Public Health England

NHS

Blood Clotting following COVID-19 Vaccination

Information for Health Professionals

As with all COVID-19 programme resources, this publication is subject to extensive and regular revisions and we recommend linking to the latest version to ensure that you are giving the most up-to-date clinical advice and guidance.

A range of resources have been developed and updated to support this decision making and are available at **www.gov.uk/government/collections/covid-19-vaccination-and-blood-clotting**.

1. What is the condition that has been reported following COVID-19 vaccination?

In recent weeks, there have been a small number of reports from the UK and internationally of an extremely rare condition characterised by thromboembolic events (blood clots) accompanied by thrombocytopenia (low platelets) following the first dose of the AstraZeneca (AZ) COVID-19 vaccination.

The most notable presentation is cerebral venous sinus thromboses (CVST) where blood clots develop in the cerebral veins occurring together with low platelet counts. These cases are particularly unusual because despite low platelets, there is progressive thrombosis (formation of blood clots which block blood vessels). Whilst the cases reported to date have primarily been venous clots, arterial clots have also been reported. All cases reported in the UK to date have occurred after the first dose of AZ vaccine.

Typical laboratory features include a low platelet count, very raised D Dimer levels – above the level expected for venous thromboembolism (VTE) and inappropriately low fibrinogen. Antibodies to platelet factor 4 (PF4) have been identified and so this has similarities to heparin-induced thrombocytopenia (HIT), but is occurring without the patient receiving any heparin treatment.

Further information on the investigation and treatment of suspected cases has been published by the Expert Haematology Panel of the British Society of Haematology and is available at weblink 1.

2. What are the risk factors for developing this condition?

This condition is known to occur naturally although the underlying risk factors have not yet been fully established. A detailed review of suspected cases of this condition following COVID vaccination is ongoing by the Medicines Healthcare products Regulatory Agency (MHRA), supported by PHE and other professional groups.

This will help us to understand the risk factors for developing this condition. The current data suggests that the overall incidence is around 4 per million first doses of the AZ vaccine administered. Although cases have been reported in all ages and genders, there appears to be a trend for increasing incidence with decreasing age amongst adults, with the highest incidence reported in the younger adult age groups.

3. Is this condition only associated with the AZ vaccine?

All suspected cases following vaccination with any of the COVID-19 vaccines being used in the UK are undergoing a detailed review by the MHRA. Up to and including 31st March, the MHRA received 79 reports of thrombosis events with low platelets of which 44 were cerebral venous sinus thrombosis (CVST), out of a total of 20.2 million doses of COVID-19 Vaccine AZ given by that date.

Two cases of blood clots (thromboembolism) with thrombocytopenia were reported for the Pfizer/BioNTech vaccine up to and including 31st March, but a detailed medical review by the MHRA concluded that these were very unlikely to be related to the vaccine.

There is currently no evidence to suggest these rare events occur with the Pfizer/BioNTech vaccine. Although these extremely rare events have been associated with the AZ vaccine, further investigations are underway to understand the biological mechanisms and whether the association is related to the vaccine platform (the way in which the vaccine delivers antigen) or some other immunological mechanism.

4. How many people have developed the condition?

This condition is known to occur naturally and is thought to be extremely rare. The background rate of cerebral venous sinus thromboses (CVSTs) is estimated to be around 5 to 16 per million annually, although there is currently limited data on the background rate of CVSTs occurring without thrombocytopenia. It is currently estimated that the overall incidence following the AZ vaccine is around 4 per million first doses administered. It is also important to note that thromboses (blood clots) have been reported with natural COVID-19 infection and more than a fifth of hospitalised patients with COVID-19 have evidence of blood clots.

Internationally, there have been a very small number of reports of thromboembolic events accompanied by thrombocytopenia following AZ vaccine.

5. How many of those affected die?

A detailed review of all suspected cases is ongoing and based on the reports received by the MHRA as of 31st March, there were 19 fatal cases from the 79 events reviewed. This compares with the clear demonstrable benefits from the COVID vaccination programme.

Since the 4th January more than 20.2 million doses of the AZ vaccine have been administered across the UK. It has been estimated that the vaccine programme has prevented 6,100 deaths in adults aged 70 years and older up to the end of February with a vaccine effectiveness of a single dose against hospitalisation estimated at 80% for both the Pfizer/BioNTech and the AZ vaccines.

6. Why isn't the UK suspending use of the AZ vaccine?

Based on a review of cases reported to the Yellow Card Scheme and the evidence of effectiveness of the COVID vaccines used in the UK to prevent serious complications and deaths from COVID-19 infection, the current MHRA advice remains that the overall benefits of the vaccine programme outweighs the extremely rare adverse events reported to date following the AZ vaccine.

The Joint Committee on Vaccination and Immunisation (JCVI) has assessed the overall risk benefit of the use of the AZ vaccine in the population. This is based on data presented by the MHRA on reported adverse events through the Yellow Card Scheme and benefits (in terms of deaths, ICU and hospital admissions averted) estimated by Public Health England. Given the very small numbers of events reported overall, there is currently a high level of uncertainty in the estimates of the incidence of this condition by age group.

There appears to be a trend of increasing incidence of this condition with decreasing age amongst adults, with the highest incidence reported in the younger adult age groups. In contrast, the risks of serious disease associated with COVID-19 increases steeply with age, with the younger adults at the lowest risk of serious disease. Amongst those healthy adults under 50 years, there continues to be an age-related risk of severe complications from COVID-19. For example, the risk of dying in an individual aged 40-49 years is 3 times higher than someone aged 30-39 years and 12 times higher than someone aged 20-29 years.

Therefore, weighing the balance of benefits and risks, currently the JCVI has concluded that for adults under 30 years of age who are not in a clinical risk group, it is preferable to offer an alternative to the AZ vaccine if available (see weblink 2).

The AZ vaccine should continue to be offered to those in Phase 1 (which includes older adults, those with underlying conditions, health and social care workers over 30 years old) who have not yet been offered the vaccine. Those who have received their first dose of AZ vaccine should continue to be offered the second dose to complete the course. Individuals aged 18 to 29 years who have received their first dose of AZ vaccine as part of the Phase 1 programme, without suffering any serious side effects, should complete their course with the same vaccine. This includes those who are health and social care workers, unpaid carers and family members of those who are immunosuppressed. Healthy adults aged 30-50 years who will be offered vaccine as part of the second phase of the programme are recommended to receive any of the available COVID-19 vaccines.

Those who have received their first dose of AZ vaccine should continue to be offered the second dose to complete the course.

As the deployment of the second phase of the programme gets underway, the JCVI are committed to undertaking a detailed and ongoing review as each age group becomes eligible for vaccination based on the current epidemiology, the latest information on reported cases to the MHRA and vaccine availability.

7. Can COVID-19 infection cause the same problem?

Thrombotic events have also occurred in individuals with natural COVID-19 infection and more than a fifth of hospitalised patients with COVID-19 have evidence of blood clots.

However, this particular combination of thrombotic events and thrombocytopenia is extremely rare and not known to be a common feature of COVID-19 infection.

8. Has this condition been reported after both the 1st and 2nd dose of COVID-19 vaccine?

To date, the small number of these extremely rare events that have been reported to the MHRA have occurred after the first dose of the AZ vaccine. Whilst currently there is no evidence to suggest whether these rare events are dose specific it is important to note that most vaccines in the UK COVID programme have been administered as first doses. The JCVI advises that those who have received their first dose of AZ vaccine should continue to be offered the second dose.

9. Is it affecting both men and women?

Suspected cases have been reported in patients of all ages in men and women. Whilst reports from some countries have suggested a substantially higher number of cases amongst females, based on the events reported to the MHRA in the UK, such a distinctive gender difference has not been observed.

It is worth noting that more females have been vaccinated which may partly explain the slight excess of cases reported amongst females.

10. Is it affecting any particular community?

Suspected cases have been reported in patients of all ages and genders and currently, no specific predisposing factors have been identified.

11. What are the signs and symptoms?

While the detailed case review is ongoing, it is important to ensure all health professionals are alert to relevant symptoms which require further clinical review and investigation. Advise patients to seek urgent medical advice if they experience any of the following symptoms more than 4 days and within 28 days of coronavirus vaccination:

- new onset of severe headache, which is getting worse and does not respond to simple painkillers
- an unusual headache which seems worse when lying down or bending over, or may be accompanied by blurred vision, nausea and vomiting, difficulty with speech, weakness, drowsiness or seizures
- new unexplained pinprick bruising or bleeding
- shortness of breath, chest pain, leg swelling or persistent abdominal pain

If you have clinical concern, patients should be urgently referred to hospital and to appropriate specialist services for further assessment, particularly if the symptoms are unexplained and present in combination with thrombocytopaenia. Further guidance for secondary care are available at weblink 1.

Mild flu-like symptoms, including headache, chills and fever remain one of the most common side effects of any COVID-19 vaccine. These generally appear within a few hours and resolve within a day or two.

12. What should I do if I suspect a case?

If you have clinical concerns, patients should be urgently referred to hospital and to appropriate specialist services for further assessment, particularly if the symptoms are unexplained and present in combination with thrombocytopaenia. Further guidance for secondary care are available at weblink 1.

In the UK, the MHRA are reviewing all reported cases to the COVID-19 Yellow Card scheme. In order to support the case reporting, clinical review and investigation, PHE has established an electronic clinical reporting scheme collecting patient identifiable information on all suspected cases. All health professionals are encouraged to report any suspected case at https://cutt.ly/haem_AE with details of the clinical presentation, dates of vaccination, vaccine product received and any underlying conditions.

A data sharing process has been agreed with the MHRA which means that professionals only need to report suspected cases once through this scheme.

13. Are there any contraindications or cautions to receiving the AZ vaccine?

Contraindications to receiving the AZ vaccine are past major thrombosis with thrombocytopaenia (including those with previous reactions to AZ and those who have previously had heparin induced thrombocytopaenia). A history of thromboses on its own is not in itself a contraindication to the vaccine.

Cautions to receiving the AZ vaccine are a history of CVST, acquired or genetic thrombophilia or anti-phospholipid syndrome.

14. Should we still give people their second dose?

Yes, because of the high risk of complications and death from COVID, the MHRA, the World Health Organisation and the European Medicines Agency have concluded that the balance is very much in favour of vaccination.

All of the events reported to date have occurred after the first dose of the AZ vaccine. There are currently no known risk factors for this extremely rare condition, which appears to be an idiosyncratic reaction on first exposure to the AZ COVID-19 vaccine. The JCVI advises that those who have received their first dose of AZ vaccine should continue to be offered the second dose.

15. What if someone has had a cerebral or major blot clot with low levels of platelets following the first dose of AZ vaccine?

Anyone who experienced cerebral or other major blood clots occurring with low levels of platelets after their first vaccine dose of COVID-19 Vaccine AZ should not have their second dose of AZ vaccine.

16. What if somebody under 30 years has had AZ for their first dose – should they have the second?

The AZ vaccine should continue to be offered to those in Phase 1 who have not yet been offered the vaccine. This includes older adults, those with underlying conditions, health and social care workers over 30 years old.

All of the events reported to date have occurred after the first dose of the AZ vaccine. There are currently no known risk factors for this extremely rare condition, which appears to be an idiosyncratic reaction on first exposure to the AZ COVID-19 vaccine.

Those who have received their first dose of AZ vaccine should continue to be offered the second dose. Individuals aged 18 to 29 years who have received their first dose of AZ vaccine as part of the Phase 1 programme, without suffering any serious side effects, should complete their course with the same vaccine. This includes those who are health and social care workers, unpaid carers and also family members of those who are immunosuppressed.

There is currently no evidence on the interchangeability of the COVID-19 vaccines although studies are underway. Therefore, every effort should be made to determine which vaccine the individual received and to complete with the same vaccine. Please see the Green Book for further advice on vaccination.

17. What if my patient refuses the AZ vaccine?

To make an informed decision it is important that all individuals are provided with the relevant information, including the benefits and risks, and that they have the opportunity to discuss this with their healthcare provider if they wish.

If the patient is under 30 an alternative vaccine will become available but they may have to wait for other supplies.

18. What if my patient under 30 years old wants to have the AZ vaccine?

Patients under 30 who decide to go ahead after they have considered all the risks and benefits can be vaccinated with the AZ vaccine.

You should document that you have had a full conversation with the patient and that you have provided them with sufficient information for them to give informed consent to vaccination.

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Sources

Guidance produced from the Expert Haematology Panel (EHP) focussed on syndrome of Thrombosis and Thrombocytopenia occurring after coronavirus Vaccination Guidance produced from the Expert Haematology Panel (EHP) focussed on syndrome of Thrombosis and Thrombocytopenia occurring after coronavirus Vaccination | British Society for Haematology (b-s-h.org.uk)

COVID-19: the green book, chapter 14a COVID-19 Greenbook chapter 14a (publishing.service.gov.uk)

Use of the AstraZeneca COVID-19 vaccine: JCVI statement www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement

MHRA issues new advice, concluding a possible link between COVID-19 Vaccine AstraZeneca and extremely rare, unlikely to occur blood clots www.gov.uk/government/news/mhra-issues-new-advice-concluding-a-possible-link-between-covid-19-vaccine-astrazeneca-and-extremely-rare-unlikely-to-occur-blood-clots

Coronavirus Yellow Card reporting site Official MHRA side effect and adverse incident reporting site for coronavirus treatments and vaccines | Coronavirus (COVID-19)

Public Health England – reporting Thrombotic events with thrombocytopenia following immunisation to COVID-19 https://cutt.ly/haem_AE

COVID-19 vaccination and blood clotting resources www.gov.uk/government/collections/covid-19-vaccination-and-blood-clotting

Weblink 1: https://b-s-h.org.uk/about-us/news/guidance-produced-from-the-expert-haematology-panel-ehp-focussed-on-syndrome-of-thrombosis-and-thrombocytopenia-occurring-after-coronavirus-vaccination/

Weblink 2: https://www.gov.uk/government/publications/use-of-the-astrazeneca-covid-19-vaccine-jcvi-statement

Vaccination, helping to protect those most vulnerable.