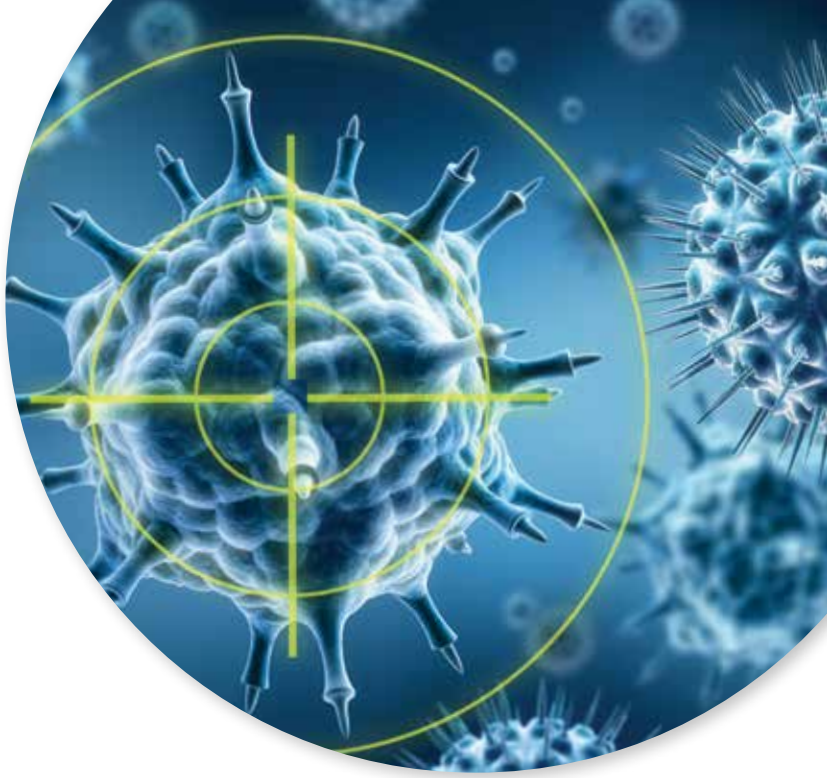

Keeping up with vaccinations

What's new, what's available and who to ask for help

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NICHOLAS WOOD MB BS, MPH, PhD

Vaccination is crucial in maintaining individual and population health. Australia's National Immunisation Program has been active since 1997 and is regularly updated as new vaccines, technology and surveillance data become available. It is therefore important that GPs have access to the most up-to-date information and resources to best advise patients, especially more vulnerable groups including children, older people, pregnant women and Aboriginal and Torres Strait Islander people.

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Immunisation in Australia started in 1804 with the first smallpox vaccine, culminating in the National Immunisation Program (NIP), which began in 1997. Since then the program has expanded to include new vaccines, altered schedules and novel monitoring tools as new technology and evidence have become available. Since early 2019, there have been a number of changes to immunisation recommendations and this article aims to inform GPs on what is new, who to ask for help and where to find further information. Some practice points on vaccination are summarised in Box 1.

Influenza

Influenza is a viral illness of the respiratory tract caused by influenza A and B viruses. These viruses cause major and minor epidemics of seasonal influenza in most years, usually during the winter months but can be present throughout the year (Figure 1), especially with increasing overseas travel.[1] Severe complications of influenza include pneumonia, myocarditis, bacterial coinfection, encephalitis and death. Children, older people, pregnant women, Aboriginal and Torres Strait Islander (Indigenous) people and people with comorbidities have a higher risk of complication from influenza compared with the general population.[2,3]

Influenza vaccination for people of Aboriginal or Torres Strait Islander background

Aboriginal and Torres Strait Islander people have a high burden of disease from influenza and influenza-related complications.[2,3] The risk of influenza-related hospitalisations between 2006 and 2010 was two to six times higher among people of Indigenous background compared with non-Indigenous people.[2] Until 2019, the seasonal influenza vaccine was nationally funded for Indigenous children aged 6 months to 5 years and Indigenous people aged 15 years and over. To close the gap, the seasonal influenza vaccine is now funded for all Aboriginal and Torres Strait Islander

1. PRACTICE POINTS ON VACCINATION

- The flu vaccine is free for all Indigenous people and will be funded for all children aged 6 months to 5 years from 2020
- The flu vaccine is safe for egg-allergic patients
- The MMR vaccine can be given to patients as young as 6 months of age for travel
- dTpa can be given as early as 20 weeks' gestation with every pregnancy
- Q fever vaccination is recommended for anyone working with animals
- Immunisation recommendations change – always refer to the updated online *Australian Immunisation Handbook*
- Immunisation specialists are available in every state for clinical assistance

people aged 6 months and over.[4] In July 2019, the Pharmaceutical Benefits Advisory Committee recommended listing of the quadrivalent influenza vaccine on the NIP for all children aged 6 months to 5 years from 2020.[5]

Influenza vaccination for older people

People aged 65 years and over have the highest influenza-related mortality and decreased effectiveness to standard trivalent influenza vaccine (TIV) compared with the younger population.[2,6] To improve the immune response to the influenza vaccine in this age group, 'enhanced' TIVs were developed. Two types of enhanced vaccine are available in Australia: a high-dose influenza vaccine that contains four times the haemagglutinin content of standard TIVs; and an adjuvanted influenza vaccine that contains adjuvant MF59 in addition to the standard haemagglutinin dose of each strain.[4,7] These vaccines increase protection compared with standard-dose TIVs, especially against influenza A (H3) strain, which causes a more common and severe disease in older people.[4,6,8-10] Clinical trials have shown reduced laboratory-confirmed influenza and influenza-related deaths in people aged 65 years and over who were vaccinated with enhanced TIVs compared with standard TIVs.[8-10] Moreover, the improved efficacy of enhanced TIVs against influenza A is likely to offset the loss of protection against the additional influenza B lineage found in the quadrivalent vaccine.[4]

In 2018, enhanced TIVs were recommended in preference to the quadrivalent influenza vaccines for people aged 65 years and over. Active surveillance of the safety of the 2019 influenza vaccine in people aged 65 years and over commenced on 1 April 2019, with data showing reported events following immunisation were consistent with expected outcomes: most people (94%) did not have any adverse reaction; of the 6% with reactions, the most common adverse effects were injection site reactions, fevers and rash; only 0.3% required medical attendance.[11,12] The adjuvanted TIV is funded through the NIP for people aged 65 years and over and the high-dose TIV is available privately.[4]

Influenza vaccination for people with egg allergy

Influenza vaccines in Australia are grown in embryonated chicken eggs and historically there have been concerns regarding the risk of anaphylaxis following influenza vaccination in people with egg allergy. However, manufacturing processes ensure that only a trace amount of ovalbumin remains within the vaccine formulation (usually less than 1 mcg of ovalbumin per dose), which is insufficient to cause anaphylaxis.[4]

In a 2014 review of 28 studies encompassing 4315 people with egg allergy (including 656 people with a history of anaphylaxis), no severe reactions were reported after influenza vaccination.[13] Vaccine allergy testing, split dosing or graded administration are no longer recommended when vaccinating people with egg allergy as they have shown no difference in the rate of adverse reactions.[14] People with egg allergy do not need to be referred to specialist hospital-based vaccination clinics for influenza vaccination; however, anyone administering a vaccine should have training and equipment for the rapid recognition and treatment of anaphylaxis.[4] The Australasian Society of Clinical Immunology and Allergy has developed guidelines on vaccinating egg-allergic people (www.allergy.org.au/hp/

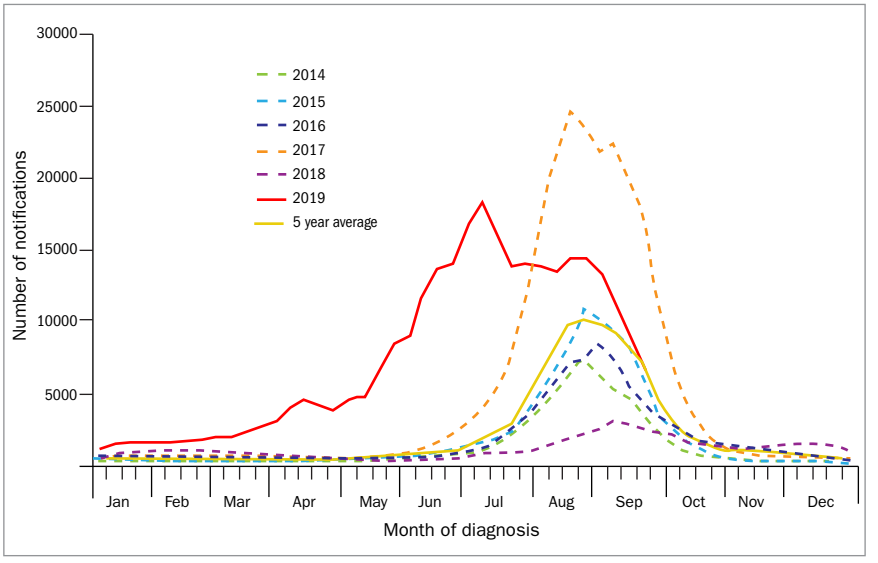


Figure 1. Notifications of laboratory confirmed influenza in Australia from 1 January 2013 to 22 September 2019, by month of diagnosis.

Reproduced with permission from the Australian Government Department of Health, 2019. Australian Influenza Surveillance Report 2019 No 11. Available online at: www1.health.gov.au/internet/main/publishing.nsf/Content/3CE94FB1E75C4A08CA2584820016014O/$File/flu-11-2019.pdf (accessed October 2019).

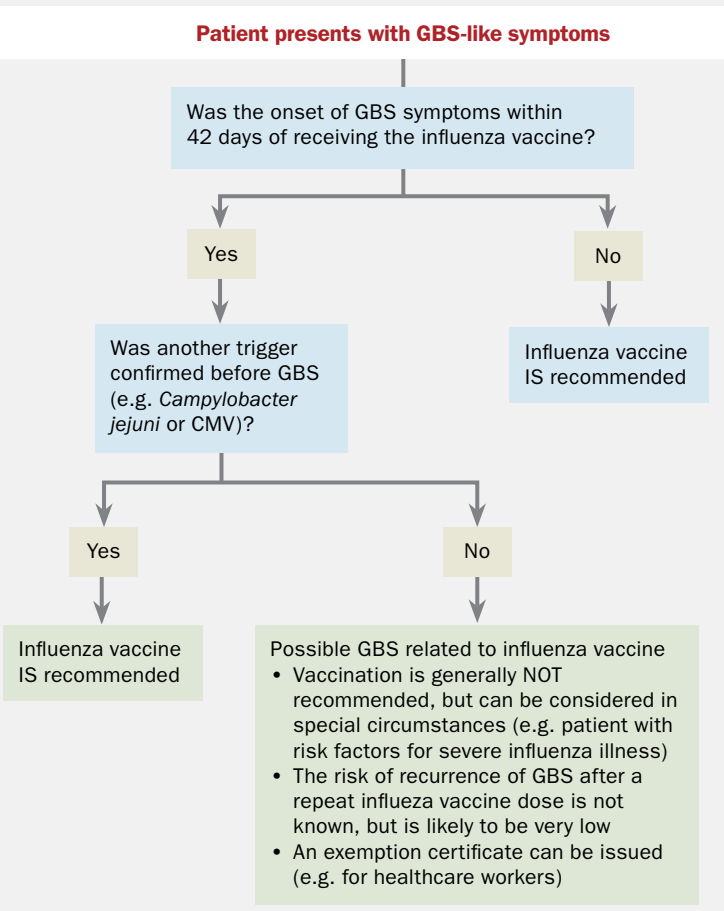
papersvaccination-of-the-egg-allergic-individual).[14]

Influenza and Guillain-Barré syndrome

Guillain-Barré syndrome (GBS) is a rare, acute immune-mediated polyneuropathy, commonly preceded and thought to be triggered by gastrointestinal or respiratory infections, including influenza. Concerns about the association between GBS and influenza vaccination arose after an increased number of cases of GBS were reported following swine flu vaccination in 1976.[15] Further studies have shown that GBS is rare after seasonal influenza vaccination, and at most may account for one additional case of GBS per million vaccine doses.[15-17]

The risk of developing GBS after influenza is 15 times higher than after influenza vaccination. Therefore, in patients with a history of GBS, the benefits of vaccination may outweigh the risk of recurrent GBS after vaccination.[18] Reassuringly, no recurrences of GBS were reported in 214 patients with a history of GBS, pooled from three studies, who received a total of 1195 doses of influenza vaccine after their GBS diagnosis.[19-21] Another study reported a recurrence of GBS-like symptoms following influenza vaccination in eight out of 211 patients with a history of GBS, but formal diagnosis of a relapse was not confirmed, most symptoms were mild and no patient required treatment or hospitalisation.[22] When considering vaccination of a patient with a past history of GBS, GPs should consider the patient's risk factors for severe influenza illness such as diabetes, any respiratory or cardiac condition, temporal association with the influenza vaccine and the possibility of a reasonable alternative trigger such as *Campylobacter* gastroenteritis. Vaccination is recommended unless the previous onset of GBS, without a potential alternative trigger, occurred within six weeks (42 days) of receiving the influenza vaccine (Flowchart).

APPROACH TO INFLUENZA VACCINATION IN PATIENTS WITH A HISTORY OF GUILLAIN–BARRÉ SYNDROME



Abbreviations: CMV = Cytomegalovirus; GBS = Guillain-Barré syndrome.
Reproduced with permission from the National Centre for Immunisation Research and Surveillance.

Measles

Measles is a highly infectious disease caused by a paramyxovirus and spread by aerosolised or droplet respiratory secretions. Complications of measles include otitis media, diarrhoea, pneumonia and encephalopathy, and measles remains one of the leading causes of death among young children.[23] Measles outbreaks have increased globally over the past few years, with the WHO estimating a 300% increase in reported cases in the first three months of 2019 resulting from gaps in vaccine coverage.[24]

In Australia, children are typically vaccinated against measles from 12 months of age, and therefore most measles cases are imported, occurring in unvaccinated or undervaccinated individuals infected while travelling to endemic or outbreak regions. Due to the constant importation of measles, there is a risk of spread to unvaccinated individuals, in particular children under the age of 1 year, in people who have not received two doses of measles-containing vaccine and immunocompromised individuals who cannot receive live vaccines.[25] As a consequence, to improve measles immunity in the community, the *Australian Immunisation Handbook* has updated its recommendations as follows:

- children as young as 6 months of age can receive the measles, mumps and rubella (MMR) vaccine
- all Australians should receive two doses of the MMR vaccine.

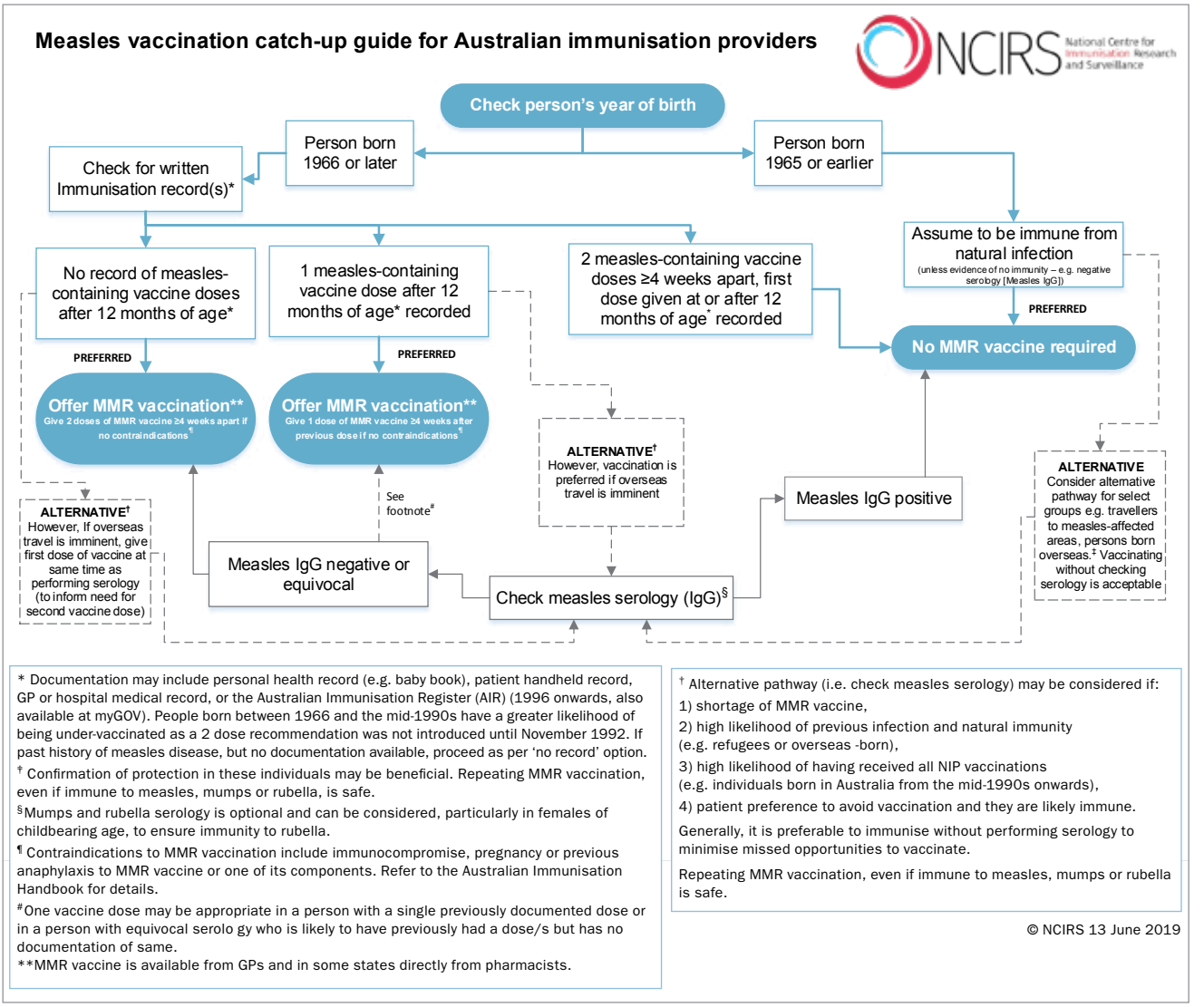


Figure 2. Measles vaccination catch up guide for Australian immunisation providers.[35] Reproduced with permission from the National Centre for Immunisation Research and Surveillance.

Measles vaccination from age 6 months

The *Australian Immunisation Handbook* has lowered the recommended age that children can receive the MMR vaccine from age 9 months to 6 months for children travelling to endemic areas, in outbreak situations and for postexposure prophylaxis in line with WHO and Centers for Disease Control and Prevention (CDC) recommendations.[4] The change in recommendation comes as a result of increasing evidence suggesting that vaccinated women have an earlier decline in circulating antibodies compared with women who have been infected with measles, resulting in lower titres of maternal antibodies being transferred to the fetus during pregnancy.[26-29] These lower titres result in a shorter period of protection in infants and a longer period of time that they are at risk of measles infection before their first dose of MMR vaccine. Countries that have lowered the recommended age of measles vaccination to as young as 6 months of age, including the US, Canada, UK and New Zealand, have reported no additional safety concerns.[30] Vaccinating infants between 6 and 11 months of age provides short-term protective antibody levels in a large proportion of infants and should be considered in addition to the routine two-dose schedule at 12 and 18 months to ensure long-term immunity.[24]

Two doses of the MMR vaccine for all

To prevent measles outbreaks, it is essential that all eligible individuals living in

Australia are immune to measles. Before 1966, the measles virus was circulating in the community and individuals born before that year are likely to have a natural immunity to measles.[31] People who were born between 1966 and 1994 may have received only a single dose of a measles-containing vaccine and, therefore, a proportion may not be immune to measles.[32]

One dose of measles-containing vaccine is 95 to 96% effective. Effectiveness increases to 99% after a second dose.[33,34] It is therefore recommended that all eligible individuals born after 1966 who are living in or visiting Australia receive two doses of a measles-containing vaccine. This requires that some patients receive catch-up vaccinations.[4] A flow chart (Figure 2) has been created by NCIRS to aid GPs in advising patients on catch-up vaccinations.[35] When it is uncertain whether a person has natural immunity or has received two doses of measles-containing vaccine, an additional MMR vaccine should be administered. There is no known increase in adverse events from vaccinating people with pre-existing immunity to measles.[4]

Routine serological testing for measles IgG to assess immunity from either natural infection or vaccination is not recommended in lieu of vaccination, but may be an alternative way to confirm measles immunity, particularly in populations where the MMR vaccine is contraindicated.[4,35] Sensitivity of the test varies by assay and time since vaccination.[36-38]

Pregnancy and vaccination

Vaccination needs should be assessed for women planning pregnancy and those who are pregnant. It is important that GPs discuss immunisation with women planning pregnancy and ensure that they are up-to-date on their immunisation schedules, particularly against rubella and chicken pox. These live vaccines can harm the fetus if contracted during pregnancy and should be given before pregnancy not during. Influenza and diphtheria-tetanus-acellular pertussis (dTpa) vaccines are recommended for pregnant women and are funded by the NIP.

Whooping cough vaccination in pregnancy

The pertussis vaccine (dTpa) is an inactivated vaccine provided free for pregnant women under the NIP, and recommended to be given in each pregnancy (even pregnancies that are closely spaced). Vaccination in pregnancy allows for maternal antibody production and in utero transfer to the fetus, protecting up to 90% of infants until the age of 3 months against hospitalisation from pertussis when the mother is vaccinated at least seven days before delivery.[39-41] The vaccine also protects pregnant women from contracting pertussis and reduces the likelihood of it spreading to other adults and their children. The recommended timing of the pertussis vaccination in pregnancy has expanded from between 28 and 32 weeks to between 20 and 32 weeks. This allows greater opportunities for health services to offer vaccination to pregnant women, to protect premature infants and to improve vaccine coverage.[4]

If the vaccine has not been given by 32 weeks of pregnancy it can still be given at any time during the third trimester. Additionally, if a pregnant woman receives the vaccine earlier than 20 weeks, she does not need a repeat dose during the same pregnancy. Evidence shows transfer of pertussis antibodies to the infant in women who received dTpa vaccine as early as 13 weeks' gestation.[42]

The vaccine is safe and well tolerated in pregnancy. Safety studies suggest that vaccination in the second and third trimester is not associated with clinically significant harm to the fetus or the mother.[42] Active surveillance of 5085 pregnant Australian women between 1 July 2018 and 30 June 2019 showed 94% had no adverse effects following dTpa vaccination. The most common adverse event was injection site pain (2.4%), followed by injection site swelling or erythema (1.7%). Fever occurred in 0.8% of women and only 0.5% of women required any medical attendance.[43] The only absolute contraindication to dTpa in pregnancy is a history of anaphylaxis to the vaccine.[4]

Influenza vaccination in pregnancy

Influenza in pregnant women and children less than 6 months of age is related to increased disease severity and risk of complications such as premature delivery and neonatal or perinatal death.[44-47] Vaccination during pregnancy ensures protection for both the mother and her infant up to 6 months of age, after which children are eligible to receive their own vaccine.[48-52] The seasonal influenza vaccine has been shown to decrease influenza cases in pregnant women by 50% and hospitalisation by 35 to 40%.[46,51,53,54] Infants less than 6 months of age were half as likely to develop influenza and 72% less likely to require hospitalisations when their mother received the influenza vaccine in pregnancy.[48] The seasonal influenza vaccine is safe throughout all trimesters of pregnancy and only one dose is recommended each season.[4,50,55] Pregnant women are advised to receive a second dose of the influenza vaccine if their first dose was the previous year's seasonal influenza vaccine.[12]

Despite the efficacy and safety data, influenza vaccine uptake is still not universal, and data from Australian states and territories estimate a minimum of 25%, and up to 60%, of pregnant women may not receive the vaccine.[56-58] GPs play a significant role in increasing vaccine uptake as women are more likely to receive the influenza vaccine if recommended by their healthcare provider.[59-61]

Pneumococcal disease

Pneumococcal disease is an infection caused by the Gram-positive encapsulated bacterium *Streptococcus pneumoniae*. Invasive pneumococcal disease (IPD) refers to severe infection usually causing sepsis, bacteraemic pneumonia or meningitis. Young children, older people, people of Aboriginal or Torres Strait Islander descent, patients who have or are at risk of cerebrospinal fluid leak or people who are immunocompromised have the highest increased risk of IPD.[62] Protection against pneumococcal disease is serotype specific. Two vaccines exist in Australia: a 13-valent

pneumococcal conjugate vaccine (13vPCV) and a 23-valent pneumococcal polysaccharide vaccine (23vPPV).[4,63] The 13vPCV is funded in the NIP infant vaccination schedule as it induces long-lasting immune responses, even in children under 2 years of age.[64] The 23vPPV offers protection, albeit shorter lasting, to more pneumococcal serotypes and is currently recommended for Indigenous people at 50 years of age and non-Indigenous people at 65 years of age.[62] This recommendation is likely to change in the next 12 months as the Pharmaceutical Benefits Advisory Committee has proposed, based on cost-effective analysis, that the 13vPCV replace the first dose of 23vPPV for Aboriginal and Torres Strait Islander adults at 50 years of age and for all other healthy adults at 70 years of age.[65]

Recommendations on the infant pneumococcal immunisation schedule were updated in July 2018. The current recommendation for children with no risk factors is to receive 13vPCV at age 2 months (or 6 weeks), 4 months and a booster at 12 months of age (2+1 schedule) to generate longer lasting immunity and improved herd immunity in children compared with the original 3+0 schedule (2, 4, 6 months of age).[4] Children of Indigenous background or with risk factors for IPD are funded through the NIP to receive four doses (3+1) of the 13vPCV at 2, 4, 6 and 12 months of age and 23vPPV at 5 years of age.[4] Additional pneumococcal vaccines, as detailed in the *Australian Immunisation Handbook*, continue to be recommended for adults and children aged 5 years and over, with risk factors for IPD, depending on the severity of risk and history of previous pneumococcal vaccination.[4,62]

The PneumoSmart vaccination tool

The PneumoSmart vaccination tool was developed by the Immunisation Coalition to help immunisation providers correctly provide pneumococcal vaccination for people aged 5 years or over, based on the recommendations from the *Australian Immunisation Handbook*. The algorithm incorporates a person's age, Indigenous status, comorbidities and previous pneumococcal vaccinations to develop a table recommending the type of vaccine, intervals between doses and whether the vaccine is funded through the NIP (https://immunisationcoalition.org.au/pvt).[66]

2. USEFUL RESOURCES FOR GPs ON VACCINATION

The following resources are useful for GPs to refer to when looking for information on immunisation.

The Australian Immunisation Handbook (https://immunisationhandbook.health.gov.au) is a free, up-to-date online reference that uses the best scientific evidence available to provide clinical guidelines for healthcare professionals.[4] The handbook provides information on vaccine preventable diseases, vaccines available in Australia, immunisation schedules and methods of administering vaccines safely and effectively. The online handbook is continually updated and supersedes the current 2014 print edition.

National Centre for Immunisation Research and Surveillance (NCIRS) (ncirs.org.au) offer numerous useful resources for GPs and the general public.

- Fact sheets on vaccine preventable diseases, vaccine safety and clinical resources have been developed principally for immunisation providers (http://ncirs.org.au/health-professionals/ncirs-fact-sheets-faqs).
- NCIRS also run a series of webinars on current topics around immunisation and vaccine preventable diseases about every six weeks (http://ncirs.org.au/NCIRSSeminars).
- Sharing knowledge about immunisation (SKAI) is a set of online vaccination communication support tools designed to assist patient-centred communication around immunisation (www.ncirs.org.au/our-work/sharing-knowledge-about-immunisation). The parent-focused website 'Talking about immunisation' contains information about common concerns around vaccination in both written and video format (www.talkingaboutimmunisation.org.au).

AusVaxSafety (www.ausvaxsafety.org.au) is an NCIRS-led collaboration established in 2014 to monitor adverse events in children following immunisation with influenza vaccines through responses solicited via automated SMS or email on a wide range of infant, pregnancy, adolescent and elderly vaccines.[11] Data on current event rates are reported via safety surveillance graphs and compared to expected rates according to existing data.

The **Immunisation Coalition** (www.immunisationcoalition.org.au) is an independent, not-for-profit organisation that works in close collaboration with consumer advocacy groups and professional and government bodies to provide current information on immunisation. The website provides the PneumoSmart calculator, fact sheets and webinars on vaccine-preventable diseases.

The Melbourne Vaccine Education Centre (MVEC) (https://mvec.mcri.edu.au) is based at the Murdoch Children's Research Institute and provides information on immunisation on a range of topics aimed at immunisation providers and members of the public including regularly updated fact sheets, links to the National Immunisation Schedule, information on how to plan catch-up immunisation schedules using the Australian Immunisation Register (AIR) and information on how to manage vaccination adverse events. The webpage also alerts clinicians to schedule updates, new guidelines and proposed changes to the childhood immunisation arrangements for family assistance payments.

The National Vaccine Storage Guidelines (Strive for 5) (www.health.gov.au/resources/publications/national-vaccine-storage-guidelines-strive-for-5) are updated national vaccine storage guidelines prompting all immunisation service providers, including GPs, to strive to keep vaccines stored at 5°C – the halfway point between the recommended temperature range of 2 to 8°C, with a permanent data logger in place to measure temperature at preset 5-minute intervals. Useful printable tools such as checklists and refrigerator temperature charts are included in the guideline.

Q fever

Q fever is a zoonotic disease caused by the intracellular bacterium *Coxiella burnetii*. Although the disease can be asymptomatic, it can often present with severe flu-like symptoms and be complicated by

pneumonia and hepatitis. Some people go on to develop chronic Q fever, which may manifest as endocarditis. Ruminants such as cattle, sheep and goats are the main reservoir for human infection but a wide variety of animals including birds, ticks and marsupials can be infected. The environmental form of *C. burnetii* is resistant to heat and desiccation. The bacteria can persist for long periods in the environment and be transported long distances by wind and dust. Humans are infected via direct contact with animals or inhalation of contaminated aerosols.[67,68]

Early diagnosis and vaccination

Q fever, despite being undernotified, remains a highly vaccine-preventable disease, especially for rural residents. A large serosurvey reported a seropositivity of 3.6% among blood donors in NSW and Queensland, with higher seroprevalence among those living in rural areas. However, 0.9% of urban dwellers with no risk factors also had evidence of exposure.[69]

People who are at high risk of contracting Q fever and for whom the vaccine is recommeded include those who work on farms, in veterinary practice or in abattoirs, manage or breed animals or handle veterinary specimens. The Q fever vaccine is licensed for use in people from 15 years of age but studies are underway to assess its safety and efficacy in children as young as 10 years of age.[70]

Candidates require prevaccination testing with serum antibody and skin testing to ensure there has been no past exposure to *C. burnetii* and to minimise adverse effects following vaccination.[4] Test results can be uploaded onto the Australian Q fever register (https://qfever.org/findvaccinator), and authorised users (usually meat processors and medical practitioners) are able to check a person's Q fever immune status.[71] The register also provides a list of medical practitioners who are experienced in testing and vaccinating against Q fever.

A study found that 40% of people for whom the vaccination is recommended were aware of the vaccine, and only 10% were vaccinated, with a perceived lack of risk being the main reported reason for not being vaccinated.[69] To increase awareness of Q fever and vaccination among GPs, a new Q fever educational resource has been developed by the Australian College of Rural and Remote Medicine (ACRRM).[72] This two-hour online course updates providers on Q fever diagnosis and vaccination and is available for free to all ACRRM members and subscribers. Nonmembers can also enrol for a fee. The module provides education about pathogenesis and the clinical presentation of Q fever, exposure risks in Australia, treatment, prevaccination testing and Q fever vaccination.[72]

Catch-up vaccinations

Free catch-up vaccinations are available for all people under 20 years of age and to all refugees and humanitarian entrants regardless of age.[4]

Immunisation calculator

A web-based immunisation calculator is available through South Australian Health to help clinicians draft a catch-up schedule for children under 10 years of age who have missed or received delayed vaccination (https://immunisationcalculator.sahealth.sa.gov.au/ImmuCalculator.aspx).[73] A similar calculator is being developed for the online *Australian Immunisation Handbook* and checking the catch-up resources on their website (https://immunisationhandbook.health.gov.au/catch-up-vaccination) on a regular basis is strongly recommended.

Adverse events following immunisation

Although vaccines are generally safe, occasionally a patient may experience a reaction following vaccination. Any negative reaction that follows immunisation is considered an adverse event following immunisation (AEFI). The adverse event does not need to be causal for it to be classified as an AEFI and may be any unfavourable or unintended sign or symptom, disease or abnormal laboratory finding. Up to 10% of people can experience a common AEFI such as an injection site reaction, pain or fever.[4,74]

AEFI reporting

In the event of a serious, uncommon or rare AEFI, the immunisation provider should seek advice from their local specialist immunisation clinic or contact their state or territory health authorities. This advice is important to determine the relationship of the adverse event to vaccination and the benefit and risks of further vaccination and to ensure the development of a plan for future vaccination. Methods of reporting vary between each state and territory. Information can be found on the NCIRS website (www.ncirs.org.au/health-professionals specialist-immunisation-services).[43]

All states and territories offer specialist clinic review for patients who have experienced AEFIs. Most clinics will see children, others will also review adults and some have teleconferencing abilities. Information can be found at www.ncirs.org.au/health-professionals specialist-immunisation-services.

Conclusion

There are some constants to immunisation such as a comprehensive and methodical immunisation schedule, and nationwide and global immunisation coverage to stop the spread of vaccine-preventable diseases. That said, with novel technology, research and surveillance methods, new vaccines are being developed and tested, and there is the ability for constant review of disease epidemiology, vaccine efficacy and adverse events. Immunisation programs are therefore constantly evolving. As such, we encourage GPs to stay updated and informed using key web resources and tools. Useful resources for GPs on vaccination are summarised in Box 2. MT

References

A list of references is included in the online version of this article (www.medicinetoday.com.au).

COMPETING INTERESTS: None.

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What's new, what's available and who to ask for help

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