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One Health

One Health: much more than a slogan

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We are in an era when public health slogans abound; we have had 'the new public health', 'emerging infectious diseases', and now 'One Health' joins this lexicon.

So, what is 'One Health'? How does this concept help us think through, and perhaps solve, public health problems? One Health places disease, particularly infection, in a broad ecological context. Many agents of infection target hosts beyond humans, and One Health seeks to understand and explain the public health implications of broad host ranges.¹ One Health is a modern restatement of the old epidemiological triad of host, agent and environment.

It has long been known that many infections cross the species barriers between humans, domesticated animals and wildlife. Our view of this has traditionally been somewhat compartmentalised; those who work in food production and regulation are aware of the importance of *Salmonella* infections and how modern intensive agriculture, food production, trade and marketing interact to determine their epidemiology. The more complex interactions between domesticated animals and wildlife that govern the spread of well-known infections such as influenza, rabies, Ross River and other arbovirus infections, and newly recognised infections such as Nipah and Hendra virus infection still tease expert minds.²

There are some specific puzzles. What determines pathogenicity of agents, with species specificity? What, in particular, makes bats an efficient vector of so many newly described infections? How do we determine whether an agent is a true pathogen? What factors determine whether an infection will cross a species barrier? What measures will most effectively limit the burden placed on veterinary and human health? The solutions to these problems will come only from cross-disciplinary work involving epidemiologists, epizootiologists of both wild and domesticated animals, veterinarians, public health practitioners, laboratory scientists and clinicians.

The One Health concept is focused on infectious diseases and their transmission. However, this is not the only way that health can be affected across species. To date, we have focused largely on animal infection, but microbiological and plant infections also impact health. An example of a crossspecies impact on health was potato blight with its first impact directly on plants, and a second impact through starvation of humans. Global warming is also predicted to have an enormous impact on agricultural production (most of which will not be due to infection), while having a secondary health impact on humans.

The One Health concept has largely been the domain of microbiologists and wildlife ecologists. More exploration and discussion of the epidemiological and epizootiological background is needed to characterise the importance of these infections to human and animal public health. This special edition of the NSW Public Health Bulletin begins to explore One Health issues of recent or emerging importance in New South Wales. Adamson et al reflect on the level of coordination that already exists between state health, veterinary and primary industry players, and Dwyer et al demonstrate how this partnership strengthened the response to the 2009 influenza pandemic and calls for expansion of these collaborative efforts. Hendra virus is a classic example of an emerging infectious disease with potentially profound human and animal health consequences, and Hess et al provide practical management advice while highlighting the need for a One Health partnership to gain a better understanding of this virus and its ecology. Paterson et al argue that current surveillance systems do not provide reassurance for early detection and characterisation of emerging pathogens that present with an encephalitis syndrome. Their argument for a standardised algorithm for diagnostic work up would allow the remarkable developments in virological science, elucidated by Wang, to rapidly

Box 1. The first International One Health Congress

The first International One Health Congress was held in Melbourne on 14–16 February 2011 with the aim of exploring the interdependencies between human, animal and wildlife health. Over the 3 days of the Congress, about 150 papers were presented on these issues, and the Congress concluded that a practical program of collaboration was needed to address the scientific, policy and social questions raised by these interdependencies.

An overview of the Congress and copies of the papers are available at the Congress website at: http://www. onehealth2011.com/index.php

characterise new pathogens, to be harnessed for directing human and veterinary public health action.

NSW Health staff recently contributed to the first International One Health Congress. Box 1 contains a link to the Congress website where copies of the papers presented are available for further information. Also presented is a glossary to assist the reader with terms that are used in this issue (Box 2).

Emerging disease threats demand a team approach that capitalises on the complementary expertise and knowledge of animal and human health professionals. The One Health approach has the potential to improve the lives of all species, whether human or animal.

An update on Hendra virus infection from the Editors

Hendra virus infection is carried by Flying-foxes in Australia. Occasionally the infection is passed to horses, presumably through exposure to virus excreted by Flyingfoxes. There have been seven human infections with Hendra virus (including four deaths) identified in Australia to date, all following significant exposures to infectious horses. No human infections have followed direct exposure to a Flying-fox or another person with the infection.

On 1 July 2011, the NSW Department of Primary Industries reported a confirmed case of Hendra virus infection in a horse that had died on a property near Wollongbar on the NSW North Coast. On 6 July, the Department of Primary Industries reported a second unrelated Hendra virus infection in a horse that died on a property near Macksville on the Mid North Coast. The horses were buried and the properties placed in quarantine. Several Queensland properties were also quarantined around the same time following confirmation of unrelated Hendra virus infections in horses there.

Nine people were identified as having potential contact with the first NSW horse while it was potentially infectious, and six with the second horse. NSW Health urgently convened expert panels including public health and infectious disease expertise from NSW and Queensland after the diagnosis was confirmed in each horse and the contacts

Box 2. Glossary of terms used in this issue

Ardeid waterbirds: the Ardeidae family of birds encompass the herons, egrets, night herons and the bitterns. They are geographically widespread and are found on all continents (except Antarctica) and islands around the world. These birds feed in water and usually live in wetlands, including swamps but also near tidal areas and streams. They like to roost and build their nests in trees. (http://tolweb.org/Ardeidae/26331)

Enzootic: of, relating to, or denoting a disease that regularly affects animals in a particular district or at a particular season. (*Oxford Dictionary*)

Epizootiology: the study of the character, ecology and causes of outbreaks of animal diseases. (*Webster Medical Dictionary*)

Novel virus: newly discovered virus.

One Health: the collaborative effort of multiple disciplines – working locally, nationally and globally – to attain optimal health for people, animals and our environment. (American Medical Veterinary Association)

Vector: in infectious disease epidemiology, an insect or any living carrier that transports an infectious agent from an infected individual or its wastes to a susceptible individual or its food or immediate surroundings. The organism may or may not pass through a developmental cycle within the vector. (*A Dictionary of Epidemiology*, 4th edition – John M. Last)

Zoonosis: an infection or infectious disease transmissible under natural conditions from vertebrate animals to humans. Examples include rabies and plague. May be enzootic or epizootic. (*A Dictionary of Epidemiology*, 4th edition – John M. Last)

had been interviewed. The panels evaluated the risk of infection to each person based on their exposures to the horses according to national protocols (see: http://www. health.nsw.gov.au/factsheets/guideline/hendra.html).

All 15 potential contacts were assessed as having had either no, negligible, low or medium level risk of exposure to the infectious horses. All previous human Hendra virus infections have occurred following high level exposures to infected horses. North Coast Public Health Unit staff counselled contacts about their risk and the disease, and initiated symptom monitoring for the incubation period for Hendra virus infection in humans (3 weeks from last exposure).

For further information on Hendra virus infection see: http://www.dpi.nsw.gov.au/agriculture/livestock/horses/ health/general/hendra-virus and http://www.health.nsw. gov.au/factsheets/infectious/hendra.html

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A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia

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Abstract: Human encephalitis in Australia causes substantial mortality and morbidity, with frequent severe neurological sequelae and long-term cognitive impairment. This review discusses a number of highly pathogenic zoonotic viruses which have recently emerged in Australia, including Hendra virus and Australian bat lyssavirus which present with an encephalitic syndrome in humans. Encephalitis surveillance currently focuses on animals at sentinel sites and animal disease or definitive diagnosis of notifiable conditions that may present with encephalitis. This is inadequate for detecting newly emerged viral encephalatides. Hospital-based sentinel surveillance may aid in identifying increases in known pathogens or emergence of new pathogens that require a prompt public health response.

Human encephalitis causes substantial morbidity and mortality in Australia, frequently resulting in severe neurological sequelae and long-term cognitive impairment. While herpes simplex virus is the most commonly identified causative pathogen, the majority of adult encephalitis hospitalisations (70%, range 62–79%) have no specific pathogen identified¹ and an increasing proportion of encephalitis deaths are due to 'unknown' causes – from 47% between 1979 and 1992 to 57% between 1993 and 2006.² Recently emerged or resurging pathogens in Australia, including Murray Valley encephalitis virus, West Nile virus (Kunjin clade), Japanese encephalitis virus, Hendra virus and Australian bat lyssavirus, cause a human encephalitis syndrome; consequently, encephalitis surveillance may be useful for signalling the emergence of novel infectious diseases, particularly viral zoonoses that may impact on human health.

Emerging infectious diseases pose a substantial threat in Australia and globally due to increased urbanisation, climate change, new farming practices, virus re-assortment and changes in human behaviours.^{3–5} The close interaction between animals and humans has provided opportunities for viruses to jump between species with 60% of known human infectious diseases and 75% of emerging infectious diseases being of animal origin.^{5,6} A One Health approach, which recognises the interdependence of human and animal health and the environment, is required to improve the surveillance of and response to Australian emerging infectious diseases.

Surveillance for viral zoonotic encephalitis

Surveillance for human viral zoonotic encephalitis in Australia depends on four different systems: notifications of specific infections to state and Commonwealth governments under public health legislation; serological surveillance of sentinel animals for flaviviruses; confirmatory testing of bats submitted after human contact for Australian bat lyssavirus; and mosquito surveillance for flaviviruses.

Although the encephalitis syndrome per se is not notifiable in Australia, specific diagnosis of a number of viral zoonotic encephalitides (Murray Valley encephalitis virus, West Nile virus (Kunjin clade), Japanese encephalitis virus, other flavivirus encephalitides and Australian bat lyssavirus) are notifiable by all states and territories, using common case definitions, to the Australian Government Department of Health and Ageing National Notifiable Diseases Surveillance System.⁷ Human Hendra virus infection is only notifiable in Queensland, although equine infections have occurred in both Queensland and northern New South Wales (NSW).⁸ Unfortunately, mandatory notification does not guarantee comprehensive reporting as it is based on detection of a causative organism. Therefore encephalitis due to rare or emerging pathogens may go unrecognised, which has led to proposals for systematic surveillance of the encephalitis syndrome.^{2,9}

Zoonotic encephalitis viruses

Zoonotic encephalitis viruses fall into two groups, each with their own particular wildlife hosts, transmission mechanisms and ecologies. The first are the vectorborne and transmitted flaviviruses: Japanese encephalitis virus, Murray Valley encephalitis virus and West Nile virus (Kunjin clade). The second are the batborne viruses where bats act as the reservoir host: Hendra virus and Australian bat lyssavirus.

Vectorborne flaviviruses

The three flaviviruses Japanese encephalitis virus, Murray Valley encephalitis virus and West Nile virus (Kunjin clade) are closely related members of the Japanese encephalitis serological complex. Their maintenance hosts are ardeid waterbirds and their vectors are *Culex* spp. mosquitoes.

Japanese encephalitis virus (JEV)

JEV is the major cause of childhood viral encephalitis and associated disability in Asia.^{10,11} Only 1:25–1:300 infections result in clinical disease^{12,13} but 25% of clinical cases are fatal and 50% of affected humans experience neurological sequelae. Transmission cycles involve *Culex* spp. mosquitoes (especially *Cx. tritaeniorhynchus*), ardeid birds, such as black-crowned night herons (*Nycticorax nycticorax*), and pigs as vertebrate amplifying hosts.¹⁴ Humans become infected by a bite from an infected mosquito but they are incidental, dead-end hosts. It is worth noting that JEV also causes encephalitis in horses, and they too are incidental, dead-end hosts.

JEV emerged unexpectedly in the Torres Strait in 1995 (probably following importation from Papua New Guinea), causing three human cases of encephalitis in Badu, two of whom died. A further case occurred in Badu in 1998, as well as the first human JEV case on mainland Australia near the mouth of the Mitchell River, Cape York.¹⁵ Virus activity has been detected in the Torres Strait in almost all years since 1995, and in Cape York on the Australian mainland in 1998 and 2004.

Sentinel pig herds were kept on various Torres Strait islands and locations in northern Cape York for serological surveillance but, as these sites were usually close to human habitation and pigs are major virus amplifiers, the sentinel pig program was discontinued except for a single site on Cape York. Sporadic opportunistic mosquito collections are made by Queensland Health for virus isolation. Future JEV activity surveillance may be incorporated in the National Arbovirus Monitoring Program of Animal Health Australia, as cattle are safe animals for surveillance.¹⁶

A safe and effective inactivated, cell culture propagated JEV vaccine is available for those living or travelling in endemic areas,¹⁷ and several newer vaccines with

potentially greater efficacy and safety are undergoing clinical trial.

Murray Valley encephalitis virus (MVEV)

Encephalitis outbreaks due to MVEV were first detected on Australia's east coast in the early 20th century, and then re-emerged as epidemics in the Murray-Darling River basin in 1951 and 1974.¹⁸ MVEV is now considered enzootic in the Kimberley and possibly the adjacent areas of the Northern Territory. The virus is maintained in a cycle primarily involving Cx. annulirostris and ardeid waterbirds, and variable activity occurs every year in these areas.¹⁸ Virus activity outside these enzootic areas generally follows heavy rainfall and flooding within normally arid areas of northern and central Australia, as infected waterbirds migrate across the flooded areas.^{19,20} This may explain the reappearance of MVEV encephalitis in central Australia and western NSW in 2000–2001.²¹ It now appears that low level MVEV activity may occur occasionally in NSW, and may have resulted in a locally acquired human infection in 2008.²² MVEV throughout Australia is predominantly genetically homogeneous, consistent with a single major enzottic source.^{23,24}

Clinical MVEV encephalitis cases are uncommon in Australia with an average of 2–3 cases each year since the late 1970s. The incubation period ranges from 1 day to 4 weeks, and most infections are either asymptomatic or the patient only develops a self-limiting febrile illness with or without headache. Encephalitis occurs in only 1:500–1:1000 infected individuals with a mortality rate of 20%; about half of all survivors have significant residual neurological deficits, with worse outcomes in the very young and elderly.

Infection risk depends on the degree of mosquito exposure during a period of MVEV activity. Generally, all residents and travellers are susceptible, with cases in all ages, except amongst Indigenous communities where there is regular virus activity, with infection more likely in young Indigenous children due to protective immunity in older children and adults.^{25,26}

Currently, there is neither a vaccine nor any specific antiviral therapy for MVEV. Sero-surveillance is carried out using sentinel chicken flocks in Western Australia, the Northern Territory, NSW and Victoria,²⁷ and by opportunistic mosquito sampling for virus isolation.

West Nile virus (Kunjin clade) (WNV-KUN)

WNV-KUN was first detected in northern Queensland in 1960 and is widely dispersed across tropical northern Queensland, the Northern Territory and Western Australia, being maintained in enzootic cycles similar to MVEV between *Culex* spp. mosquitoes and ardeid waterbirds. WNV-KUN activity is regularly detected in south-eastern Australia, but usually without recognised human cases. WNV-KUN is believed to have caused 11% of encephalitis cases in the 1974 Murray Valley outbreak.²⁸ During the following three decades, three encephalitis cases caused by WNV-KUN were reported (all non-fatal), while 68 MVEV encephalitis cases were confirmed. The incubation period appears similar to MVEV infection but the encephalitic illness is more benign with complete or near complete recovery.²⁹

Currently, there is neither a vaccine nor any specific antiviral therapy for WNV-KUN infection. MVEV sentinel chicken flocks are also tested for WNV-KUN infection.

Batborne viruses Hendra virus (HeV)

HeV was first described in 1994 during an outbreak of severe respiratory disease amongst racehorses and humans in Brisbane.^{30,31} A second outbreak occurred at the same time but was unrecognised for a further 13 months. A Mackay farmer, infected while assisting with an equine autopsy, suffered mild meningitis and recovered, but 13 months later relapsed with fatal encephalitis.³² There have been 12 further outbreaks;^{33,34} 11 in Queensland and one near Murwillumbah in NSW. There have been seven confirmed human HeV infections, with four deaths, Flving foxes of the genus *Pteropus* are the reservoir host,³⁵ but all human infections to date have been epidemiologically linked to horses, the major spill-over host. Horses are believed to become infected after grazing on pastures contaminated with bat urine, birthing fluids or spats (fibrous plant material remaining after mastication by bats). Humans become infected by the virus entering through cuts or grazes after exposure to equine bodily fluids, but humans are dead-end hosts and there is no evidence of human-to-human infection.

HeV is one of two members of the genus Henipavirus, the other being Nipah virus, the cause of fatal encephalitis affecting pigs and humans in Malaysia in 1999.³³ Nipah virus, like HeV, is a virus of Pteropid bats, but with pigs as the spill-over hosts. Very recent studies have indicated that pigs could also potentially act as spill-over hosts for HeV.³⁶ Human-to-human transmission with Nipah virus resulting in cases of clinical disease has been documented, with some of the cases probably being due to ingestion of bat-contaminated palm juice, whereas others may be due to other routes of infection.^{33,37} Human-to-human transmission of HeV has not been reported. Over the past decade, sero-epidemiological studies have shown that HeV and Nipah virus, or closely related viruses, are widely distributed over the range of Pteropid bats.^{33,34,38}

There is no active surveillance for HeV in Australia, in either humans or animals, and spill-over infections are uncovered when there is clinical evidence of infection in horses. Veterinarians and others likely to be exposed to infected bats or horses should take appropriate personal protection measures. It is not practical to prevent all interactions between flying foxes and horses, and no vaccines are available, although post-exposure prophylaxis is currently being investigated and shows promise.

Australian bat lyssavirus (ABLV)

ABLV was first isolated in 1996 in NSW from the brain of a black flying fox (Pteropus alecto) which was behaving strangely.³⁹ It is closely related to rabies virus,⁴⁰ but is distinguishable genetically and thus classified as lyssavirus serotype 1, genotype $7.^{34,41}$ ABLV has been found in all four species of Australian flying fox (genus Pteropus) throughout their geographic range, and in at least one species of insectivorous microbat, the yellow-bellied sheath-tailed bat (Saccolaimus flaviventris), in Queensland.^{34,42} Serological evidence of infection has also been found in a number of other genera, and the ecology and diversity of this virus is yet to be fully understood. Less than 1% of flying foxes in the wild are infected with ABLV, but this increases to as many as 15% of sick or injured flying foxes and about 3% of yellow-bellied sheath-tailed bats.⁴³ Limited studies to infect terrestrial wildlife have failed, although experimental exposure of domestic cats and dogs can produce mild signs and seroconversion but with no evidence of viral persistence.⁴⁴

ABLV has caused two human deaths in Australia. The first was a bat carer who had been scratched by a yellow-bellied sheath-tailed bat 5 weeks earlier^{45,46} and the second, a woman bitten 2 years prior by a flying fox.⁴⁷ In both patients the disease was similar to classical rabies, with non-suppurative encephalitis accompanied by hypersalivation, aggression and agitation. Currently available cell-culture derived vaccines appear efficacious in protecting against ABLV infection in exposed humans.^{48,49} Bat carers and others at risk of ABLV exposure are offered pre-exposure vaccination and those exposed are given standard preparations of vaccine and the rabies immune globulin.^{17,43} It is important that, wherever possible, the bat responsible for the potential exposure is sent for testing.

Discussion

Globally, many of the recently emerged Australian zoonotic viruses have presented with an encephalitic syndrome in humans,^{6,50} including the highly pathogenic HeV and ABLV.^{51,52} Other zoonotic viral encephalitides have appeared in new Australian regions, including JEV, MVEV and WNV-KUN.⁵³ Current Australian surveillance, which focuses on seroconversion in sentinel animals in a limited number of sentinel sites (pigs for JEV and chickens for MVEV and WNV-KUN), definitive diagnosis in reservoir hosts (culled bats that have had potential transmission contact with humans for ABLV or horses for HeV), or definitive diagnosis in humans, has the potential to miss encephalitis cases caused by notifiable conditions, and is particularly inadequate for detecting newly emerged viral encephalitides.² A recent study examining the diagnostic assessment of encephalitis in three Regional Referral Hospitals in NSW determined that only 15% of encephalitis patients were tested for flaviviruses and 0–7% were tested for specific zoonotic encephalitis viruses.⁵⁴

Conclusion

Given that viral encephalitis generally causes relatively serious illness resulting in hospitalisation,⁵⁵ the utility of hospital sentinel surveillance of adults or paediatric medicine inpatients deserves prompt investigation, as does the use of a standardised diagnostic and testing algorithm which includes viral zoonotic encephalitides. Improvements in encephalitis surveillance at the animal, human, environment interface would aid in earlier identification of known pathogens and in alerting authorities to the emergence of new pathogens or outbreaks that may require public health investigation and action.

Editor's note

During 2011 there has been a resurgence in MVE across Australian states with 14 confirmed cases notified in the National Notifiable Diseases Surveillance System, including one in NSW, and two deaths. Canadian authorities also confirmed the additional death of a Canadian tourist who was infected in the Northern Territory.^{56–59}

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One Health in NSW: coordination of human and animal health sector management of zoonoses of public health significance

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Abstract: Zoonoses of public health significance may occur in wildlife, livestock or companion animals, and may be detected by the human or animal health sectors. Of particular public health interest are foodborne, arboviral and emerging zoonoses (known/unknown, endemic/exotic). A coordinated One Health approach to the management of zoonoses in NSW uses measures including: mutually agreed intersectoral procedures for detection and response; surveillance and notification systems for defined endemic and exotic diseases; joint meetings and exercises to ensure currency of response plans; and intersectoral communication during a response. This One Health approach is effective and ensures the interests of both the human health and animal health sectors are addressed.

Zoonoses are infectious diseases that are transmissible between vertebrate animals and humans under natural conditions.¹ Zoonoses are caused by a wide variety of microorganisms and a subset of zoonotic infections may have significant public health implications that require a coordinated approach across human health and animal health sectors.

People who are exposed to animals at home, at work or elsewhere tend to be at greatest risk of zoonotic diseases. Examples of people who are especially at risk of exposure to zoonotic diseases include veterinarians and veterinary staff, wildlife officers, zoo keepers, farmers, shooters, abattoir workers, animal carers and pet owners. Because pathogens tend to have specific host species, certain infections tend to be associated with certain animal species.

This paper provides an overview of how the human and animal health sectors work collaboratively in New South Wales (NSW) to manage zoonoses. Planning for and responding to zoonotic public health threats and incidents requires an integrated, intersectoral approach that recognises the interrelationships between humans, animals and the environment, and the different interests of the sectors. This is sometimes described as the One Health approach.

Methods

Zoonotic diseases of public health significance in NSW were identified (Table 1). The arrangements for preparedness, detection, analysis and response activities across both the human and animal health sectors were compared, with particular focus on the comparative roles of NSW Health and the NSW Department of Primary Industries. Local and statewide strategies for prevention and preparedness, detection of individual clinical cases and surveillance, analysis of data, response and control were included.

Results

Management of zoonoses in NSW occurs in both the human and animal health sectors at the local and state level using the following strategies (Table 2).

General arrangements Human health sector

NSW Health, including local health districts, has the main responsibility for human health issues in NSW, including zoonotic diseases. The Centre for Health Protection within the Population Health Division oversees both communicable diseases and environmental health issues. The Communicable Diseases Branch coordinates surveillance and response activities for statewide infectious disease issues, including zoonotic diseases, and coordinates policy development.

Operationally, NSW public health units linked with local health districts detect and respond to local infectious

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Ross River virus	Endemic	¥	>				
Bovine spongiform encephalopathy/new variant Craint-feldt-labob disease	Exotic		~	7	≻	~	
Botulism	Endemic	>	>				
Brucellosis – any human infection	Endemic/exotic	- >	- >				>
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Swine influenza	Sporadic			> :	> :	> :	
Equine influenza	Exotic			Y	7	~	
Leptospirosis	Endemic	>	> 1		:		۲
Lyssavirus (NEC)	Exotic	¥	Y		۲	~	
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Listeriosis	Endemic	~	Y		:		Y
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Nipah virus infection	Exotic	:	:	> :	> :	~	:
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Plague (Yersinia pestis)	Exotic	> :	> :				:
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Severe acute respiratory syndrome	Exotic		~	:	:		
Trichinellosis	Exotic			Y	Y	~	
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DAFF: Department of Agriculture, Fisheries and Forestry. DoH: NSW Department of Health. DoHA: Department of Health and Ageing. DPI: NSW Department of Primary Industries. NAHIS: National Animal Health Information System. NCIMS: Notifiable Conditions Management System. NEC: Not elsewhere classified. NNDSS: National Notifiable Diseases Surveillance System.

Prevention and preparefuses Surveillance - International, Jurisdictional Dissecurity - quaratrite, Infection control, immunisation Surveillance - International, Internot Dissecurity - quaratrite, Infection control, environment Plans/supporting documents CONA, State of Nathoul Guidelines (SONGS) (e.g. Hendra virus Guidelines for Vereinarian Indunerad and other Immunisation - Australian Vereinarian Indunerad internor guidelines for Vereinarian Indunerad and other Immunisation - Australian Vereinarian Indunerad internor guidelines for Vereinarian Indunerad and other Immunisation - Australian Vereinarian Indunerad internor Justralian Pathonand Indunerad - Australian Vereinarian Indunerad Indunerad - Australian Vereinarian Indunerad - Australian Vereinarian Indunerad NSW VERV NSW - Australian Indunerad - Australian Vereinarian Indunerad - Australian Vereinarian Indunerad NSW NSW - Australian Indunerad - Australian Vereinarian Indunerad - Australian Vereinarian Indunerad - Au	je Actic	on	Human health	Animal health
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disease issues of public health significance and forge relationships with local stakeholders; for zoonoses, this includes those in the animal health sector.

Animal health sector

The animal health sector includes wildlife, livestock and companion animals. Overseeing the health of livestock and companion animals falls under the jurisdiction of the Department of Primary Industries (DPI). Although primarily concerned with minimising any adverse impact of disease on productivity and trade, the DPI is also interested in ensuring that human health is not compromised by zoonotic diseases. The DPI works closely with Livestock Health and Pest Authorities who employ veterinarians to undertake disease control work predominately with livestock.

District Veterinarians with Livestock Health and Pest Authorities and Veterinary Officers within the DPI detect and respond to local incidents of infectious disease, including zoonotic diseases of public health significance. Regional Veterinary Officers within the DPI forge relationships and undertake most of the contact with local stakeholders, such as the local public health unit.

The health of wildlife and zoo animals falls under the jurisdiction of the NSW Office of Environment and Heritage. However, most wildlife diseases are reported through the Australian Wildlife Health Network which maintains a register of wildlife diseases and provides coordination and guidance on these diseases. The Australian Registry of Wildlife Health laboratory services include investigation of zoonoses in wildlife. The DPI coordinates significant diseases in wildlife and assists with diagnostic and field investigations.

Other sectors

Human health and safety in the workplace is the primary concern of the WorkCover Authority of NSW. WorkCover NSW is part of the Compensation Authorities Staff Division and sits within the Treasury portfolio.

The NSW Food Authority provides the regulatory framework for industry to produce safe foods and reports to the NSW Minister for Primary Industries.

Prevention and preparedness

Mutually agreed policies and procedures for managing zoonoses of public health significance are in place in both the national and jurisdictional human and animal health sectors. These are developed and maintained for currency through intersectoral agency links with contributions from other professional organisations, research facilities and universities, such as those involved with human and animal health, microbiology, epidemiology, infection control, agriculture, environment and food manufacture. Plans for managing human and animal health emergencies, including zoonoses, are supplemented by disease-specific plans, policies, guidelines and factsheets (Table 2) which are targeted to appropriate audiences (e.g. general public, human/animal health professionals, other animal workers and carers). An important part of the management of zoonoses is the prevention of transmission, and these plans and advice sheets include recommendations for measures such as infection control and biosecurity, as well as prophylaxis through immunisation.

The national and NSW plans are tested in periodic intersectoral exercises, which in recent years have examined the response to avian influenza (*Exercise Eleusis* and *Exercise Hippolytus*) and pandemic influenza (*Exercise Cumpston*).^{2–4} They have also been tested in NSW in recent emergencies including equine influenza, pandemic (H1N1) 2009 influenza in humans and swine, and a suspected equine Hendra virus infection investigation.

Detection

Human health sector

Zoonotic diseases in humans are diagnosed by clinicians, and selected zoonotic diseases are notifiable by clinicians and laboratories under the NSW *Public Health Act 1991*. Public health units enter data into a statewide database, the Notifiable Conditions Information Management System (NCIMS) and these data are analysed for the local area, the state and nationally. Data are reported daily to the Australian Government Department of Health and Ageing through the National Notifiable Diseases Surveillance System. In addition, the Public Health Real-time Emergency Department Syndromic Surveillance system is occasionally used to provide complementary surveillance data arising from attendances at selected emergency departments across NSW.

Public health units also report any significant zoonotic event to the Communicable Diseases Branch when it may be of statewide significance or if the incident may have ramifications for other sectors. The Communicable Diseases Branch maintains open communication lines with counterparts in the DPI, and nationally.

In addition, public health units maintain good working relationships with DPI Regional Veterinary Officers; these officers are often the source of information about local zoonotic incidents that may have health consequences for humans.

Animal health sector

Zoonotic diseases in animals may be detected by agricultural or other animal workers, and diagnosed by Livestock Health and Pest Authorities' District Veterinarians, DPI Veterinary Officers, veterinarians in private practice, industry or education, or through government, private and industry-specific laboratories.

National and jurisdictional surveillance and notification systems are used by the DPI to monitor the occurrence of defined endemic and exotic infectious diseases, including zoonoses, and to comply with international reporting requirements.⁵ Surveillance in the animal health sector is also used widely to demonstrate freedom from defined diseases for export and interstate trade purposes.

Nationally, notifiable diseases are reported quarterly by the DPI to the Australian Government Department of Agriculture, Fisheries and Forestry through the National Animal Health Information System administered by Animal Health Australia. Some additional diseases are only reported within NSW to the DPI. Some notifiable diseases are also defined as emergency animal diseases with a specific response prescribed in AUSVETPLAN.^{6,7} Syndromic surveillance is not currently available in the animal health sector, although a national pilot is in progress.

Targeted surveillance programs

Targeted surveillance is also used in both sectors in NSW (e.g. by human health for arboviruses and waterborne diseases, and by animal health for arboviruses through the National Arbovirus Monitoring Program, and for avian influenza in wild birds).

Analysis

Human health sector

Analysis of routinely collected data on human zoonotic notifications occurs regularly at local, statewide and national levels. Single case reports of selected notifiable zoonoses prompt individual risk assessment which may involve public health unit staff interviewing the case or contacts to ascertain possible exposures, site visits, workplace assessment, enhanced surveillance and further laboratory characterisation of the organism. The outbreak management function of NCIMS facilitates additional targeted and enhanced surveillance where necessary. Geomapping capability in NCIMS, while currently limited is being developed and will be a useful epidemiological tool.

Where a risk assessment is complex or involves several local health districts, the Communicable Diseases Branch offers advice and coordinates the risk assessment.

Animal health sector

The outbreak management system used by the DPI, the Biosecurity Surveillance, Incident, Response and Tracing (BioSIRT) system, is a relatively new surveillance system with geomapping capability that is being introduced for routine use in most states to record on-farm animal health events. BioSIRT is currently being used in NSW for emergency situations and there are plans to link it with the Wildlife Health Information System (eWHIS), the national real-time reporting system used for wildlife incidents. BioSIRT will also link with other databases including laboratory information management systems for uploading test results (this will be facilitated through the Sample Tracking and Reporting System project), and the NSW Property Identification Codes database which can provide information about a property's ownership, location and livestock.

Although these surveillance and notification systems are primarily used to record incidents of defined notifiable diseases, eWHIS in the wildlife animal health sector may indicate the occurrence of known or unknown emerging infectious diseases, including zoonoses. The national Wildlife Event Investigations Team may be convened by the Australian Chief Veterinary Officer to support the investigation of emerging infectious diseases in wildlife, including the potential for zoonotic disease.

Response

A zoonotic disease may be detected in the human or animal health sector. Table 3 describes examples of some recent zoonotic disease incidents not elsewhere described in this issue. Timely communication between the sectors during a response ensures coordinated risk assessment and effective management and that the different interests of each sector are addressed.

Human health sector

Management of notifiable diseases, including zoonoses, by public health units follows disease-specific protocols found in the *NSW Notifiable Diseases Manual*.⁸ For some notifications, the DPI is notified as part of the routine response. Depending on the nature of the zoonosis, the public health intervention may be to disseminate information to the case and others who may have been exposed, or to recommend or arrange treatment or prophylaxis for cases or contacts.

In recent times, the Communicable Diseases Network Australia has recognised the need to harmonise public health responses across all Australian states and territories and this has led to the development of the *Series of National Guidelines* (SoNGs) for selected diseases. Currently, SoNGs are being developed for Hendra virus infections and for rabies/Australian bat lyssavirus infections and exposures to animals potentially infected with rabies/Australian bat lyssavirus.

Animal health sector

For notifiable diseases the DPI response follows defined national and jurisdictional procedures, and for zoonoses includes liaison with the human health sector.

Incident type	Detection	Response
Foodborne	Human illness/laboratory detection (e.g. salmonellosis, listeriosis, VTEC)	NSW Health investigation includes notifying the NSW Food Authority and OzFoodNet. If required, there may also be a response by animal health authorities, which may include examining animal feed sources.
	Abattoir detection of Cysticercus bovis	C. bovis (the intermediate stage of <i>Taenia saginata</i>) was recently detected in cattle carcasses in an abattoir, and is now a notifiable disease when detected in cattle. Discussions between the DPI, the NSW Department of Health, the NSW Food Authority and the Australian Quarantine and Inspection Service ensured that all potentially infected cattle from the source property were inspected, carcasses dealt with appropriately, and all animals traced using the National Livestock Identification System.
Wildlife – known zoonosis	Psittacosis – detected first in humans or birds	A large outbreak of psittacosis occurred in the Blue Mountains in NSW in 2002. Prior to the outbreak, residents had reported an increase in the number of dead wild birds in the subsequently identified as a significant risk factor in a case control study.
	Australian bat lyssavirus – sick or dead bats, laboratory confirmation	There have now been approximately 43 confirmed cases of Australian bat lyssavirus in bats in NSW, but no cases in humans, although two human fatalities have occurred in Queensland. Advice is provided to all bat carers and people involved with bats regarding the need for vaccination, and caution and appropriate personal protective equipment when handling sick or dead bats.
Wildlife – emerging infectious disease	Magpie deaths in NSW	In 2006, deaths occurred in magpies and some other wild bird species in the Sydney area. This coincided with a worldwide alert for West Nile virus, and was extensively investigated, but no cause was found and a zoonosis was not suspected. As emerging infectious diseases are likely to arise in wildlife, investigations follow a defined pathway in NSW: a wildlife incident which exceeds an established trigger level is reported by, for example, the Office of Environment and Heritage and/or the Australian Wildlife Health Network to the DPI who notify the NSW Department of Health; the NSW Chief Veterinary Officer may declare an alert, convene a Steering Committee which develops an Emergency Animal Disease Response Protocol, and may also request that the Wildlife Event Investigations Team be convened.
Livestock – emergency animal disease	Anthrax – detected first as sudden animal death, with laboratory confirmation, or occasionally in humans as cutaneous anthrax	Human cases of anthrax are notified to the DPI. Animal cases are notified to NSW Health. Anthrax is an emergency animal disease, so the animal health response is according to animal health policy. NSW has approximately five anthrax incidents in livestock per year in a defined area of NSW. All humans involved with these cases are given information about the risks of human infection. There have been two case reports of cutaneous anthrax in sheep farmers working in the NSW anthrax belt in recent years. Both cases were treated effectively. The detection of human anthrax prompted a joint risk assessment between NSW Health and the DPI.
Livestock – non-emergency	<i>Brucella suis</i> – laboratory detection of human cases	<i>Brucella suis</i> has been found in feral pigs in Queensland however whilst suspected it has never been found in feral pigs in NSW. It has been found in feral pigs in the area.
animal disease	Leptospirosis – clinical/ laboratory detection in humans or animals	Leptospirosis infection in humans is notifiable under the NSW <i>Public Health Act 1991</i> . Most cases occur in people with occupational exposures to animals. Occasionally cases occur in people who have been exposed to flood waters or mud that have been contaminated with the urine of infected animals. Urine from infected dairy cows can also infect farm workers, and vaccination of dairy cattle can help reduce the risk of human infection.
Companion animals	Q fever in cats – clinical/ laboratory detection in humans	Several cases of Q fever have been reported in veterinarians with exposures to parturient cats. There is a need to raise awareness amongst the veterinary community about use of personal protective equipment and vaccination to prevent infection.
	Hydatid surveys of dogs	Periodic surveys indicate that hydatids are not uncommon in some dog populations. Information from these studies is shared with NSW Health to allow for a better understanding of the interaction that is occurring between dogs and people in this area.
DPI: NSW Departm	nent of Primary Industries. VTEC: verot	oxin-producing <i>Escherichia coli</i> infections.

The response to emergency animal diseases may include convening a specific Consultative Committee on Emergency Animal Disease with a representative from the human health sector.

Discussion

The collaborative intersectoral approach to the management of zoonotic diseases in NSW ensures a timely and effective response. Established relationships between key officers in the different sectors are a major factor in ensuring effective communication. Regular joint meetings help ensure that this occurs, and that each agency understands the needs and constraints on the other agencies.

Management of endemic and exotic zoonoses continues to utilise significant resources in both the human and animal health sectors in NSW; this is particularly so for the investigation of foodborne diseases. Recent exotic zoonoses responses have included the provision of post-exposure prophylaxis against rabies for a number of people returning from Bali following dog bites, and the DPI involvement with rabies control projects in Bali. A positive outcome of collaborative management has been the implementation of improved infection control and biosecurity procedures for veterinarians and others associated with animal care and handling. For example, the occurrence of Hendra virus in horses and the fact that the symptoms in horses are not specific has resulted in more horse practitioners using personal protective equipment. It is also now recognised by veterinarians that Q fever is not just a disease of farm animals and that cases have been recorded in companion animals. This has necessitated the need for routine personal protective equipment/infection control use in a wider range of situations.

The following offer the potential to improve zoonotic disease management:

- The introduction of BioSIRT could potentially enable the collation of real-time reporting in a single national database which will be particularly useful for crossborder incidents.
- Currently, human and animal health surveillance and laboratory data are held within each sector, but data regarding zoonotic incidents could be shared (e.g. through automated intersectoral real-time alerts).
- Due to the different interests of each sector in zoonoses, and variable regional incidence, zoonosis notification is inconsistent between and within the sectors, and could be aligned to ensure timely and effective management.
- Arbovirus monitoring programs are conducted in mosquitoes and animals for each sector in NSW, but are targeted for diseases specific to that sector. There is potential for greater collaboration (e.g. sharing of specimens to look for diseases of interest to the other sector).

Conclusion

A coordinated One Health approach by the human and animal health sectors in NSW provides effective management of zoonoses of public health significance, and ensures the different interests of each sector are addressed. National health reforms and consequent reorganisation of the NSW Health system is likely to change some of the arrangements for delivering public health services in the state. It will be important for both sectors to maintain effective working relationships as the organisational structures within the health system evolve. Particular challenges include detection and management of emerging zoonoses, especially in wildlife, and the changing humananimal interface with increasing urbanisation.

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Discovering novel zoonotic viruses

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Abstract: From the emergence of Hendra virus and Menangle virus in Australia to the global pandemics of severe acute respiratory syndrome and influenza viruses (both H5N1 and H1N1), there has been a surge of zoonotic virus outbreaks in the last two decades. Although the drivers for virus emergence remain poorly understood, the rate of discovery of new viruses is accelerating. This is due to a combination of true emergence of new pathogens and the advance of new technologies making rapid detection and characterisation possible. While molecular approaches will continue to lead the way in virus discovery, other technological platforms are required to increase the chance of success. The lessons learnt in the last 20 years confirm that the One Health approach, involving inclusive collaborations between physicians, veterinarians and other health and environmental professionals, will be the key to combating future zoonotic disease outbreaks.

Globalisation of travel and trade, changes in agricultural practice (e.g. intensive farming and land use) and climate change are some of the drivers responsible for the emergence of novel pathogens affecting humans and livestock.¹ Early detection and/or identification of the causative agent plays a pivotal role in minimising the impact of any infectious disease outbreak, especially for those caused by previously unknown pathogens. This review describes some of the recent zoonotic viral disease outbreaks both in Australia and abroad and focuses on the approaches and impact of virus discovery during disease investigation. It also summarises current virus discovery strategies and future trends in this area. While this review focuses on the importance of molecular techniques in virus discovery, it should be emphasised that virus isolation and serological investigation is equally important in the investigation of diseases caused by previously unknown viruses.

A brief review of virus discovery with or without associated diseases Hendra virus

In September 1994, a mysterious disease outbreak, with primarily respiratory presentation, occurred in a horse stable in Hendra, Brisbane. It claimed the life of the horse trainer and 13 of his high value horses. A stable hand on the property also suffered a severe respiratory illness, but survived the infection. Three days after receiving horse specimens at the CSIRO Australian Animal Health Laboratory, cytopathic effect was observed in cultures of Vero cells inoculated with lung homogenates from deceased horses. Similar results were observed with human specimens a few days later. Electron microscopic analysis indicated the presence of a viral agent with a morphology resembling paramyxovirus. Further polymerase chain reaction (PCR) analysis using degenerate primers demonstrated a partial sequence of the matrix protein gene most similar to the cognate genes of morbilliviruses in the family Paramyxoviridae. A challenge experiment conducted under stringent biocontainment conditions at the CSIRO Australian Animal Health Laboratory demonstrated that the isolated virus was able to kill horses 4-5 days after infection and a similar clinical presentation, and the virus was re-isolated from infected animals, fulfilling all four requirements of the original Koch's postulate. Hendra virus was therefore the causative agent of the zoonotic viral disease outbreak.² About a year later it was determined that flying foxes are the natural reservoir of this novel virus.³ Since 1994, there have been 14 recorded Hendra virus outbreaks, together responsible for the death of more than 40 horses and four humans.

Nipah virus

From late 1998 to early 1999 in peninsular Malaysia, an unusual surge of encephalitic disease was detected in people dealing with live pigs. The incidents coincided with outbreaks of respiratory disease in pigs. A novel virus was isolated from human patients, which was closely related to the Hendra virus.⁴ It was named Nipah virus after the name of the village of the index case, and later proved to be the causative agent of both the human and pig disease. It is now known that different strains of Nipah virus are widely distributed in bats from Indonesia, Malaysia, Thailand, India, Bangladesh, Madagascar and west African nations.⁵ Since the Malaysian outbreaks, Nipah virus has emerged almost annually in Bangladesh. In total, the virus has claimed the lives of more than 250 humans with mortality rates ranging from 40 to 100%.

To confirm that Nipah virus also uses bats as its natural reservoir, field surveillance studies were carried out to detect virus in bat urine on Tioman Island in Malaysia. In addition to the isolation of Nipah virus, two new viruses were discovered: Tioman virus (a paramyxovirus) and Pulau virus (a reovirus). The significance of these 'accidental' discoveries will be explored later in this paper.

Menangle virus

Menangle virus was isolated in 1997 from stillborn piglets with deformities at a large commercial piggery in New South Wales.⁶ The virus was found to be responsible for a single outbreak of reproductive disease, causing reduced farrowing rate and stillbirths with deformities. Serum samples from two humans, who were in close contact with infected pigs and suffered a flu-like illness, were found to have high levels of convalescent neutralising antibodies to Menangle virus. Extensive serological testing showed no evidence of any alternative cause. It is believed therefore that the human illness was caused by Menangle virus, demonstrating a zoonotic potential that is yet to be fully characterised. Although the exact origin of the virus was not known at the time of the outbreak, serological studies indicated the presence of neutralising antibodies in bats. The bat origin was further corroborated by comparative genome sequencing, which indicated that the Menangle virus is highly related to the batborne Tioman virus identified in Malaysia.7

SARS virus

The severe acute respiratory syndrome (SARS) coronavirus was responsible for the first serious and widespread zoonotic disease outbreak of the 21st century, having a huge global impact on health, travel and economy.⁸ The great global impact of the SARS outbreak was in some ways intensified by the delay in identifying the causative agent of the disease. From November 2002, a mysterious disease known as 'atypical pneumonia' was rapidly spreading in southern China, exacerbated by several intensive nosocomial transmissions. It took almost 6 months before a novel coronavirus was isolated by the joint effort of the WHO SARS Collaborative Network.⁸ Within a few weeks of virus identification, the whole genome sequence was determined. This in turn facilitated the development and distribution of molecular and serological tests which played an essential role in the eventual control of the global pandemic. It is important to note that the global outbreak was under control within 3 months of the discovery of the causative agent. The genomic sequence information also played an important role in the identification of civets as the main intermediate host responsible for transmitting the virus to humans and bats as a potential natural reservoir of the SARS virus and other highly related coronaviruses.^{8,9}

Melaka virus

Reoviruses (respiratory enteric orphan viruses) were first discovered in the 1950s and named orphan viruses due to

the failure to associate them with any known human disease. As mentioned previously, Pulau virus was isolated during a search for Nipah virus in bat urine samples, which is closely related to Nelson Bay virus isolated from Australian bats in the early 1970s.¹⁰ The disease-causing potential of neither virus was known. In 2006, during an investigation of a small cluster of patients in a Malaysian family suffering from severe flu-like symptoms, a virus was isolated and named Melaka virus. Electron microscopic examination revealed a reovirus-like structure. Using the sequence information and reagents developed for Pulau and Nelson Bay viruses, rapid confirmation of Melaka virus as a zoonotic reovirus was achieved within 2 weeks. Melaka virus represents the first reovirus known to cause severe acute disease in humans. Since then, at least two additional bat reoviruses have jumped species to infect humans and cause respiratory disease.¹¹

A new arenavirus

In 2008, three Australian recipients of a visceral organ transplant from a single donor died of a febrile illness 4–6 weeks after transplantation. Due to the nature of the disease, involvement of an infectious agent was suspected. However, bacterial and viral culture revealed no candidate pathogens. PCR assays for most known human viral and bacterial pathogens, and pan-viral and pan-microbial oligonucleotide microarray analyses also failed to identify any potential agent. Eventually, the causative agent was identified by unbiased high-throughput sequencing.12 Out of 103 632 sequencing reads obtained from total RNA extracted from different organ tissues of two patients, 14 sequences were shown to be related to Old World arenaviruses, with lymphocytic choriomeningitis virus being the most related. Subsequent virus isolation from frozen kidney samples was successful. While not all of Koch's postulate conditions were fulfilled, the fact that all four patients (donor and three recipients) had virusspecific antibodies and all recipients had viral RNA in their circulation was considered compelling evidence that the arenavirus was the cause.¹²

Reston Ebola virus

Ebola viruses are members of the family *Filoviridae* associated with acute fatal haemorrhagic diseases of humans and non-human primates. Among the five known species of Ebola viruses, Reston Ebola virus is the only one thus far not associated with disease in humans although nonsymptomatic infection has been observed in humans in the United States and Philippines. Recently it has been shown that African fruit bats are the likely natural host of the African species of Ebola virus. It is not known whether this is also the case for Reston Ebola virus, so far only detected in non-human primates in the Philippines. During an investigation for respiratory and reproductive disease syndrome in domestic pigs in the Philippines, multiple cell

Technology	Principle	Applications	Major advantage	Major disadvantage
Species-specific PCR	PCR amplification of any specific region of a known virus sequence	Rapid diagnosis and investigation of new host range of a known virus	Low cost, high specificity and sensitivity, easy to operate	Not suitable for virus variants or new viruses
Group- or family-specific PCR	PCR amplification of a highly conserved region of a group of viruses, usually involving the use of degenerate primers	Surveillance and discovery of related viruses	Lost cost and easy to operate	Not as sensitive or specific as virus-specific PCR, not suitable for new viruses
Multiplex PCR-MS assays	Simultaneous detection of multiple targets using multiplex PCR followed by mass determination of amplified PCR products and database matching	Surveillance and discovery of related viruses	Multiplicity and sensitivity	High cost and requirement for specific capital equipment that few laboratories can afford
Microarray	Detection of viral nucleic acid through hybridization with probes designed using conserved sequences of all known viruses on a microarray chip	Discovery of any new viruses which share sufficient sequence identity with any of the known viruses	No prior knowledge is required and can be applied to viruses of different origin (e.g. human, animal, plant or insect viruses)	lssues with sensitivity and specificity when used to probe samples from tissue origin
Subtractive hybridization	Removal of host nucleic acid sequences by hybridization before sequencing the enriched random nucleic acid pool	Discovery of any new viruses which share minimal sequence identity with any of the known viruses	Highly sensitive and specific	Very time consuming and requires highly skilled operators
High-throughput sequencing	Identification of new viruses by bioinformatic process to match random sequence reads with database of all known viral sequences	Discovery of any new viruses which share minimal sequence identity with any of the known viruses	Unbiased, highly sensitive and specific and can be used on samples of any origin	Substantially more expensive than other methods and requirement for highly trained operators
PCR: polymerase chain reaction. PCR-MS: polymerase chain reaction m	ass spectroscopy.			

Table 1. Comparison of current molecular technologies used in virus discovery

lines were used for virus isolation. In addition to the isolation of the porcine reproductive and respiratory syndrome virus, which was the main suspected causative agent, cytopathic effect was unexpectedly detected in Vero cells which are nonpermissive to the porcine virus. To investigate the identity of this virus, viral nucleic acid materials were tested using a pan-viral microarray. It was revealed that this unknown agent was the Reston Ebola virus.¹³ This is a highly significant discovery, widening the host range of Ebola virus to domestic pigs. Of the 141 individuals who worked on pig farms or with swine products, six had Ebola-specific antibodies, confirming pig-to-human transmission.¹³

Different pathways to virus discovery

The examples of virus discovery reviewed in this paper were selected to highlight two points: (1) most are associated with bats; and (2) virus discovery goes beyond finding previously unknown viruses: it is equally important to discover related viruses or new hosts of known viruses.

Although most of the discoveries of new viruses were made as a result of disease investigation, there are also examples where orphan viruses were 'accidentally' discovered, and later proved to be highly useful in the investigation of disease outbreaks caused by viruses closely related to them. Faced with the rapid technology advances in virus discovery, it is expected that more and more orphan viruses will be discovered. The appropriate sharing of orphan virus reagents and information in the international community will be crucial for effective future responses to infectious disease caused by novel viruses.

It should also be noted that the causal relationship between a virus and disease may be established by modern technologies without fulfilling all four conditions specified in the original Koch's postulates.¹⁴ This was best illustrated by the description of the identification of a new arenavirus as the causative agent of a disease that resulted in the deaths of three transplant patients from the same donor.¹²

Increasing importance of molecular approaches to virus discovery

It is evident from all the cases reviewed in this paper that molecular techniques played a pivotal role in the discovery of new viruses. The various molecular techniques currently being used for virus discovery are summarised in Table 1. While virus-specific PCR is a powerful tool for diagnosis and investigation of new host ranges of known viruses, its usefulness in the discovery of new viruses is rapidly being superseded by more advanced molecular technologies. Multiplex PCR-MS (mass spectroscopy) assays such as the Ibis T500 biosensor system¹⁵ and the MassTag PCR¹⁶ are extremely powerful tools for investigating multiple microbe targets,¹⁷ however very few laboratories can afford the high cost equipment required. Microarrays containing oligonucleotide probes to all known viruses were at one stage considered the future of virus discovery,^{18,19} but their performance has not met initial expectations due to issues with sensitivity and specificity when tissue samples are used. Currently, the most powerful and promising method of rapid agent identification is the unbiased highthroughput sequencing strategy.^{12,17} Although currently expensive, its application is expected to increase and with this the cost will decrease. Also, consideration of its speed (within days) and definitive nature will likely outweigh the cost, especially during the investigation of emergency disease outbreaks. The success rate of virus discovery in raw tissue samples can be increased by combining subtractive cDNA hybridization⁷ and high-throughput sequencing.

Conclusion

The most advanced molecular tools described in this paper are available in only a small number of specialised laboratories around the world. Their effective application is therefore dependent on close international collaboration and networks involving both human and animal health professionals, and laboratories in both developed and developing nations. Technology advance in other areas will also play a role in shaping the future of virus discovery; these include the development of more efficient sequence data management and bioinformatics tools, the development of specialised cell lines to increase the chance of successful isolation of live viruses,²⁰ and the development of high density protein or peptide arrays for serological examination of antibodies cross-reactive with highly conserved epitopes of all known viral proteins.¹⁷

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Hendra virus: what do we know?

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Abstract: Hendra virus infection is an emerging infectious disease that is not well understood. Most cases of Hendra virus infection have occurred in Queensland, with one case in a horse in NSW. Hendra virus infection has a high mortality rate in horses and humans and as cases could occur anywhere in Australia it is important to be ready for prompt action should an outbreak occur in NSW. This paper: reviews the current knowledge on Hendra virus infection including methods for preventing the disease; explains the animal health and human health response for an outbreak within NSW; and discusses possible future avenues for post-exposure prophylaxis and prevention by vaccination.

Hendra virus infection is an emerging infectious disease in horses and humans and, due to its high mortality rate, is attracting extensive media and public interest.

Hendra virus was first described in September 1994 during an outbreak in Hendra, Brisbane.¹ This outbreak involved 18 horses and two humans (a horse trainer and a stable hand). One person and 14 horses died from what was a mystery disease. A novel equine virus belonging to the family Paramyxoviridae was isolated;² first named equine morbillivirus, the novel virus was later renamed Hendra virus.³

In August 1994 at Mackay in north Queensland, a person caring for two ill horses and then assisting in their autopsies developed aseptic meningitis.⁴ He recovered fully but developed severe encephalitis 13 months later and died. Retrospectively he and the horses were found to have been

infected with Hendra virus. There were no known links between the two outbreaks.

This paper reviews the existing knowledge about the virus, outlines the planned outbreak response in NSW, and discusses possible future avenues for post-exposure prophylaxis and prevention by vaccination.

Methods

A literature review was conducted using Ovid Medline and Google Scholar. The search terms used were 'Hendra', 'equine morbillivirus', 'paramyxoviridae' and 'horse'. Article abstracts were reviewed and the articles which met the selection criteria (English-language, Australian or international studies, peer-reviewed empirical or descriptive literature, published since 1994) were retrieved. The reference lists of these articles were searched for further appropriate articles which were located using Ovid Medline.

Results of literature review

Outbreaks of disease

Fourteen outbreaks of Hendra virus infection have occurred to March 2011: 13 in Queensland and one in Murwillumbah, northern NSW. Five of these outbreaks involved humans with four deaths among a total of seven human cases.^{1,4–6}

Australian Flying-foxes

All four species of Australian Flying-foxes (*Pteropus* spp., also called fruit bats) have been found to have serological evidence of previous exposure to Hendra virus. The virus was also detected in uterine fluid and foetal tissue, confirming Flying-foxes as the natural host.⁷

Australian Flying-foxes live along much of the Australian coast (Figure 1). Hendra virus infection could theoretically occur anywhere in Australia where there are Flying-foxes.⁸ Frequent horse movements between states and territories mean that cases could also occur outside the geographic distribution of the Flying-fox populations.

Transmission between species

It is not yet clear how the virus spills over from Flyingfoxes to horses. Research suggests the most likely route is ingestion by horses of pasture or feed contaminated with the urine, faeces, saliva or birthing products from infected Flying-foxes.^{9,10} The risk of transmission to horses was found to be increased during Flying-fox reproductive periods and at times when the colonies were undergoing nutritional stress.⁹ Spill-over to horses seems to be a rare



Figure 1. Distribution of four species of Flying-foxes in Australia.

Source: Adapted from Hall and Richards (2000) by HE Field (2004). The ecology of Hendra virus and Australia bat lyssavirus (thesis).

event; over 2000 horses were tested in Queensland in 1995 after the first two outbreaks of Hendra virus, and none had serological evidence of previous infection.¹¹

Transmission of Hendra virus between horses appears to be more likely in horses kept in close proximity in stables; however, companion horses in paddocks have also been infected on three occasions.¹⁰ Hendra virus may survive on fomites for short periods of time, assisting spread between horses. Further, infected horses can excrete viral RNA through nasal discharge prior to the onset of clinical signs.¹²

Extensive serological testing of people in contact with known infected horses and humans showed negative results, indicating that the virus is not easily transmitted to humans.¹³ Direct physical contact with the secretions or body fluids (such as nasal discharge or blood) from an infected or dead horse appears to be necessary.

To date, there is no evidence of human-to-human, humanto-horse or Flying-fox-to-human¹⁴ transmission of Hendra virus. Other species do not seem to be affected, however, experimentally, cats, guinea pigs and pigs can be infected.^{15,16}

Clinical features and management Horses

Infection in horses usually causes acute onset of respiratory and/or neurological signs, but signs can be variable. The first signs include fever, tachycardia, discomfort, weight shifting and depression (lethargy, unresponsiveness). There may be laboured breathing and frothy nasal discharge. The rapid deterioration of the horse's condition is considered an important sign in determining the likelihood of Hendra virus infection. Most cases are fatal,¹⁰ with a mortality rate greater than 70%.¹⁷ Horses are considered potentially infectious from 72 hours prior to the onset of disease until their death and the safe disposal of their carcass.¹⁰

Humans

Hendra virus disease in humans is characterised by influenza-like illness, which can progress to severe pneumonia and death, or encephalitis including symptoms such as headache, high fever and drowsiness.¹⁸ Further, Hendra virus can lead to encephalitis following a symptom-free period after an initial illness.^{4,19} The incubation period has been estimated at 5–21 days and the human case fatality rate is over 50%.¹⁸ Current treatment for Hendra virus is supportive and includes intravenous therapy and mechanical ventilation. Antiviral therapy has not been effective.

Laboratory testing

In acute cases of disease, Hendra virus genome is readily detected by quantitative real-time reverse transcriptase polymerase chain reaction (qRT-PCR) assays of blood or urine samples, nasal or oropharyngeal swabs or tissue samples collected at post-mortem. However, samples taken very early during the incubation period may test negative by qRT-PCR and it may be necessary to repeat the sampling to exclude transmission. Hendra virus qRT-PCR testing is available: in NSW for horses at the Elizabeth MacArthur Agricultural Institute (NSW Department of Primary Industries); in Victoria for horses and humans at the Australian Animal Health Laboratory in Geelong (Commonwealth Scientific and Industrial Research Organisation) and; in Queensland for humans at Queensland Health Forensic and Scientific Services.

Serological tests such as an indirect enzyme-linked immunosorbent assay (ELISA) are methods for screening sera of humans and horses for the presence of antibodies to Hendra virus, and a virus neutralisation test may be used for antibody detection in any species. The diagnostic sensitivity of the ELISA is not well established. ELISA testing for horses is available at the Elizabeth MacArthur Agricultural Institute and the Australian Animal Health Laboratory for both horses and humans.

In order to exclude Hendra virus infection in humans, qRT-PCR is performed for symptomatic contacts. For asymptomatic contacts serological testing is performed at baseline and at 3 and 6 weeks after last exposure (earlier if symptomatic). Results from initial testing are usually available within 24–48 hours.

Prevention of infection

Infection of horses can be prevented by minimising contact with Flying-foxes and their excretions.^{17,19} Feed and water troughs should be placed under cover and away from trees where Flying-foxes might feed or roost and horse feed that might attract them (such as apples, carrots or anything sweet) should be avoided. As loss of habitat contributes to nutritional stress of Flying-foxes, removal of fruit trees on horse paddocks is not recommended;⁹ however access beneath trees while flowering and fruiting should be prevented.

Flying-foxes are a protected species so culling is inappropriate and is unlikely to be a feasible or effective prevention strategy.^{9,20} Habitat loss and alteration, roost disturbance, urbanisation and being hunted stress Flying-fox colonies, which may magnify the problem.⁹

To prevent infection in humans it is important to control viral spread from diseased horses, including horses that are incubating Hendra virus but not yet showing clinical signs. People most at risk include horse owners, veterinary personnel, horse dentists, farriers and any other persons in close contact with horses. The routine use of personal protective equipment by horse health workers handling/ contacting horses that may have been exposed to fluids from Flying-foxes will minimise the risk of exposure. Horse handlers should always apply general good hygiene practices such as covering cuts and abrasions, especially on arms and hands, and hand washing after handling a horse.¹⁷

When examining ill horses, an initial risk assessment should be conducted for the likelihood of Hendra virus to avoid unnecessary exposure and to instigate appropriate infection control procedures as described in *Guidelines for veterinarians handling potential Hendra virus infection in horses*.¹⁰

The outbreak response in NSW

Hendra virus infection in horses is a notifiable disease in NSW.¹⁷ The Department of Primary Industries notifies the NSW Department of Health of any highly suspect or confirmed cases. Hendra virus infection in humans is currently not notifiable in NSW.

Animal health response

When Hendra virus infection is suspected in a horse, a Livestock Health and Pest Authority or Department of Primary Industries inspector must be notified. An experienced veterinary officer conducts a risk assessment and classifies the case according to the likelihood of Hendra virus:

- Not/Unlikely priority green
- Possible priority amber
- Likely priority red.

All priority amber and red cases are promptly investigated. The horse should be isolated and handling minimised. If the horse is deceased, post-mortem examination is not recommended due to the high risk of viral exposure but, as a minimum, blood and nasal swabs should be collected. The Department of Primary Industries provides advice on the dispatch of samples. Horses shown to have been infected but surviving the infection are euthanased as they may pose an ongoing risk to humans. The property where the horse case/s is/are located is quarantined and other properties that may require risk assessment and quarantine are identified.

Public health response

The public health response involves close collaboration of the NSW Department of Health with the local health services where the horse case has occurred. The response follows the Hendra Virus National Guidelines for Public Health Units.²¹ These Guidelines were developed by public health and veterinary experts in Australia, including people with direct experience in the management of Hendra outbreaks. An outbreak control team undertakes a prompt epidemiological investigation to identify all persons at risk of Hendra virus infection and to minimise any further exposure. The infection risk will be assessed for all people who may have been exposed to infected horses or people; in some cases this can be a large number.⁵ For all people at risk, information is provided and testing is arranged on a case by case basis. If possible, infectious disease specialists should be involved in patient management. Close follow up of all people tested is important and may be managed by local general practitioners.

Hendra virus investigations can generate intense media interest and may evoke fear amongst the public. Open and transparent communication is therefore important. An experienced spokesperson should be nominated and all enquiries referred to them. Community meetings with public health professionals and animal health specialists may be necessary to inform the public on risks and outbreak management.

Rural areas

Hendra virus infection may be more likely in rural and peri-urban areas due to the greater prevalence of both Flying-foxes and horses. Further, the larger geographical distances and smaller social distances²² mean that people are often closely connected locally but are far from services. A collaborative approach across the public health network will be needed to implement the required response.

Future treatment and vaccination

There are presently no licensed therapeutics available to treat infection caused by Hendra virus. However, a neutralising human monoclonal antibody that recognises the Hendra virus G surface glycoprotein has recently been extensively characterised. Administration of the antibody early after exposure to Nipah virus has prevented the development of significant clinical disease in laboratory animals²³ and is under review for Hendra infections in humans.

A potential mechanism for controlling the disease is equine vaccination. The most promising approaches to Hendra virus vaccine development are based on the expression of the F and/or G envelope glycoproteins through recombinant canarypox viruses or recombinant Hendra G as subunit vaccines; candidate vaccines are currently being formulated for immunogenicity and efficacy studies in horses. Preliminary work suggests that both approaches will provide protection from Hendra virus disease and significantly reduce the viral loads in vaccinated animals,²⁴ but the necessity of completing efficacy studies at a physical containment level 4 facility means that progress is both costly and slow.

Conclusion

Hendra virus infection is an emerging infectious disease that is still not well understood. Further research is needed to determine what factors cause the virus to spill over from Flying-foxes to horses to humans. Diagnosis in horses is difficult due to the variable signs and symptoms and people at risk can be unwittingly exposed to infected horses. As there is no effective treatment or vaccination for humans good hygiene practices and appropriate personal protective equipment are therefore important to prevent disease transmission.

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Influenza: One Health in action

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Abstract: Influenza highlights the relevance of One Health, where experts in animal, human and environmental health combine to solve interrelated problems. Human disease due to pandemic (H1N1) 2009 influenza and avian and human disease due to influenza A/H5N1 are recent examples of new zoonoses with significant global impact. Management and prevention of influenza and other emerging infectious diseases requires the expansion and continuing support of collaborations between human and animal health experts at the clinical, diagnostic laboratory, public health, research and training levels.

A strong driver of One Health was the emergence of the new influenza viruses A/H5N1 and A/H7N7 from birds,¹ as well as other respiratory viruses, such as severe acute respiratory syndrome (SARS) and henipa viruses from bats.^{2,3} The appearance of the pandemic (H1N1) 2009 influenza virus further galvanized discussions about the need for understanding the interactions between human and animal health.⁴ The general population understand these connections, as 'bird flu' and 'swine flu' have entered the lexicon in the past few years.

The clues to the origins of human pandemics are found in the study of influenza viruses in birds and animals, study that is justified by the local and global economic, social and health impacts of influenza. This paper describes the emergence of the two influenza viruses, influenza A/H5N1 and pandemic (H1N1) 2009, that have caused recent international public health concern, and considers how an understanding of One Health contributes to managing future influenza epidemics in Australia.

Influenza viruses

Influenza viruses are naturally present in migratory water birds and spillover into human (and animal) populations may cause pandemics. The influenza viruses are members of the Orthomyxoviridae family, enveloped viruses that contain a segmented single-stranded RNA genome. The important antigenic features of influenza are the external glycoproteins, haemagglutinin (H), responsible for virus attachment to the target cell, and neuraminidase (N), needed for virion maturation and release. The sixteen H and nine N influenza A subtypes all circulate, often asymptomatically, in water birds.⁵ Some viruses move across into domestic poultry, with A/H5N1 and A/H7N7 strains particularly associated with high pathogenicity. Influenza A subtypes can infect and become established in animals, including horses (as demonstrated by the costly equine influenza A/H3N8 outbreak in eastern Australia in 2007) and pigs.⁶ In 2010, an A/H10N7 virus affected poultry in New South Wales (NSW), with zoonotic transfer to a number of humans in close contact with infected poultry. However, only three H (H1, H3, H2) and two N (N1 and N2) influenza A subtypes independently circulate in humans. Influenza B viruses are only present in humans.

The two influenza viruses of most public health concern in recent years have been influenza A/H5N1 and pandemic (H1N1) 2009.

Influenza A/H5N1

Influenza A/H5N1, first isolated in 1996 from a goose in Guangdong Province in China, caused severe poultry losses and occasional human infections in Hong Kong in 1997. The main human public health response that controlled this outbreak was an aggressive poultry cull. However, from 2003 the virus has moved throughout south east and eastern Asia, to Russia, central Asia and the Middle East (in 2005), Europe (2005), Africa (2006) and the Indian subcontinent (2006), making it the largest recorded epizoonosis in poultry (both commercial and backyard) and migratory birds. The combination of legal and illegal poultry and wild bird trade, and migratory water birds, contributed to its rapid spread.⁷ This has caused significant economic and social impact in affected countries.

Influenza A/H5N1 has infected humans following contact with infected poultry, causing severe disease with a high mortality. Fortunately, human-to-human transmission is rare, preventing pandemic spread of this potentially devastating pathogen.⁸

Concerns about the spread of avian influenza A/H5N1 and the 2003 SARS outbreak dominated pandemic planning until the emergence in 2009 of 'swine flu'. These concerns are reflected in the Australian Health Management Plan for Pandemic Influenza,⁹ and the World Health Organization (WHO) pandemic plan.¹⁰

The pandemic (H1N1) 2009 influenza virus

The first descriptions of pandemic (H1N1) 2009 influenza virus infection occurred in the southwestern United States and Mexico in April 2009.¹¹ This virus, quickly given the moniker 'swine flu', was identified to have animal origins, with reassortment of influenza gene segments from North American and Eurasian swine, avian and human viruses. Although seasonal A/H1N1 viruses had been circulating for many years, this novel reassortant A/H1N1 virus was not covered by current seasonal influenza vaccines.¹² As the world population was not immune to the pandemic (H1N1) 2009 influenza virus, it spread quickly. The first Australian human case was identified in Queensland on 8 May 2009 in a traveler returning from North America, but the first evidence of significant community transmission was identified in Victoria in late May and early June 2009.13,14 The epidemic then spread nationally, taking approximately 7 weeks for peak activity to be reached in Western Australia. There was variability in urban and rural attack rates, and within cities. For example, in Sydney, activity was focused in the western and southwestern suburbs, with rates of hospitalisation due to pandemic (H1N1) 2009 influenza virus infection approximately three times higher than those seen in the eastern and northern regions of the city.¹⁵

The origins and exact timing of the emergence of this new pandemic virus remain uncertain. It may have been circulating, but unrecognised, in pigs for some years, as there is minimal influenza surveillance in most commercial pig populations. Interestingly, transmission of the pandemic (H1N1) 2009 influenza virus from humans to pigs has occurred in Australia and other countries. This is, however, not unique. In the United States a number of strains of influenza A are endemic in the pig population and have been frequently transferred to humans and vice versa.

For the most part, pandemic (H1N1) 2009 influenza virus infection caused a relatively mild disease. However hospital or intensive care unit (ICU) admissions, and deaths, were proportionally higher in younger populations compared to seasonal influenza. Risk factors for severe pandemic (H1N1) 2009 influenza infection included morbid obesity, pregnancy and immunosuppression, although approximately one-third of ICU admissions and deaths occurred in otherwise healthy individuals.^{16,17}

A locally produced monovalent pandemic (H1N1) 2009 influenza vaccine was available after the first pandemic wave in Australia, and now a trivalent formulation that includes pandemic (H1N1) 2009, seasonal A/H3N2 and B viruses has been distributed worldwide. Although vaccination accessibility and uptake varies significantly between countries, the 'herd' immunity induced by infection during the first and subsequent waves, and the availability of specific vaccination (and possibly use of antiviral drugs) mean that the subsequent waves are likely to be less severe than those seen during earlier pandemics.

Where to from here?

What do the concepts of One Health mean for managing future influenza epidemics in Australia, using pandemic (H1N1) 2009 influenza and influenza A/H5N1 as examples? How should these concepts be supported? Some of the approaches to enhancing One Health are listed in Box 1.

Box 1. One Health approaches to influenza

- Enhanced surveillance
 - clinical human and veterinary disease
 - o combination of clinical and laboratory surveillance
 - co-ordination of local, regional, national and international surveillance programs
 - $\circ \;\;$ genetic and antigenic variation of viruses.
- Rapid, 'real time' dissemination of surveillance data.
- Understanding patterns of transmission: human-tohuman (and animal), animal-to-animal (and human).
- Understanding pathogenesis of disease in animals and humans.

Clinical surveillance

In human health, clinical networks in Australia allowed the risk factors and clinical presentations of severe pandemic (H1N1) 2009 influenza to be identified and managed quickly.^{16–18} Advances in diagnostic laboratory techniques meant that diagnoses and characterisation of the pandemic (H1N1) 2009 influenza virus, including antiviral drug resistance, was rapid.^{19–21}

With most respiratory tract viral infections there is more mild (or asymptomatic, or non-specific) disease than severe clinical disease. This means that serological testing is needed to determine the true rate of influenza infection.²² The impact of infection varies by season, age group and underlying health status. This makes all-encompassing clinical surveillance difficult, especially as laboratory testing is needed to differentiate the various viral causes of disease. The quality of human surveillance for clinical presentations of new respiratory tract infections in Australia is patchy. Investment in comprehensive surveillance systems that capture, in real time, severe disease (e.g. ICU admissions, or hospitalisations for pneumonia) or outbreaks (e.g. in aged-care facilities) is required.

Laboratory surveillance

As influenza is a notifiable disease (and pandemic (H1N1) 2009 and A/H5N1 are quarantinable diseases) in NSW, passive (but not active) laboratory surveillance is already in place. The widespread use of rapid antigen tests and nucleic acid testing has improved clinical diagnosis of influenza. Paradoxically this may cause a problem: virus isolation is now performed less frequently, but isolates are needed for antigenic and genetic surveillance of influenza strains.^{23,24}

Worldwide, surveillance of influenza isolates is undertaken by the WHO Global Influenza Network, which consists of five Collaborating Centres and some 110 National Influenza Centres. Australia has a WHO Collaborating Centre in Melbourne and three National Influenza Centres: in Sydney (Institute of Clinical Pathology and Medical Research, Westmead), Melbourne (Victorian Infectious Diseases Reference Laboratory) and Perth (PathWest Laboratory Medicine WA). These, and other laboratories in the Australian Public Health Laboratory Network and in the Asia-Pacific region, contribute influenza strains to the WHO Collaborating Centre in Melbourne and contribute to the international surveillance of influenza strains.

Veterinary surveillance

In contrast to the situation in birds and pigs in most overseas countries, the Australian animal and bird populations are currently believed to be free of infection with highly pathogenic influenza viruses.²⁵ The exception is likely to be semi-free range duck populations that have regular opportunity for contact with wild aquatic birds. Generally, Australian chicken populations are completely free of infection with influenza A viruses. When A/H5 or A/H7 infections have occurred in poultry, overt disease outbreaks have rapidly followed. These have been quickly followed by interventions, usually with bird depopulation of the infected farms. The current knowledge of risks posed to humans from infected birds and the established links between animal and public health agencies reduce the chance of human disease.

Even though Australian pigs have been free of infection and so are highly susceptible, pandemic (H1N1) 2009 influenza virus infection mostly passed unnoticed, with little or no disease. In most situations, people posed a greater risk to infection in pigs than the converse. The A/H3N8 virus that infected horses and dogs in Australia presented many challenges for the veterinary profession and laboratories but passed unnoticed from a public health perspective. Despite exposures to massive doses of virus, there was no record of human infection.

From a laboratory perspective, the A/H5N1 epidemics that occurred overseas were invaluable as a stimulus for enhancing the diagnostic capacity and preparedness of veterinary and public health laboratories. In addition, communication and interaction between human and animal health laboratories has improved. Ongoing support of human and veterinary laboratories is required, especially to undertake the specialised reference laboratory analyses needed to characterise new outbreaks.

Human and veterinary collaborations

Continually enhancing the communication between the various national and state human and animal health groups responsible for influenza and communicable diseases will assist in supporting rapid containment of zoonotic threats, and to this end there is veterinary representation on committees such as the Australian Public Health Laboratory Network and the Communicable Diseases Network of Australia. Expansion of collaborations between human and animal health experts should be encouraged at the clinical, diagnostic laboratory, research and training levels. An example of this in NSW is the formation in 2010 of the Sydney Emerging Infections and Biosecurity Institute (located at the Sydney Medical School and Westmead Hospital), a multi-disciplinary and multi-faculty approach to One Health.

Conclusion

While the One Health stimulus from recent epidemic/ pandemic events may be abating recent experience has demonstrated that well-coordinated animal and human surveillance for influenza viruses (and other respiratory pathogens) is required for pandemic planning and management.

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Automated data extraction from general practice: influenza-like illness surveillance

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In *Global Agenda for Influenza Surveillance and Control*, the World Health Organization (WHO) articulates the need for improved capabilities in influenza surveillance.¹ Enhanced intelligence about influenza improves our understanding of both the health burden and the economic burden posed and informs both seasonal influenza response and pandemic preparedness and response.

Two of the WHO's global thematic aims for influenza surveillance and control are:

- · improved quality and coverage of influenza surveillance
- more rapid communication and information exchange between Influenza Network Members and key partners and stakeholders on local, state, national and international levels.

Meeting these aims in gathering intelligence about influenza-like illness (ILI) in the community is a complex task, requiring multiple approaches. Building public health intelligence involves gathering data from a range of sources, interfacing the various pieces of information to facilitate broad analysis leading to intelligence.

New South Wales (the pandemic response in 2009) The focus in New South Wales (NSW) during the 2009

pandemic influenza season was largely on emergency department presentations and hospital and intensive care unit admissions. This provided a view of ILI activity in hospitals.² Based on epidemiological assumptions, this sample examines only a portion of all ILI cases in the community (Pentinnen P, senior influenza expert at the European Centre for Disease Prevention and Control, pers. comm, Nov. 2009). A missing piece of the data puzzle in NSW is general practice records.

General practice surveillance for ILI has been conducted in Australia in a variety of ways. The Australian Sentinel Practices Research Network, operated by the Royal Australian College of General Practitioners and the University of Adelaide is engaging general practitioners (GPs) in national level surveillance.³ A recent report from the Australian Department of Health and Ageing⁴ showed that GP participation in this program remains low. Informal feedback from general practice networks within the former Northern Sydney Central Coast Area Health Service (NSCCAHS) has identified some issues with the extra demands being placed on GP workloads with current surveillance systems.

NSW Health carried out a general practice sentinel surveillance program during the pandemic (H1N1) 2009 influenza response. This effort gained support from GPs and divisions, but provided inconsistent results.² Participating GPs within NSCCAHS indicated that the paper-based report system used in this program was time consuming and resulted in lack of compliance.

A possible public health intelligence enhancement

The Canning Division of General Practice has designed a software package applied in practices nationally.⁵ The Canning Data Extraction Tool has been used to collect de-identified data about chronic diseases and appears to be well accepted by GPs. A pilot study in the former NSCCAHS will explore the adaptation of the Canning Tool to extract ILI data from routine general practice records.

Post scriptum

The aforementioned study has now been completed and a report published in BioMed Central Public Health: Liljeqvist G, Staff M, Puech M, Blom H, Torvaldsen S. Automated data extraction from general practice records in an Australian setting: Trends in influenza-like illness in sentinel general practices and emergency departments. *BMC Public Health* 2011; 11: 435. Available from: http:// www.biomedcentral.com/1471-2458/11/435.

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Dengue

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Dengue is one of the most important mosquito-borne diseases.^{1,2} Predominantly an urban disease, mosquitoes that spread the virus are closely associated with human habitation and humans act as the reservoir host. With current estimates of up to 100 million infections each year, there is concern that predicted climate change and continuing urbanisation may result in a continued upward trend in the number of dengue infections worldwide. In Australia, locally acquired cases of dengue occur only in far north Queensland where populations of vector mosquitoes are present. Annual activity has occurred in the region since the 1980s with the largest Australian epidemic in 50 years occurring in 2009 when approximately 1000 cases were reported.³

Dengue viruses

Dengue fever and its more serious form, dengue haemorrhagic fever, are caused by one of four closely-related viruses. Dengue virus belongs to the family Flaviviridae and infection with one serotype does not provide crossprotective immunity. Infection with dengue viruses produces a spectrum of clinical illness ranging from a non-specific mild febrile illness to severe and potentially fatal dengue haemorrhagic fever. Older children and adults may have a mild febrile syndrome but more typically experience high fever, severe headache, pain behind the eves, muscle and joint pains and rash. The incubation period ranges from 3 to 14 days.⁴ Once recovered, a person develops immunity to this single serotype. However, upon infection with a different serotype, the person stands a greater risk of developing dengue haemorrhagic fever, characterised by high fever, haemorrhagic phenomena, enlarged liver and circulatory failure. There is no specific treatment or vaccine for dengue fever, but close medical attention and clinical management saves many lives.^{1,4} Without treatment, the average fatality rate for dengue haemorrhagic fever can be as high as 5%.

Vectors

The most important vector of dengue virus globally is *Aedes aegypti*. This species is a very efficient epidemic vector because of its adaptation to water-holding containers found in urban environments, and its preference for feeding on humans. A secondary vector is the Asian tiger mosquito, *Ae. albopictus*, which is also associated with human

activity and has been introduced to many parts of the world over the last 30 years, primarily through international movement of used tyres. The immature stages of both species can be commonly found in water-holding containers. *Ae. albopictus* will often also utilise natural environments (e.g. tree holes). Mosquitoes ingest viruses when feeding on an infective individual. Once infected, a mosquito remains infective for life.⁴

Control

Demographic and societal changes over the past 50 years have contributed to a global resurgence of dengue. Population growth and modern transportation have been forces. Control of mosquito populations remains the key to dengue management. Few new and effective mosquito control methods have been developed in the past 30 years. Reductions in the availability of suitable habitats, chemical use, biological control and changes in human behaviour can all assist in reducing the risk of dengue.

Dengue in New South Wales (NSW)

There have been no records of local activity of *Ae. aegypti* or the dengue virus in NSW since the late 1940s.⁵ While there is debate surrounding the factors contributing to the retreat of *Ae. aegypti* from NSW, there is concern regarding the possible reintroduction of the species into urban areas in light of increasing domestic water storage. In addition, a widespread infestation of *Ae. albopictus* has been documented from the Torres Strait and computer modelling has suggested that there is the potential for this species to become established and widespread in coastal Australia.⁵

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Communicable Diseases Report, NSW, March and April 2011

Communicable Diseases Branch NSW Department of Health

For updated information, including data and facts on specific diseases, visit www.health.nsw.gov.au and click on **Public Health** and then **Infectious Diseases**. The communicable diseases site is available at: http://www.health.nsw.gov.au/publichealth/ infectious/index.asp.

Figure 2 and Tables 1 and 2 show notifications of communicable diseases received in March and April 2011 in New South Wales (NSW).

Enteric infections

Outbreaks of foodborne disease

Eight outbreaks of suspected foodborne disease were investigated in March and April 2011. These outbreaks were identified through surveillance of laboratory notifications, or complaints to the NSW Food Authority (NSWFA) or the local public health unit (PHU). In three of these outbreaks the causative organism was established: one as *Salmonella enterica* serovar Typhimurium, one as norovirus and one as *Clostridium perfringens*.

The *S*. Typhimurium outbreak was identified through a complaint to the NSWFA. Interviews with the five affected people found illness to be associated with consuming chicken, beef or mixed kebabs from a takeaway food van. Two of these people were admitted to hospital and one of them had a stool specimen collected which tested positive for *S*. Typhimurium. The NSWFA inspected the businesses, took food and environmental swabs and issued an improvement notice due to some concerns with the potential for cross contamination between raw and cooked ingredients. All samples tested negative for any pathogens.

Salmonella infections can occur after eating undercooked food made from eggs, meat or poultry.¹ Sometimes it can be spread by contact with a person with the infection, or if an infected person has prepared food for others. Thorough cooking of food kills Salmonella bacteria. The best way to avoid contracting a Salmonella infection is to avoid raw or undercooked meat, poultry or eggs. Poultry and meat – such as hamburgers, sausages, and rolled roasts – should not be eaten if pink in the middle.

The norovirus outbreak reported in this period was identified through a complaint to the NSWFA. The complaint reported 45 of 83 people with vomiting and diarrhoea 24–40 hours after attending a christening held at a function centre. The menu consisted of a chicken schnitzel meal for children, and various meals including steak, chicken and pasta dishes for adults. One child was admitted to hospital and was one of three people who submitted stool specimens which tested positive for norovirus. The limited information available from the affected people meant the PHU was not able to determine whether the outbreak was due to person-to-person spread or to food contamination.

The *C. perfringens* outbreak was in a long-term care facility for disabled men. Five residents and one staff member reported diarrhoea. Cases of gastroenteritis appeared in three clusters occurring 2 weeks apart. Two stool specimens were positive for *C. perfringens* with spore counts of 5.8 and 6.5×10^7 /g. Faecal spore counts greater than 10^6 /g are suggestive of food poisoning.² The local council inspected the facility and the local PHU provided advice on cleaning and hygiene measures. A mechanism for spread for the pathogen was not identified.

Outbreaks of gastroenteritis in institutional settings

During March and April, 107 outbreaks of gastroenteritis in institutions were reported, affecting 1434 people. Fortysix outbreaks occurred in child care centres, 41 in aged care facilities, 16 in hospitals, and one each in a camp, family care centre, psychiatric care facility and rehabilitation facility. These outbreaks appear to have been caused by person-to-person spread of a viral illness. In 53 outbreaks (50%) one or more stool specimens were collected. Norovirus was detected in 18 of these outbreaks (34%), three of which also detected incidental findings of *C. difficile* and one of which also detected *Campylobacter* bacteria. Other pathogens were detected in another six outbreaks (11%), including rotavirus in four outbreaks and *C. difficile* in two. Stool specimens for laboratory testing were not available for the remaining 54 outbreaks.

The number of outbreaks for March and April is double the average number of outbreaks for the same period over the previous 5 years (n = 53). Viral gastroenteritis increases in incidence in winter months. There were also more outbreaks of gastroenteritis than expected in January and February 2011 (Figure 1). It is possible however that some of the increase could be due to improved reporting by some institutions. PHUs encourage institutions to submit stool specimens for testing during outbreaks to help determine the cause of these outbreaks.

Respiratory and other infections

Legionnaires' disease (update)

During March and April, 22 cases of *Legionella pneumo-phila* infection were notified compared to 13 cases for the same period in 2010. The majority of notifications (86%) were from residents of metropolitan Sydney. No common source of infection had been identified at the time of writing. PHUs are working with councils to ensure cooling towers are maintained and to investigate possible common sources of infection.³

Legionnaires' disease is a form of pneumonia caused by infection with *Legionella* bacteria. These bacteria can proliferate in environmental sources such as the warm water of cooling towers (in the case of *Legionella pneumophila*) or in soil and potting mix (in the case of *L. longbeachae*).⁴ People can acquire the infection if they breathe in contaminated water vapours or dust.

Zoonoses

Leptospirosis

In March and April there were eight cases of leptospirosis notified from farming regions in NSW. Leptospirosis is an infectious disease caused by bacteria called leptospires (*Leptospira borgpetersenii* sv. Arborea) that are transmitted from animals to humans. Urine of infected animals can contaminate the environment and leptospires survive well in moist conditions.

Humans become infected through broken or abraided skin or mucous membrane contact with water, food, soil or vegetation that is contaminated with the urine from infected animals.¹ Leptospirosis is unusual in southern NSW and is most likely related to a mouse plague that is sweeping across western NSW (occurring in the context of recent flooding). There are a number of ways to prevent leptospirosis during the current mouse plague:

- cover cuts and abrasions with waterproof dressings, especially before coming into contact with soil, mud or water that may be contaminated with mouse urine
- wear footwear outdoors, especially when walking in mud or moist soil
- wear gloves when removing dead mice and when gardening, to protect your hands
- control rodents by cleaning up rubbish and removing food sources close to housing
- wash hands with soap, as *Leptospira* bacteria is quickly killed by soap, disinfectants and drying.

Vaccine-preventable diseases Measles

There were 36 cases of measles notified in NSW in March and April (32 in March and four in April), compared with two cases for the same period in 2010. Five of these cases were associated with overseas travel (two unrelated cases from the Philippines, one from Italy, one from France, and one from Bangladesh). Seven cases in this period were notified from people with no links to known cases and four secondary cases were subsequently notified from people in contact with two of these cases. A further 20 cases notified were associated with three measles clusters in the Western Sydney and Illawarra regions. The age of cases ranged between 0 and 44 years and included 11 unvaccinated children aged less than 5 years.

Measles is an especially infectious virus and is easily spread among unvaccinated or partially vaccinated people. The virus is spread through the air by someone who is unwell with the disease. Symptoms include fever, sore eyes and a cough followed a few days later by a rash.¹

Measles vaccine is recommended for infants at 12 months and at 4 years of age, and this provides long-lasting immunity in 99% of recipients.⁵ Many people who were born during or since 1966 may not be immune to measles because they have neither been infected with measles nor received two doses of a measles-containing vaccine. People who are planning overseas travel should ensure they have received two doses of the free measles-mumpsrubella vaccine (at least 1 month apart) from their general practitioner (GP) or at a travel health clinic.

Meningococcal disease

Eleven cases of meningococcal disease were notified in NSW in March and April 2011 (nine in March and two in April). The age of these cases ranged between 1 and 80 years and included four cases aged less than 5 years. One death was notified in this period, an adult from regional NSW (compared to three deaths for the same period in 2010). Six cases were caused by *Neisseria meningitidis* serogroup B, one case by *N. meningitidis* serogroup Y, and for four cases the serogroup was unable to be determined.

A free vaccine for serogroup C meningococcal disease is available for infants at 12 months of age.⁵ Consequently, serogroup C meningococcal disease is now mainly seen in adults and in unimmunised children. In NSW this year, 81% of cases of meningococcal disease (where the serogroup was known) have been caused by *N. meningitidis* serogroup B, for which there is no vaccine. No cases of serogroup C disease have been reported to date this year.

Pertussis (whooping cough)

During March and April, 1940 cases of pertussis were notified in NSW compared with 696 for the same period in 2010. To date, the number of cases has been highest in children aged 5–9 years (1257 cases) and 0–4 years (987 cases). In total 9276 cases were notified in 2010 compared with 12 577 in 2009.

A free vaccine is recommended for infants at 2, 4 and 6 months at age, although the first dose can be given as early as 6 weeks of age. A booster dose is recommended at 4 years but this can be given as early as 3 years and 6 months of age.⁶

Immunisation reduces the risk of infection, however the vaccine does not provide lifelong protection and reinfection can occur.⁵ Because pertussis immunity wanes over time, many older children and adults are susceptible to infection and can be the source of new infections in infants.⁷ For a limited time, NSW Health is providing free pertussis (dTpa) vaccine through GPs to all new parents, grandparents and any other adults who will regularly care for infants less than 12 months of age. Free vaccine boosters are also provided in high school as part of NSW Health's School-Based Vaccination Program.

Sexually transmissible infections Gonorrhoea

Notifications of gonorrhoea decreased during March and April 2011, following a rise in notifications in the first 2 months of the year. In total, 389 cases of gonorrhoea were notified (226 in March and 163 in April) in this period, compared to 389 (197 in March and 192 in April) in 2010. The majority of cases continue to occur in men. However, there has been a recent increase in cases notified among women, with 80 cases notified in March and April 2011, compared to 62 cases for the same period in 2010.

Gonorrhoea is a bacterial infection spread through unprotected vaginal, oral or anal sex. Infection in men can present as discharge from the penis, irritation or pain on urinating. Infections of the cervix, anus and throat usually cause no symptoms.¹

Syphilis

Notifications of infectious syphilis cases continued to decrease during March and April 2011, following a significant decrease at the end of 2010. In total, 31 cases of infectious syphilis were notified in this period



Figure 1. Number of outbreaks of gastroenteritis in institutions notified in NSW by month for each year in the period January 2006–April 2011.

(24 in March and seven in April). This is a decrease of approximately 30% compared with the same time period in 2010 (36 in March and 28 in April). The majority of cases continue to occur in men aged between 20 and 50 years.

Syphilis is a highly infectious sexually transmitted disease that is spread through vaginal, anal or oral sex through skin-to-skin contact. Syphilis is highly contagious during the primary and secondary stages when the sore or rash is present.¹ Those most at risk include men who have sex with men, people with HIV/AIDS, and people living in Aboriginal communities that are remote or have poor access to health care services.

Lymphogranuloma venereum

An outbreak of lymphogranuloma venereum (LGV) was identified in NSW in 2010 with a peak in cases notified between May and August (32 cases). Since then, the number of cases has dropped significantly but increased during January and February 2011 with 10 cases notified. The increasing trend did not continue in this period with only 10 cases notified in March and April 2010 (seven in March and three in April).

LGV is a sexually transmitted infection. It is caused by a rare, severe strain of *Chlamydia trachomatis* which generally causes more severe symptoms than chlamydia. LGV

is spread through unprotected vaginal, anal or oral sexual contact.¹

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Table 1. Notifications of scheduled medical conditions received in March 2011 by local health district in NSW

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	al above and many and and a later of a later of a	aa amaalan diinaaa	atendo																

Table 2. Notifications of scheduled medical conditions received in April 2011 by local health district in NSW

2						+	Local	Health Dis	trict (201	(1							Tota	اد
NI Condition	urrumpiagee	NSW	NSW 1	Vest P	Vew dew dand	NSW N	North Ce	oast Sy	dney Ea	astern S volnev	hoalhaven	syaney	Western	Sydney	Blue Mountaine	Health	Apr ^b	to date ^b
Bloodborne and sexually transmitted				5	giaira		-0431		5	yuncy			Juney	-				
Chamcroid Chlamvdia (genital) ^a	- 66	39 -	- 99	1 6	- 002	- 99	32	- 89	118	- 258	- 82	168	- 133	- 139	- 12	- 23	- 1521	- 6621
Gonorrhoea ^a	-	-	-	ı.	13	m ·	-	2	12	51	5	40	10	6	13	-	163	779
Hepatitis B – acute viral ^a Henatitis B – other ^a	10	1 1	7 -	- 0		- m	10	- 0	- 1	33 1	- 0	- 22	46	- 55	1 9		4 217	13 886
Hepatitis C – acute viral ^a	L I S	1	• • •		. 7			;		3 1 3	L I I	; ' ;	2 1 3	3 1 3		. 1	5	15
Hepatitis C – other" Henatitis D – unsnerifiad ^a	10	= '	01	- 1	25 -	× 1	4 1	14	ı م	24	<u>0</u> 1	34 1	26 -	27	∞ ı	1 1	221	1115
Lymphogranuloma venereum	I	I	I	I	I	I	I	I	I	I	I	£	I	• 1	I	I	- m	17
Syphilis	I.	,	r.	I.	4	r.	ı.	m	2	14	m	=	m	2	2	ı.	4	194
Vectorborne Bermeh Eoroct virue ^a	~	ſ	÷	c	v	v	d				-				-		36	שאנ
Baintian Forest virus Ross River virus ^a	15 1	→ ←	- 0	n n	0 <u>8</u>	25	12		5	· 	t 1		·				6 6	348
Arboviral infection (other) ^a	1	I I	L	I.	l n		L	I.	-	m		1.	1 -		-	I	~ ~	54
					,							-	-	-	-	'	`	2
Anthrax ^a	I	1	I	T	1	I	I	1	I	I	I	I	I	I	I	I	I	I
Brucellosis ^a	IV	ı.	ı.	I.	I.	1 -	I.	I.	I.	I.	I.	I.	i.	i.	I.	I	11	- ç
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Respiratory and other Blood lead level ^a	14	I	m	1	I	I	1	-	I	-	I	4	m	-	2	I	29	89
Influenza ^a	- c	υ	90	1.0	7	7	-	1 -	13	6,	4 (4	~ '	18	6,	I	85	839
Invasive pneumococcal infection ^a <i>Leaionella Ionabeachae</i> infection ^a	7 -	m I	7 -	7 -	- 1	1 1	1 1	- 1	<-	4 1	7 -	1 1	4 1	γι	- 1	1 1	22	104
Legionella pneumophila infection ^a	I	i.	I.	I.	I.	I.	I.	I.	5	9		, -,	4	 .	I.	I	18	27
Legionnaires' disease (other)" Lenrosv	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	1 1	- 1	1 1	- 1	1 1	1 1	7 1	0 1
Meningococcal infection (invasive) ^a	I	I	I	I	 .,	I	I	I	1 -	10	,	14	I	1 4	-	I	2 00	23
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Vaccine-preventable Adverse event after immunisation	2	ŝ	2	-	2	ı.	i.	1	2	9	1	-	I.	6	2	I	31	89
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Mumps ^a	1	6	۱ţ	1.	I Ş		1.	1 6	ŝ	1 (1 0	- :	- ;	2 20	25	I	10	18
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Tetanus	I	I.	I.	I.	I.	I.	I.	I.	I.	I.	I.	1	I.	I.	I.	I	1	1
Enteric Botulism											1				1		1	1
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Listeriosis ^a	1 1	1 1	1 1	1 1	I 	1 1	1 1		1 1	1 1	1 1	1 1	1 1	1	1 1	1 1	v ←	0 Г
Rotavirus ^a	2	-	2	T	6	4	-	2	19	9	-	m	5	9	m	1.	64	261
Salmonellosis" Shinallocic ^a	20	D	~ -	1	42	12	=	<u>n</u>	48 8 c	- 28	01	ء 78	38	35 1	= -	7	323 o	1960
Typhoid ^a			- 1		-				۱m	- 1	1	4 1	-	- 7	- 1		2	52
Verotoxin producing <i>E. coli^a</i>	I.	ı.	I.	I.		I.	ı.	1	I.	I.	I.	I.	ı.	ı.	-	I.	2	2
Miscellaneous Creutzfeldt–Jakob disease	I	I	I	1	1	I	1	I	I	I	I	I	I	I	I	I	I	4
Meningococcal conjunctivitis	I.	I.	I.	I.	I.	I.	I.	I.	I.	I.	I	I.	I.	I.	I.	I.	I.	-
^a Laboratory-confirmed cases only. ^b Includes case	es with unknown J	postcode.														-		
NB: Data are current and accurate as at the prep NB: HIV and AIDS data are reported separately ir Data is renorted as of nublic bathh unit office	aration date. The l the Public Health	number of cas Bulletin quart	erly.	s, however,	subject to	change, as ca	ases may be	entered at a	later date o	or retracted	upon further ir	vestigation.						

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