water e-journal
Online Journal of the Australian Water Association
ISSN 2206-1991
Volume 2 No 2 2017
https://doi.org/10.21139/wej.2017.012

UNDERSTANDING *NAEGLERIA FOWLERI*

A Different Type of Pathogen, An Increasing Climate Change Threat

C Laydon

ABSTRACT

Naegleria fowleri is warm water environmental pathogen which, in contact with the internal nasal passage, can cause a rare but fatal infection called Primary Amoebic Meningoencephalitis (PAM). While Australia was one of the first countries to investigate this pathogen in the context of potable water risks and mitigation, there is a mixed level of understanding and awareness in the current industry.

With a climate of increasing temperature trends, this pathogen has the potential to become more prevalent within Australia and internationally. With recent cases in America being the first to be attributed to potable water supplies, the Centers for Disease Control and Prevention (CDC) is currently assessing the potential for climate-related changes to expand the geographical range of the organism.

This paper presents information on the pathogen, its infection pathway and resulting disease, as well as the Australian historical study that provided the basis of the current potable water advice within the Australian Drinking Water Guidelines (ADWG) and results of more recent disinfection studies. The key objective of this paper is to provide a comprehensive review of the available information, so as to provide a greater understanding of the pathogen, its risks, and mitigation measures regarding potable water management.

INTRODUCTION TO NAEGLERIA

Naegleria is a natural environmental water borne organism (free moving amoeba) that lives in warm fresh water conditions, and is part of the 'Thermophilic Amoeba' group.

Naegleria prefers warm water and grows optimally at approximately 45°C. However, at cooler temperatures (20°C to 12°C) the amoeba will revert to a cyst form (Chang, 1978) (spherical 7-15 μm in diameter) which can protect the organism until more favourable warmer conditions return. (Figure 1) When water is warm and organic material is available the organism will undergo excystation into the trophozoite form (10-35 μm long). If food becomes scarce the amoeba can also transition into a temporary non feeding flagellated state (10-16 μm in length) (CDC, 2015).

While there are numerous species within the *Naegleria* genus, *Naegleria fowleri* is the primary pathogen of human concern. Unlike most water borne pathogens of concern, *Naegleria fowleri* does not use a mammal host to complete its lifecycle nor does it cause any symptoms if ingested. Instead if the trophozoite form of the organism is exposed to the nasal track, the trophozite will penetrate the nasopharyngeal mucosa, migrate to the olfactory nerve, and invades the brain through the cribriform plate (Marshall, 1997), refer to Figure 2. There have also been studies that indicate that if an infectious cyst is inhaled the cyst can undergo excystation and the trophozoite follows the same route for infection (Marshall, 1997). However it is noted that this cyst infection pathway has also been disputed by other studies (Dorsch, 1982). As a result, it is accepted that the most common and likely infection exposure pathway is direct contaminated water exposure to the inside of the nasal track.

Once infection occurs, due to warm body temperatures and the presence of organic matter, the brain provides optimal living conditions for *Naegleria fowleri* and as a result the organism starts to feed on the brain tissue, causing cell inflammation and degradation.

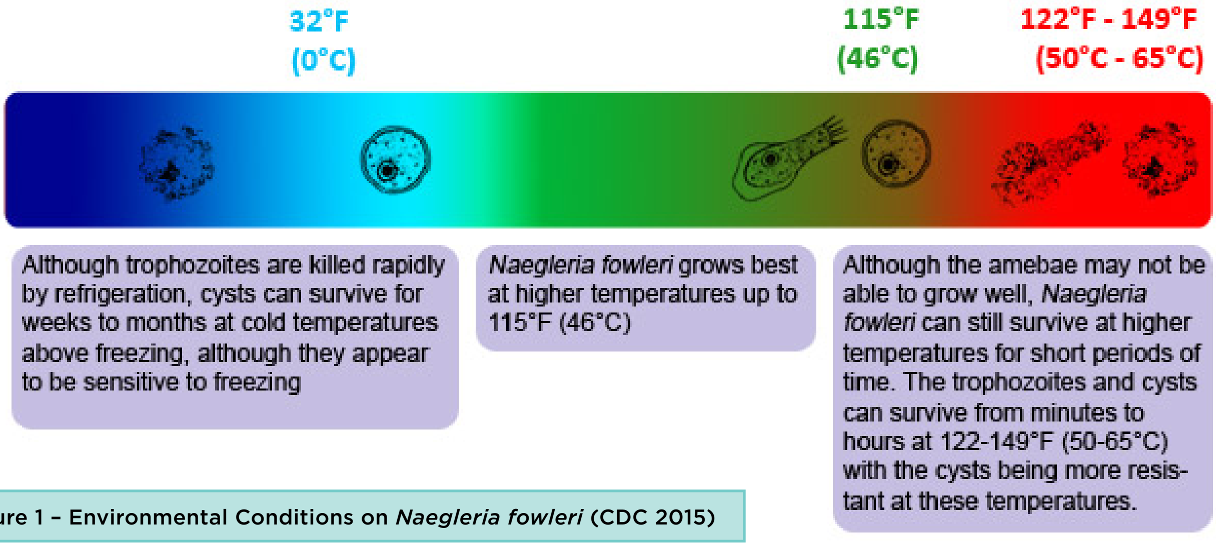


Figure 1 – Environmental Conditions on *Naegleria fowleri* (CDC 2015)

This infection is called Primary Amoebic Meningoencephalitis (PAM), and in the majority of cases death occurs within 1-2 weeks of infection (Healthdirect, 2015). While fatal, given the right conditions, the disease is considered rare. Within the United States (U.S.) there have been only 138 cases of PAM from 1962 to 2015 (CDC 2015).

The majority of PAM cases worldwide occur due to exposure to contaminated recreational water, such as seasonally warmed fresh water lakes and dams, hot springs, etc. Infections do occur more commonly in children and males. There is uncertainty regarding the distribution pattern of infections, but it is suspected, as the cribriform plate is not fully fused in small children, this can increase infection potential. Water activities which could lead to exposure may also reflect the types of water activities (such as diving or water sports) that might be more common among children, particularly young boys (CDC, 2015).

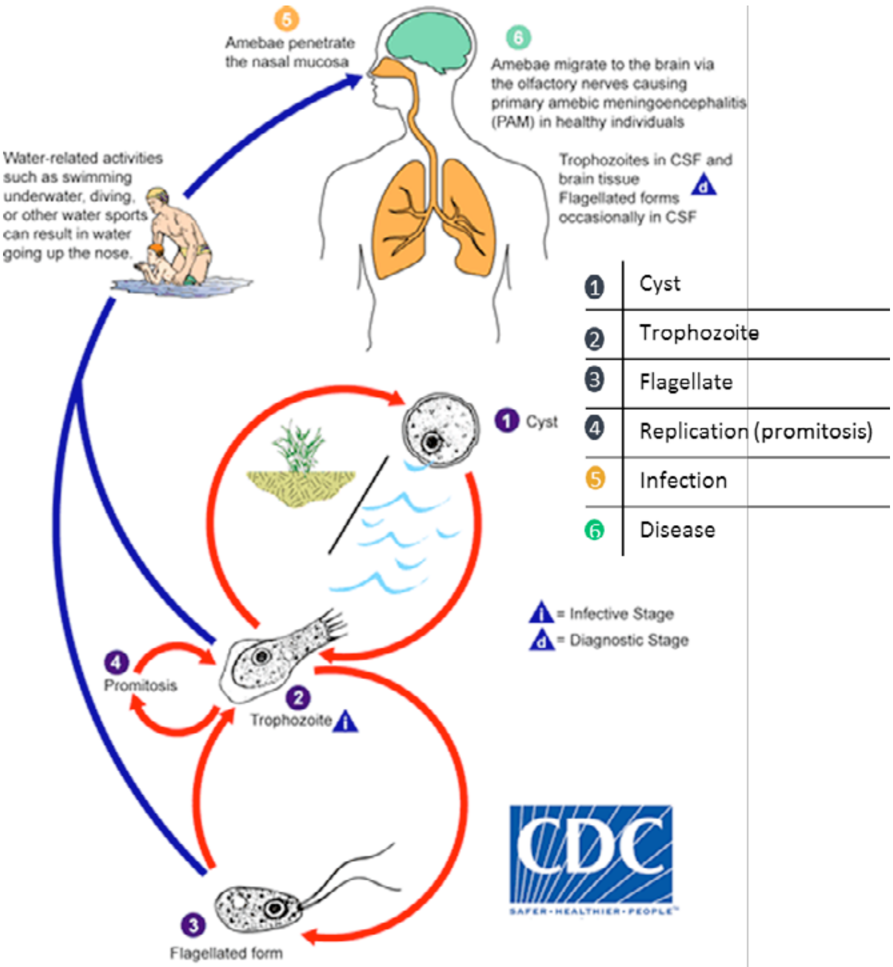


Figure 2 – Lifecycle and infection path for *Naegleria fowleri* (CDC 2015)

Symptoms of infection include high fever, severe and persistent headache, stiff neck, confusion or hallucinations, sleepiness, sore throat, nausea and vomiting, disturbances of taste and smell, seizures (fits) (Healthdirect, 2015), ultimately in the great majority of cases the infection results in death.

The disease is diagnosed using specific and specialised laboratory tests. PAM and *Naegleria fowleri* infection can be diagnosed in the laboratory by detecting *Naegleria fowleri* organisms in cerebrospinal fluid (CSF), biopsy, or tissue specimens, by detecting *Naegleria fowleri* nucleic acid in CSF, biopsy, or tissue specimens, or by detecting *Naegleria fowleri* antigen in CSF, biopsy, or tissue specimens. (CDC, 2016).

Due to the rarity of the infection, speciality tests required for detection, difficulty in identifying the pathogen, and the rapid nature of the disease, PAM is difficult to treat. As a result, the great majority of the cases (greater than 97%) are fatal, and 75% of diagnoses are made after the death of the patient. (CDC, 2016).

More recently there have been two known survivors of the infection in 2013 within Northern America. The first, a 12-year-old girl, was diagnosed with PAM approximately 30 hours after becoming ill and was started on the recommended treatment within 36 hours. She also received the investigational drug miltefosine, and her brain swelling was aggressively managed with treatments that included therapeutic hypothermia (cooling the body below normal body temperature). This patient made a full neurologic recovery and returned to school. Her recovery has been attributed to early diagnosis and treatment and novel therapeutics including miltefosine and hypothermia.

A second 8-year-old child is also considered a PAM survivor, although he has suffered what is likely permanent brain damage. He was also treated with miltefosine but was diagnosed and treated several days after his symptoms began. Therapeutic hypothermia was not used in this case. Overall, the outlook for people who get this disease is poor, although early diagnosis and new treatments might increase the chances for survival (CDC, 2016).

DISCUSSION OF CURRENT AUSTRALIAN GUIDELINES

As outlined, the key findings from the Dorsch 1982 study has provided the basis for the recommendations within the current ADWGs. The Dorsch study reviewed PAM cases within Australia from 1955 to 1981, as shown in Figure 3, to identity the causes of the infections, and to review the potable water management approaches used in those affected supplies. Based on these findings the ADWGs have include a dedicated factsheet on the pathogen. However, within the material the ADWG does not set a health limit guideline value for the pathogen. Instead it provides a number of key recommendations regarding monitoring, trigger levels and response approaches.

The ADWG have outlined that water supplies that seasonally exceeds 30°C or that continually exceeds 25°C can support the growth of *Naegleria fowleri.* (ADWG, 2016). The ADWG also recommends prospective studies on those water supplies with elevated temperatures, which could then lead to more regular testing if detections are found.

In testing for *Naegleria fowleri,* the first detection test is for the Thermophilic Amoeba group, following which the genus is identified, and then if *Naegleria* is detected further, testing and identification is undertaken to determine *Naegleria fowleri*. The ADWG notes that any detection of any thermophilic amoeba is evidence that conditions are suitable for *Naegleria fowleri,* should it be introduced, and if samples include any *Naegleria* remedial action should be taken immediately without waiting for specific identification (ADWG 2016).

Further the ADWG outline that a density of 2 organisms per litre (or detection in a 500 mL sample) is an appropriate threshold for action, given the rapid density changes that can occur. (ADWG, 2016) and that other thermophilic *Naegleria* can be useful 'proxy' organisms for *Naegleria fowleri,* allowing early remedial action. (ADWG, 2016)

In this regard, as per the ADWGs, water authorities which have water at the correct temperatures, anywhere within the water supply system, should consider a study or periodic testing to review if they have the supporting conditions and presence of thermophilic amoeba and *Naegleria*. If detections are made then this warrants 'remedial' action and notification and advice from the relevant health authority (such as the State's Department of Health).

Remedial action is not defined in the ADWG, however there is clear guidance that a free chlorine or chloramination level of 0.5 mg/L should be targeted throughout the entire network (ADWG, 2016) to manage the pathogen. This is based on the key findings from the Dorsch 1982 study.

It is noted that in a practical application achieving a free chlorine of 0.5 mg/L throughout the entire network can be difficult, and often requires higher dose rates at the dosing plant, which can cause aesthetic issues to close customers and also makes the management of disinfection by-products more challenging.

From the behaviour of the organism, as supported in the Dorsch 1982 study, thermophilic amoeba, *Naegleria* and *Naegleria fowleri* can be more difficult to isolate in routine samples. Amoeba are free moving (when in trophozoite form) and can move throughout a water system. The organisms also prefer biofilm, sludge layers and filter media, where they can be protected from chlorine and able to colonise. Due to the colonisation in these environments, samples of sludge, such as in the bottom of reservoirs, pipeline slimes, biofilms and backwash water, can provide elevated levels of amoeba, as compared to reticulated water samples. These results, while not truly representative of the supplied water, are useful in determining the organism's presence in the system. Further it can also drive increased operational activities to improve reservoir and pipeline cleanliness to reduce conducive environments for the pathogen.

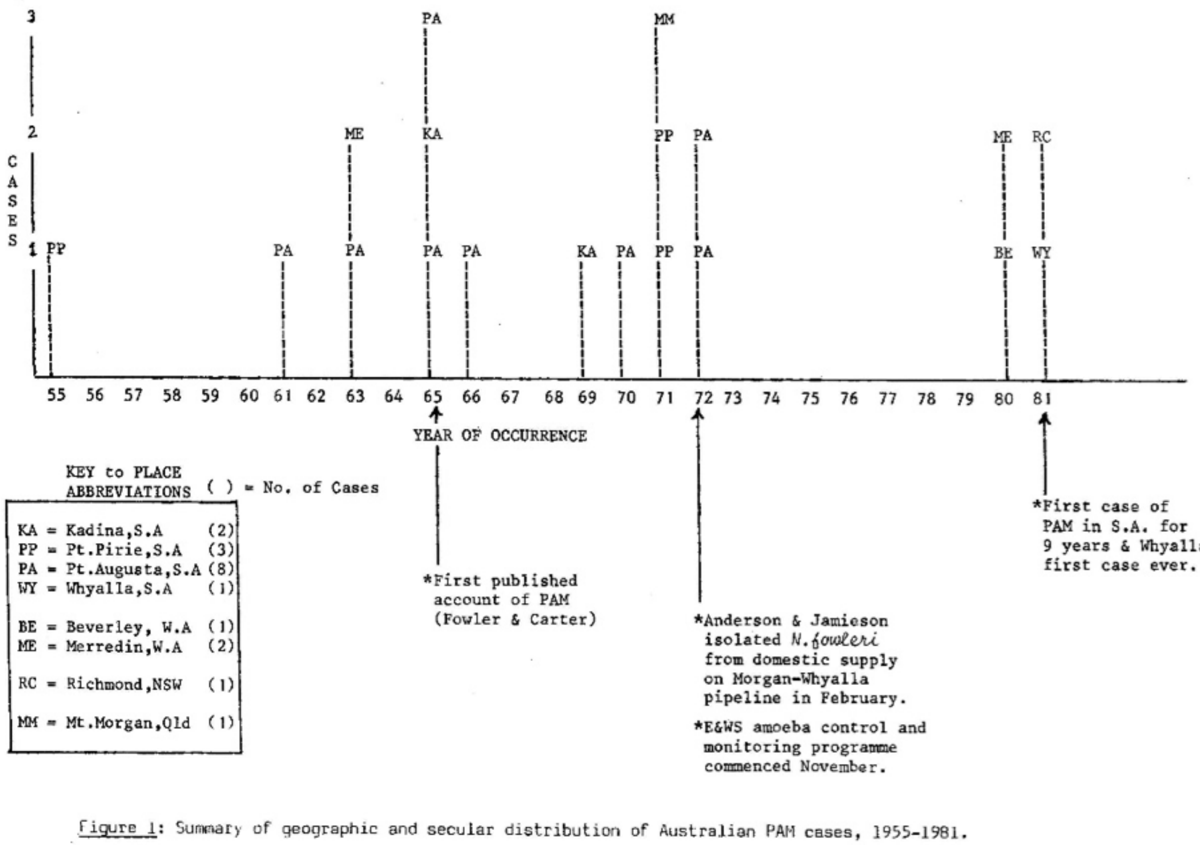


Figure 3 – Summary of geographic and secular distribution of Australian PAM cases, 1955 – 1981 (Dorsch, 1982)

DISCUSSION OF RECENT DISINFECTION STUDIES AND RISK ASSESSMENTS

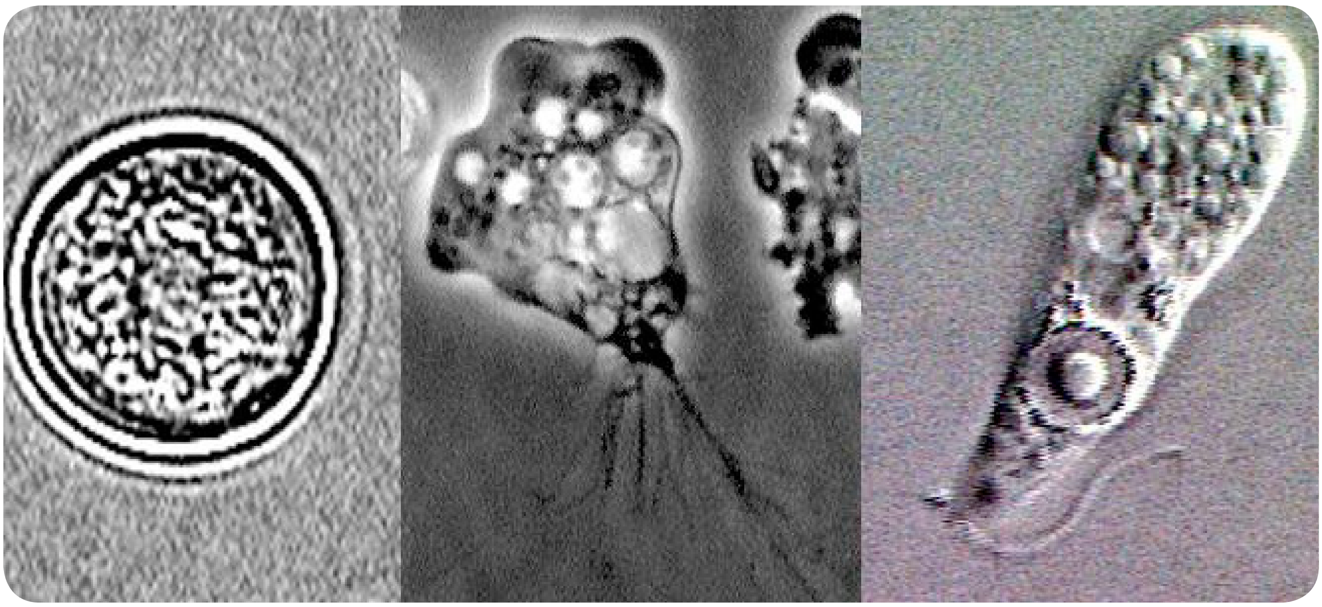
Although Australia had till recently the most comprehensive information regarding potable water management of *Naegleria fowleri*, the United States (U.S.) has been undertaking a number of new studies and investigations.

This is following a number of PAM deaths that have been directly linked to potable water supplies in the U.S. for the first time. Six infections in the U.S. have been associated with using water from drinking water systems. (CDC, 2016).

This more recent American research has resulted in the determination of Ct and log removal values using chlorine and UV for the amoeba, both in open trophozoite and cyst from Arizona bore waters (Sarkar and Gerba, 2012). It should be noted that the bore waters used in this study had a, pH of 7.3 – 8.2, turbidity of 0.04 NTU and a total organic content of 0.7 – 1 mg/L.

The findings from this study indicate that the chlorine Ct of 15 mg-min/L, as sighted by Dorsch 1982, would provide a greater than 4 log reduction for *Naegleria fowleri* trophozoite, but would not be sufficient for a 2 log reduction of cysts.

As with many amoeba, the cyst state provides *Naegleria fowleri* with an additional protection from environmental stresses, and as result increases the disinfection requirements. As a result, cooling the contaminated water below 20°C (Chang, 1978) causes encystation and as a result will require higher chlorine Ct and UV doses to ensure adequate disinfection, however maintaining chlorine in warmer waters is also challenging as it increases rates of chlorine volatilisation. As with general chlorination maintaining the pH under 9, is also important to ensure higher chlorination (hypochlorous acid; HOCl) efficiencies.



Naegleria fowleri **lifecycle stages**

The key results from Sarkar and Gerba, 2012 are from the expanded summary paper and are shown in Table 1 and Table 2.

The risk profile of this pathogen in municipal water supplies is likely to remain at a lower risk level compared to traditional water borne gastroenteritis pathogens. However, there is a question regarding the prevalence of this pathogen in current water supplies that have the correct environmental conditions which have not been previously tested for the amoeba. Further, there is a potential with a warming climate that this amoeba may become more widespread over an already warm continent such as Australia.

The ADWG support a risk assessment approach in reviewing pathogenic risk in potable water supplies and it is important that water authorities consider this pathogen during these assessments. In addition, within Australia there are a number of reticulated non chlorinated, recycled water and raw water systems as well as individually managed household supplies, such as rainwater tanks and bores which could be at risk. In these cases, conditions could be suitable for *Naegleria fowleri* and although many of these schemes may be deemed as non-potable, the water could be used in a manner which could lead to an infection. In these cases, those with the responsibility for community health may need to consider the risk profile of these supplies with a specific focus on *Naegleria fowleri*.

Table 1 – Chlorine contact times and log reduction values for *Naegleria fowleri* (Sarkar and Gerba, 2012)

Cx Tvalues for *Naegleria fowleri* trophozoites and cysts in buffered water			
PH	Log_{10} Inactivation	C x T for Trophozoites	C x T for Cysts
7.5	2	6	31.2
	3	9	42.5
	4	12.2	53
9.0	2	18	37
	3	23	50
	4	27.5	62
C x T—concentration x exposure time			

Table 2 – Ultraviolet dose and log reduction values for *Naegleria fowleri* (Sarkar and Gerba, 2012)

Dose of ultraviolet light required to inactivate *Naegleria fowled cysts* and trophozoites in mW.s/cm² at 24°C			
Life Stage	$2Log_{10}$	$3Log_{10}$	$4Log_{10}$
Trophozoite	12.6	18.1	24
Cyst	63	104.3	121

DISCUSSION ON PRACTICAL MANAGEMENT

A number of Australian state departments have developed supporting medical and potable water advice. This includes the Western Australian Department of Health (WA DoH), who have developed specific Amoeba Response Protocols (WA DoH, 2014), to support WA water suppliers by providing information, monitoring and response guidance on the pathogen.

The Amoeba Response Protocols (WA DoH, 2014) recommend a slightly lower temperature threshold for testing at 20°C compared to the ADWG of 25°C, South Australia and Queensland Health (SAH, 2012 and QLD Health 2015) identified waters within the range of 25°C to 40°C are at risk, which is in line with the ADWG.

In addition, the Western Australia Water Corporation (WaterCorp, 2008) who manage a number of supplies which have had detections of *Naegleria* use management practices which reflect the ADWGs, such as by ensuring adequate disinfection and on ongoing free chlorine residual.

Water Corporation targets a chlorine contact time of greater than 30 mg/L-min and in many cases the chlorine contact time ranges from 50 to 500 mg/L-min. The ADWG free chlorine residual target of 0.5 mg/L, in some cases due to practicality, has been effectively reduced to maintain a free residual, at or greater than, 0.2 mg/L. Under circumstances which have previously lead to detections such as after burst mains, tanks running empty, valve operations or flow reversals the residual levels are increased to 0.5 mg/L. (WaterCorp, 2008) This is coupled with ongoing monitoring to ensure there are no detections which would require an increase in residual. As well as optimising pH and reticulation and reservoir cleanliness to reduce biofilms and sediment layers. (WaterCorp, 2008)

For those water supplies that may fall into the risk temperature profile it is advised to discuss any concerns of with the local and state health departments to determine an appropriate course of action. This may include initially undertaking a monitoring program for thermophilic amoeba and reviewing chlorination contact times, residual and reticulation management practices.

While this pathogen has a long history in Australia, and is being effectively managed by a number of water authorities, it has been on the peripheries of industry awareness. Therefore, it is important that with the increasing risk management approaches, and improvements in water quality safety that this pathogen be considered as we currently have the tools to effectively monitor and manage this pathogenic risk.

CONCLUSION

With the likelihood of increased temperatures due to climate change, *Naegleria fowleri* could become even more prevalent in Australian water supplies. Australia has historically been at forefront of managing *Naegleria fowleri* in potable water supplies and it is important that we continue to use the best management approaches, and review the most recent studies and data, to continue to control this deadly pathogen to protect public health.

THE AUTHOR

Clara Laydon is a senior process engineer at Hunter H2O. Clara focus on drinking water quality management and has worked with municipal water schemes which have had to consider the risk of *Naegleria fowleri* since 2008. Clara has also presented on *Naegleria fowleri* at a number of Australian conferences and internationally.

Email: clara.laydon@hunterh2o.com.au

REFERENCES

Chang, 1978, Resistance of pathogenic Naegleria to some common physical and chemical agents, Applied and Environmental Microbiology, 35(2) page 369, Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC242840/?page=2 [8 February 2017].

CDC 2015, Naegleria fowleri — Primary Amebic Meningoencephalitis (PAM) — Amebic Encephalitis, Pathogen & Environment, 7 December 2015, Centers of Disease Control and Prevention. Available from: https://www.cdc.gov/parasites/naegleria/pathogen.html [19 January 2017]

Healthdirect 2015, Primary amoebic meningoencephalitis (PAM), Australian Government Department of Health, November 2015. Available from: https://www.healthdirect.gov.au/primary-amoebic-meningoencephalitis-pam [19 January 2017]

CDC 2016, Naegleria fowleri — Primary Amebic Meningoencephalitis (PAM) — Amebic Encephalitis, Illness and Symptoms, 12 April 2016, Centers of Disease Control and Prevention. Available from: https://www.cdc.gov/parasites/naegleria/pathogen.html [19 January 2017]

Dorsch 1982, Primary Amoebic Meningoencephalitis: An Historical and Epidemiological perspective with Particular Reference to South Australia, Epidemiology Branch South Australian Health Commission, January 1982.

ADWG 2016, Australian Drinking Water Guidelines, National Health and Medical Research Centre, 2011 – Updated November 2016. Available from https://www.nhmrc.gov.au/guidelines-publications/eh52 [25 January 2017]

Sarkar and Gerba 2012, Inactivation of Naegleria fowleri by Chlorine and Ultraviolet Light, March 2012, Journal - American Water Works Association, Volume 104, Number 3 Pages E173-E180.

Miller et al 2015, Haylea C. Miller†‡, Jason Wylie‡, Guillaume Dejean‡§, Anna H. Kaksonen‡∥, David Sutton∥, Kalan Braun⊥, and Geoffrey J. Puzon, Reduced Efficiency of Chlorine Disinfection of Naegleria fowleri in a Drinking Water Distribution Biofilm, Environmental Science and Technology, August 19, 2015), pages 11125–11131

ABC 2015, Australian Story - Out of the Water, Australian Broadcasting Corporation, 10 November , 2015. Available from http://www.abc.net.au/austory/content/2015/s4338006.htm [25 January 2017]

WA DoH 2014, Amoeba response protocol, Water Unit, Environmental Health Directorate

Public Health Division, Department of Health, Available from http://ww2.health.wa.gov.au/~/media/Files/Corporate/general%20documents/water/PDF/Amoeba-Response-Protocol.ashx [7 February 2017]

SAH 2016, Naegleria fowleri, South Australian Department of Health, Last Modified: 21 Dec 2016. Available from:

http://www.sahealth.sa.gov.au/wps/wcm/connect/public+content/sa+health+internet/protecting+public+health/water+quality/naegleria+fowleri [13 February 2017]

QLD Health 2015, Naegleria fowleri: Qs and As, Queensland Department of Health, Last modified 5 November 2015,

http://conditions.health.qld.gov.au/HealthCondition/condition/14/165/101/Naegleria-fowleri-Qs-As [[13 February 2017]

(WaterCorp, 2008), Operational management of Naegleria spp. in drinking water supplies in Western Australia, Water Corporation, Trolio, Bath, Gordon and Wyber, July 2008.