Japanese encephalitis

A learning resource for registered nurses and midwives

3 August 2023



Disclaimer



- This resource provides information on Japanese encephalitis (JE) and the vaccines available to reduce the risk of spread of the JE virus.
- This resource is intended as an education tool to support registered nurses and midwives administering the JE vaccine.
- Immunisation providers must work within their scope of practice. Please review the relevant authorisations for immunisation in your state or territory.
- Information has been sourced from <u>The Australian Immunisation Handbook (the</u> <u>Handbook)</u> and <u>ATAGI clinical guidance on Japanese encephalitis virus vaccines.</u>
- Immunisation providers should also refer to information about JE specific to their state or territory. This is particularly important in regards to eligibility criteria and any accelerated vaccination program in high-risk settings.
- Some states and territories may require completion of a formal eLearning module before administering JE vaccines. Refer to your relevant state or territory health department website.



This resource has been developed using information and case studies from the Victoria Department of Health Japanese encephalitis eLearning module.

Section 1: Background





Topics covered in this resource include:

- key facts about JE, including how the Japanese encephalitis virus (JEV) is spread, signs and symptoms of infection, and strategies to reduce the spread of the virus.
- different JE vaccine brands, dosing schedule and route of administration for JE vaccines.
- precautions and contraindications for JE vaccines
- key resources available to support the safe use and delivery of JE vaccines.

Section 2: JE overview





- Japanese encephalitis (JE) is caused by a mosquito-borne RNA flavivirus called Japanese encephalitis virus (JEV).
- The virus circulates in nature in pigs and wading birds. It is not transmitted directly from human to human.
- Most JEV infections are asymptomatic. However, around 1% of people infected will develop an acute neurological illness (encephalitis) characterised by:
 - headache, fever, convulsions, altered level of consciousness and/or focal neurological deficits, called JE.
- JE may lead to death or permanent disability.
- JE can occur in people of any age if they are not immune to the virus from past infection and/or vaccination.

Epidemiology - 2018



Japanese encephalitis, countries or areas at risk



Source: World Health Organization



JE in Asia

- JE is a significant public health problem in many parts of Asia, including China, the Indian subcontinent and southeast Asia.
- The disease is also present in eastern Indonesia (including Bali) and Papua New Guinea.

JE in Australia

- JEV outbreaks have occurred sporadically in northern Australia (mainly the Torres Strait islands) since the mid-1990s.
- Between 2001 and 2014, only nine cases of JE were notified in Australia, and in all of these cases, the virus was acquired overseas.

Source: Australian Immunisation Handbook. Japanese encephalitis.



- More recently, in 2022, there have been 42 human cases of JE notified in Australia, with 7 deaths (as at 19 October 2022).
- People most at risk of JEV infection include people who:
 - live in a higher risk region
 - work in specific occupations (including piggery workers and those working with mosquitoes)
 - spend significant time outdoors in the eastern states of Australia, South Australia and the Northern Territory.
- While it is important to be aware of the presence of JEV in specific geographical areas, the risk of contracting JE and developing serious illness remains low.

Useful resource: Japanese encephalitis virus (JEV) health professionals kit

Clinical features



- Symptoms of JE usually develop 5 to 15 days after being bitten by an infected mosquito.
- More than 90% of JEV infections are asymptomatic. Severe disease occurs in less than 1% of cases.
- Common symptoms of mild disease are:
 - headache
 - fever
 - muscle aches
 - neck and/or back stiffness
 - sensitivity to light (photophobia)

Clinical features



- Common symptoms of serious (encephalitic) disease can be any combination of mild symptoms, plus:
 - severe headache
 - seizures
 - confusion
 - reduced level of consciousness
 - focal neurological impairment.
- Diagnosis can be challenging, as these symptoms are similar to many other diseases (including other viral illnesses).
- Diagnosis requires a combination of clinically compatible symptoms, evidence of JEV immune response on pathology tests (taken at least 2 weeks apart) and evidence of exposure to JEV.

Complications



- Most people who are infected with JEV are asymptomatic. Those who develop symptoms, mostly present with only mild disease and can recover well at home.
- Severe disease as a result of JEV infection is very rare, but for the small percentage of people who develop neurological disease, the consequences can be very serious.
- For those with encephalitic (severe) disease, mortality rate is approximately 30%. Of those who survive the acute illness, around 30-50% will have ongoing neurological symptoms.
- Severe disease is usually associated with a prolonged hospital admission, and often requires long-term functional rehabilitation.
- There is no specific treatment for JE, and the goal of medical treatment is to reduce the effects of the symptoms it causes.

Source: Australian Immunisation Handbook Japanese encephalitis





- JEV transmission occurs primarily in rural agricultural areas.
- The normal lifecycle of JEV is between waterbirds and Culex mosquitoes, which may then transfer to pigs and horses.
- Animals and people become infected with the virus through the bite of infected mosquitoes.



Japanese encephalitis disease spread pathway



Image source: Department of Agriculture, Water and the Environment (DAWE).

- Mosquitoes transmit the virus between waterbirds, pigs, horses and humans.
- Pigs and wading birds are 'amplifying hosts' for JEV.
 - This means that the virus replicates in the animal and causes high levels of virus in the bloodstream.
- Humans and horses are dead-end hosts.
 - Meaning they usually do not develop high enough concentrations of JEV in their bloodstreams to infect feeding mosquitoes

Prevention strategies



- For people living in high-risk areas, the best strategies for preventing infection are:
 - avoiding mosquito bites through the use of long and light-coloured clothing, adequate footwear, mosquito repellent and mosquito screens/netting
 - staying indoors when mosquitoes are most active, including at dawn and dusk.
- Vaccination is also a key prevention strategy for JE.



- JE disease is caused by infection with the mosquito-borne JEV.
- JEV cannot be spread directly from person to person, or from person to mosquito to person.
- JEV cannot be caught through eating pork or pig products.
- There is no specific treatment available for JE only supportive care and symptom management.

Section 3: JE vaccination



Who should be vaccinated?



Vaccination is a key prevention strategy for JE



Who should be vaccinated?



- Before recommending or administering a JE vaccine, you should first check that individual meets the current eligibility requirements in your state or territory.
- JE vaccine is not currently part of the National Immunisation Program (NIP).
- There are routine recommendations for vaccination for travellers to endemic areas and residents of the Torres Strait islands.
- The Australian Technical Advisory Group on Immunisation (ATAGI) <u>recommends</u> <u>vaccination of people ≥2 months of age in high-risk settings in Australia</u>.
- JE vaccine is free for people who are at high risk and recommended for vaccination.
- Check the current priority groups eligible for free vaccination in your state or territory.

Note: It is possible the list of priority groups eligible for free JEV vaccination evolves, as more is known about the virus.

Current priority groups for vaccination



Please refer to current priority groups in your state or territory.



- People who do not meet the eligibility criteria for the JE vaccine may present to immunisation providers seeking the vaccine.
- If this occurs, immunisation providers should carefully understand the purpose of the request and seek to educate the person about their relative risk of infection.
- If people do not meet the eligibility criteria and are concerned about possible infection, they may be referred to a general practitioner (GP) to discuss if JE vaccination is appropriate for them.

About JE vaccines



- There are two JE vaccines registered for use in Australia:
 - Imojev
 - JEspect (also known as lxiaro)
- ATAGI advises that Imojev, which requires only a single dose, should be prioritised during the management of JE and is suitable for people from 9 months of age.
- Vaccination against JE is safe and effective.
- JE vaccines have been used extensively over many years in Australian Defense Force personnel, residents of the Torres Strait islands and travellers to southeast Asia.
- More than 95% of people develop a protective immune response to the virus approximately 28 days after completing the primary vaccination schedule.

Section 4: Preparation and administration of JE vaccine





Determine eligibility

- Before administering or recommending a JE vaccine, you should check that the individual meets the current eligible priority group requirements for free JE vaccine in your jurisdiction.
- People who do not meet the free vaccine eligibility requirements should not be vaccinated and be directed to information about the disease, risk of transmission and other preventive measures they can take.
- People who have further questions may also be referred to a GP or the state or territory immunisation service.

Useful links: Australian Government Department of Health and Aged Care - Information about JE for the public



Conduct pre-vaccination screening and obtain valid consent

- A pre-vaccination screening checklist is available in the Handbook.
- Refer to <u>Responses to conditions or circumstances identified through the</u>
 <u>pre-vaccination screening checklist</u>

Pre-vaccination screening considerations



When completing the pre-vaccination screening process for JE vaccines, consider the following:

- Immediate health: Check if the person to be vaccinated is unwell today. People with minor illnesses, such as a cold, can be vaccinated. People who are moderately or severely ill should usually wait until they recover before getting the JE vaccine.
- Check eligibility requirements: ensure that you have the right person to be vaccinated.
- Check vaccination history: Consider whether the individual has previously had a JE vaccine check the Australian Immunisation Register. (Note: IXIARO now has its own vaccine code on AIR.)
- Check dose intervals: Ensure minimal interval requirements are maintained for JEspect vaccine
- **Consider contraindications or precautions:** Note JE vaccine recommendations for people who are immunocompromised or people who are pregnant or breastfeeding and note advice for people who have recently received immunoglobulins or immunoglobulin-containing blood products or live attenuated vaccines.
- **Previous adverse events following immunisation:** Check whether the person to be vaccinated has had a severe reaction following any vaccine. JE vaccines are contraindicated in people who have had anaphylaxis after a previous dose of any JE vaccine, or anaphylaxis after any component of a JE vaccine (including protamine sulfate for JEspect).
- Age: Ensure that the person to be vaccinated is the appropriate age for the vaccines they are receiving.

Further information: Recommended doses of Japanese encephalitis vaccines, Australian Immunisation Handbook

Vaccine storage and product information



- Prior to each vaccination event, ensure that vaccines have been stored within the temperature range of +2°C to +8°C.
- All immunisation providers must adhere to the latest edition of <u>National Vaccine</u> <u>Storage Guidelines: Strive for 5.</u>
- Product information:
 - Imojev is distributed by Sanofi: The <u>product information</u> is available on the Therapeutic Goods Administration (TGA) website.
 - JEspect is distributed by Seqirus. The product information is available on the TGA website.

Imojev vaccine preparation



- Imojev requires reconstitution
- It presents as one dose of freeze-dried white to creamy-white vaccine powder and one dose of clear diluent in separate vials with one syringe and two needles, one for preparation and one for injection.

Step 1

- Imojev comes in a vial with lyophilised powder in a monodose vial with separate diluent.
- Store at +2°C to +8°C. Do not freeze. Protect from light.

Step 2

• Add the entire contents of the diluent container to the vial and shake until the powder completely dissolves.

Step 3

• After reconstitution, the vaccine should be a colourless to amber suspension.

The reconstituted vaccine should be administered within one hour.

Imojev vaccine

 Imojev is a live attenuated vaccine. This means it contains a weakened version of the live JE virus.

Doses and schedule

- Imojev is given as a single dose via subcutaneous injection.
- Recommended for use in people aged ≥9 months.



Image courtesy of Sanofi



Imojev vaccine



Imojev cannot be used in:

- people with immunocompromise
- people who are pregnant or breastfeeding
- infants aged less than 9 months.

Important:

Assess whether a person has altered immune status before vaccinating because people who have compromised immunity may have:

- reduced response to vaccines, so they may need extra doses
- an increased risk of vaccine preventable diseases or complications
- an increased risk of adverse events, particularly from live vaccines.

Note: JEspect (another JE vaccine) is not a live vaccine and can be safely administered to people who are identified as being immunocompromised, pregnant women and infants from 2 months of age.

Source: Australian Immunisation Handbook

Immunocompromising conditions



A person may be considered immunocompromised if they:

- have active leukaemia or lymphoma, or other generalised malignancy
- have received recent chemotherapy or radiotherapy
- have HIV (certain people only)
- had a solid organ transplant or haematopoietic stem cell transplant (HSCT) less than 2 years ago, or are still immunocompromised or taking immunosuppressive drugs, or have graft-versus-host disease (GVHD)
- are taking highly immunosuppressive therapy, including bDMARDs or tsDMARDs (biological or targeted synthetic disease-modifying anti-rheumatic drugs) e.g. rituximab, or high-dose corticosteroids e.g. prednisone
- have certain autoimmune diseases, particularly if they are on highly immunosuppressive therapy
- have aplastic anaemia
- have congenital immunodeficiency



- Administration of live vaccines (such as the JE vaccine Imojev) to an immunocompromised person may increase their risk of adverse effects. This is primarily a safety concern.
- Live vaccines should be deferred until immune function has been assessed.
- If there is any uncertainty about how severe the person's immunocompromising condition is and whether they can safely receive live attenuated vaccines, defer vaccination, pending discussion with your state or territory immunisation service or the patient's treating specialist.

Imojev vaccine: important considerations



- People who can become pregnant should avoid pregnancy for 28 days after Imojev vaccination.
- Do not give Imojev within 6 weeks of treatment with immunoglobulins or immunoglobulin-containing blood products. Imojev should be delayed until 3 months after these treatments.
- Imojev can be co-administered (given on the same day) as other live vaccines such as MMR and yellow fever. Give in separate limbs if possible, or if this is not possible, separate sites by at least 2.5 cm.
- If Imojev or other live vaccines are not co-administered, they should be given at least 4 weeks apart. You must check if a person has recently received any live vaccines before administering Imojev, and delay vaccination if required.

JEspect vaccine



- JEspect is an inactivated vaccine
- It can be used for individuals who are unable to have Imojev, including:
 - people who are pregnant or breastfeeding
 - immunocompromised people
 - infants aged ≥ 2 months (Note: Imojev is only suitable in babies ≥ 9months)

Doses and schedule:

- JEspect is given as **two injections** 28 days apart **by intramuscular injection**. The pre-filled syringe contains 0.5mL The dose required depends on the age of the person:
 - Infants and children aged ≥2 months to <3 years should receive 2 doses, each **0.25 mL**, 28 days apart. Discard the remaining half dose.
 - Children aged ≥3 years and adults should receive 2 doses, **each 0.5 mL**, 28 days apart

Ixiaro is the same product as JEspect (both manufactured by the same manufacturer but have different trade names)



Image courtesy of Seqirus



- ATAGI recommends that the interval between the 2 doses of JEspect for the primary course should be **7 days** for adults who are at a high risk of immediate exposure (e.g. residents of or farm workers on affected piggeries).
- Check with your relevant state or territory for information about accelerated schedules.





- Children and adolescents aged <18 years should maintain a 28-day interval between doses.
- People who have a weakened immune system (immunocompromised), people who are pregnant or breastfeeding or infants aged ≥ 2 months can receive this vaccine.
- JEspect comes in a pre-filled syringe of 0.5 ml with one needle included. It should be stored at +2°C to +8°C, protected from light and should not be frozen.
- JEspect is distributed by Seqirus. The <u>product information</u> is available on the TGA website.
- Ixario is an equivalent brand product of the JEspect vaccine.

Variation from product information



- The Australian Product Information for JEspect currently states that this vaccine is for use in people aged ≥18 years.
- However, ATAGI recommends that children and adolescents aged ≥2 months to <18 years can receive this vaccine.

Source: ATAGI clinical guidance on Japanese encephalitis virus vaccines

Booster dose recommendations



As of 23 September 2022

- Booster doses are recommended for certain individuals if there is an ongoing risk of JEV infection.
- Considerations:
 - Individual's age when they received the primary course, and the vaccine used.
- A booster dose (of either Imojev or JEspect) is recommended for people who are at risk of JEV infection (as advised by the local public health authority) and more than 1 year has passed since their primary JE vaccine course in childhood or as an adult.
- The exception is people who have evidence that they received a dose of Imojev when they were aged ≥18 years, for whom a booster dose of a JE vaccine is not required.
- The Handbook recommends the same JE vaccine be used for the booster dose as was used for the primary course.

Sources

ATAGI clinical guidance on Japanese encephalitis virus vaccines Australian Immunisation Handbook: Japanese encephalitis



Age at vaccination	Vaccine	Number of doses	Boosters	Notes
≥2 months to <18 years	JEspect – intramuscular injection	2 doses (0, 28 days)	>1 year after primary dose if ongoing risk of JEV exposure	Each dose of JEspect in infants and children aged ≥2 months to <3 years is 0.25 mL. Discard the remainder of the dose.
≥9 months to <18 years	Imojev – subcutaneous injection	1 dose	>1 year after primary dose if ongoing risk of JEV exposure	Live vaccine. Check contraindications prior to administration.
≥18 years	Imojev – subcutaneous injection	1 dose	Not required	Live vaccine. Check contraindications prior to administration.
≥18 years	JEspect – intramuscular injection	2 doses (0, 28 days)*	>1 year after primary dose if ongoing risk of JEV exposure	The interval between the 2 doses of JEspect for the primary course should be 7 days for adults who are at a high risk of immediate exposure (e.g. residents of or farm workers on affected piggeries.



- Imojev is administered via subcutaneous injection
- JEspect is administered via intramuscular injection
- The deltoid muscle is the recommended site for intramuscular vaccination in adults and children aged ≥12 months.

Administering Imojev vaccine



- Imojev is given as a single dose via subcutaneous injection:
 - over the deltoid muscle
 - over the anterolateral thigh
- Skin cleaning is only required if the skin is not visibly clean
- If alcohol or other disinfecting agents are used to clean skin that is visibly dirty, the skin must be allowed to dry before injecting the vaccine.



Figure: Subcutaneous injection into the deltoid area

Source: Australian Immunisation Handbook

Administering JEspect vaccine



- JEspect is given by intramuscular injection
- Skin cleaning is only required if the skin is not visibly clean
- If alcohol or other disinfecting agents are used to clean skin that is visibly dirty, the skin must be allowed to dry before injecting the vaccine.

See next slides for vaccination sites

Source: Australian Immunisation Handbook

Vaccination site for infants aged <12 months

Recommended site for injection in infants aged <12 months

- The vastus lateralis muscle in the anterolateral thigh is the recommended site for intramuscular injection and subcutaneous injection in this age group.
- It is a large muscle and is free of neurovascular structures that could be harmed by vaccine administration.

Source: Anatomical markers used to identify the vastus lateralis injection site on the anterolateral thigh, Australian Immunisation Handbook





Vaccination site for children aged 12 months and older and adults

- The deltoid muscle is the recommended site for intramuscular and subcutaneous vaccination in adults and children aged ≥12 months.
- Correct injection technique and positioning will assist in <u>avoiding shoulder injury related to</u> <u>vaccine administration.</u>



Source: Anatomical markers used to identify the deltoid injection site, AIH

Useful link: Avoiding shoulder injury related to vaccine administration, Australian Immunisation Handbook



Co-administration with other vaccines



- Imojev or JEspect can be co-administered with other vaccines, if required.
- If a person does not receive Imojev and another live vaccine at the same time, they should receive them 4 weeks apart.
- Use separate syringes and inject in separate limbs for vaccines being co-administered.
- Refer to the <u>Handbook</u> for further information.

Vaccine safety



- Vaccination against JE is safe and effective.
- Common adverse events following JE vaccination are:
 - injection site pain and/or redness
 - headache
 - fatigue
 - Malaise
- Children may also experience:
 - fever
 - appetite loss
 - irritability
 - abnormal crying



- Most symptoms resolve within three days.
- Severe reactions to JE vaccines are very rare. As with any medicine, there is a very small chance of a vaccine causing a severe allergic reaction.
- As for all vaccines, observe the vaccine recipient for 15 minutes after vaccination.
- Adverse events reported following a booster dose of JEspect were similar to those reported following the primary course.

Visit the Australian Government Department of Health and Aged Care website for information about how to report an adverse event following immunisation.

Use in pregnant and breastfeeding people



- JEV infection during the first and second trimesters of pregnancy has been associated with miscarriage.
- No adverse outcomes of pregnancy have been attributed to vaccination with JEspect.
- <u>ATAGI recommends</u> JEspect in preference to Imojev for breastfeeding women who are at increased risk of acquiring JE. Imojev is not contraindicated in breastfeeding.
- Refer to the <u>Handbook</u> for further information regarding JE vaccine precautions and contraindications.



- It is recommended that the individual being vaccinated remains under observation for a minimum of 15 minutes following vaccination.
- It is also recommended that the individual (or their parent/guardian) is provided with appropriate information regarding potential adverse events, preferably in writing, and the date their next vaccination is due (where applicable).
- Consumer medicines information are available for <u>JEspect</u> and <u>Imojev</u>.

Reporting adverse events following immunisation



- Any adverse event felt to be significant following JE immunisation, regardless of whether the symptoms were known to be related to the vaccine or not, should be reported.
- Information about reporting adverse events following immunization is available on the <u>Australian Government Department of Health and Aged Care</u> website.

Recording JE vaccines on the Australian Immunisation Register

- JE vaccines should be reported to the • Australian Immunisation Register (AIR) via practice management software or directly on the AIR site.
- Reporting these vaccinations to AIR means • that the register contains a complete and reliable dataset, and immunisation coverage and administration can be monitored.
- Reporting to AIR will ensure individuals have ٠ a complete record of their vaccinations.

Useful link: Recording vaccines given to your patients





Learning check



1. How is JEV transmitted?

- Human mosquito human
- Pig/waterbird mosquito human mosquito
- Mosquito pig/waterbird mosquito human
- Mosquito pig/waterbird human
- 2. Preventing JEV is the most effective way to avoid severe disease. Prevention can be accomplished by which of the following?
 - · Wearing long -sleeved, light coloured clothing
 - Using mosquito repellent
 - JE vaccination
 - All of the above

3. Which of the following statements about JE virus is correct?

- JE virus can be transmitted between humans via respiratory droplets.
- JE virus is primarily found in built up areas, such as high rise apartment blocks.
- JE virus is asymptomatic in most people; however, it can be fatal in serious cases.
- Eating pork products may increase the chance of contracting JE virus.
- 4. Which of the following is not a contraindication to JE vaccination?
 - · Anaphylaxis after a previous dose of any JE vaccine
 - · Anaphylaxis after any component of a JE vaccine
 - Having a minor cold

The correct answers are available on subsequent slides

Japanese encephalitis learning resource_August 2023

Learning check - answers



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- Mosquito pig/waterbird mosquito human
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 - Having a minor cold

The correct answer is highlighted in red

Learning check – case study



The correct answers are available on subsequent slides

Joseph and his family work and reside at a property that has been confirmed to be infected with the JE virus. He presents at your clinic to ask some questions about JE and to determine whether he requires JE vaccination.

1. You identify that Joseph is eligible to have the JE vaccine, and agree to administer Imojev. Select the correct statement

- One dose required, intramuscular injection
- One dose required, subcutaneous injection
- Two doses required, intramuscular injection
- Two doses required, subcutaneous injection

Learning check – case study



Joseph and his family work and reside at a property that has been confirmed to be infected with the JE virus. He presents at your clinic to ask some questions about JE and to determine whether he requires JE vaccination.

- 2. Joseph had a covid-19 booster vaccination one month ago. Can he still have the JE vaccine?
 - Yes
 - No

3. Joseph's wife Lakshmi is 16 weeks pregnant. What recommendation would you suggest for Lakshmi?

- Lakshmi should defer JE vaccination until after giving birth.
- Lakshmi can be administered Imojev.
- Lakshmi can be administered JEspect.
- · Lakshmi can be administered either Imojev or JEspect

Learning check – case study answers

The correct answer is highlighted in red

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 - One dose required, intramuscular injection
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Further information



- ATAGI clinical guidance on Japanese encephalitis virus vaccines
- Australian Government Department of Health and Aged Care JEV resources
- <u>Australian Immunisation Handbook</u>
- National Centre for Immunisation Research and Surveillance <u>Japanese</u> <u>encephalitis</u>

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