MJA
The Medical Journal of Australia

Supporting Information

Supplementary material

This appendix was part of the submitted manuscript and has been peer reviewed.
It is posted as supplied by the authors.

Appendix to: Kurcheid J, Gordon CA, Clarke N, et al. Neglected tropical diseases in Australia: a narrative review. *Med J Aust* 2022; doi: 10.5694/mja2.51533.

Section 1

A previously endemic NTD: yaws

Yaws is caused by the bacterium *Treponema pallidum* sub-species *pertenue*. Other treponemal diseases include syphilis, pinta, and bejel.[1] The disease can be effectively treated with penicillin or azithromycin. However, untreated cases can result in disfiguring lesions of skin, bones and cartilage.[2] Yaws thrives only in tropical areas with mean annual temperatures above 27 degrees Celsius;[3] although previously endemic in Northern Australia, the last reported case was in 1972.[4]

The introduction of penicillin and improvements to primary health care led to a substantial reduction in the prevalence of yaws in Australia between 1950 and 1980 and the WHO subsequently removed Australia from the list of countries endemic for the disease.[5] There are some cases identified in Australia among people who have migrated from endemic areas and who still have positive serology; cross reactivity occurs with syphilis, pinta, and yaws.[6] A close Australian neighbour, Papua New Guinea (PNG), is still endemic for yaws although there is little current data post-2010 on infection prevalence but there is the possibility of the disease crossing into remote communities in Northern Australia.[7,8]

NTDs not endemic in Australia but their vectors/reservoirs are present

Rabies

Rabies in Australia is a variant of rabies termed Australian bat lyssavirus (ABLV) of the family *Rhabdoviridae* and genus *Lyssavirus*, only occurs in bats.[9,10] However the disease in humans caused by infection with either classical rabies or ABLV is indistinguishable.

ABLV was first identified in 1996 and has been associated with three reported human fatalities, two adults and a child.[11,12] Since 2001 there has only been one notification, in 2013, of human infection.[13] Unlike rabies, dogs and cats seem to be less susceptible to ABLV infection, and therefore their potential role in transmission is low.[14] The distribution of flying foxes and microbat species that have been shown to carry ABLV covers most of the eastern side of Australia, northern Australia, and coastal Western Australia.[15] Despite this wide distribution of bats, the actual risk of ABLV from these animals is low, as studies on wild bats show the prevalence of the virus is less than 1%.[14] This risk increases when examining sick bats, which are more likely to be handled by humans[15] (**Box 1**). To date, all human fatalities have occurred in Queensland.

Foxes (*Vulpes vulpes)* are important reservoirs of rabies in other countries.[16] Foxes occur throughout Australia with the exception of the far north,[17] are common in both urban and rural environments, and have proved extremely resistant to eradication attempts.[18,19] There is also a risk of zoonotic incursion of canine rabies from neighbouring countries including Indonesia and PNG.[9,20,21]

Chikungunya and dengue

Chikungunya

Chikungunya is a mosquito-borne viral disease caused by chikungunya virus (CHIKV). Occurring predominantly in Africa, India, South-East Asia and the Western Pacific, it is also considered to be emerging or re-emerging in many other regions of the world. Significant outbreaks of chikungunya have become more frequent in many areas, including a number of Indian Ocean and Pacific Island nations, such as PNG.[22,23] CHIKV is spread to humans through the bite of infected mosquitos, mainly *Aedes aegypti* and *Ae. albopictus. Ae. aegypti* is present in the tropics and sub-tropics; in Australia it is found in parts of Queensland. *Ae. albopictus* occurs in some temperate regions as well as the tropics and subtropics; in terms of Australia, *Ae. albopictus* is currently confined to the Torres Strait islands.[24] There is no record to date of locally acquired chikungunya in Australia. However, the increasing numbers of infected travellers from endemic regions have become an important public health consideration for areas where the vectors are established, particularly in northern Queensland.[25,26] Cases of imported chikungunya cases have occurred regularly in Australia since 2008.[13,25-27] Therefore, the presence of susceptible vectors with the occasional importation of CHIKV by travellers points to the risk of an outbreak in the future (**Box 1**). [26]

Dengue

Dengue virus, belonging to the family flaviviridae and transmitted by *Ae. aegypti* and *Ae. albopictus*,[28] is not considered endemic in Australia but there are annual cases reported and occasional outbreaks (**Box 1**).[13] Four large dengue epidemics which swept through Queensland and New South Wales between 1897 and 1926 infected up to 90% of the urban population in each outbreak and were responsible for a reported 733 deaths.[29] In recent years, imported dengue cases have led to autochthonous dengue outbreaks in north and central Queensland,[22,30,31] including an outbreak in 2009 that led to more than 900 locally acquired cases.[32,33] In 2016, there was an outbreak of dengue on the islands of Erub and Badu in the Torres Strait.[34] If all outbreaks are considered, the cost of the introduction of *Ae. aegypti* into Australia, including lost work and vector control costs, has been considerable, estimated at around $17 million per annum.[26] *Aedes albopictus* is already established in the Torres Strait; consequently, there is a risk of introduction to mainland Australia.[35] *A. albopictus* is also highly invasive, capable of surviving in

temperate zones, and is an aggressive biter.[35] It is thus a major concern for not only Dengue but also transmission of other local flaviviruses. There is a risk of further outbreaks of dengue in Australia because of importation due to arriving travellers; with the exception of 2020, when there were 222 notifications of Dengue infection in Australia (down from 1465 in 2019), hundreds to thousands of cases are recorded every year.[13,36] The presence of competent vectors in Queensland, and other areas of the country, is also a risk factor for Dengue becoming endemic (**Box 1**).[25] Viral sequencing has shown that the majority of dengue cases are imported from PNG and Indonesia, two of Australia's closest neighbours with considerable movement between these two countries. [36]

NTDs not present or sporadic in humans but found in animals

There is a group of NTDs that do not currently cause locally acquired infections in Australia, but are present in domestic or wild animals, thus potentially posing a risk of emergence in humans (**Box 1**).

Foodborne trematodiases – fascioliasis

Phylum: Platyhelminthes; **Class:** Trematoda; **Order:** Plagiorchiida

Foodborne trematodiases include *Clonorchis sinensis*, *Opisthorchis viverrini*, *Fasciola hepatica*, *F. gigantica*, and *Paragonimus* spp. and are uncommon in Australia.

There have been a very small number of reported cases of paragonimiasis, clonorchiasis, and opisthorchiasis, all occurring in immigrants from endemic countries. On the other hand, *Fasciola hepatica* is known to be endemic in livestock in Australia, including sheep and cattle, in New South Wales and Victoria, and the parasite has also been reported in marsupials.[37] *F. gigantica*, which is common in South-East Asia, is not endemic to Australia. Human fascioliasis occurs only sporadically but can lead to complications including pancreatitis, gallstones, and cholangitis[38] Treatment involves the anti-parasitic agent triclabendazole, which is the only medicine recommended by WHO to treat human fascioliasis. [39] Case reports of human fascioliasis acquired in Australia have shown it predominantly occurs in farmers or those living in rural areas with a history of eating wild watercress on which the metacercarial infective stage encysts.[40-42] One such case occurred following consumption of wild water cress purchased in an urban setting,[43] and in two instances the source of infection was unclear. [44] There have also been a number of cases reported in which the disease was acquired overseas.[45,46] As indicated, given the presence of the disease in Australian livestock, there remains a risk of human infection if contaminated plants such as watercress are ingested.

Taeniasis and Cysticercosis

Phylum: Platyhelminthes; **Class:** Cestoda**; Order:** Cyclophyllidea

Taeniasis is caused by *Taenia solium* (pork tapeworm) and *T. saginata* (beef tapeworm) and *T. asiatica*. These species are not currently endemic in Australia and any cases are from returned travellers from endemic areas. The first case of locally acquired neurocysticercosis, caused by infection with *T. solium*, was reported in 2020.[47] No definitive mode of transmission was determined but it is likely the individual acquired the infection from a human carrier who was infected outside of Australia.

T. saginata has occasionally been identified in cattle in Australia. An outbreak of taeniasis in Australian cattle in 2013 was traced back to 'copra meal', a commercially available feed imported from Papua New Guinea.[48] Mitigation efforts include not grazing animals on pastures irrigated with sewerage, and meat inspections help keep the risk of infection low.[49]

Chagas disease

Chagas disease (also known as American trypanosomiasis) is a zoonotic, parasitic disease transmitted through the faeces and urine of blood-feeding triatomine bugs; it predominantly occurs in Latin America and is caused by the protozoan parasite *Trypanosoma cruzi.*[50-52] Healthcare costs associated with the disease can be very high, particularly if the disease has developed into the chronic stages with clinical manifestations, which occur in approximately 30 – 40% of cases.[50,53,54] Chronic manifestations of Chagas disease include mega colon and mega oesophagus, and heart rhythm abnormalities which can lead to heart failure.

Due to the often lengthy asymptomatic nature of the disease, infected individuals can unknowingly act as carriers. The disease is now emerging in many previously non-endemic regions including Europe, North America and the Western Pacific Region (WPR), specifically Japan and Australia, due to increased emigration from Latin America, including some people infected with *T. cruzi*[51,53] Estimates of infection numbers in Australia range from between 1,000 and 10,000 cases at a rate of 16 per 1000 immigrants from Latin America.[53,55]

No vector transmission of *T. cruzi* has occurred in Australia, although *Triatoma leopoldi*, a potential vector, occurs in Northern Australia.[56] In addition there are several species of *Trypanosoma* in native wildlife such as bandicoots and bettongs.[57]

Transmission can still occur via congenital transfer or blood transfusions. The Australian Red Cross Blood Service conducts limited screening of blood and plasma donors by way of a questionnaire to identify at-risk individuals; there is no routine testing of blood for *T. cruzi* infection.[58] The generally low prevalence and non-specific clinical signs of Chagas disease in Australia mean that many physicians may not recognize the clinical presentation, delaying diagnosis and treatment for infected patients and potentially resulting in progression to more severe forms of the disease.[58] Currently, Australia does not stock either of the antiparasitic drugs (benznidazole and nifurtimox) for treating Chagas disease, nor is there a policy in place to identify at-risk individuals.

Leishmaniasis

Leishmaniasis, transmitted by sand flies, is caused by zoonotic and anthroponotic protozoan parasites belonging to the genus *Leishmania*.[659] Whilst most human infections are asymptomatic, clinical disease of varying severity can also develop which can be highly disfiguring, exacerbating the negative social and economic burden of the disease. [59,60]

Australia harbours a unique species, *L. australiensis* (also known as *L. macropodum*), and a potential vector other than phlebotomine sandflies.[61,62] Evidence suggests that day-feeding midges from the subgenus *Forcipomyia* (*Lasiohelea*) spp., family Ceratopogonidae, and possibly a similar species, *F.* (*L.*) *peregrinator*, are responsible for transmitting *Leishmania* between macropods in the Northern Territory.[61] These day-feeding midge species also feed on humans, although no human transmission has been reported.[61] Leishmaniasis is a notifiable disease in animals in Australia. [63]

Human cases of leishmaniasis in Australia, caused by various *Leishmania* species from Africa and the Middle East, are limited to imported cases with increasing numbers recorded in recent years due to international tourism, military service in endemic areas, and the migration of refugees from endemic regions.[63-65] There are three main manifestations of leishmaniasis which are dependent on the infecting species. They are, cutaneous leishmaniasis (most commonly *L. tropica, L. major,* and *L. mexicana*,), muco-cutaneous leishmaniasis (most commonly *L. braziliensis* and *L. guyanensis*), and visceral leishmaniasis (most commonly *L. donovani* and *L. infantum*). Dogs imported from endemic regions have been found to harbour *Leishmania infantum*, and while there is currently no evidence for vector transmission, there is a concern that Australia is at risk of an incursion of leishmaniasis due to these increased numbers of imported cases in humans and canines.[64,66] It is unknown what public health impact such an introduction might have but there is a need in Australia for surveillance in people and animals, and maintaining awareness of leishmaniasis symptoms among physicians.

References

1. Marks M, Mitjà O, Vestergaard LS, Pillay A, Knauf S, Chen C-Y, et al. Challenges and key research questions for yaws eradication. The Lancet Infect Dis. 2015;15(10):1220-5.
2. Marks M. Yaws: towards the WHO eradication target. Trans R Soc Trop Med Hyg. 2016;110(6):319-20.
3. Kazadi WM, Asiedu KB, Agana N, Mitjà O. Epidemiology of yaws: an update. Clin Epidemiol. 2014;6:119-28.
4. Garner M, Backhouse J, Moddie P, Tibbs G. Treponemal infection in the Australian Northern Territory aborigines. Bull World Health Organ. 1972;46:285-93.
5. World Health Organization. Eradication of Yaws. Geneva: WHO; 2018.
6. de Caprariis PJ, Della-Latta P. Serologic cross-reactivity of syphilis, yaws, and pinta. Am Fam Physician. 2013;87(2):80.
7. Mitjà O, Hays R, Lelngei F, Laban N, Ipai A, Pakarui S, et al. Challenges in recognition and diagnosis of yaws in children in Papua New Guinea. Am J Trop Med Hyg. 2011;85(1):113-6.
8. Capuano C, Ozaki M. Yaws in the Western pacific region: a review of the literature. J Trop Med. 2011;2011:642832.
9. Sparkes J, Ballard G, Fleming PJS. Cooperative hunting between humans and domestic dogs in eastern and northern Australia. Wildl Res. 2016;43(1):20-6.
10. Walker PJ, Blasdell KR, Calisher CH, Dietzgen RG, Kondo H, Kurath G, et al. ICTV Virus Taxonomy Profile: Rhabdoviridae. J Gen Virol. 2018;99(4):447-8.
11. Francis JR, Nourse C, Vaska VL, Calvert S, Northill JA, McCall B, et al. Australian Bat Lyssavirus in a child: the first reported case. Pediatrics. 2014;133(4):e1063-7.
12. Hanna JN, Carney IK, Smith GA, Tannenberg AE, Deverill JE, Botha JA, et al. Australian bat lyssavirus infection: a second human case, with a long incubation period. Med J Aust. 2000;172(12):597-9.

13. Australian Government. National notifiable diseases surveillance system 2021. Access Date. 23.02.2021. Available from: http://www9.health.gov.au/cda/source/rpt_3.cfm.
14. McColl KA, Chamberlain T, Lunt RA, Newberry KM, Westbury HA. Susceptibility of domestic dogs and cats to Australian bat lyssavirus (ABLV). Vet Microbiol. 2007;123(1-3):15-25.
15. Si D, Marquess J, Donnan E, Harrower B, McCall B, Bennett S, et al. Potential Exposures to Australian Bat Lyssavirus Notified in Queensland, Australia, 2009−2014. PLoS Negl Trop Dis. 2016;10(12):e0005227.
16. Finnegan CJ, Brookes SM, Johnson N, Smith J, Mansfield KL, Keene VL, et al. Rabies in North America and Europe. J R Soc Med. 2002;95(1):9-13.
17. Australian Government. European red fox (*Vulpes vulpes*). In: Department of Sustainability E, Water, Population and Communities, editor. Canberra, ACT2010.
18. Coman BJ. Simulated rabies eradication: the lessons from two exercises in Victoria. Bureau of Rural Resources Proceedings. 1992;11:91-5.
19. Marks C, Bloomfield T. Distribution and density estimates for urban foxes (Vulpes vulpes) in Melbourne: Implications for rabies control. CSIRO Wildlife Research. 1999;26:763-75.
20. Degeling C, Brookes V, Lea T, Ward M. Rabies response, One Health and more-than-human considerations in Indigenous communities in northern Australia. Soc Sci Med. 2018;212:60-7.
21. Hudson EG, Brookes VJ, Ward MP. Assessing the Risk of a Canine Rabies Incursion in Northern Australia. Frontiers in veterinary science. 2017;4:141.
22. Roth A, Mercier A, Lepers C, Hoy D, Duituturaga S, Benyon E, et al. Concurrent outbreaks of dengue, chikungunya and Zika virus infections - an unprecedented epidemic wave of mosquito-borne viruses in the Pacific 2012-2014. Euro Surveill. 2014;19(41).
23. Arima Y, Matsui T. Epidemiologic update of dengue in the Western Pacific Region, 2010. Western Pacific surveillance and response journal : WPSAR. 2011;2(2):4-8.
24. Knope K, Doggett SL, Jansen CC, Johansen CA, Kurucz N, Feldman R, et al. Arboviral diseases and malaria in Australia, 2014-15: Annual report of the National Arbovirus and Malaria Advisory Committee. Communicable diseases intelligence (2018). 2019;43.
25. Suhrbier A, Devine G. Chikungunya virus, risks and responses for Australia. Aust N Z J Public Health. 2016;40(3):207-9.
26. Viennet E, Knope K, Faddy HM, Williams CR, Harley D. Assessing the threat of chikungunya virus emergence in Australia. Communicable diseases intelligence quarterly report. 2013;37(2):E136-43.
27. Johnson DF, Druce JD, Chapman S, Swaminathan A, Wolf J, Richards JS, et al. Chikungunya virus infection in travellers to Australia. Med J Aust. 2008;188(1):41-3.
28. WHO. Comprehensive Guidelines for Prevention and Control of Dengue and Dengue Haemorrhagic Fever. revised and expanded edition ed. India: World Health Organization Regional Officer for South East Asia; 2011. 212 p.
29. Canyon DV. Historical analysis of the economic cost of dengue in Australia. J Vector Borne Dis. 2008;45(3):245-8.
30. Ritchie SA, Long S, Smith G, Pyke A, Knox TB. Entomological investigations in a focus of dengue transmission in Cairns, Queensland, Australia, by using the sticky ovitraps. J Med Entomol. 2004;41(1):1-4.
31. Queensland government. Dengue outbreaks 2018. Access Date. 28.01.2018. Available from: https://www.health.qld.gov.au/clinical-practice/guidelines-procedures/diseases-infection/diseases/mosquito-borne/dengue/dengue-outbreaks.
32. Ritchie SA, Pyke AT, Hall-Mendelin S, Day A, Mores CN, Christofferson RC, et al. An Explosive Epidemic of DENV-3 in Cairns, Australia. PLoS ONE. 2013;8(7):e68137.
33. Imrie A. Dengue introduced by travellers, Australia. Microbiology Australia. 2018;39(2):67-71.
34. Ciocchetta S, Prow NA, Darbro JM, Frentiu FD, Savino S, Montarsi F, et al. The new European invader Aedes (Finlaya) koreicus: a potential vector of chikungunya virus. Pathog Glob Health. 2018;112(3):107-14.
35. van den Hurk AF, Nicholson J, Beebe NW, Davis J, Muzari OM, Russell RC, et al. Ten years of the Tiger: Aedes albopictus presence in Australia since its discovery in the Torres Strait in 2005. One health (Amsterdam, Netherlands). 2016;2:19-24.

36. data.gov.au. Number of people requiring interventions against neglected tropical diseases 2018. Access Date. 17.03.2021. Available from: https://data.gov.au/data/dataset/number-of-people-requiring-interventions-against-neglected-tropical-diseases.
37. Mas-Coma S. Epidemiology of fascioliasis in human endemic areas. J Helminthol. 2005;79(3):207-16.
38. Sripa B, Kaewkes S, Intapan PM, Maleewong W, Brindley PJ. Food-borne trematodiases in Southeast Asia: epidemiology, pathology, clinical manifestation and control. Adv Parasitol. 72: Elsevier; 2010. p. 305-50.
39. WHO. Foodborne trematode infections 2018. Access Date. 17.07.2019. Available from: https://www.who.int/foodborne_trematode_infections/en/.
40. Croese J, Chapman G, Gallagher N. Evolution of fascioliasis after eating wild watercress. Aust N Z J Med. 1982;12(5):525-7.
41. Laird P, Boray J. Human fascioliasis successfully treated with triclabendazole. Aust N Z J Med. 1992;22(1):45-7.
42. WOOD IJ, STEPHENS WB, PORTER DD. Fascioliasis causing hepatitis in two eaters of water cress. Med J Aust. 1975;2(22):829-31.
43. Hughes AJ, Spithill TW, Smith RE, Boutlis CS, Johnson PD. Human fasciolosis acquired in an Australian urban setting. The Medical Journal of Australia. 2003;178(5):244-5.
44. Prociv P, Walker JC, Whitby M. Human ectopic fascioliasis in Australia: first case reports. Med J Aust. 1992;156(5):349-51.
45. Figtree M, Beaman MH, Lee R, Porter M, Torey E, Hugh TJ, et al. Fascioliasis in Australian travellers to Bali. Med J Aust. 2015;203(4):186-8.
46. Mangos P, Menzies S. Human fascioliasis in Australia. Med J Aust. 1973;1(6):295-6.
47. Forster D, Ko DK, Koehler AV, Kranz S, Goh C, Fleming B, et al. Case Report: Neurocysticercosis Acquired in Australia. Am J Trop Med Hyg. 2020;103(6):2318-22.
48. Jenkins DJ, Brown GK, Traub RJ. 'Cysticercosis storm' in feedlot cattle in north-west New South Wales. Aust Vet J. 2013;91(3):89-93.
49. Kiermeier A, Hamilton D, Pointon A. Quantitative risk assessment for human Taenia saginata infection from consumption of Australian beef. Microbial Risk Analysis. 2019;12:1-10.
50. Lidani KCF, Andrade FA, Bavia L, Damasceno FS, Beltrame MH, Messias-Reason IJ, et al. Chagas disease: From discovery to a worldwide health problem. Frontiers in Public Health. 2019;7(166).
51. Guhl F. 5 - Geographical distribution of Chagas disease. In: Telleria J, Tibayrenc M, editors. American Trypanosomiasis Chagas Disease (Second Edition). London: Elsevier; 2017. p. 89-112.
52. Martins-Melo FR, Carneiro M, Ribeiro ALP, Bezerra JMT, Werneck GL. Burden of Chagas disease in Brazil, 1990-2016: findings from the Global Burden of Disease Study 2016. Int J Parasitol. 2019;49(3-4):301-10.
53. Bonney KM. Chagas disease in the 21st century: a public health success or an emerging threat? Parasite (Paris, France). 2014;21:11-.
54. Nunes MCP, Beaton A, Acquatella H, Bern C, Bolger AF, Echeverría LE, et al. Chagas Cardiomyopathy: An Update of Current Clinical Knowledge and Management: A Scientific Statement From the American Heart Association. Circulation. 2018;138(12):e169-e209.
55. Schmunis GA, Yadon ZE. Chagas disease: a Latin American health problem becoming a world health problem. Acta Trop. 2010;115(1-2):14-21.
56. Monteith GB. Confirmation of the presence of Triatominae (Hemiptera: Reduviidae) in Australia, with notes on Indo-Pacific species. J Aust Entomol Soc. 1974;13:89-94.
57. Thompson CK, Godfrey SS, Thompson RC. Trypanosomes of Australian mammals: A review. International journal for parasitology Parasites and wildlife. 2014;3(2):57-66.
58. Jackson Y, Pinto A, Pett S. Chagas disease in Australia and New Zealand: risks and needs for public health interventions. Trop Med Int Health. 2014;19(2):212-8.
59. Burza S, Croft SL, Boelaert M. Leishmaniasis. The Lancet. 2018;392(10151):951-70.
60. Torres-Guerrero E, Quintanilla-Cedillo MR, Ruiz-Esmenjaud J, Arenas R. Leishmaniasis: a review. F1000Research. 2017;6:750-.

61. Dougall AM, Alexander B, Holt DC, Harris T, Sultan AH, Bates PA, et al. Evidence incriminating midges (Diptera: Ceratopogonidae) as potential vectors of Leishmania in Australia. Int J Parasitol. 2011;41(5):571-9.
62. Rose K, Curtis J, Baldwin T, Mathis A, Kumar B, Sakthianandeswaren A, et al. Cutaneous leishmaniasis in red kangaroos: isolation and characterisation of the causative organisms. Int J Parasitol. 2004;34(6):655-64.
63. Department of Agriculture WatEA. National list of notifiable animal diseases. 2019.
64. Stark D, van Hal S, Lee R, Marriott D, Harkness J. Leishmaniasis, an emerging imported infection: report of 20 cases from Australia. J Travel Med. 2008;15(5):351-4.
65. Roberts T, Barratt J, Sandaradura I, Lee R, Harkness J, Marriott D, et al. Molecular Epidemiology of Imported Cases of Leishmaniasis in Australia from 2008 to 2014. PLoS ONE. 2015;10(3):e0119212.
66. Department of Primary Industries NSW (Australia). Leishmaniasis in Dogs: Guidelines for Veterinarians. 2017.

Table 1. Clinically relevant laboratory-based diagnostic methods for NTDs in Australia (modified with permission from Rogers et al;[1] additional references [ref] are indicated)

		Microscopy	Immunodiagnostics	DNA-based	Other/notes
Endemic NTDs					
Scabies	Sample type/s	Skin scrapings/biopsy			Clinical diagnosis based on itch, plaque, location (interdigital spaces, skin folds)[1]
Soil-transmitted helminths (STH)	Sample type/s	Stool		Stool	Multiplex PCR panels often combine STH with intestinal protozoa detection[1]
	Test name/s	Formalin-ethyl acetate concentration, Parasep		Multiplex qPCR	
Strongyloidiasis	Sample type/s	Sputum, stool, bowel biopsy	Serum	Stool, blood/serum	Larvae in stool and sputum. Clinical symptoms and epidemiological data key for initial evaluation. Microscopy often has low sensitivity, serology recommended. A number of molecular diagnostics have been developed and are used in some diagnostic laboratory tests[1]
	Test name/s	Formalin-ethyl acetate concentration, Parasep, agar plate culture, sputum smear, histopathology	IFA, ELISA	qPCR, LAMP	
Echinococcosis	Sample type/s	Cyst aspirate (if performed, risk of secondary seeding of infection) or tissue	Serum	Cyst fluid or tissue	Visualization of cysts (CT, MRI, ultrasonography), confirmed with serology or antigen testing. ELISA appears most sensitive and specific of available assays. Antibody detection is more sensitive than antigen detection in diagnosing *E. granulosus*[1]
	Test name/s	Direct microscopy, histopathology	ELISA, Immunoblot	qPCR, PCR	
Buruli ulcer (Daintree/ Bairnsdale ulcer)	Sample type/s	Ulcer swab		Ulcer swab/aspirate, tissue biopsy	Differential diagnosis to rule out other conditions that present with indurated ulcers (ie, cutaneous leishmaniasis, diabetes mellitus), nodules (onchocerciasis, lipoma), plaques (eczema, Kaposi sarcoma), and/or oedema (cellulitis, lymphatic filariasis). Diagnosis usually on clinical symptoms
	Test name/s	Acid-fast staining, histology, culture		PCR, qPCR, OSCPH	
	[ref]	2,3		2	
Leprosy	Sample type/s	Skin biopsy	Serum	Skin biopsy	Considered with chronic skin lesions, especially with sensory loss. No reliable tests are available. PCR useful for identification when clinical or histology signs are inconclusive
	Test name/s	Histology	ELISA	PCR, qPCR	
	[ref]	4	5	6-8	
Trachoma	Sample type/s	Conjunctiva	Blood, serum	Blood, conjunctiva	Clinical diagnosis is largely based on clinical manifestations. Differential diagnosis of conjunctivitis from other causes (viral, bacterial, allergy)
	Test name/s	Microscopy (Giemsa staining), tissue culture	IFA, EIA, ELISA	PCR, qPCR	
	[ref]	9	10,11	10,12	
Snakebite envenoming	Sample type/s		Blood, bite site swab, urine		Diagnosis is often made on confirmation of bite from a dangerous snake, swelling of bite site, local blistering or bruising, persistent oozing of blood, enlarged, painful lymph nodes near bite, systemic symptoms.[13] Australia is the only country that has a snake venom detection kit
	Test name/s		EIA (snake venom detection kit)		
	[ref]		14		
A previously endemic NTD					
Yaws	Sample type/s		Serum	Swabs or exudate	Serological tests are the same as those to diagnose syphilis, does not differentiate between the two diseases. Several serological based rapid POC tests available for out of the laboratory testing — most are primarily for detecting syphilis[15-17]
	Test name/s		RPR, VDRL, TPHA, TPPA, FTA-Abs, EIA	PCR	
	[ref]		16-19	20,21	
Not endemic in Australia but their vectors are present					
Rabies	Sample type/s		Serum, CSF	Neck skin biopsy, serum, saliva, urine)	Diagnosis suspected in patients with acute progressive encephalitis, hydrophobia and aerophobia. Antibodies in serum may appear after onset of clinical symptoms, later in CSF[22]
	Test name/s		DFA, IFA, RFFIT	RT-PCR	
	[ref]		23	22,23	
Chikungunya	Sample type/s		Serum	Serum	Diagnosis suspected on acute onset of polyarthritis and epidemiological exposure.

	Test name/s		IFA, ELISA, LFA	RT-PCR	RT-PCR can be used within first week of infection. Negative RT-PCR does not rule it out, and serology should be performed. IgM antibodies present up to three months, IgG persists for years[24]
	[ref]		25,26	27,28	
Dengue	Sample type/s	Tissue (usually post-mortem)	Serum	Serum	Four dengue serotypes: DENV-1, DENV-2, DENV-3, DENV-4. In areas of high endemicity positive predictive value of clinical criteria is high. RT-PCR can be used within first week of infection. Serology can be confounding after infection of vaccination of other flaviviruses[29,30]
	Test name/s	Viral particle visualisation IHC staining	LFA, MAC-ELISA	RT-PCR	
	[ref]	31	32-34	35	
NTDs not present or sporadic in humans but found in animals					
Fascioliasis	Sample type/s	Stool, bile, duodenal aspirates, liver biopsies	Serum		Serological diagnostics can lack specificity, cross-react with other parasites including schistosomiasis
	Test name/s	Formalin-ethyl acetate concentration, histopathology	IHA, IFA, ELISA, immunoblot		
Taeniasis and cysticercosis	Sample type/s	Stool (taeniasis only)	Serum	Plasma, CSF	Taeniasis can be diagnosed as eggs in faeces via microscopy or PCR. Cysticercosis diagnosed from imaging (cysts) via CT and MRI, with confirmation via serology. Poor performance identified with commercially available ELISA.[1] MAT available in Europe, limited availability in USA. qPCR may be useful in diagnosing subarachnoid NCC[1]
	Test name/s	Formalin-ethyl acetate concentration	EITB, ELISA	qPCR	
Chagas	Sample type/s	Blood, buffy coat (acute disease)	Serum (chronic disease)	Blood/buffy coat (acute disease)	PCR can be used for monitoring patients for reactivation risk; sensitive detection in acute disease. Parallel antigen based tests required to improve accuracy of diagnosis[1]
	Test name/s	Giemsa stain	ELISA, IFA, TESA, IHA, Abbott TESA Chagas	PCR, qPCR	
East African trypanosomiasis (*Trypanosoma brucei* subsp. *rhodesiense*)	Sample type/s	Blood, buffy coat, CSF, lymph node aspirate		Blood/buffy coat, skin biopsy of tsetse fly bite site eschar	*T. b. rhodesiense* and *T. b. gambiense* cannot be differentiated by microscopy or 18s rRNA PCR, but the diseases are clinically distinct and are not sympatric, although both subspecies are present in Uganda[1,36]
	Test name/s	Giemsa stain thick and thin film microscopy on blood, CSF or lymph node aspirates		PCR, qPCR	
West African trypanosomiasis (*Trypanosoma brucei* subsp. *gambiense*)	Sample type/s	Blood, buffy coat (acute phase), CSF	Serum	Blood/buffy coat (acute phase)	Positive serology requires confirmatory testing via visualization of parasites. PCR may complement serology and parasite visualization if available PCR, direct microscopy and are insensitive for West African trypanosomiasis due to the low number of circulating trypomastigotes. Rapid test serology combined with clinical presentation is the preferred diagnostic method[1,36]
	Test name/s	Giemsa stain thick and thin film microscopy on blood, CSF or lymph node aspirates	Rapid test, ELISA	PCR, qPCR	
Cutaneous/mucocutaneous leishmaniasis	Sample type/s	Skin/lesion biopsies		Skin/lesions	Parallel tests (histology, culture, PCR) for best diagnostic accuracy. RFLP-PCR distinguishes species[1]
	Test name/s	Histology, NNN media culture		PCR, qPCR, RFLP-PCR	
Visceral leishmaniasis	Sample type/s	Bone marrow, whole blood, lymph node, splenic aspirate	Serum	Bone marrow, whole blood, lymph node, splenic aspirate	Bone marrow aspirate is preferred specimen. Consider serology for suspected VL with negative or inconclusive histopathology, culture, and PCR. Immunocompromised individuals may have lower sensitivity to serological tests; PCR and culture recommended[1]
	Test name/s	Giemsa stain microscopy, NNN media culture	ICT, IFA, ELISA, DAT	qPCR, PCR	

CT = computed tomography; CSF = cerebral spinal fluid; DAT = direct agglutination test; DFA = direct fluorescent antibody test; EIA = enzyme immunoassay; ELISA = enzyme-linked immunosorbent assay; EITB = enzyme-linked immunoelectrotransfer blot; FTA-Abs = fluorescent treponemal antibody absorption; ICT = immunochromatographic test; IFA = immunofluorescent antibody test; IHA = indirect haemagglutination assay, IHC = immunohistochemistry; LAMP = loop mediated isothermal amplification; LFA = lateral flow immunoassay; MAC-ELISA = IgM antibody capture enzyme-linked immunosorbent assay; MRI = magnetic resonance imaging; OSCPH = oligonucleotide-specific capture plate hybridization; Parasep = brand name faecal concentrator; PCR = polymerase chain reaction; qPCR = real-time PCR, RT-PCR = reverse transcriptase PCR; RFLP-PCR = restriction fragment length polymorphism PCR ; RFFIT = rapid fluorescent focus inhibition test; RPR = rapid plasma regain; TPHA = *Treponema pallidum* haemaglutination assay, TPPA = Treponema pallidum particle agglutination assay; TESA = trypomastigote excreted-secreted antigen; VDRL = venereal disease research laboratory.

References

1 Rogers MJ, McManus DP, Gordon CA. Membrane technology for rapid point of care diagnostics for parasitic neglected tropical diseases. Clin Microbiol Rev. 2021; 34(4).
2 Portaels F, Agular J, Fissette K, Fonteyne PA, De Beenhouwer H, de Rijk P, et al. Direct detection and identification of Mycobacterium ulcerans in clinical specimens by PCR and oligonucleotide-specific capture plate hybridization. J Clin Microbiol. 1997; 35(5): 1097-100.
3 Guarner J, Bartlett J, Whitney EA, Raghunathan PL, Stienstra Y, Asamoa K, et al. Histopathologic features of Mycobacterium ulcerans infection. Emerg Infect Dis. 2003; 9(6): 651-6.
4 Pires CA, Miranda MF, Bittencourt Mde J, Brito AC, Xavier MB. Comparison between histopathologic features of leprosy in reaction lesions in HIV coinfected and non-coinfected patients. An Bras Dermatol. 2015; 90(1): 27-34.
5 Parkash O, Kumar A, Pandey R, Franken K, Ottenhoff THM. Detection of Mycobacterium leprae infection employing a combinatorial approach of anti-45 kDa and modified anti-PGL-I antibody detection assays. J Med Microbiol. 2007; 56(Pt 8): 1129-30.
6 Martinez AN, Talhari C, Moraes MO, Talhari S. PCR-based techniques for leprosy diagnosis: from the laboratory to the clinic. PLoS Negl Trop Dis. 2014; 8(4): e2655.
7 Han XY, Sizer KC, Thompson EJ, Kabanja J, Li J, Hu P, et al. Comparative sequence analysis of Mycobacterium leprae and the new leprosy-causing Mycobacterium lepromatosis. J Bacteriol. 2009; 191(19): 6067-74.
8 Gillis T, Vissa V, Matsuoka M, Young S, Richardus JH, Truman R, et al. Characterisation of short tandem repeats for genotyping Mycobacterium leprae. Lepr Rev. 2009; 80(3): 250-60.
9 Taylor HR, Burton MJ, Haddad D, West S, Wright H. Trachoma. Lancet. 2014; 384(9960): 2142-52.
10 Senyonjo LG, Debrah O, Martin DL, Asante-Poku A, Migchelsen SJ, Gwyn S, et al. Serological and PCR-based markers of ocular Chlamydia trachomatis transmission in northern Ghana after elimination of trachoma as a public health problem. PLoS Negl Trop Dis. 2018; 12(12): e0007027.
11 Martin DL, Saboyà-Díaz MI, Abashawl A, Alemayeh W, Gwyn S, Hooper PJ, et al. The use of serology for trachoma surveillance: Current status and priorities for future investigation. PLoS Negl Trop Dis. 2020; 14(9): e0008316.
12 Solomon AW, Holland MJ, Burton MJ, West SK, Alexander ND, Aguirre A, et al. Strategies for control of trachoma: observational study with quantitative PCR. Lancet. 2003; 362(9379): 198-204.
13 Warrell DA. Snake bite. Lancet. 2010; 375(9708): 77-88.
14 UoM. Snake venom detection kits The University of Melbourne2021. (viewed Aug 2021). https://biomedicalsciences.unimelb.edu.au/departments/department-of-biochemistry-and-pharmacology/engage/avru/advice-and-resources/for-clinicians/snake-venom-detection-kits.
15 Marks M, Goncalves A, Vahi V, Sokana O, Puiahi E, Zhang Z, et al. Evaluation of a rapid diagnostic test for Yaws infection in a community surveillance setting. PLoS Negl Trop Dis. 2014; 8(9): e3156.
16 Marks M, Yin YP, Chen XS, Castro A, Causer L, Guy R, et al. Metaanalysis of the performance of a combined treponemal and nontreponemal rapid diagnostic test for syphilis and yaws. Clin Infect Dis. 2016; 63(5): 627-33.
17 Ayove T, Houniei W, Wangnapi R, Bieb SV, Kazadi W, Luke LN, et al. Sensitivity and specificity of a rapid point-of-care test for active yaws: a comparative study. The Lancet Global health. 2014; 2(7): e415-21.
18 Menke HE, Veldkamp J, Brunings EA, Niemel PL, Notowicz A, Stolz E. Comparison of cardiolipin and treponemal tests in the serodiagnosis of yaws. Br J Vener Dis. 1979; 55(2): 102-4.
19 Garner MF, Backhouse JL, Daskalopoulos G, Walsh JL. Treponema pallidum haemagglutination test for yaws. Comparison with the TPI and FTA-ABS tests. Br J Vener Dis. 1972; 48(6): 479-82.
20 Marks M, Fookes M, Wagner J, Butcher R, Ghinai R, Sokana O, et al. Diagnostics for yaws eradication: Insights from direct next-generation sequencing of cutaneous strains of Treponema pallidum. Clin Infect Dis. 2018; 66(6): 818-24.
21 Harper KN, Liu H, Ocampo PS, Steiner BM, Martin A, Levert K, et al. The sequence of the acidic repeat protein (arp) gene differentiates venereal from nonvenereal Treponema pallidum subspecies, and the gene has evolved under strong positive selection in the subspecies that causes syphilis. FEMS Immunol Med Microbiol. 2008; 53(3): 322-32.
22 Dacheux L, Reynes JM, Buchy P, Sivuth O, Diop BM, Rousset D, et al. A reliable diagnosis of human rabies based on analysis of skin biopsy specimens. Clin Infect Dis. 2008; 47(11): 1410-7.
23 CDC. Infectious diseases laboratory test directory 2021. (viewed Aug 2021). https://www.cdc.gov/laboratory/specimen-submission/cdc-lab-tests.pdf.
24 Weaver SC, Lecuit M. Chikungunya virus and the global spread of a mosquito-borne disease. N Engl J Med. 2015; 372(13): 1231-9.
25 Reddy A, Bosch I, Salcedo N, Herrera BB, de Puig H, Narváez CF, et al. Development and validation of a rapid lateral flow E1/E2-antigen test and ELISA in patients infected with emerging Asian strain of chikungunya virus in the Americas. Viruses. 2020; 12(9).
26 Fumagalli MJ, de Souza WM, Espósito DLA, Silva A, Romeiro MF, Martinez EZ, et al. Enzyme-linked immunosorbent assay using recombinant envelope protein 2 antigen for diagnosis of Chikungunya virus. Virol J. 2018; 15(1): 112.
27 Edwards T, Del Carmen Castillo Signor L, Williams C, Larcher C, Espinel M, Theaker J, et al. Analytical and clinical performance of a Chikungunya qRT-PCR for Central and South America. Diagn Microbiol Infect Dis. 2017; 89(1): 35-9.
28 Simmons M, Myers T, Guevara C, Jungkind D, Williams M, Houng HS. Development and validation of a quantitative, one-step, multiplex, real-time reverse transcriptase PCR assay for detection of dengue and chikungunya viruses. J Clin Microbiol. 2016; 54(7): 1766-73.
29 Plennevaux E, Moureau A, Arredondo-García JL, Villar L, Pitisuttithum P, Tran NH, et al. Impact of dengue vaccination on serological diagnosis: insights from phase III dengue vaccine efficacy trials. Clin Infect Dis. 2018; 66(8): 1164-72.
30 Vázquez S, Valdés O, Pupo M, Delgado I, Alvarez M, Pelegrino JL, et al. MAC-ELISA and ELISA inhibition methods for detection of antibodies after yellow fever vaccination. J Virol Methods. 2003; 110(2): 179-84.
31 Jessie K, Fong MY, Devi S, Lam SK, Wong KT. Localization of dengue virus in naturally infected human tissues, by immunohistochemistry and in situ hybridization. J Infect Dis. 2004; 189(8): 1411-8.
32 Welch RJ, Chang GJ, Litwin CM. Comparison of a commercial dengue IgM capture ELISA with dengue antigen focus reduction microneutralization test and the Centers for Disease Control dengue IgM capture-ELISA. J Virol Methods. 2014; 195: 247-9.
33 Lu Y, Sengvilaipaseuth O, Chanthongthip A, Phonemixay O, Vongsouvath M, Phouminh P, et al. Comparison of two commercial ELISA kits for the detection of anti-dengue IgM for routine dengue diagnosis in Laos. Trop Med Infect Dis. 2019; 4(3).
34 Xiong Y, Luo Y, Li H, Wu W, Ruan X, Mu X. Rapid visual detection of dengue virus by combining reverse transcription recombinase-aided amplification with lateral-flow dipstick assay. Int J Infect Dis. 2020; 95: 406-12.
35 Santiago GA, Vergne E, Quiles Y, Cosme J, Vazquez J, Medina JF, et al. Analytical and clinical performance of the CDC real time RT-PCR assay for detection and typing of dengue virus. PLoS Negl Trop Dis. 2013; 7(7): e2311.
36 Bradbury R, Benedict T, Rivera H. Trypanosomiasis. Washington DC2019.

Table 2. Search terms used for data collection

Disease name/commonly used term	AND	Australia
Dengue		
Chikungunya		
Rabies, bat lyssavirus		
Trachoma, trichiasis, Chlamydia trachomatis		
Buruli ulcer, Bairnsdale ulcer, Searls ulcer, Daintree ulcer, Mycobacterium ulcerans		
Yaws, Treponema pallidum pertenue		
Leprosy, Hansen's disease, Mycobacterium lepr*		
Chagas disease, Trypanosoma cruzi, American trypanosomiasis		
Human African trypanosomiasis, sleeping sickness, Trypanosoma brucei		
Leishmania*, Leishmaniosis		
Taenia*, tapeworm, cysticercosis, neurocysticercosis, solium, saginatum, asiatica		
Dracuncul*, guinea worm		
Echinococc*, hydatid disease		
Foodborne trematod*, Clonorch*, Opisthorch*, Fasciol*, Paragonim*, liver fluke, lung fluke		
Onchocerc*, river blindness, Robles disease		
Schistosom*, bilharzia, blood fluke		
Soil-transmitted helminth*, geohelminth*, nematode*, hookworm, Ascari*, Necator, Ancylostoma, Trichuri*, Strongyloid*		
Mycetoma		
Scabies, ectoparasite*, Sarcoptes scabiei		
Snakebite, snake bite, snake envenoming, snake venom		

WHO = World Health Organization.