vasovagal	Autonomic dysfunction	First 30 minutes,	

Table 2: Efficacy of various Covid-19 vaccines

Covaxin	Oxford-AstraZeneca (Covishield)	Pfizer-BioNTech	Moderna	J&J/Janssen	Sputnik V
2nd interim analysis of Phase 3 trial Overall, 78% efficacy 100% efficacy against severe Covid-19 70% efficacy against asymptomatic infection	66.7% efficacy against symptomatic disease 100% effective in preventing hospitalisations. Efficacy is 54.9% when time between doses was ≤6 weeks apart *but* 82.4% when given ≥12 weeks apart. *(India is administering the 2nd dose between 4 to 6 weeks after the 1st dose)*	95% effective in preventing symptomatic disease. 100% effective in preventing hospitalisations. Equally protective across age groups	94.1% effective in preventing symptomatic Covid-19 after 2nd dose. 89% effective in preventing hospitalisations. Efficacy slightly low in ≥65 years	Phase 3 trial conducted in USA, Latin America, and South Africa Overall, 66% effective in protecting against moderate to severe Covid-19: • USA (72%) • Latin America (66%) • South Africa (57%) 85% effective in preventing severe disease. 100% effective in preventing Covid-19-related hospitalization and death, 28 days after vaccination	Interim analysis of the phase 3 data 91.6% efficacy against symptomatic infection 100% protection against moderate/severe COVID-19 Efficacy seen across all age groups, including older adults (≥60 years)

Since the pandemic began, I have been holding daily virtual meetings and counselling sessions with diverse groups of people – those who have Covid-19; patients in home isolation; the general public; Resident Welfare Associations (RWAs), NGOs, teachers, principals and students of schools and colleges including doctors, to educate them about the disease and then the Covid-19 vaccine, and remove their fear and dispel prevailing myths.

Herein, we look at some anecdotal and visual accounts of adverse events experienced by vaccine recipients. These have been reported to me in my meetings with them.

The sole purpose of sharing them here is to sensitize doctors, including the general public, about the possible adverse effects and not to dissuade anyone from taking the vaccine. This way they can be anticipated and timely and the right steps can be taken to prevent them as "Forewarned is forearmed".

Vaccines can cause immediate type I hypersensitivity reactions, which occur within few minutes of exposure. These allergic reactions are due to the vaccine excipients such as polyethylene glycol (PEG) or polysorbate 80. Anaphylaxis occurs with 15-30 minutes of the vaccine; hence, the mandatory 30 minute waiting period at the vaccination center after taking the vaccine. Serious allergic reactions occur one in a million vaccine recipients.

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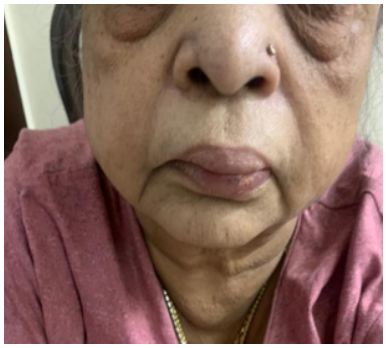
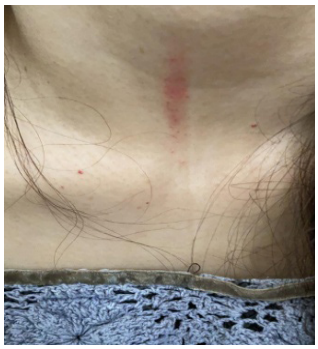
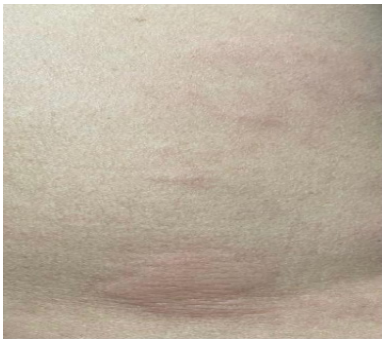


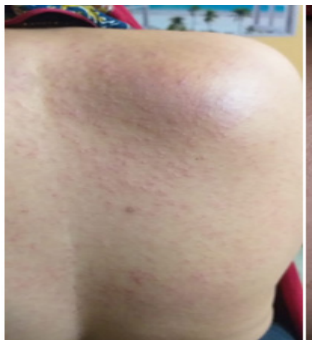
Angioneurotic edema after 6 hours



Rash on the neck on the second

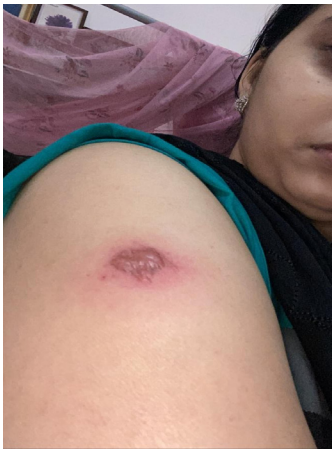


Urticaria on the second day after the vaccine



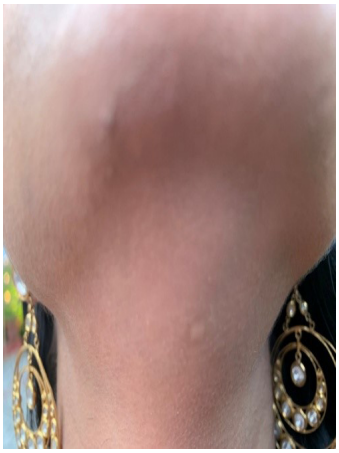
Rash seen on 5th day in a patient with history of allergy

Type IV hypersensitivity reactions at the local injection site (similar to lepromin or tuberculin test) are very common and can be confused with local cellulitis. They appear as indurated raised inflammatory skin lesion usually between 2nd and 4th day at the injection site or even remotely from the injection site on the same hand.

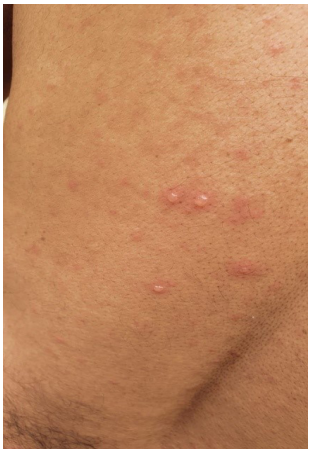


5 days after the vaccine

Rash away from the site of injection on 14th day



Painful lymphadenitis



Chickenpox rash 10 days after the vaccine

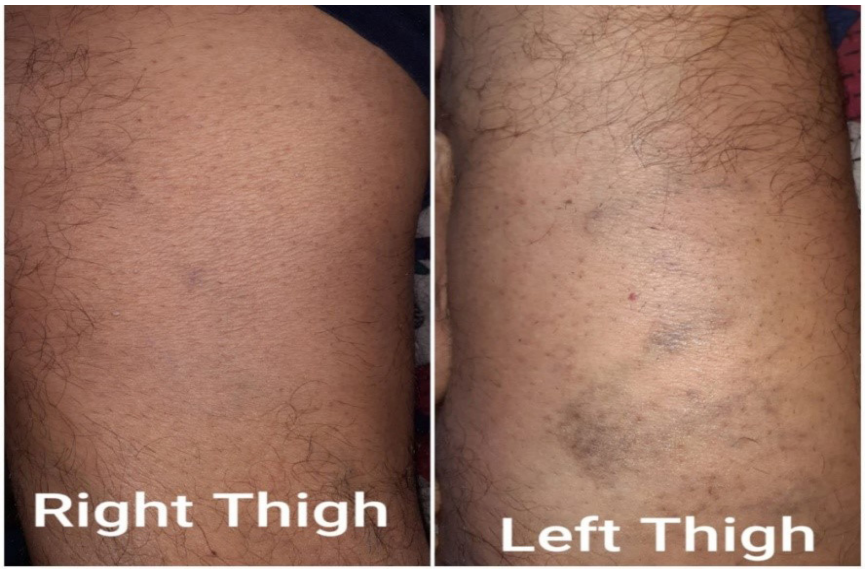
The vaccine can precipitate underlying inflammation or autoimmune disease via Th1 and Th 17 responses: rheumatoid arthritis, adult chickenpox, herpes zoster, painful lymphadenitis, episcleritis, left eye conjunctivitis, psoriasis. Patients have also reported flaring up of their Crohn's disease and irritable bowel syndrome with diarrhea (IBS-D).

Patient with history of psoriasis since 15yrs suffered a relapse on the second day after the 1st dose.

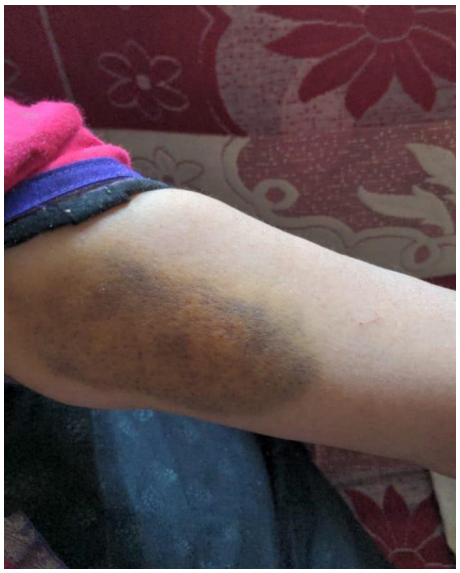
The vaccine may also cause neuroinflammation triggering seizures (focal or generalized), transient ischemic attack (TIA). Patients have reported increased tinnitus, blurred vision and neurological pain.

Vaccine can cause thromboinflammation. Patients have developed vaccine-induced thrombocytopenia with superficial clots. This reaction is quite similar to heparin-induced thrombocytopenia (HIT). Such patients need rivaroxaban and not heparin. Check platelets after the 4th day. If platelets start decreasing after day 4, immediately start rivaroxaban.

Vaccine may cause thrombosis



Vaccine-induced thrombocytopenia with venous thrombosis: Superficial venous clots in lower limbs 14 days after the vaccine; platelets dropped from 3 lakhs to 1.5 lakhs.



Blood clot in the arm 3 weeks after the vaccine

Vaccine may cause sympathetic overactivity, which can manifest as accelerated hypertension and transient atrial fibrillation (AF). A 76-year-old female developed accelerated hypertension (190/120) and transient AF, which reverted. Another elderly patient reported atrial fibrillation.

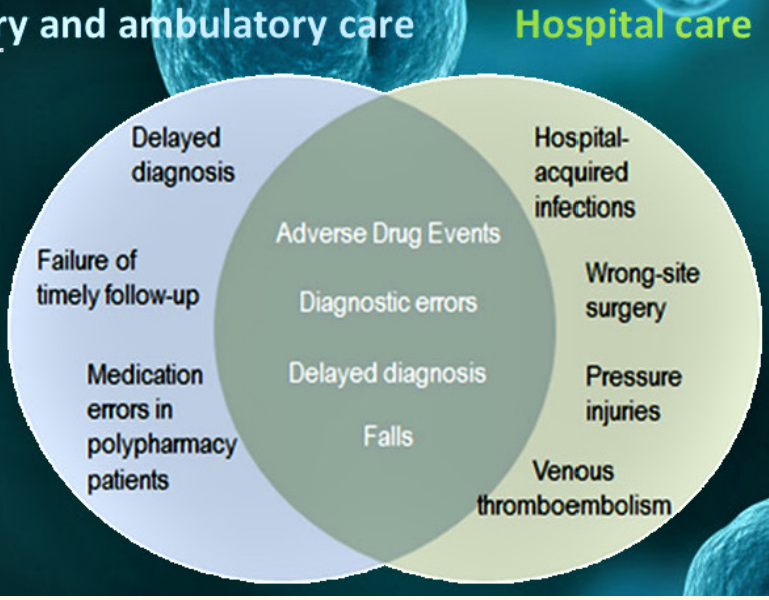
Vaccine can act as trigger to Covid-19. Few patients have reported testing positive for Covid-19 after the first dose of vaccine, from second day to up to 15th day. This can cause severe inflammation presenting as high fever and rising C-reactive protein (CRP) levels.

As doctors, we can evaluate the risk in every person before they take the vaccine. Assess your patient and ask yourself the following questions:

- Will he/she develop & tolerate vasovagal reaction? If the patient has a history of syncope, ask them to take the vaccine while lying down and stay hydrated.
- Will he/she develop and tolerate immediate (IgE) and or delayed (Non IgE) allergy? If likely (non IgE mediated): pre-load with Montelukast + H1 + H2 blocker. If known IgE allergy: Get eosinophilic count and IgE levels, do a scratch test/ intra dermal challenge.
- Will he/she get exacerbation of thrombo-inflammation? If baseline CRP >1 mg/L, it will cause rise in CRP, IL-6, IL-1β). In such cases, preload the patient with ACS (aspirin, colchicine and statin). CRP may rise by 30% on day 2. If rise is more or CRP is >10 mg/L, then add mefenamic acid or any other immunomodulator.
- Will he/she get overactive sympathetic response? (abnormal HR variability, 6 MWD/T less than 700 feet or over sympathetic response to walking) pre-load such patients with a β-blocker.
- Advise patients to continue all their medications unless contraindicated on the day of vaccination.

Improve patient safety by eliminating adverse events in health care settings

It is estimated that every year more than 300,000 patients acquire a healthcare associated infection (HCAI, HAI or nosocominal infection)as a result of care with in the NHS.



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