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LETTER



# Arthritis as an adverse event of special interest post COVID-19 vaccine implementation

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## Dear Editor,

COVID-19 vaccines are currently in development or being rolled out as a public health response to manage the pandemic. While vaccines selected for mass public immunization programs would have demonstrated safety and efficacy in Phase 3 trials, vaccine safety monitoring including reporting of adverse events following immunization (AEFI) and investigation of reported cases are still required for safety surveillance. Monitoring of AEFI post COVID-19 vaccination is quite relevant to clinicians.

All clinicians play a role in reporting suspected AEFI to national pharmacovigilance centers. These reports are submitted to Vigibase, the World Health Organisation's database of adverse drug reactions, which is utilized for international safety signal detection. This approach for vaccine safety monitoring is of particular importance for COVID-19 vaccines, given the rapid implementation via Emergency Use Authorisation and the planned administration to large populations over a short period of time [1].

For some AEFI, it may be intuitive that the adverse event was a direct consequence of the vaccination. For example, a case report described a patient presenting with an acutely painful right shoulder after receiving a Pneumovax injection. The pseudo skeptic arthritis was postulated to have developed from an accidental intra-articular administration, given the proximity of deltoid injections to the glenohumeral joint [2].

However, some AEFI may not be easily attributable to vaccinations and may manifest as possibly unrelated conditions. Clinicians should have a low threshold to report suspected AEFI, as this may lead to signal detection and trigger further investigations and causality assessment. This was previously experienced with the rubella vaccine. In 1991, the Institute of Medicine reviewed a wide range of information sources and published a report concluding a causal relationship between the rubella vaccine with acute and chronic arthritis in adult women [3]. Subsequent to this, claims for chronic arthropathy post-rubella vaccination were submitted to the National Vaccine Injury Compensation Programme. The majority of the claims were for symptoms between one and six weeks after vaccination, ranging from arthralgia and fibromyalgia to multiple symptoms with minimal arthralgia or myalgia [4].

While a large retrospective cohort study did not find any associated risk for new-onset chronic arthropathies in women receiving the RA27/3 rubella vaccine [5], idiosyncratic reactions are usually rare and identified during post-marketing surveillance. A systematic review evaluating the association between vaccinations to incident arthritis or worsening of arthritis conditions found that studies were also quite heterogenous and incomplete for rigorous causality assessment to be performed [6].

Due to this previous experience, acute aseptic arthritis was identified as an Adverse Event of Special Interest (AESI). For clinicians, this means that cases of acute aseptic arthritis warrant reporting to national pharmacovigilance centers, particularly if there is a temporal relationship to receiving a COVID-19 vaccine. The case definition for acute aseptic arthritis and a guideline template for reporting is available from the Brighton Collaboration [7]. In addition to arthritis, there are also frequently reported autoimmune manifestations post-vaccination, such as vasculitis, encephalitis, thrombocytopenia and Guillain-Barre syndrome. However, it should be noted that controlled studies of autoimmunity following viral vaccines did not identify evidence of an association [8].

Overall, while the occurrence of arthritis and autoimmune conditions after vaccines remain controversial, clinicians should report all suspected AEFI. Acute aseptic arthritis constitutes an AESI, which should be reported as part of vaccine safety surveillance for COVID-19 vaccine recipients. These will contribute towards signal detection and trigger further investigations if warranted.

## Declarations

**Conflict of interest:** The author declares no conflict of

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interest.

## References


1. World Health Organization. Covid-19 vaccines: safety surveillance manual. 2020. Available on: https://www.who.int/vaccine_safety/committee/Module_Stakeholders.pdf?ua=1
2. McColgan B P, Borschke F A. Pseudoseptic arthritis after accidental intra-articular deposition of the pneumococcal polyvalent vaccine: a case report. The American journal of emergency medicine, 2007, 25(7): 864. e1-864. e3.
3. Howson C P, Fineberg H V. Adverse events following pertussis and rubella vaccines: summary of a report of the Institute of Medicine. Jama, 1992, 267(3): 392-396.
4. Weibel R E, Benor D E. Chronic arthropathy and musculoskeletal symptoms associated with rubella vaccines. A review of 124 claims submitted to the National Vaccine Injury Compensation Program. Arthritis & Rheumatism: Official Journal of the American College of Rheumatology, 1996, 39(9): 1529-1534.
5. Ray P, Black S, Shinefield H, et al. Risk of chronic arthropathy among women after rubella vaccination. Jama, 1997, 278(7): 551-556.
6. Panozzo C A, Pourmalek F, Pernus Y B, et al. Arthritis and arthralgia as an adverse event following immunization: A systematic literature review. Vaccine, 2019, 37(2): 372-383.
7. Woerner A, Pourmalek F, Panozzo C, et al. Acute aseptic arthritis: case definition and guidelines for data collection, analysis, and presentation of immunisation safety data. Vaccine, 2019, 37(2): 384-391.
8. Schattner A. Consequence or coincidence?: The occurrence, pathogenesis and significance of autoimmune manifestations after viral vaccines. Vaccine, 2005, 23(30): 3876-3886.


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