Chapter 23. Diplostomiasis (*Diplostomum spathaceum* and related species)

Anssi Karvonen[1*] & David J. Marcogliese[2,3]

[1]University of Jyväskylä, Department of Biological and Environmental Science, P.O. Box 35, FI-40014 University of Jyväskylä, Finland. Email: anssi.t.karvonen@jyu.fi

[2]Aquatic Contaminants Research Division, Water Science and Technology Directorate, Science and Technology Branch, Environment and Climate Change Canada, St. Lawrence Centre, 105 McGill, 7th floor, Montreal, Quebec H2Y 2E7, Canada. Email: david.marcogliese@canada.ca

[3]St. Andrews Biological Station, Fisheries and Oceans Canada, 125 Marine Science Drive, St. Andrews, NB E5B 0E4, Canada.

23.1 Introduction

Diplostomum spp. (Trematoda) are widespread parasites of freshwater and brackish water fishes (Chappell, 1995), and they infect different parts of the fish eyes such as lens, humour and retina (Marcogliese *et al.*, 2001a; Karvonen *et al.*, 2006b; Désilets *et al.*, 2013; Padros *et al.*, 2018). In the ecological literature, species infecting the lens are commonly grouped as a single species, *Diplostomum spathaceum*. However, morphological (Niewiadomska, 1984, 1986; Niewiadomska and Kiseliene, 1994) and particularly molecular studies (Niewiadomska and Laskowski, 2002; Locke *et al.*, 2010a; Locke *et al.*, 2010b; Rellstab *et al.*, 2011; Blasco-Costa *et al.*, 2014; Locke *et al.*, 2015) indicated that *Diplostomum* is a species complex with a number of different species infecting specific parts of fish eyes. However, details of life histories and ecological differences of many of the species are not known. Our present focus is on species infecting the lens and causing diplostomiasis. Most of the published literature is on *D. spathaceum* (in the light of the current knowledge possibly including more than one species) or *D. pseudospathaceum* (the species was described by Niewiadomska (1984) and verified by Niewiadomska and Laskowski (2002) using molecular techniques). For simplicity and due to the lack of data, we assume here that effects of all parasite species possibly co-infecting a lens are similar and they respond roughly the same way to climate change.

The life cycle of lens-infecting *Diplostomum* spp. includes an avian definitive host, a molluscan first intermediate host and fish second intermediate host (Chappell *et al.*, 1994; Karvonen, 2012) (Fig. 23.1). Parasites reproduce sexually in the gut of the bird and start producing eggs in three days after establishment (Chappell *et al.*, 1994). Eggs are released into the aquatic environment through bird faeces. They hatch to free-swimming miracidia that are non-feeding and short-lived stages, which infect the molluscan intermediate host. This is typically a snail of the genus *Lymnaea*. Within a snail, each miracidium gives rise to a mother sporocyst, which then replicates asexually to multiple daughter sporocysts. Larval cercariae are formed in the sporocyst through asexual reproduction. Thus, cercariae from a single-miracidial infection in a snail are genetically identical. However, one snail can be infected with multiple miracidia (Rauch *et al.*, 2005; Louhi *et al.*, 2013) and produce cercariae of different genotypes at the same time. Cercariae are released from an infected snail to surrounding water in very high numbers (Lyholt and Buchmann, 1996; Karvonen *et al.*, 2004a). Free-swimming cercariae in the water column do not feed after leaving the snail, but rely on glycogen reserves, which last for approximately 24 hours (Karvonen *et al.*, 2003). Afterwards, cercariae lose their infectivity and die. If a cercaria encounters a fish, it penetrates gills or skin and migrates as a diplostomulum to the eye lens. Details of the route and mechanisms of migration are unknown (Ratanarat-Brockelman, 1974). The migration typically takes place within 24 h, but this depends on the water temperature (Lyholt and Buchmann, 1996). Diplostomulum that fails to complete the migration exhausts its energy reserves and is eliminated by the fish immune system. Those that reach the lens are at least partly protected from the host immune system, as the eye lens is not directly connected to blood circulation of the fish. In the lens, parasites develop to the final larval stages, metacercariae, within a few weeks and afterwards can probably survive in the lens for years. Consequently, numbers of metacercariae in fish tend to increase with time (Marcogliese *et al.*, 2001b). The life cycle is completed when a fish-eating bird consumes an infected fish.

INSERT FIGURE 23.1 HERE

Figure 23.1 Life cycle of *Diplostomum* spp. includes three hosts. Parasites mature in the intestine of a definitive host (1) and release eggs (2) into the aquatic environment with faeces. Eggs hatch into miracidia (3) that seek the first intermediate host, an aquatic snail. Within the snail (4), parasites reproduce asexually producing high numbers of cercariae (5) that are released to water. Cercariae are short-lived and await a fish host. They penetrate the epithelium of the fish, migrate to the eye lenses, and develop to metacercariae (6). The life cycle is

completed when the definitive host consumes an infected fish. Reproduced with permission from Karvonen (2012).

Diplostomum spathaceum has been reported from eye lenses of over 100 fish species in Europe (Chappell, 1995), while the global distribution of the *Diplostomum* spp. probably includes many more host species. Thus, the genus is considered one of the most common and abundant parasites of freshwater fishes. Species belonging to Cyprinidae, Percidae, Salmonidae, Coregonidae, Catostomidae, and Gasterosteidae which inhabit littoral waters are commonly infected (Margolis and Arthur, 1979; McDonald and Margolis, 1995; Valtonen and Gibson, 1997; Seppälä *et al.*, 2011). *Diplostomum* spp. have also been reported from marine fish species in brackish waters including Gadidae and Pleuronectidae (Buchmann, 1986; Koie, 1999). However, the prevalence and abundance of the infection is typically highly variable and can depend, in addition to fish species, on the geographical location, type of water body, habitat within a water body, season, host age and community structure of all the other hosts in the life cycle (Pennycuick, 1971; Sweeting, 1974; Burrough, 1978; Balling and Pfeiffer, 1997; McKeown and Irwin, 1997; Valtonen and Gibson, 1997; Valtonen *et al.*, 1997; Marcogliese and Compagna, 1999; Marcogliese *et al.*, 2001a; Marcogliese *et al.*, 2001b; Karvonen *et al.*, 2004b; Karvonen *et al.*, 2015). For example, locations within a single lake can have different infection levels (Balling and Pfeiffer, 1997), possibly reflecting on factors such as differences in abundance of infected snails. Also, infections in the higher latitudes are seasonal and mainly take place during summer months (McKeown and Irwin, 1997; Marcogliese *et al.*, 2001a; Karvonen *et al.*, 2004b), which results in first infections in eye lenses of young fish and accumulation of infections with fish age.

23.2 Diagnosis

Metacercariae of *Diplostomum* spp. are soft-bodied, flat, bilateral and round or oval-shaped, with a body length of approximately 0.3-0.4 mm when fully-developed (note that the morphology and size strongly depend on the age of the metacercaria, (see Sweeting (1974)). Infections are clearly visible from a dissected eye lens under a microscope (Fig. 23.2) and identification is straightforward as all parasite species in eye lenses of a fish belong to this same genus. However, identification at species level is notoriously difficult. Different species are morphologically very similar, especially as larval stages (miracidium, cercaria, metacercaria), and their identification requires particular expertise and experience (Niewiadomska, 1986;

Niewiadomska and Kiseliene, 1994). More recently, species identification has been aided using molecular techniques (Niewiadomska and Laskowski, 2002; Moszczynska *et al.*, 2009), while these have resulted in a significant increase in the number of *Diplostomum* species (Locke *et al.*, 2010b; Blasco-Costa *et al.*, 2014).

INSERT FIGURE 23.2 HERE

Figure 23.2 Three metacercariae of *Diplostomum* sp. in an eye lens of Atlantic salmon. Photo courtesy of Ines Klemme.

23.2.1 Parasitic cataracts (diplostomiasis)

The most notable sign of infection in an eye lens is cataract formation due to metacercarial movement and metabolism which damage the structure of the lens. If there are many metacercariae, the damage accumulates and can result in the chronic stage of infection, known as diplostomiasis. A severe condition can be observed visually as the eye lens becomes opaque, grey or whitish. In extreme cases, the lens capsule can rupture or the lens becomes dislocated, when the fish host loses its eyesight. Fewer cataracts (e.g. small clouds of granules or thread-like formations (Shariff *et al.*, 1980)) and their early stages following development of the metacercariae can be seen reliably only using a microscope, such as an ophthalmoscope (Karvonen *et al.*, 2004c). This type of infections occur in most of the infected fish species worldwide.

Cataracts gradually impair the vision of fish and the degree of impairment is linearly related to the number of parasites in the lens (Karvonen *et al.*, 2004c) (Fig. 23.3). In other words, few parasites rarely cause severe cataracts, except in small fishes, although parasites can remain in the lens for years. However, there are no detailed data on long-term dynamics of cataracts recorded from individual fish. Development of cataracts is also related to the size of the fish and, consequently, size of the eye lens. In a small fish, even a low number of parasites can be sufficient to cause severe pathology (Karvonen and Lindström, 2018). Further, recent evidence suggest that fish may also show differences in their ability to tolerate the deleterious effects of the parasites, i.e., the same number of parasites results in different degree of cataract formation (Klemme and Karvonen, 2017). Infection can also decrease the lens size directly (Karvonen and Seppälä, 2008a), but the significance of such effects for visual ability of fish needs further study.

INSERT FIGURE 23.3 HERE

Figure 23.3 Relationship between cataract coverage and the number of *Diplostomum pseudospathaceum* in the eye lenses of whitefish (*Coregonus lavaretus*). Data from Karvonen and Seppälä (2008b). Reproduced with permission from Karvonen (2012).

Infections in the eye lens and the subsequent cataract formation can have significant implications for the well-being of fish. Gradual deterioration of eyesight with increasing infection intensity can cause several physiological and behavioural effects in fish. One notable phenotypic sign of infection is darkening of the fish skin as the light intensity entering the eye decreases. This impairs the cryptic colouration of the fish particularly against a light background (Seppälä *et al.*, 2005a), which can lead to increased detection by predators. Eye infection can also decrease the efficiency of fish to detect and harvest prey items (Crowden and Broom, 1980; Owen *et al.*, 1993), which can result in decreased growth (Karvonen and Seppälä, 2008b). Impaired visual abilities have also a range of other effects that relate to social interactions of fish and susceptibility to avian predation, the latter of which is essential for completion of the parasite life cycle. For example, infection reduces group cohesion of shoaling fish (Seppälä *et al.*, 2008), which can render individual fish detectable by predators. Infected fish may also swim closer to the water surface (Crowden and Broom, 1980), although this evidence is not conclusive (Seppälä *et al.*, 2004). Further, infection and cataracts increase catchability of fish in experiments mimicking predation from fish-eating birds plunging into water from the air. These effects also coincide with the metacercariae becoming fully developed (Seppälä *et al.*, 2004, 2005b), which supports the idea that cataracts can enhance parasite transmission to the definitive hosts.

23.2.2 Implications of climate change for the parasite life cycle

Parasitism and disease in aquatic animals may increase with climate change, principally in response to rising temperatures that accelerate parasite development (Marcogliese, 2001, 2008; Lõhmus and Björklund, 2015), although general predictions are difficult to make as effects are species specific, context dependent and may vary among hosts (Marcogliese, 2008; Rohr *et al.*, 2011; Marcogliese, 2016). The existence of extreme weather events, confounding factors, and non-linear thresholds further complicate matters (Marcogliese, 2008; Rohr *et al.*, 2011; Altizer *et al.*, 2013; Marcogliese, 2016) and some diseases may actually decrease in occurrence with

climate change (Lafferty, 2009; Karvonen *et al.*, 2010b). Nevertheless, temperature is considered the most important abiotic factor that influence parasitic platyhelminths in ectothermic hosts, including fish (Chubb, 1979). In parasites with complex life cycles, such as *Diplostomum* spp., temperature affects all free-living life cycle stages as well as those in ectothermic hosts. Higher temperatures are generally expected to lead to faster growth, development and reproduction, earlier transmission and development in the spring, prolonged transmission in the autumn and more generations per year. However, it may also increase mortality rate among parasites in the aquatic environment (Marcogliese, 2001). Thus, it is important to consider the net effects of temperature within the entire parasite life cycle. As there are no data on relationships between temperature and cataracts (diplostomiasis) *per se*, and because cataracts are related to parasite numbers (Fig. 23.3), it is relevant to consider temperature-related factors that control the latter.

Our current discussion includes the effects of temperature on potential spread of *Diplostomum* spp., followed by temperature effects on production and transmission of the life cycle stages. Throughout, we will explore evidence on temperature effects on *Diplostomum* spp. and other trematode taxa and on general trematode biology, while discussing the net effects of increasing temperature for the parasite life cycle. We will also consider ecological evidence from field studies, and explore effects of temperature on the physiology and the resistance of snails and fish. Besides temperature, we will also focus on other environmental changes that are associated with climate change and likely to either increase or decrease parasite population. Finally, we will discuss the implications of climate warming for parasite prevention strategies in aquaculture.

23.3 Potential spread of *Diplostomum* spp. with increasing water temperature

Range shifts of aquatic biota are expected with climate change (Settele *et al.*, 2014). However, given that *Diplostomum* spp. are already widespread in the northern hemisphere (*e.g.*, see Fig. 1 in Locke *et al.* (2015)), large range shifts are unlikely. Lens-infecting *Diplostomum* spp. are generalists infecting a range of fish species (Locke *et al.*, 2010a; Locke *et al.*, 2010b; Rellstab *et al.*, 2011; Locke *et al.*, 2015), so changes in fish species composition as a result of fish host range expansion or contraction should not have large effects on the parasite's distribution. However, the host spectrum in any given habitat could change. For example, increasing temperatures are predicted to have significant negative effects on cold-water stenotherms, such

as salmonids and coregonids, contracting their range (Marcogliese, 2001; Chen *et al.*, 2016). These high-latitude cold-water stenotherms may experience an increase in their northern range, but a contraction of their southern boundaries with the expansion northward of temperate fishes (Ficke *et al.*, 2007; Settele *et al.*, 2014). In addition, warm- and cool-water fishes may displace native species as they migrate into higher latitudes in the northern hemisphere and lower latitudes in the southern hemisphere (Ficke *et al.*, 2007). Another potential complicating factor is that snail intermediate host populations may be at risk because freshwater molluscs are predicted to be unable to track high rates of climate change (Settele *et al.*, 2014). Their populations are further compromised by invasive species, habitat modification, and contaminants (Settele *et al.*, 2014).

In addition to range shifts of resident fish and invertebrate species, increasing temperature is expected to lead to the invasion of new and potentially susceptible hosts (Marcogliese, 2001; Altizer *et al.*, 2013), including those for *Diplostomum* spp. For example, there have already been numerous introductions of warm-water fish species into the lower Great Lakes, expanding their distributions northward (Marcogliese, 2001). Further warming should facilitate the introduction and expansion of warm-water invaders (Collingsworth *et al.*, 2017). There are at least two possible outcomes. First, invasive species can facilitate parasite transmission by effectively acting as new susceptible hosts and boost the life cycle completion. Second, new hosts can be resistant to infections and act as sinks of infection while diluting infection risk among the native hosts. In Europe, round gobies (*Neogobius melanostomus*) and bighead gobies (*Ponticola kessleri*) were heavily infected with *Diplostomum* spp. in their introduced range in the Danube River, the Rhine River, and parts of the south-western Baltic Sea, potentially enhancing transmission of *Diplostomum* spp. to piscivorous birds (Ondračková *et al.*, 2009; Muhlegger *et al.*, 2010; Francová *et al.*, 2011; Kvach and Winkler, 2011; Ondračková *et al.*, 2015). In contrast, following the introduction of the round goby in the St. Lawrence River, Canada, abundance of *Diplostomum* spp., which at one time was one of the most common fish parasites in that river, declined to extremely low levels within five years or less in yellow perch, *Perca flavescens*, golden shiner (*Notemigonus crysoleucas*) and the spottail shiner, *Notropis hudsonius* (Gendron and Marcogliese, 2017). The authors suggested this was due to gobies acting as incompetent decoy hosts for cercariae and diluting the risk of infection to the native fish. The difference between the capacity of gobies as hosts for *Diplostomum* spp. in Europe and North America may be because invasive gobies in Europe were exposed to widespread European species, while those in North America were exposed to new parasites

with which they had no previous experience. This idea is supported by the increase in abundance of *Diplostomum* spp. in round gobies over time (15 years) since their initial invasion into the Great Lakes (Gendron *et al.*, 2012).

23.4 Implications of increasing temperature for the parasite life cycle stages

23.4.1 Effects of elevated temperature on life cycle stages

Life cycle stages of *Diplostomum* spp. outside the endothermic avian host (miracidia, cercariae, and the larval forms residing in ectothermic snails and fish) are potentially influenced by increasing water temperature. However, it is important to note that in general, physiological tolerance of parasites to temperature not only varies among species, but also among stages of the same species (Chubb, 1979; Marcogliese, 2001). Overall, there are a few experimental studies on effects of temperature on different life cycle stages of *D. spathaceum* and related species (Table 23.1), although much more information is needed to make reliable predictions. For example, swimming velocity of the miracidia hatching from eggs increased at higher temperatures, but the life span declined (Harris, 1986). While the latter result is likely due to faster depletion of the finite glycogen reserves, the net effects on transmission are unknown. Considering these effects alone, an increase in temperature should likely promote the encounter between miracidia and potential snail hosts, but decrease the infective time-period. Further evidence on the snail host has shown that the time to patency decreased and cercarial output increased at higher temperatures (Harris, 1986; Waadu and Chappell, 1991), both of which should promote transmission to the fish host. However, both cercarial activity time and life span were reduced at higher temperatures, which should limit transmission (Harris, 1986; Sous, 1992; Lyholt and Buchmann, 1996). Moreover, cercarial penetration and speed of migration to the eyes increased at higher temperatures (Whyte *et al.*, 1988; Lyholt and Buchmann, 1996), but infectivity peaked at the mid-range of the experimental exposure temperatures (Stables and Chappell, 1986b). The latter results suggest that infection success would decrease eventually as temperature increases. To sum up, the contrasting effects of higher temperature would increase parasite reproduction, but decrease longevity and infectivity of the transmission stages. Consequently, it is at present difficult to predict the overall effects of temperature on the parasite transmission success (Fig. 23.4).

270 Table 23.1 Experimental studies on effects of temperature on free-living stages of *Diplostomum*
271 *spathaceum* and other species as well as on those stages in gastropod (*Lymnaea* spp.) and
272 rainbow trout (*Oncorhynchus mykiss*). Parasites are *D. spathaceum* unless otherwise indicated.
273

Trait	**Temperature**	**Comment**	**Reference**
Egg hatch	Delayed at 4 °C in *D. phoxini*	At 4 °C, 6 d delay in hatch, but equals rate at 20 °C by 14 d	Harris (1986)
Miracidial swimming velocity	Increases with temperature to a maximum at 25 °C, then declines in *D. phoxini*	Examined velocity between 5 and 40 °C	Harris (1986)
Miracidial life span	Maximum at 4 °C, then declines with increasing temperature in *D. phoxini*	No survival at 40 °C	Harris (1986)
Miracidial infectivity to snails	Declines if exposed at lower temperatures (<14 °C) and switched to 20 °C	Effect lost if snails all exposed at same temperature (20 °C), then switched to lower temperatures	Waadu and Chappell (1991)
Time to patency in snails	Faster at higher temperatures in *D. phoxini*	75h at 10 °C vs. 40 hr at 20 °C	Harris (1986)
	Affected by snail maintenance temperature	Delayed in snails infected at 20 °C if held at 14 °C, not 20-25 °C	Waadu and Chappell (1991)
Cercarial shedding (minimum temperature)	None < 10 °C		Bauer (1959)

	Occurs at 4-6 °C	Stops at 3-5 °C	Lyholt and Buchmann (1996)
	None < 9 °C	Field-based study	Sous (1992)
Cercarial output	Increases with temperature, peaks at 18 °C		Bauer (1959)
	Declines at temperatures < 10 °C	Gradual decline to 5-6 °C, then drops rapidly.	Lyholt and Buchmann (1996)
	Rate of output increases between 10 and 20 °C in *D. phoxini*		Harris (1986)
	Rate of output increases between 10 and 27 °C	<100/hr at 4-14 °C 20-1100/hr at 15-20 °C 100-4700 at 20-27 °C	Sous (1992)
Cercarial activity	None < 9-10 °C	Move to upper waters at 18-22°C	Bauer (1959)
	Peaks at intermediate temperatures in *D. phoxini*	None at 4 °C, maximum at 15 °C, then declines	Harris (1986)
Cercarial life span	Shorter at higher temperatures (e.g., 72 hr at 20 °C vs. 240 hr at 4 °C	Consistent decline between 4 and 25 °C	Harris (1986); Sous (1992); Lyholt and Buchmann (1996)
Cercarial penetration	Increases at higher temperatures	*In vitro* system; occurs as low as 4 °C	Whyte *et al.* (1988)
	Occurs at 7.5 °C		Stables and Chappell (1986b)
Cercarial migration to fish eyes	Faster at higher temperature		Lyholt and Buchmann (1996)

	Inhibited at <10 °C		Stables and Chappell (1986b)
Cercarial establishment in eyes	Highest at ≥ 18 °C	Occurs at 13-16 °C	Bauer (1959)
	Maximum in mid-range (17.5 °C)	No infections at < 10 °C if fish maintained at < 10 °C, but infections obtained at 5 °C if fish maintained at 15 °C	Stables and Chappell (1986b)
	Greater at high temperature (15 °C)	No infections at 5 °C	Lyholt and Buchmann (1996)

INSERT FIGURE 23.4 HERE

Figure 23.4 A dense swarm of cercariae of *Diplostomum pseudospathaceum* released from snail (*Lymnaea stagnalis*). Production and release of cercariae increase significantly from 10 to 20 °C. However, cercarial infectivity and lifespan deplete faster at higher temperatures. Photo by Anssi Karvonen.

An early meta-analysis by Poulin (2006) suggested that cercarial emergence could increase 200-fold with a 10°C increase in temperature, prompting the author to suggest climate change could have a huge influence on parasite populations. However, in a subsequent meta-analysis that accounted for the minimum emergence temperature threshold (the temperature where emergence rates decrease to almost zero) and acclimation status of infected molluscs, temperature above a particular threshold actually does not appear to affect cercarial development (Morley and Lewis, 2013). In addition, cercarial emergence from molluscan hosts shows a peaked pattern with temperature, at first increasing within low temperature ranges. It was unaffected within the optimum temperature ranges (thermostability), which correspond to the latitudinal range inhabited, but then declined at higher temperatures (Morley and Lewis, 2013). However, there were also geographic strain-specific differences in thermostability within *D. spathaceum* in two lymnaeid species (Morley and Lewis, 2013), which underscores the complexity of making predictions and establishing general rules for *Diplostomum* spp.

294

295 Thermostability over a range equivalent to typical summer temperatures for a particular species
296 also was observed for most trematode species in cercarial mortality and glycogen utilization
297 rate over normal temperature ranges encountered (Morley, 2011). A more recent meta-analysis
298 of over 30 trematode species including *D. spathaceum* demonstrated an optimal temperature
299 for both cercarial output and infectivity, while mortality was directly related to temperature
300 (Studer and Poulin, 2014). Specifically, cercarial mortality and glycogen utilization rate
301 increased linearly with temperature in *D. phoxini* (Morley, 2011). Furthermore, temperature
302 had little influence on miracidial survival and metabolism over normal temperature ranges,
303 suggesting that miracidia are more resistant to temperature changes than cercariae (Morley,
304 2012). Interestingly, there was little correlation in thermal responses between miracidia and
305 cercariae within geographic strains of the same species (Morley, 2012). Using metabolic
306 measures, Morley and Lewis (2015) showed that in general, trematode miracidia and cercariae
307 show increased infectivity with temperature, maximizing over optimal temperature ranges and
308 then declining at higher temperatures. Infectivity of metacercariae to definitive hosts, in
309 contrast, was highest at low temperatures and declined as temperature increased. The overall
310 conclusion is that temperature is not hugely important for the survival and function of
311 trematode free-living transmission stages. Rather, transmission may depend more on thermal
312 effects of climate change on the target hosts, among other factors (Morley and Lewis, 2015).
313 For example, it is possible that any higher production of infective stages with temperature
314 would be compensated for by their higher mortality, resulting in a roughly stable risk of
315 infection to fish regardless of temperature. Under such conditions, factors such as host age, size
316 and physiological state may affect infectivity more than direct effects of temperature on
317 miracidia or cercariae (Morley and Lewis, 2015).
318
319 *23.4.2 Ecological evidence from field studies*
320
321 Comparisons of parasite infections in fish inhabiting areas of elevated temperatures with those
322 under ambient conditions may provide insight into effects of temperature increases at the scale
323 of an entire host-parasite relationship (Marcogliese, 2001, 2008). For example, infection of
324 European perch (*Perca fluviatilis*) by *D. baeri* occurred earlier in Biotest Lake, a semi-enclosed
325 area in the Baltic Sea heated by nuclear power plant thermal effluent, than at an ambient site,
326 and infections accumulated there to a higher degree at an increased prevalence in 1986-87
327 (Höglund and Thulin, 1990). Additionally, fish were presumed to show increased mortality in

328 the heated area due to selective predation on heavily infected hosts. In another example of a
329 similar system, the release of cercariae by infected snails (*Helisoma trivolvis*) and recruitment
330 of metacercariae of the eyefluke *Tylodelphys scheuringi* in the mosquitofish (*Gambusia affinis*)
331 were prolonged into the winter months in a thermally-altered reservoir compared to ambient
332 areas in South Carolina, USA (Aho *et al.*, 1982). Cercarial release also ceased during the
333 warmest months (e.g. July and August), implying an upper thermal limit to this trait, in
334 agreement with Morley and Lewis (2013). The trematode *Ornithodiplostomum ptychocheilus*
335 released cercariae from infected *Physa* sp. year-round in the same thermally altered reservoir,
336 also with the exception of the warmest months (Camp *et al.*, 1982). However, recruitment by
337 mosquitofish did not differ between the thermally altered and ambient areas, showing that there
338 can be distinct different responses to temperature between phylogenetically related parasites in
339 the same fish host at the same sites.
340
341 Systems with natural elevation in water temperature compared to that in the ambient
342 environment may also provide interesting comparisons on the effect of temperature. Karvonen
343 *et al.* (2013) examined *Diplostomum* spp. in threespine sticklebacks (*Gasterosteus aculeatus*)
344 from two Icelandic lakes that possess natural temperature gradients due to groundwater inflow
345 and geothermic activity. In both lakes, sticklebacks from the warm areas showed a much higher
346 abundance of *D. baeri* than those from cold regions. A second species of *Diplostomum* also
347 had much higher prevalence and abundance in the warm part of one lake compared to the colder
348 part, although it was absent from the second lake (Karvonen *et al.*, 2013).
349
350 **23.5 Population dynamics of the hosts**
351
352 Since fish growth is temperature-dependent, an extended growing season and reduction in
353 overwintering stress could lead to increases in fish productivity in temperate fishes that are
354 currently limited by sub-optimal temperatures for their growth (Ficke *et al.*, 2007). This,
355 however, assumes that temperatures remain within optimal ranges and other conditions are
356 adequate and food is not limiting. However, reproduction could be negatively affected in those
357 fishes requiring low overwintering temperatures for spawning, such as salmonids (Ficke *et al.*,
358 2007). However, the duration of optimal temperatures for growth will likely increase for all
359 thermal guilds of fishes (Collingsworth *et al.*, 2017). Furthermore, recruitment and production
360 of spring and summer spawners can be promoted (Collingsworth *et al.*, 2017). Fish populations
361 also could be negatively affected not only by increased temperatures, but by decreased levels

of dissolved oxygen, and changes in contaminant concentrations, disease dynamics, and hydrography, along with any other associated habitat modifications (Ficke *et al.*, 2007; Collingsworth *et al.*, 2017). Besides fish, similar processes could apply also to other hosts in parasite life cycles, such as snails in case of *Diplostomum* spp. Without long-term data or epidemiological modelling, however, it is not possible to predict how these changes could affect levels of *Diplostomum* spp. in fishes. Nevertheless, given that most lens-infecting species of *Diplostomum* are generalists, any decrease in the availability of fish intermediate hosts likely will be offset by increases in others.

23.6 Effect of temperature on parasite mortality

Diplostomum spp. metacercariae are generally well protected within the fish eye lens, both from the host immune attacks and from the external environment, and there are no experimental data showing metacercarial mortalities in fish directly following environmental perturbations. Thus, effects of the ambient environment on the parasite population are more likely to concern the free-living infective stages, miracidia and cercariae, as well as processes related to host physiology and resistance. As discussed earlier, increasing temperature tends to decrease the longevity of the infective stages as their finite energy reserves are exhausted more rapidly in higher water temperatures (Table 23.1). Similarly, temperature could enhance host immune function to prevent parasites migration in host tissues towards the eye (see below). Whether this results in negative net effects on the parasite population given the probable increase in parasite replication with temperature needs elucidation.

23.6.1 Effects of climate warming on host physiology and immunological resistance

Temperature also controls the physiological functions (e.g. immunity) in the fish hosts, some of which have direct relevance to parasite infections. Early work examining the immune response in fish to *Diplostomum* spp. used the rainbow trout (*Oncorhynchus mykiss*)-*D. spathaceum* system, while more recent studies have explored ecological immunology in threespine stickleback. In general, immune responses in the eye lenses of fish are considered weak or non-existent as the lens is not directly connected to blood circulation (Sitjá-Bobadilla, 2008). Therefore, the time window for fish to fight off an initial infection is very narrow and consists of the time diplostomules are migrating to the lens, typically within 24 hr from exposure (Chappell *et al.*, 1994; Sitjá-Bobadilla, 2008). Given that not all diplostomules reach

396 the eye in an initial exposure, non-specific immune responses of the fish are likely responsible
397 for partly preventing the infection (Whyte *et al.*, 1991). In rainbow trout, these responses
398 include, for example, activity of the alternative-pathway of the complement cascade (Whyte *et*
399 *al.*, 1988, 1989) as well as macrophages (Whyte *et al.*, 1989; Chappell *et al.*, 1994). Fish also
400 display antibody-mediated specific responses to infection with *Diplostomum* spp. that develop
401 within a few weeks from the first exposure and significantly reduce the number of parasites
402 establishing in subsequent exposures (Stables and Chappell, 1986a; Höglund and Thuvander,
403 1990; Whyte *et al.*, 1990; Karvonen *et al.*, 2005; Karvonen *et al.*, 2010a; Rellstab *et al.*, 2013).
404 In sticklebacks, *in vitro* experiments have demonstrated that head kidney leucocytes (HKL)
405 exhibit a strong respiratory burst when exposed to antigens of *D. pseudospathaceum* (Franke
406 *et al.*, 2014). However, the HKL respiratory burst activity also drops 1.5 days after exposure,
407 implying that phagocytic cell activation is important for the immune response to *D.*
408 *pseudospathaceum* (Scharsack and Kalbe, 2014). These authors suggested that the innate
409 immune response, but not the acquired immune response, was activated to defend against *D.*
410 *pseudospathaceum* in threespine sticklebacks (Scharsack and Kalbe, 2014). There was also
411 evidence supporting parasite genotype-specific innate immune activity in *G. aculeatus* (Haase
412 *et al.*, 2014), while other studies found no evidence of genotype-specificity in the acquired
413 responses (Rellstab *et al.*, 2013; Haase *et al.*, 2016). Further, the immune response in threespine
414 sticklebacks against *Diplostomum* spp. varies among populations and habitats (Scharsack and
415 Kalbe, 2014; Scharsack *et al.*, 2016). For example, fish sympatric with *D. pseudospathaceum*
416 show a stronger innate response against initial infection than those from uninfected populations
417 (Kalbe and Kurtz, 2006).
418
419 Temperature basically affects all physiological functions in ectotherms (Bowden, 2008). In
420 fish, the immune response is stimulated or at least positively correlated with temperature, as
421 shown by lysozyme activity, concentration of circulating IgM, and major histocompatibility
422 complex and cytokine gene expression (Tort *et al.*, 2003; Bowden, 2008; Martin *et al.*, 2010;
423 Uribe *et al.*, 2011). Circulating IgM concentration increases in salmonids when acclimated to
424 19 °C (Uribe *et al.*, 2011). However, it is not known if these processes play a role in defence
425 against *Diplostomum* spp. In contrast, temperature effects on complement activity are
426 inconclusive, effects on haematology vary with cell type, and phagocytosis is not greatly
427 affected (Bowden, 2008; Uribe *et al.*, 2011), processes and functions which do play a role in
428 the immune response against *Diplostomum* spp. In most fish species examined, acquired
429 immune activity and immune gene expression are enhanced while innate immune activity is

suppressed at the highest temperatures tested (Dittmar *et al.*, 2014). Nevertheless, one might expect resistance to parasites such as *Diplostomum* spp. to increase with climate change (Scharsack *et al.*, 2016). However, higher temperatures also accelerate parasite growth, development and life cycle completion, and it is not clear whether the host or the parasite benefits more under these circumstances (Scharsack *et al.*, 2016). Again, the above aspects well illustrate the complex nature of temperature effects; they potentially elevate transmission and can result in higher parasite numbers (Fig. 23.5), but also interact with different types of temperature effects on the host as well as with many other ecological and evolutionary factors determining host resistance.

INSERT FIGURE 23.5 HERE

Figure 23.5 Timing and temperature-dependence of transmission of *Diplostomum* spp. to fish in natural conditions. Data show the mean number of new *Diplostomum* spp. infections (±SD) in eye lenses of fish caged in an oligotrophic lake during two-week periods in May-October. The solid line indicates water temperature of the lake. Infections peak naturally in July-August when water temperature exceeds 15 °C. Climate warming could potentially enhance parasite reproduction in the snail intermediate hosts and transmission to fish resulting in higher number of infections within the current window on transmission. Additionally, higher water temperatures in spring and autumn could prolong the optimal infection period from both ends of the range. Reproduced with permission from Karvonen *et al.* (2004b).

Extreme weather events are also predicted to increase with climate change (Marcogliese, 2001). Examination of how host-parasite systems respond to extreme weather such as heat waves and drought may provide insight into how climate change will affect outbreaks of diseases in ecosystems (Hudson *et al.*, 2006; Poulin and Mouritsen, 2006; Morley and Lewis, 2014). Studies have shown that acute temperature changes experienced during heat waves can cause immunosuppression in fish (Uribe *et al.*, 2011; Scharsack *et al.*, 2016). Generally, in ectotherms, such changes can suppress various immune functions such as phagocytosis, respiratory burst and antibody production (Martin *et al.*, 2010). Immune function is more efficient if fish are acclimated to higher or varying temperatures (Martin *et al.*, 2010; Scharsack *et al.*, 2016). Indeed, in simulated heat wave experiments, innate and adaptive immune functions were optimal at 13-17 °C compared to 18-24 °C in threespine stickleback (Dittmar *et al.*, 2014). Exposure to a simulated heat wave also caused long-lasting deleterious effects on immune function, but less so if fish were from presumably better-adapted populations (Dittmar

464 *et al.*, 2014). Sticklebacks maintained in artificial enclosures with the lowest parasite load and
465 an intermediate level of MHC class IIb sequence variation survived best, while those with the
466 highest parasite burdens perished during the 2003 European heat wave. This suggests a link
467 between MHC diversity and fitness (Wegner *et al.*, 2008).
468
469 In addition to fish, higher water temperatures can influence resistance of the other
470 poikilothermic intermediate host of *Diplostomum* spp., the snail. Compared to fish, however,
471 there is little information on the immune response of snails to the infection. It has been
472 established that the susceptibility of *Lymnaea stagnalis* to *D. spathaceum* varies with age -
473 young snails being susceptible and older snails more resistant to infection (Chappell *et al.*,
474 1994). Haemocyte profiles also differ between infected and uninfected snails with haemocytes
475 from infected snails displaying reduced phagocytotic capability, and serum showing lower
476 opsonic and agglutinating abilities (Riley and Chappell, 1992). This is consistent with the
477 suggestion that the initial infection decreases immune function in snails, making them more
478 susceptible to accumulate further infections (Louhi *et al.*, 2013).
479
480 Evidence on the effect of temperature on snail immune function comes mostly from parasite
481 systems other than *Diplostomum* spp. For example, exposure of *L. stagnalis* to simulated heat
482 waves of 25 °C increased infection success of the trematode *Echinoparyphium aconiatum*
483 (Leicht and Seppälä, 2014). Exposure of the snails to 23.5-25 °C for more than one week also
484 reduced their haemocyte concentration and phenoloxidase-like activity, an oxidative defence
485 against parasites (Leicht *et al.*, 2013; Leicht *et al.*, 2017; Salo *et al.*, 2017). It is likely that
486 similar processes could influence also infections of *Diplostomum* spp. in *L. stagnalis* and in
487 other lymnaeids. Overall, this evidence suggests that increasing temperature could impair the
488 ability of snails to prevent infections, likely resulting in increasing prevalence of *Diplostomum*
489 spp. and other trematode infections. As these infections typically castrate the host, increased
490 likelihood of parasitism would undoubtedly influence also the snail populations, which again
491 would be reflected in the net effects of temperature on the parasite life cycle.
492
493 *23.6.2 Net effects of increasing temperature on the parasite life cycle*
494
495 Overall, there are no detailed studies on the net effects of temperature on transmission and
496 pathology of *Diplostomum* spp. However, studies on a similar host-parasite system may shed
497 some light on the question of net effects. *Ribeiroia ondatrae* has a three-host life cycle,

498 infecting snails and birds. One fundamental difference is that amphibian tadpoles are second
499 intermediate hosts, where the parasite causes limb malformations. Nevertheless, the second
500 intermediate host is a freshwater ectothermic vertebrate with pathological consequences.
501 Studies on net effects of temperature on different life history aspects of *R. ondatrae* may
502 provide informative for *Diplostomum* spp. Paull and Johnson (2011) and Paull *et al.* (2012)
503 demonstrated differential effects on different parasite and host life history characteristics (see
504 Marcogliese (2016)). For example, cercarial survival and establishment in the tadpole peaked
505 at low temperatures, while egg development rate, cercarial development rate and cercarial
506 penetration to tadpoles peaked at high temperatures, but metacercarial numbers in the tadpoles
507 were lowest at high temperatures. Growth of snails (*Planorbella trivolvis*), infected or not, and
508 Pacific chorus frog (*Pseudacris regilla*) tadpoles peaked at high temperatures, along with snail
509 fecundity. However, fecundity of infected snails peaked at intermediate temperatures. Their
510 crucial finding was that pathology in the snail in terms of castration and gigantism peaked at
511 high temperatures, but malformations in the tadpoles were maximised at intermediate
512 temperatures and were lowest at high temperatures (Paull and Johnson, 2011; Paull *et al.*,
513 2012). In a year-long mesocosm study, a temperature increase of 3 °C induced snails to release
514 cercariae of *R. ondatrae* nine months earlier than at ambient conditions and increased snail
515 mortality four-fold (Paull and Johnson, 2014). However, infections in bullfrog (*Lithobates*
516 *catesbeianus*) tadpoles peaked two months earlier. In chorus frogs (*Pseudacris triserata*),
517 infections were reduced by half and malformations by two-thirds (Paull and Johnson, 2014).
518 After one year, 92% fewer adult snails were releasing cercariae in the thermally-altered
519 mesocosm compared to the ambient one (Paull and Johnson, 2014). These results suggest that
520 changes in the impact of parasites on their hosts following global warming depend on the
521 timing and temporal overlap of the temperature-driven changes in the host and parasite
522 populations.
523
524 To conclude, the above examples highlight the need to understand the net effects of temperature
525 increases on parasite transmission in general and on *Diplostomum* spp. in particular (Altizer *et*
526 *al.*, 2013; Marcogliese, 2016). It seems clear that elevated temperatures will influence both
527 parasites and hosts, patterns that could show contrasting effects on parasite prevalence and
528 abundance. Untangling these relationships requires rigorous experimental approaches in
529 laboratory and under field conditions. Due to multiple underlying factors, interpreting the
530 overall effect of climate warming also emphasises the importance of long-term time-series data
531 on parasite population dynamics. Such data are not available for most systems, but would be

532 invaluable as they capture the outcome of the entire process within a host-parasite interaction.
533 Furthermore, the current evidence on temperature effects needs to be interpreted with caution,
534 as they may not have accounted for acclimation of both hosts and parasites, in addition to
535 infected hosts, or variation in temperature (Morley and Lewis, 2013; Raffel *et al.*, 2013; Rohr
536 *et al.*, 2013; Raffel *et al.*, 2015; Altman *et al.*, 2016). This is important, as organisms generally
537 acclimate their performance after a temperature shift, which could change the interpretation of
538 the temperature effects. Moreover, natural temperatures are rarely constant but variable and
539 even a short-term variation in temperature will change the outcome of a host-parasite
540 interaction (Paaijmans *et al.*, 2010; Raffel *et al.*, 2013). Indeed, variation in temperature is
541 expected to increase with climate warming (Jiménez Cisneros *et al.*, 2014; IPCC, 2018), which
542 emphasises the importance of incorporating temperature dynamics into studies on disease
543 occurrence. Undoubtedly, short-term temperature variation plays an important role in
544 epidemics of directly transmitted pathogens. However, implications of the temperature
545 variation for macroparasites with complex life cycles, such as *Diplostomum* spp., may be
546 challenging and difficult to predict.
547
548 **23.7 Other associated consequences of climate change**
549
550 Freshwater ecosystems can be expected to undergo numerous changes aside from increased
551 temperature associated with climate change. These include changes in precipitation, salinity
552 eutrophication, acidification, hydrology and water levels, reduced ice cover, habitat loss,
553 fragmentation, pollution, ultraviolet (UV) radiation, and invasive species (Marcogliese, 2001,
554 2008, 2016), all of which could affect the distribution and abundance of *Diplostomum* spp.
555 (Table 23.2). There is no general unidirectional effect of these environmental changes; they
556 can lead to parasite population increases or declines, emphasizing the importance of
557 confounding factors and context dependency (Rohr *et al.*, 2011; Altizer *et al.*, 2013).
558
559 Table 23.2 Putative effects of environmental or biological changes associated with climate
560 change derived from Table I in Marcogliese (2008) on populations of *Diplostomum* spp. in
561 fishes based on information in Marcogliese (2001, 2004, 2005, 2008), Marcogliese *et al.* (2010)
562 and Tully *et al.* (2019).
563

Environmental or biological change	**General response of *Diplostomum* spp.**	**Putative cause**
Species introductions with change in host range	Population increase or decrease	Introduction of host species should increase generalist and specialist *Diplostomum* species of introduced hosts, but decrease specialist *Diplostomum* species of native hosts at risk
Loss of habitat due to temperature	Population decline	Applies to specialist species whose hosts lose habitat
Reduced flow rates	Population increase	Retention of free-living infective stages, increased infectivity of fish, promotion of snail habitat
Eutrophication	Population increase	Promotes parasites, which use snails as intermediate hosts and birds as definitive hosts
Increased stratification	Population decline	Reduction in snail habitat due to seasonal anoxia in bottom waters
Reduced ice cover	Population increase	Promotes transmission of *Diplostomum* spp. to avian definitive hosts over longer period
Increased acidification in headwater streams	Population decline	Reduced survival of snail intermediate hosts sensitive to acidification
Decreased acidification in lakes	Population increase	Promotes survival of snail intermediate hosts
Increased ultraviolet (UV) radiation	Population decline	Mortality of free-living infective stages
Decrease in salinity due to increased precipitation	Population increase	Increase in available habitat due to lower salinity
Rise in sea level	Population decline	Loss of habitat due to saltwater intrusion
Increased concentration of contaminants	Population decline	Combined effects of contaminants and *Diplostomum* spp. infection reduces

		fish health; transmission to fish reduced through effects on cercariae
Socioeconomic adaptation (dam construction)	Population increase	Replacement of lotic conditions with still or slow-moving waters (see altered hydrology above)
(modifying water withdrawal or delivery)	Population decrease	Increased stream flow

564

565 There are some examples of impacts of these factors on *Diplostomum* spp. that may be
566 illuminating. For example, abundance of *Diplostomum* spp. in mudpuppies (*Necturus*
567 *maculosus*) in the St. Lawrence River was highest in a regulated fluvial lake with stable water
568 levels compared to two other fluvial lakes where levels fluctuated (Marcogliese *et al.*, 2000).
569 Experimental studies also demonstrated that transmission of *D. spathaceum* to rainbow trout
570 was greatly reduced at higher flow rates, with a ten-fold increase in flow rate decreasing
571 infections thirty-fold (Stables and Chappell, 1986b). Abundance of a similar parasite,
572 *Posthodiplostomum minimum*, also increased under low-flow conditions, but was severely
573 reduced under high flow conditions associated with snowmelt in *Fundulus zebrinus* in the
574 Platte River, Nebraska (Janovy *et al.*, 1997). Further, infection of eye flukes in the snail
575 *Lymnaea peregra* plummeted in a reservoir after it was filled to maximum volume (Moody and
576 Gaten, 1982). Thus, regulation of water bodies and flow rates, coupled with declining water
577 levels, should potentially serve to increase infection levels of *Diplostomum* spp. Indeed,
578 reservoir construction is considered a means of helping to mitigate or adapt to effects of climate
579 change on streams, rivers and wetlands (Jiménez Cisneros *et al.*, 2014; Muller, 2019).
580
581 Contaminant concentration may increase under low water conditions and climate change
582 (Johnson *et al.*, 2009; Jiménez Cisneros *et al.*, 2014; Landis *et al.*, 2014; Morley and Lewis,
583 2014). Lethal and sub-lethal effects of combined exposure of animals to both parasites and
584 contaminants can be greater than the effects of either stressor alone (Marcogliese and Pietrock,
585 2011). For example, the combined exposure to municipal, agricultural and industrial pollution
586 and infection with *Diplostomum* spp. increased oxidative stress in yellow perch, *Perca*
587 *flavescens* (Marcogliese *et al.*, 2010). Moreover, exposure to increasing temperature

588 concurrently with another stressor may negatively impact an organism's health, leading to
589 population declines in ectotherms (Rohr and Palmer, 2013). Survival of naturally infected
590 snails (*L. stagnalis* and *L. peregra*) was reduced when exposed to cadmium compared to
591 controls (Morley *et al.*, 2003a). Free-living stages of a parasite also are sensitive to
592 environmental contaminants (Morley *et al.*, 2003c; Pietrock and Marcogliese, 2003). Exposure
593 of cercariae of *Diplostomum* spp. to cadmium, chromium, mercury and sediment extracts from
594 the polluted Oder River reduced their life span (Pietrock *et al.*, 2001; Pietrock *et al.*, 2002a;
595 Pietrock *et al.*, 2002b). Exposure to mixtures of cadmium and zinc, however, increased survival
596 in *D. spathaceum* (Morley *et al.*, 2001, 2002). Notably, cercarial activity of *D. spathaceum* was
597 reduced following exposure to zinc, cadmium, and zinc-cadmium mixture at all concentrations
598 tested and were vulnerable during the period of maximal cercarial infectivity (Morley *et al.*,
599 2003b). Infectivity of cercariae of both *Posthodiplostomum minimum* and *Ornithodiplostomum*
600 *ptychocheilus* to fathead minnows (*Pimephales promelas*) was reduced following exposure to
601 cadmium (Pietrock and Goater, 2005). Climate change can also increase the toxicity of
602 chemical contaminants as well as their uptake and an animal's susceptibility (Schiedek *et al.*,
603 2007; Noyes *et al.*, 2009; Hooper *et al.*, 2013; Stahl *et al.*, 2013). Furthermore, exposure to
604 contaminants may decrease an organism's thermal tolerance to increasing temperature (Noyes
605 *et al.*, 2009), as well interact with other climate-associated stressors (Moe *et al.*, 2013). Thus,
606 any increase in contaminants may decrease *Diplostomum* spp. infections in fish and snail
607 intermediate hosts.
608
609 Nutrient pollution is also expected to increase in fresh waters (Ficke *et al.*, 2007; Jiménez
610 Cisneros *et al.*, 2014; Collingsworth *et al.*, 2017), which can have significant implications for
611 parasitism. For example, occurrence of limb malformations and abundance of *R. ondatrae* in
612 anurans in agricultural wetlands was associated with eutrophication through effects on snail
613 species composition and biomass (Johnson and Chase, 2004; Johnson *et al.*, 2007).
614 Eutrophication combined with high temperatures leads to more frequent blooms of harmful
615 algal blooms (HABs) of cyanobacteria (Paerl *et al.*, 2011; Moe *et al.*, 2013; Jiménez Cisneros
616 *et al.*, 2014). HABs produce toxins and hypoxic conditions, detrimental to aquatic life (Moe *et*
617 *al.*, 2013). Interestingly, exposure to low concentrations of the cyanobacterial toxin
618 microcystin-LR (MC-LR) increased infection intensities of larval trematodes in leopard frogs,
619 *Rana pipiens* (Milotic *et al.*, 2018). While it did not affect growth or survival, exposure of the
620 snail *L. stagnalis*, the intermediate host for *Diplostomum* spp., reduced fecundity of adult snails
621 (Gérard *et al.*, 2005). Therefore, eutrophication associated with climate change may promote

infections of *Diplostomum* spp. in fish, but if allowed to progress, resulting in anoxia and the proliferations of HABs, infections may decrease (see also Budria (2017)). Similar effects of more frequent and widespread hypoxia in the benthos is expected in several water bodies because of longer periods of stratification during summer (Ficke *et al.*, 2007; Collingsworth *et al.*, 2017). Such developments would also negatively affect populations of snail and fish intermediate hosts of *Diplostomum* spp. in deeper waters (Table 23.2).

Exposure to ultraviolet (UV) radiation in freshwater ecosystems is expected to increase due to enhanced penetration under certain conditions, and it may be most problematic in clear, shallow waters (see Marcogliese (2001)). UV is harmful to invertebrates, including parasites, whose free-living stages such as cercariae are sensitive to environmental stressors (Pietrock and Marcogliese, 2003). While exposure to UV radiation may negatively affect free-living stages of *Diplostomum* spp., it also is immunosuppressive in fish. Exposure of rainbow trout to UV radiation led to increased numbers of *D. spathaceum* compared to controls, presumably because of reduced resistance (Markkula *et al.*, 2007). Exposure to UV is expected to increase in streams with climate change following reduced discharge, lower stream depth, and reduced dissolved organic carbon (Clements *et al.*, 2008; Moe *et al.*, 2013). However, conflicting effects on parasites and hosts make any predictions problematic.

Other abiotic parameters that may be affected by climate may also negatively or positively impact the immune response in fish (Uribe *et al.*, 2011). For example, an increase in hypoxia decreased the respiratory burst activity of macrophages and lowered the level of circulating antibodies. In contrast, elevated salinity increased lytic enzyme activity, macrophage respiratory burst activity, HKL phagocytic activity, plasma lysozyme concentration and circulating IgM (Bowden, 2008; Uribe *et al.*, 2011). Effects of pH on immune response, on the other hand, have provided conflicting results (Bowden, 2008; Uribe *et al.*, 2011). Temperature stress combined with contaminants such as nickel and chlorine also causes immunosuppression in fishes, including reduced spleen cellularity, erythrocyte and leukocyte counts, and increased superoxide production (Prophete *et al.*, 2006; Verma *et al.*, 2007).

23.8 Control and prevention of *Diplostomum* spp.

The lens-infecting *Diplostomum* species also occur in pond-aquaculture as all the necessary hosts of the parasite are commonly present. For example, fish farms typically attract fish-eating

656 birds, the definitive hosts of *Diplostomum* spp., to feed. Earth ponds with vegetation used in
657 rearing aquaculture fish also provide favourable habitats for snail intermediate hosts that
658 become readily infected following parasite output from birds attracted to the ponds. Prevalence
659 of infection in the snails can be high, which results in high infection also in fish (Stables and
660 Chappell, 1986c; Field and Irwin, 1994; Karvonen *et al.*, 2006a). Parasite cercariae can also be
661 brought into a facility with incoming water from upstream water bodies, but this is considered
662 not as significant source of infection in fish compared to transmission occurring within the
663 facility (Field and Irwin, 1994; Karvonen *et al.*, 2006a). High numbers of metacercariae and
664 resulting pathology in the eyes of fish may become a problem if they reduce the desired growth
665 in fish intended for market. Similarly, infected fish for stocking to support natural fish
666 populations may have lower success in the wild, although detailed data on the effects of
667 *Diplostomum* spp. infections in natural fish populations are not available.
668
669 It is likely that problems associated with *Diplostomum* spp. in aquaculture are also likely to
670 increase. These may be through increased rate of parasite replication, prolonged period of
671 parasite transmission and metacercarial development, or impaired ability of cold-water species
672 such as salmonids to resist the infection (Hakalahti *et al.*, 2006). Such effects may be
673 manifested as longer and later outbreaks of the disease in the autumn (Fig. 23.5), thus
674 necessitating extra control measures. Control of *Diplostomum* spp. infections, however, can be
675 challenging as there is no effective treatment of the infection in fish and immunizing fish
676 against the infection provides only partial protection against later infections (Höglund and
677 Thuvander, 1990; Karvonen *et al.*, 2005). Studies have shown that immunization alone does
678 not protect fish from the deleterious effects of infection and other means of defence, such as
679 behavioural avoidance of cercariae, may be needed to complement any immune-mediated
680 response (Karvonen *et al.*, 2004b; Karvonen *et al.*, 2010a). However, such behavioural
681 avoidance is often impossible in the confined space of aquaculture tanks and ponds. In addition,
682 other types of control measures such as treatment or filtering of water are not feasible because
683 of large water volumes and the continuous output of parasite cercariae during summer months.
684 Removal or chemical eradication of snails from the rearing ponds is generally considered as
685 the only viable option to control and prevent the infections in fish (Stables and Chappell, 1986c;
686 Field and Irwin, 1994), although this can be system-specific and depends on the magnitude of
687 cercarial input from upstream water bodies. Nevertheless, eradication of snails as the main
688 preventative method should work equally well even with increasing water temperatures,
689 although positive effect of temperature on reproduction of snails may necessitate more frequent

use of the eradication protocols. However, constructing the tanks and ponds in a way that limits establishment of vegetation and snail populations should help in longer-term prevention of infections.

23.9 Conclusions

The current evidence on the relationships between climate warming and infections of *Diplostomum* spp. strongly highlight the difficulty of determining the net effects on the complex parasite life cycle. This is because most, if not all, of the life cycle stages in the aquatic environment likely respond to temperature by increasing parasite replication and infectivity. However, elevated temperature will likely result in increased mortality of the infective stages, and possibly accompanied by higher resistance in the fish hosts. Increasing temperature also acts in concert with many other interrelated environmental changes such as alteration in hydrology, increasing eutrophication, pollution and UV-radiation, loss of habitats and higher risk of invasive species. All these factors working in concert illustrates the magnitude and scope of environmental effects on *Diplostomum* spp., and on many other host-parasite systems covered in this book. The high number of variables emphasises the importance of long-term time-series studies, which would adequately provide the influence of all related factors. Pinpointing the importance of individual factors, on the other hand, requires rigorous experimental approaches supported by mathematical models on parasite dynamics with changing temperature. One area of experimental research needed concerns the effect of temperature and the other related factors (Table 23.2) on the severity of *Diplostomum* spp.-induced pathology in fish, which has received relatively little attention. Alongside the effects on the parasite life cycle, it is one of the key factors determining the impact of the parasite on fish populations in nature and in units of intensive aquaculture.

Acknowledgements

D.J.M. would like to thank Neil Morley for providing essential information from the Harris (1986) thesis. A.K. was supported by a grant (#310632) from the Academy of Finland.

724

725 **23.10 References**

726

727 Aho, J.M., Camp, J.W. and Esch, G.W. (1982) Long-term studies on the population biology
728 of *Diplostomulum scheuringi* in a thermally altered reservoir. *Journal of Parasitology,*
729 68, 695-708. doi:10.2307/3280931.
730 Altizer, S., Ostfeld, R.S., Johnson, P.T.J., Kutz, S. and Harvell, C.D. (2013) Climate change
731 and infectious diseases: From evidence to a predictive framework. *Science,* 341, 514-
732 519. doi:10.1126/science.1239401.
733 Altman, K.A., Paull, S.H., Johnson, P.T.J., Golembieski, M.N., Stephens, J.P., LaFonte, B.E.
734 and Raffel, T.R. (2016) Host and parasite thermal acclimation responses depend on
735 the stage of infection. *Journal of Animal Ecology,* 85, 1014-1024. doi:10.1111/1365-
736 2656.12510.
737 Balling, T.E. and Pfeiffer, W. (1997) Location-dependent infection of fish parasites in Lake
738 Constance. *Journal of Fish Biology,* 51, 1025-1032.
739 Bauer, O.N. (1959) Parasites of freshwater fish and the biological basis for their control
740 (Translated from Russian, Israel Program for Scientific Translations, Jerusalem,
741 1962). *Bulletin of the State Scientifc Research Institute of Lake and River Fisheries,*
742 49.
743 Blasco-Costa, I., Faltýnková, A., Georgieva, S., Skirnisson, K., Scholz, T. and Kostadinova,
744 A. (2014) Fish pathogens near the Arctic Circle: molecular, morphological and
745 ecological evidence for unexpected diversity of *Diplostomum* (Digenea:
746 diplostomidae) in Iceland. *International Journal for Parasitology,* 44, 703-715.
747 doi:10.1016/j.ijpara.2014.04.009.
748 Bowden, T.J. (2008) Modulation of the immune system of fish by their environment. *Fish &*
749 *Shellfish Immunology,* 25, 373-383. doi:10.1016/j.fsi.2008.03.017.
750 Buchmann, K. (1986) Prevalence and intensity of infection of *Cryptocotyle lingua* (Creplin)
751 and *Diplostomum spathaceum* (Rudolphi) - parasitic metacercariae of Baltic cod
752 (*Gadus morhua* L). *Nordisk Veterinaer Medicin,* 38, 303-307.
753 Budria, A. (2017) Beyond troubled waters: the influence of eutrophication on host-parasite
754 interactions. *Functional Ecology,* 31, 1348-1358. doi:10.1111/1365-2435.12880.
755 Burrough, R.J. (1978) Population biology of two species of eyefluke, *Diplostomum*
756 *spathaceum* and *Tylodelphys clavata*, in roach and rudd. *Journal of Fish Biology,* 13,
757 19-32. doi:10.1111/j.1095-8649.1978.tb03409.x.

758 Camp, J.W., Aho, J.M. and Esch, G.W. (1982) A long-term study on various aspects of the
759 population biology of *Ornithodiplostomum ptychocheilus* in a South-Carolina cooling
760 reservoir. *Journal of Parasitology,* 68, 709-718. doi:10.2307/3280932.
761 Chappell, L.H., Hardie, L.J. and Secombes, C.J. (1994) Diplostomiasis: the disease and host-
762 parasite interactions. *In:* Pike, A.W. and Lewis, J.W. (eds.) *Parasitic diseases of fish.*
763 Samara Publishing Limited, Dyfed, pp. 59-86.
764 Chappell, L.H. (1995) The biology of diplostomatid eyeflukes of fishes. *Journal of*
765 *Helminthology,* 69, 97-102.
766 Chen, Y.S., Todd, A.S., Murphy, M.H. and Lomnicky, G. (2016) Anticipated water quality
767 changes in response to climate change and potential consequences for inland fishes.
768 *Fisheries,* 41, 413-416. doi:10.1080/03632415.2016.1182509.
769 Chubb, J.C. (1979) Seasonal occurrences of helminths in freshwater fishes. Part II.
770 Trematoda. *Advances in Parasitology,* 17, 141-313.
771 Clements, W.H., Brooks, M.L., Kashian, D.R. and Zuellig, R.E. (2008) Changes in dissolved
772 organic material determine exposure of stream benthic communities to UV-B
773 radiation and heavy metals: implications for climate change. *Global Change Biology,*
774 14, 2201-2214. doi:10.1111/j.1365-2486.2008.01632.x.
775 Collingsworth, P.D., Bunnell, D.B., Murray, M.W., Kao, Y.C., Feiner, Z.S., Claramunt,
776 R.M., Lofgren, B.M., Hook, T.O. and Ludsin, S.A. (2017) Climate change as a long-
777 term stressor for the fisheries of the Laurentian Great Lakes of North America.
778 *Reviews in Fish Biology and Fisheries,* 27, 363-391. doi:10.1007/s11160-017-9480-3.
779 Crowden, A.E. and Broom, D.M. (1980) Effects of the eyefluke, *Diplostomum spathaceum*,
780 on the behavior of dace (*Leuciscus leuciscus*). *Animal Behaviour,* 28, 287-294.
781 doi:10.1016/s0003-3472(80)80031-5.
782 Désilets, H.D., Locke, S.A., McLaughlin, J.D. and Marcogliese, D.J. (2013) Community
783 structure of *Diplostomum* spp. (Digenea: Diplostomidae) in eyes of fish: Main
784 determinants and potential interspecific interactions. *International Journal for*
785 *Parasitology,* 43, 929-939. doi:10.1016/j.ijpara.2013.07.002.
786 Dittmar, J., Janssen, H., Kuske, A., Kurtz, J. and Scharsack, J.P. (2014) Heat and immunity:
787 an experimental heat wave alters immune functions in three-spined sticklebacks
788 (*Gasterosteus aculeatus*). *Journal of Animal Ecology,* 83, 744-757. doi:10.1111/1365-
789 2656.12175.

790 Ficke, A.D., Myrick, C.A. and Hansen, L.J. (2007) Potential impacts of global climate
791 change on freshwater fisheries. *Reviews in Fish Biology and Fisheries,* 17, 581-613.
792 doi:10.1007/s11160-007-9059-5.
793 Field, J.S. and Irwin, S.W.B. (1994) The epidemiology, treatment and control of
794 diplostomiasis on a fish farm in Northern Ireland. *In:* Pike, A.W. and Lewis, J.W.
795 (eds.) *Parasitic diseases of fish.* Samara Publishing Limited, Dyfed, pp. 87-100.
796 Francová, K., Ondračková, M., Polacik, M. and Jurajda, P. (2011) Parasite fauna of native
797 and non-native populations of *Neogobius melanostomus* (Pallas, 1814) (Gobiidae) in
798 the longitudinal profile of the Danube River. *Journal of Applied Ichthyology,* 27, 879-
799 886. doi:10.1111/j.1439-0426.2010.01582.x.
800 Franke, F., Rahn, A.K., Dittmar, J., Erin, N., Rieger, J.K., Haase, D., Samonte-Padilla, I.E.,
801 Lange, J., Jakobsen, P.J., Hermida, M.*, et al.* (2014) In vitro leukocyte response of
802 three-spined sticklebacks (*Gasterosteus aculeatus*) to helminth parasite antigens. *Fish*
803 *& Shellfish Immunology,* 36, 130-140. doi:10.1016/j.fsi.2013.10.019.
804 Gendron, A.D., Marcogliese, D.J. and Thomas, M. (2012) Invasive species are less
805 parasitized than native competitors, but for how long? The case of the round goby in
806 the Great Lakes-St. Lawrence Basin. *Biological Invasions,* 14, 367-384.
807 doi:10.1007/s10530-011-0083-y.
808 Gendron, A.D. and Marcogliese, D.J. (2017) Enigmatic decline of a common fish parasite
809 (*Diplostomum* spp.) in the St. Lawrence River: Evidence for a dilution effect induced
810 by the invasive round goby. *International Journal for Parasitology-Parasites and*
811 *Wildlife,* 6, 402-411. doi:10.1016/j.ijppaw.2017.04.002.
812 Gérard, C., Brient, L. and Le Rouzic, B. (2005) Variation in the response of juvenile and
813 adult gastropods (*Lymnaea stagnalis*) to cyanobacterial toxin (microcystin-LR).
814 *Environmental Toxicology,* 20, 592-596. doi:10.1002/tox.20147.
815 Haase, D., Rieger, J.K., Witten, A., Stoll, M., Bornberg-Bauer, E., Kalbe, M. and Reusch,
816 T.B.H. (2014) Specific gene expression responses to parasite genotypes reveal
817 redundancy of innate immunity in vertebrates. *PLoS One,* 9.
818 doi:10.1371/journal.pone.0108001.
819 Haase, D., Rieger, J.K., Witten, A., Stoll, M., Bornberg-Bauer, E., Kalbe, M. and Reusch,
820 T.B.H. (2016) Immunity comes first: The effect of parasite genotypes on adaptive
821 immunity and immunization in three-spined sticklebacks. *Developmental and*
822 *Comparative Immunology,* 54, 137-144. doi:10.1016/j.dci.2015.09.008.

823 Hakalahti, T., Karvonen, A. and Valtonen, E.T. (2006) Climate warming and disease risks in
824 temperate regions - *Argulus coregoni* and *Diplostomum spathaceum* as case studies.
825 *Journal of Helminthology,* 80, 93-98. doi:10.1079/joh2006351.
826 Harris, A.L. (1986) Larval trematode infections of the freshwater snail *Lymnaea peregra*
827 (Muller). M. Phil. Thesis. Queen Mary & Westfield College, University of London.
828 Hooper, M.J., Ankley, G.T., Cristol, D.A., Maryoung, L.A., Noyes, P.D. and Pinkerton, K.E.
829 (2013) Interactions between chemical and climate stressors: A role for mechanistic
830 toxicology in assessing climate change risks. *Environmental Toxicology and*
831 *Chemistry,* 32, 32-48. doi:10.1002/etc.2043.
832 Hudson, P.J., Cattadori, M., Boag, B. and Dobson, A.P. (2006) Climate disruption and
833 parasite-host dynamics: patterns and processes associated with warming and the
834 frequency of extreme climatic events. *Journal of Helminthology,* 80, 175-182.
835 doi:10.1079/joh2006357.
836 Höglund, J. and Thulin, J. (1990) The epidemiology of the metacercariae of *Diplostomum*
837 *baeri* and *Diplostomum spathaceum* in perch (*Perca fluviatilis*) from the warm water
838 effluent of a nuclear power station. *Journal of Helminthology,* 64, 139-150.
839 Höglund, J. and Thuvander, A. (1990) Indications of non-specific protective mechanisms in
840 rainbow trout *Oncorhynchus mykiss* with diplostomosis. *Diseases of Aquatic*
841 *Organisms,* 8, 91-97.
842 IPCC (2018) Summary for Policymakers. *In:* Masson-Delmotte, V., Zhai, P., Pörtner, H.-O.,
843 Roberts, D., Skea, J., Shukla, P.R., Pirani, A., Moufouma-Okia, W., Péan, C.,
844 Pidcock, R.*, et al.* (eds.) *Global Warming of 1.5°C. An IPCC Special Report on the*
845 *impacts of global warming of 1.5°C above pre-industrial levels and related global*
846 *greenhouse gas emission pathways, in the context of strengthening the global*
847 *response to the threat of climate change, sustainable development, and efforts to*
848 *eradicate poverty.* World Meteorological Organization, Geneva, Switzerland, pp. 32.
849 Janovy, J., Snyder, S.D. and Clopton, R.E. (1997) Evolutionary constraints on population
850 structure: The parasites of *Fundulus zebrinus* (Pisces: Cyprinodontidae) in the South
851 Platte River of Nebraska. *Journal of Parasitology,* 83, 584-592. doi:10.2307/3284228.
852 Jiménez Cisneros, B.E., Oki, T., Arnell, N.W., Benito, G., Cogley, J.G., Döll, P., Jiang, T.
853 and Mwakalila, S.S. (2014) Freshwater resources. *In:* Field, C.B., Barros, V.R.,
854 Dokken, D.J., Mach, K.J., Mastrandrea, M.D., Bilir, T.E., Chatterjee, M., Ebi, K.L.,
855 Estrada, Y.O., Genova, R.C.*, et al.* (eds.) *Climate Change 2014: Impacts, Adaptation,*
856 *and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of Working*

Group II to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change. Cambridge University Press, Cambridge, United Kingdom and New York, New York, USA, pp. 229-269.

Johnson, A.C., Acreman, M.C., Dunbar, M.J., Feist, S.W., Giacomello, A.M., Gozlan, R.E., Hinsley, S.A., Ibbotson, A.T., Jarvie, H.P., Jones, J.I., *et al.* (2009) The British river of the future: How climate change and human activity might affect two contrasting river ecosystems in England. *Science of the Total Environment,* 407, 4787-4798. doi:10.1016/j.scitotenv.2009.05.018.

Johnson, P.T.J. and Chase, J.M. (2004) Parasites in the food web: linking amphibian malformations and aquatic eutrophication. *Ecology Letters,* 7, 521-526. doi:10.1111/j.1461-0248.2004.00610.x.

Johnson, P.T.J., Chase, J.M., Dosch, K.L., Hartson, R.B., Gross, J.A., Larson, D.J., Sutherland, D.R. and Carpenter, S.R. (2007) Aquatic eutrophication promotes pathogenic infection in amphibians. *Proceedings of the National Academy of Sciences of the United States of America,* 104, 15781-15786. doi:10.1073/pnas.0707763104.

Kalbe, M. and Kurtz, J. (2006) Local differences in immunocompetence reflect resistance of sticklebacks against the eye fluke *Diplostomum pseudospathaceum*. *Parasitology,* 132, 105-116. doi:10.1017/s0031182005008681.

Karvonen, A., Paukku, S., Valtonen, E.T. and Hudson, P.J. (2003) Transmission, infectivity and survival of *Diplostomum spathaceum* cercariae. *Parasitology,* 127, 217-224. doi:10.1017/s0031182003003561.

Karvonen, A., Kirsi, S., Hudson, P.J. and Valtonen, E.T. (2004a) Patterns of cercarial production from *Diplostomum spathaceum*: terminal investment or bet hedging? *Parasitology,* 129, 87-92. doi:10.1017/s0031182004005281.

Karvonen, A., Seppälä, O. and Valtonen, E.T. (2004b) Parasite resistance and avoidance behaviour in preventing eye fluke infections in fish. *Parasitology,* 129, 159-164. doi:10.1017/s0031182004005505.

Karvonen, A., Seppälä, O. and Valtonen, E.T. (2004c) Eye fluke-induced cataract formation in fish: quantitative analysis using an ophthalmological microscope. *Parasitology,* 129, 473-478. doi:10.1017/s0031182004006006.

Karvonen, A., Paukku, S., Seppälä, O. and Valtonen, E.T. (2005) Resistance against eye flukes: naive versus previously infected fish. *Parasitology Research,* 95, 55-59. doi:10.1007/s00436-004-1246-x.

890 Karvonen, A., Savolainen, M., Seppälä, O. and Valtonen, E.T. (2006a) Dynamics of
891 *Diplostomum spathaceum* infection in snail hosts at a fish farm. *Parasitology*
892 *Research,* 99, 341-345. doi:10.1007/s00436-006-0137-8.
893 Karvonen, A., Terho, P., Seppälä, O., Jokela, J. and Valtonen, E.T. (2006b) Ecological
894 divergence of closely related *Diplostomum* (Trematoda) parasites. *Parasitology,* 133,
895 229-235. doi:10.1017/s0031182006000242.
896 Karvonen, A. and Seppälä, O. (2008a) Eye fluke infection and lens size reduction in fish: a
897 quantitative analysis. *Diseases of Aquatic Organisms,* 80, 21-26.
898 doi:10.3354/dao01918.
899 Karvonen, A. and Seppälä, O. (2008b) Effect of eye fluke infection on the growth of
900 whitefish (*Coregonus lavaretus*) - An experimental approach. *Aquaculture,* 279, 6-10.
901 doi:10.1016/j.aquaculture.2008.04.013.
902 Karvonen, A., Halonen, H. and Seppälä, O. (2010a) Priming of host resistance to protect
903 cultured rainbow trout *Oncorhynchus mykiss* against eye flukes and parasite-induced
904 cataracts. *Journal of Fish Biology,* 76, 1508-1515. doi:10.1111/j.1095-
905 8649.2010.02597.x.
906 Karvonen, A., Rintamäki, P., Jokela, J. and Valtonen, E.T. (2010b) Increasing water
907 temperature and disease risks in aquatic systems: climate change increases the risk of
908 some, but not all, diseases. *International Journal for Parasitology,* 40, 1483-1488.
909 doi:10.1016/j.ijpara.2010.04.015.
910 Karvonen, A. (2012) *Diplostomum spathaceum* and Related Species. *In:* Woo, P.T.K. and
911 Buchmann, K. (eds.) *Fish Parasites: Pathobiology and Protection.* CAB
912 International, Oxfordshire, UK, pp. 260-269.
913 Karvonen, A., Kristjansson, B.K., Skulason, S., Lanki, M., Rellstab, C. and Jokela, J. (2013)
914 Water temperature, not fish morph, determines parasite infections of sympatric
915 Icelandic threespine sticklebacks (*Gasterosteus aculeatus*). *Ecology and Evolution,* 3,
916 1507-1517. doi:10.1002/ece3.568.
917 Karvonen, A., Lucek, K., Marques, D.A. and Seehausen, O. (2015) Divergent macroparasite
918 infections in parapatric Swiss lake-stream pairs of threespine stickleback
919 (*Gasterosteus aculeatus*). *PLoS One,* 10. doi:10.1371/journal.pone.0130579.
920 Karvonen, A. and Lindström, K. (2018) Spatiotemporal and gender-specific parasitism in two
921 species of gobiid fish. *Ecology and Evolution,* 8, 6114-6123. doi:10.1002/ece3.4151.

922 Klemme, I. and Karvonen, A. (2017) Vertebrate defense against parasites: Interactions
923 between avoidance, resistance, and tolerance. *Ecology and Evolution,* 7, 561-571.
924 doi:10.1002/ece3.2645.
925 Koie, M. (1999) Metazoan parasites of flounder *Platichthys flesus* (L.) along a transect from
926 the southwestern to the northeastern Baltic Sea. *Ices Journal of Marine Science,* 56,
927 157-163. doi:10.1006/jmsc.1999.0463.
928 Kvach, Y. and Winkler, H.M. (2011) The colonization of the invasive round goby *Neogobius*
929 *melanostomus* by parasites in new localities in the southwestern Baltic Sea.
930 *Parasitology Research,* 109, 769-780. doi:10.1007/s00436-011-2321-8.
931 Lafferty, K.D. (2009) The ecology of climate change and infectious diseases. *Ecology,* 90,
932 888-900. doi:10.1890/08-0079.1.
933 Landis, W.G., Rohr, J.R., Moe, S.J., Balbus, J.M., Clements, W., Fritz, A., Helm, R., Hickey,
934 C., Hooper, M., Stahl, R.G.*, et al.* (2014) Global climate change and contaminants, a
935 call to arms not yet heard? *Integrated Environmental Assessment and Management,*
936 10, 483-484. doi:10.1002/ieam.1568.
937 Leicht, K., Jokela, J. and Seppälä, O. (2013) An experimental heat wave changes immune
938 defense and life history traits in a freshwater snail. *Ecology and Evolution,* 3, 4861-
939 4871. doi:10.1002/ece3.874.
940 Leicht, K. and Seppälä, O. (2014) Infection success of *Echinoparyphium aconiatum*
941 (Trematoda) in its snail host under high temperature: role of host resistance. *Parasites*
942 *& Vectors,* 7, 192. doi:10.1186/1756-3305-7-192.
943 Leicht, K., Seppälä, K. and Seppälä, O. (2017) Potential for adaptation to climate change:
944 family-level variation in fitness-related traits and their responses to heat waves in a
945 snail population. *BMC Evolutionary Biology,* 17, 140. doi:10.1186/s12862-017-0988-
946 x.
947 Locke, S.A., McLaughlin, J.D., Dayanandan, S. and Marcogliese, D.J. (2010a) Diversity and
948 specificity in *Diplostomum* spp. metacercariae in freshwater fishes revealed by
949 cytochrome c oxidase I and internal transcribed spacer sequences. *International*
950 *Journal for Parasitology,* 40, 333-343. doi:10.1016/j.ijpara.2009.08.012.
951 Locke, S.A., McLaughlin, J.D. and Marcogliese, D.J. (2010b) DNA barcodes show cryptic
952 diversity and a potential physiological basis for host specificity among
953 Diplostomoidea (Platyhelminthes: Digenea) parasitizing freshwater fishes in the St.
954 Lawrence River, Canada. *Molecular Ecology,* 19, 2813-2827. doi:10.1111/j.1365-
955 294X.2010.04713.x.

956 Locke, S.A., Al-Nasiri, F.S., Caffara, M., Drago, F., Kalbe, M., Lapierre, A.R., McLaughlin,
957 J.D., Nie, P., Overstreet, R.M., Souza, G.T.R., *et al.* (2015) Diversity, specificity and
958 speciation in larval Diplostomidae (Platyhelminthes: Digenea) in the eyes of
959 freshwater fish, as revealed by DNA barcodes. *International Journal for*
960 *Parasitology,* 45, 841-855. doi:10.1016/j.ijpara.2015.07.001.
961 Lõhmus, M. and Björklund, M. (2015) Climate change: what will it do to fish-parasite
962 interactions? *Biological Journal of the Linnean Society,* 116, 397-411.
963 doi:10.1111/bij.12584.
964 Louhi, K.-R., Karvonen, A., Rellstab, C., Louhi, R. and Jokela, J. (2013) Prevalence of
965 infection as a predictor of multiple genotype infection frequency in parasites with
966 multiple-host life cycle. *Journal of Animal Ecology,* 82, 191-200. doi:10.1111/j.1365-
967 2656.2012.02028.x.
968 Lyholt, H.C.K. and Buchmann, K. (1996) *Diplostomum spathaceum*: Effects of temperature
969 and light on cercarial shedding and infection of rainbow trout. *Diseases of Aquatic*
970 *Organisms,* 25, 169-173. doi:10.3354/dao025169.
971 Marcogliese, D.J. and Compagna, S. (1999) Diplostomatid eye flukes in young-of-the-year
972 and forage fishes in the St. Lawrence River, Quebec. *Journal of Aquatic Animal*
973 *Health,* 11, 275-282. doi:10.1577/1548-8667(1999)011<0275:defiyo>2.0.co;2.
974 Marcogliese, D.J., Rodrigue, J., Ouellet, M. and Champoux, L. (2000) Natural occurrence of
975 *Diplostomum* sp (Digenea : Diplostomatidae) in adult mudpuppies and bullfrog
976 tadpoles from the St. Lawrence River, Quebec. *Comparative Parasitology,* 67, 26-31.
977 Marcogliese, D.J. (2001) Implications of climate change for parasitism of animals in the
978 aquatic environment. *Canadian Journal of Zoology,* 79, 1331-1352. doi:10.1139/cjz-
979 79-8-1331.
980 Marcogliese, D.J., Compagna, S., Bergeron, E. and McLaughlin, J.D. (2001a) Population
981 biology of eyeflukes in fish from a large fluvial ecosystem: the importance of gulls
982 and habitat characteristics. *Canadian Journal of Zoology,* 79, 1102-1113.
983 doi:10.1139/cjz-79-6-1102.
984 Marcogliese, D.J., Dumont, P., Gendron, A.D., Mailhot, Y., Bergeron, E. and McLaughlin,
985 J.D. (2001b) Spatial and temporal variation in abundance of *Diplostomum* spp. in
986 walleye (*Stizostedion vitreum*) and white suckers (*Catostomus commersoni*) from the
987 St. Lawrence River. *Canadian Journal of Zoology,* 79, 355-369. doi:10.1139/cjz-79-
988 3-355.

989 Marcogliese, D.J. (2004) Parasites: small players with crucial roles in the ecological theater.
990 *EcoHealth,* 1, 151-164.
991 Marcogliese, D.J. (2005) Parasites of the superorganism: Are they indicators of ecosystem
992 health? *International Journal for Parasitology,* 35, 705-716.
993 doi:10.1016/j.ijpara.2005.01.015.
994 Marcogliese, D.J. (2008) The impact of climate change on the parasites and infectious
995 diseases of aquatic animals. *Revue Scientifique Et Technique-Office International Des*
996 *Epizooties,* 27, 467-484. doi:10.20506/rst.27.2.1820.
997 Marcogliese, D.J., Dautremepuits, C., Gendron, A.D. and Fournier, M. (2010) Interactions
998 between parasites and pollutants in yellow perch (*Perca flavescens*) in the St.
999 Lawrence River, Canada: implications for resistance and tolerance to parasites.
1000 *Canadian Journal of Zoology,* 88, 247-258. doi:10.1139/z09-140.
1001 Marcogliese, D.J. and Pietrock, M. (2011) Combined effects of parasites and contaminants on
1002 animal health: parasites do matter. *Trends in Parasitology,* 27, 123-130.
1003 doi:10.1016/j.pt.2010.11.002.
1004 Marcogliese, D.J. (2016) The distribution and abundance of parasites in aquatic ecosystems
1005 in a changing climate: More than just temperature. *Integrative and Comparative*
1006 *Biology,* 56, 611-619. doi:10.1093/icb/icw036.
1007 Margolis, L. and Arthur, J.R. (1979) Synopis of the parasites of fishes of Canada. *Bulletin of*
1008 *the Fisheries Research Board of Canada,* 199, 269.
1009 Markkula, S.E., Karvonen, A., Salo, H., Valtonen, E.T. and Jokinen, E.I. (2007) Ultraviolet B
1010 irradiation affects resistance of rainbow trout (*Oncorhynchus mykiss*) against
1011 bacterium *Yersinia ruckeri* and trematode *Diplostomum spathaceum*. *Photochemistry*
1012 *and Photobiology,* 83, 1263-1269. doi:10.1111/j.1751-1097.2007.00165.x.
1013 Martin, L.B., Hopkins, W.A., Mydlarz, L.D. and Rohr, J.R. (2010) The effects of
1014 anthropogenic global changes on immune functions and disease resistance. *Annals of*
1015 *the New York Academy of Sciences,* 1195, 129-148. doi:10.1111/j.1749-
1016 6632.2010.05454.x.
1017 McDonald, T.E. and Margolis, L. (1995) Synopsis of the parasites of fishes of Canada:
1018 Supplement (1978-1993). *Canadian Special Publication of Fisheries and Aquatic*
1019 *Sciences,* 122, 265.
1020 McKeown, C.A. and Irwin, S.W.B. (1997) Accumulation of *Diplostomum* spp. (Digenea:
1021 Diplostomatidae) metacercariae in the eyes of 0+ and 1+ roach (*Rutilus rutilus*).

International Journal for Parasitology, 27, 377-380. doi:10.1016/s0020-7519(96)00204-4.

Milotic, M., Milotic, D. and Koprivnikar, J. (2018) Exposure to a cyanobacterial toxin increases larval amphibian susceptibility to parasitism. *Parasitology Research,* 117, 513-520. doi:10.1007/s00436-017-5727-0.

Moe, S.J., De Schamphelaere, K., Clements, W.H., Sorensen, M.T., Van den Brink, P.J. and Liess, M. (2013) Combined and interactive effects of global climate change and toxicants on populations and communities. *Environmental Toxicology and Chemistry,* 32, 49-61. doi:10.1002/etc.2045.

Moody, J. and Gaten, E. (1982) The population dynamics of eyeflukes *Diplostomum spathaceum* and *Tylodelphys clavata* (Digenea, Diplostomatidae) in rainbow and brown trout in Rutland water - 1974-1978. *Hydrobiologia,* 88, 207-209. doi:10.1007/bf00008315.

Morley, N.J., Crane, M. and Lewis, J.W. (2001) Toxicity of cadmium and zinc to *Diplostomum spathaceum* (Trematoda : Diplostomidae) cercarial survival. *International Journal for Parasitology,* 31, 1211-1217. doi:10.1016/s0020-7519(01)00229-6.

Morley, N.J., Crane, M. and Lewis, J.W. (2002) Toxicity of cadmium and zinc mixtures to *Diplostomum spathaceum* (Trematoda : Diplostomidae) cercarial survival. *Archives of Environmental Contamination and Toxicology,* 43, 28-33. doi:10.1007/s00244-002-1244-x.

Morley, N.J., Crane, M. and Lewis, J.W. (2003a) Cadmium toxicity and snail-digenean interactions in a population of *Lymnaea* spp. *Journal of Helminthology,* 77, 49-55. doi:10.1079/joh2002148.

Morley, N.J., Crane, M. and Lewis, J.W. (2003b) Toxicity of cadmium and zinc to the cercarial activity of *Diplostomum spathaceum* (Trematoda : Diplostomidae). *Folia Parasitologica,* 50, 57-60. doi:10.14411/fp.2003.011.

Morley, N.J., Irwin, S.W.B. and Lewis, J.W. (2003c) Pollution toxicity to the transmission of larval digeneans through their molluscan hosts. *Parasitology,* 126, S5-S26. doi:10.1017/s0031182003003755.

Morley, N.J. (2011) Thermodynamics of cercarial survival and metabolism in a changing climate. *Parasitology,* 138, 1442-1452. doi:10.1017/s0031182011001272.

Morley, N.J. (2012) Thermodynamics of miracidial survival and metabolism. *Parasitology,* 139, 1640-1651. doi:10.1017/s0031182012000960.

1056 Morley, N.J. and Lewis, J.W. (2013) Thermodynamics of cercarial development and
1057 emergence in trematodes. *Parasitology,* 140, 1211-1224.
1058 doi:10.1017/s0031182012001783.
1059 Morley, N.J. and Lewis, J.W. (2014) Extreme climatic events and host-pathogen interactions:
1060 The impact of the 1976 drought in the UK. *Ecological Complexity,* 17, 1-19.
1061 doi:10.1016/j.ecocom.2013.12.001.
1062 Morley, N.J. and Lewis, J.W. (2015) Thermodynamics of trematode infectivity. *Parasitology,*
1063 142, 585-597. doi:10.1017/s0031182014001632.
1064 Moszczynska, A., Locke, S.A., McLaughlin, J.D., Marcogliese, D.J. and Crease, T.J. (2009)
1065 Development of primers for the mitochondrial cytochrome c oxidase I gene in
1066 digenetic trematodes (Platyhelminthes) illustrates the challenge of barcoding parasitic
1067 helminths. *Molecular Ecology Resources,* 9, 75-82. doi:10.1111/j.1755-
1068 0998.2009.02634.x.
1069 Muhlegger, J.M., Jirsa, F., Konecny, R. and Frank, C. (2010) Parasites of *Apollonia*
1070 *melanostoma* (Pallas 1814) and *Neogobius kessleri* (Guenther 1861) (Osteichthyes,
1071 Gobiidae) from the Danube River in Austria. *Journal of Helminthology,* 84, 87-92.
1072 doi:10.1017/s0022149x09990095.
1073 Muller, M. (2019) Dams have the power to slow climate change. *Nature,* 566, 315-317.
1074 Niewiadomska, K. (1984) Present status of *Diplostomum spathaceum* (Rudolphi, 1819) and
1075 differentiation of *Diplostomum pseudospathaceum* nom. nov. (Trematoda:
1076 Diplostomatidae). *Systematic Parasitology,* 6, 81-86. doi:10.1007/bf02185515.
1077 Niewiadomska, K. (1986) Verification of the life-cycles of *Diplostomum spathaceum*
1078 (Rudolphi,1819) and *D. pseudospathaceum* Niewiadomska, 1984 (Trematoda:
1079 Diplostomidae). *Systematic Parasitology,* 8, 23-31. doi:10.1007/bf00010306.
1080 Niewiadomska, K. and Kiseliene, V. (1994) *Diplostomum* cercariae (Digenea) in snails from
1081 Lithuania. II. Survey of species. *Acta Parasitologica,* 39, 179-186.
1082 Niewiadomska, K. and Laskowski, Z. (2002) Systematic relationships among six species of
1083 *Diplostomum* Nordmann, 1832 (Digenea) based on morphological and molecular
1084 data. *Acta Parasitologica,* 47, 20-28.
1085 Noyes, P.D., McElwee, M.K., Miller, H.D., Clark, B.W., Van Tiem, L.A., Walcott, K.C.,
1086 Erwin, K.N. and Levin, E.D. (2009) The toxicology of climate change: Environmental
1087 contaminants in a warming world. *Environment International,* 35, 971-986.
1088 doi:10.1016/j.envint.2009.02.006.

1089 Ondračková, M., Davidova, M., Blazek, R., Gelnar, M. and Jurajda, P. (2009) The interaction
1090 between an introduced fish host and local parasite fauna: *Neogobius kessleri* in the
1091 middle Danube River. *Parasitology Research,* 105, 201-208. doi:10.1007/s00436-
1092 009-1384-2.
1093 Ondračková, M., Hudcova, I., Davidova, M., Adamek, Z., Kasny, M. and Jurajda, P. (2015)
1094 Non-native gobies facilitate the transmission of *Bucephalus polymorphus*
1095 (Trematoda). *Parasites & Vectors,* 8. doi:10.1186/s13071-015-0999-7.
1096 Owen, S.F., Barber, I. and Hart, P.J.B. (1993) Low-level infection by eye fluke, *Diplostomum*
1097 spp, affects the vision of 3-spined sticklebacks, *Gasterosteus aculeatus*. *Journal of*
1098 *Fish Biology,* 42, 803-806.
1099 Paaijmans, K.P., Blanford, S., Bell, A.S., Blanford, J.I., Read, A.F. and Thomas, M.B. (2010)
1100 Influence of climate on malaria transmission depends on daily temperature variation.
1101 *Proceedings of the National Academy of Sciences of the United States of America,*
1102 107, 15135-15139. doi:10.1073/pnas.1006422107.
1103 Padros, F., Knudsen, R. and Blasco-Costa, I. (2018) Histopathological characterisation of
1104 retinal lesions associated to *Diplostomum* species (Platyhelminthes: Trematoda)
1105 infection in polymorphic Arctic charr *Salvelinus alpinus*. *International Journal for*
1106 *Parasitology-Parasites and Wildlife,* 7, 68-74. doi:10.1016/j.ijppaw.2018.01.007.
1107 Paerl, H.W., Hall, N.S. and Calandrino, E.S. (2011) Controlling harmful cyanobacterial
1108 blooms in a world experiencing anthropogenic and climatic-induced change. *Science*
1109 *of the Total Environment,* 409, 1739-1745. doi:10.1016/j.scitotenv.2011.02.001.
1110 Paull, S.H. and Johnson, P.T.J. (2011) High temperature enhances host pathology in a snail-
1111 trematode system: possible consequences of climate change for the emergence of
1112 disease. *Freshwater Biology,* 56, 767-778. doi:10.1111/j.1365-2427.2010.02547.x.
1113 Paull, S.H., LaFonte, B.E. and Johnson, P.T.J. (2012) Temperature-driven shifts in a host-
1114 parasite interaction drive nonlinear changes in disease risk. *Global Change Biology,*
1115 18, 3558-3567. doi:10.1111/gcb.12018.
1116 Paull, S.H. and Johnson, P.T.J. (2014) Experimental warming drives a seasonal shift in the
1117 timing of host-parasite dynamics with consequences for disease risk. *Ecology Letters,*
1118 17, 445-453. doi:10.1111/ele.12244.
1119 Pennycuick, L. (1971) Differences in the parasite infections in three-spined sticklebacks
1120 (*Gasterosteus aculeatus* L.) of different sex, age and size. *Parasitology,* 63, 407-418.
1121 Pietrock, M., Meinelt, T., Marcogliese, D.J. and Steinberg, C.E.W. (2001) Influence of
1122 aqueous sediment extracts from the Oder River (Germany/Poland) on survival of

Diplostomum sp (Trematoda : Diplostomidae) cercariae. *Archives of Environmental Contamination and Toxicology,* 40, 327-332.

Pietrock, M., Marcogliese, D.J. and McLaughlin, J.D. (2002a) Effects of cadmium upon longevity of *Diplostomum* sp (Trematoda : Diplostomidae) cercariae. *Chemosphere,* 47, 29-33. doi:10.1016/s0045-6535(01)00283-1.

Pietrock, M., Marcogliese, D.J., Meinelt, T. and McLaughlin, J.D. (2002b) Effects of mercury and chromium upon longevity of *Diplostomum* sp (Trematoda : Diplostomidae) cercariae. *Parasitology Research,* 88, 225-229. doi:10.1007/s00436-001-0529-8.

Pietrock, M. and Marcogliese, D.J. (2003) Free-living endohelminth stages: at the mercy of environmental conditions. *Trends in Parasitology,* 19, 293-299. doi:10.1016/s1471-4922(03)00117-x.

Pietrock, M. and Goater, C.P. (2005) Infectivity of *Ornithodiplostomum ptychocheilus* and *Posthodiplostomum minimum* (Trematoda : Diplostomidae) cercariae following exposure to cadmium. *Journal of Parasitology,* 91, 854-856. doi:10.1645/ge-473r.1.

Poulin, R. (2006) Global warming and temperature-mediated increases in cercarial emergence in trematode parasites. *Parasitology,* 132, 143-151. doi:10.1017/s0031182005008693.

Poulin, R. and Mouritsen, K.N. (2006) Climate change, parasitism and the structure of intertidal ecosystems. *Journal of Helminthology,* 80, 183-191. doi:10.1079/joh2006341.

Prophete, C., Carlson, E.A., Li, Y., Duffy, J., Steinetz, B., Lasano, S. and Zelikoff, J.T. (2006) Effects of elevated temperature and nickel pollution on the immune status of Japanese medaka. *Fish & Shellfish Immunology,* 21, 325-334. doi:10.1016/j.fsi.2005.12.009.

Raffel, T.R., Romansic, J.M., Halstead, N.T., McMahon, T.A., Venesky, M.D. and Rohr, J.R. (2013) Disease and thermal acclimation in a more variable and unpredictable climate. *Nature Climate Change,* 3, 146-151. doi:10.1038/nclimate1659.

Raffel, T.R., Halstead, N.T., McMahon, T.A., Davis, A.K. and Rohr, J.R. (2015) Temperature variability and moisture synergistically interact to exacerbate an epizootic disease. *Proceedings of the Royal Society B,* 282. doi:10.1098/rspb.2014.2039.

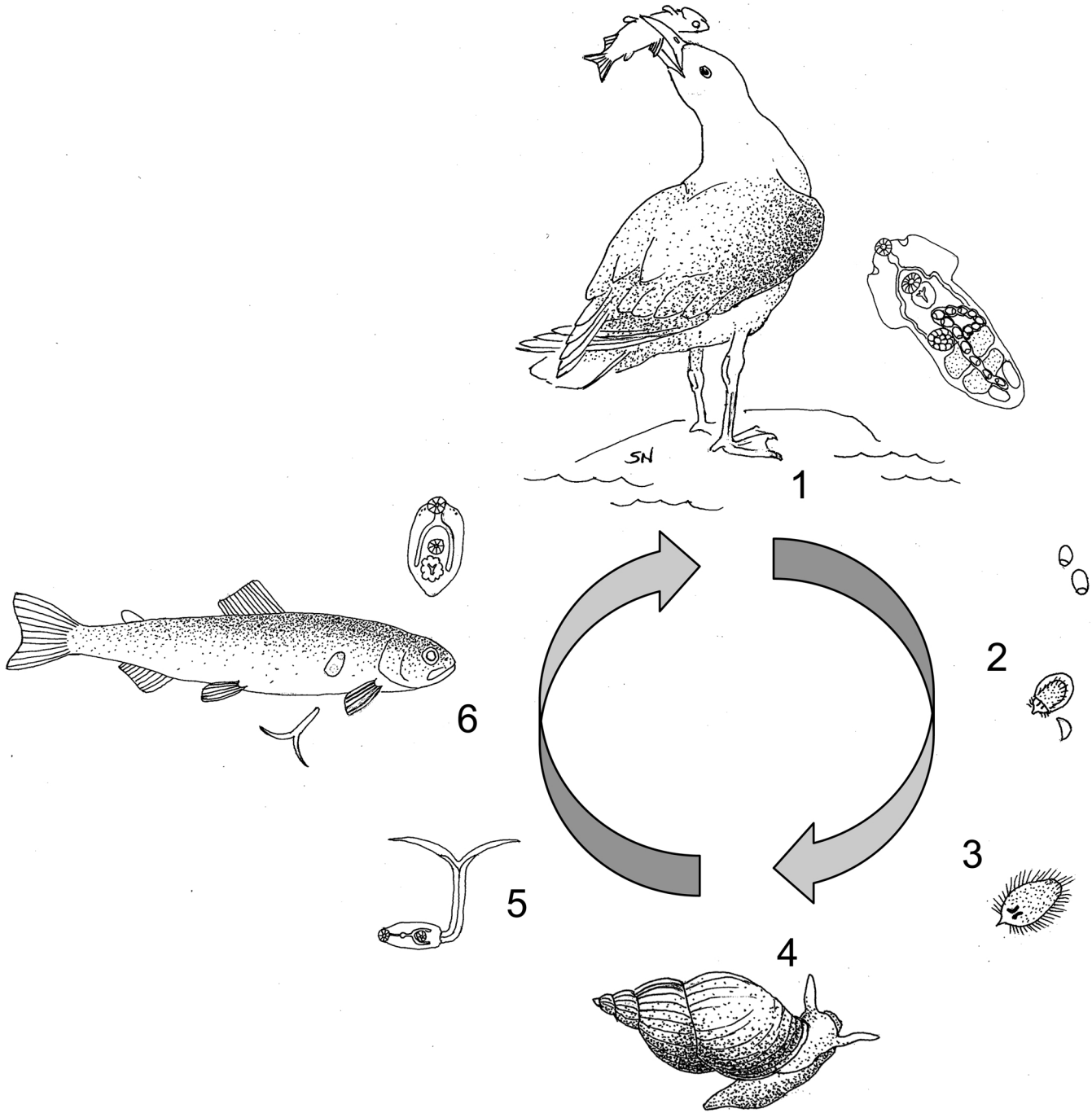
Ratanarat-Brockelman, C. (1974) Migration of *Diplostomum spathaceum* (Trematoda) in the fish intermediate host. *Zeitschrift für Parasitenkunde,* 43, 123-134.

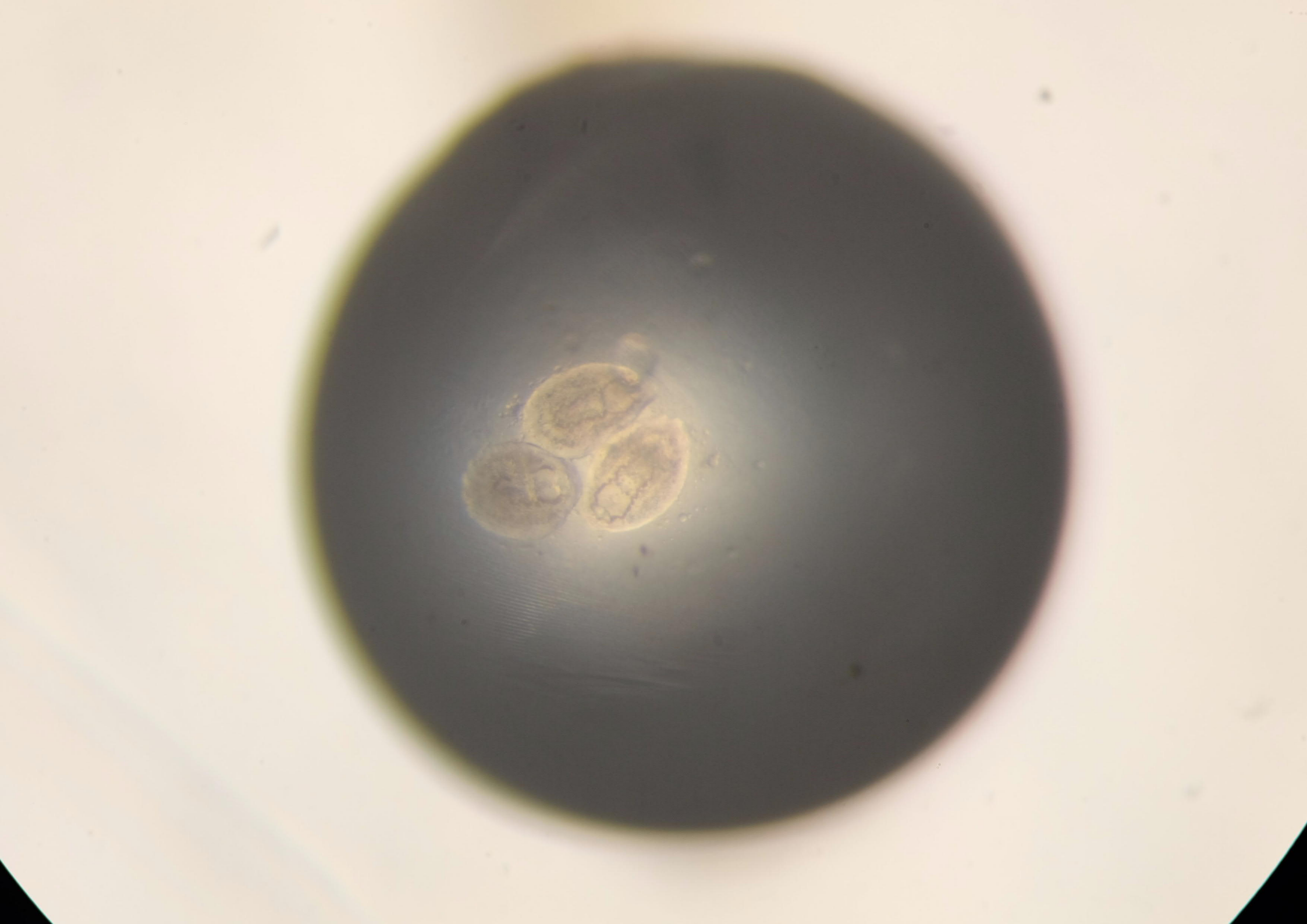
1157 Rauch, G., Kalbe, M. and Reusch, T.B.H. (2005) How a complex life cycle can improve a
1158 parasite's sex life. *Journal of Evolutionary Biology,* 18, 1069-1075.
1159 doi:10.1111/j.1420-9101.2005.00895.x.
1160 Rellstab, C., Louhi, K.R., Karvonen, A. and Jokela, J. (2011) Analysis of trematode parasite
1161 communities in fish eye lenses by pyrosequencing of naturally pooled DNA.
1162 *Infection, Genetics and Evolution,* 11, 1276-1286. doi:10.1016/j.meegid.2011.04.018.
1163 Rellstab, C., Karvonen, A., Louhi, K.-R. and Jokela, J. (2013) Genotype-specific vs. cross-
1164 reactive host immunity against a macroparasite. *PLoS One,* 8.
1165 doi:10.1371/journal.pone.0078427.
1166 Riley, E.M. and Chappell, L.H. (1992) Effect of infection with *Diplostomum spathaceum* on
1167 the internal defense system of *Lymnaea stagnalis*. *Journal of Invertebrate Pathology,*
1168 59, 190-196. doi:10.1016/0022-2011(92)90032-y.
1169 Rohr, J.R., Dobson, A.P., Johnson, P.T.J., Kilpatrick, A.M., Paull, S.H., Raffel, T.R., Ruiz-
1170 Moreno, D. and Thomas, M.B. (2011) Frontiers in climate change-disease research.
1171 *Trends in Ecology & Evolution,* 26, 270-277. doi:10.1016/j.tree.2011.03.002.
1172 Rohr, J.R. and Palmer, B.D. (2013) Climate change, multiple stressors, and the decline of
1173 ectotherms. *Conservation Biology,* 27, 741-751. doi:10.1111/cobi.12086.
1174 Rohr, J.R., Raffel, T.R., Blaustein, A.R., Johnson, P.T.J., Paull, S.H. and Young, S. (2013)
1175 Using physiology to understand climate-driven changes in disease and their
1176 implications for conservation. *Conservation Physiology,* 1, cot022.
1177 doi:10.1093/conphys/cot022.
1178 Salo, T., Stamm, C., Burdon, F.J., Räsänen, K. and Seppälä, O. (2017) Resilience to heat
1179 waves in the aquatic snail *Lymnaea stagnalis*: Additive and interactive effects with
1180 micropollutants. *Freshwater Biology,* 62, 1831-1846. doi:10.1111/fwb.12999.
1181 Scharsack, J.P. and Kalbe, M. (2014) Differences in susceptibility and immune responses of
1182 three-spined sticklebacks (*Gasterosteus aculeatus*) from lake and river ecotypes to
1183 sequential infections with the eye fluke *Diplostomum pseudospathaceum*. *Parasites &*
1184 *Vectors,* 7, 109. doi:10.1186/1756-3305-7-109.
1185 Scharsack, J.P., Franke, F., Erin, N.I., Kuske, A., Buscher, J., Stolz, H., Samonte, I.E., Kurtz,
1186 J. and Kalbe, M. (2016) Effects of environmental variation on host-parasite
1187 interaction in three-spined sticklebacks (*Gasterosteus aculeatus*). *Zoology,* 119, 375-
1188 383. doi:10.1016/j.zool.2016.05.008.

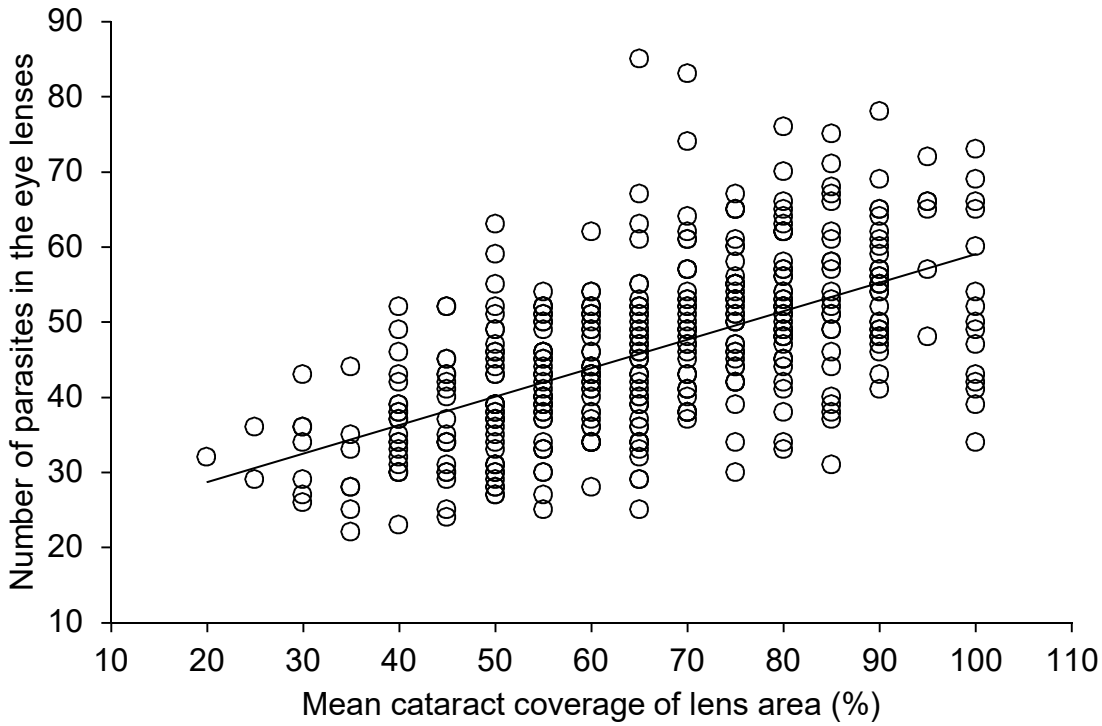
1189 Schiedek, D., Sundelin, B., Readman, J.W. and Macdonald, R.W. (2007) Interactions
1190 between climate change and contaminants. *Marine Pollution Bulletin,* 54, 1845-1856.
1191 doi:10.1016/j.marpolbul.2007.09.020.
1192 Seppälä, O., Karvonen, A. and Valtonen, E.T. (2004) Parasite-induced change in host
1193 behaviour and susceptibility to predation in an eye fluke - fish interaction. *Animal*
1194 *Behaviour,* 68, 257-263. doi:10.1016/j.anbehav.2003.10.021.
1195 Seppälä, O., Karvonen, A. and Valtonen, E.T. (2005a) Impaired crypsis of fish infected with
1196 a trophically transmitted parasite. *Animal Behaviour,* 70, 895-900.
1197 doi:10.1016/j.anbehav.2005.01.021.
1198 Seppälä, O., Karvonen, A. and Valtonen, E.T. (2005b) Manipulation of fish host by eye
1199 flukes in relation to cataract formation and parasite infectivity. *Animal Behaviour,* 70,
1200 889-894. doi:10.1016/j.anbehav.2005.01.020.
1201 Seppälä, O., Karvonen, A. and Valtonen, E.T. (2008) Shoaling behaviour of fish under
1202 parasitism and predation risk. *Animal Behaviour,* 75, 145-150.
1203 doi:10.1016/j.anbehav.2007.04.022.
1204 Seppälä, O., Karvonen, A. and Valtonen, E.T. (2011) Eye fluke-induced cataracts in natural
1205 fish populations: is there potential for host manipulation? *Parasitology,* 138, 209-214.
1206 doi:10.1017/s0031182010001228.
1207 Settele, J., Scholes, R., Betts, R., Bunn, S., Leadley, P., Nepstad, D., Overpeck, J.T. and
1208 Taboada, M.A. (2014) Terrestrial and inland water systems. *In:* Field, C.B., Barros,
1209 V.R., Dokken, D.J., Mach, K.J., Mastrandrea, M.D., Bilir, T.E., Chatterjee, M., Ebi,
1210 K.L., Estrada, Y.O., Genova, R.C.*, et al.* (eds.) *Climate Change 2014: Impacts,*
1211 *Adaptation, and Vulnerability. Part A: Global and Sectoral Aspects. Contribution of*
1212 *Working Group II to the Fifth Assessment Report of the Intergovernmental Panel on*
1213 *Climate Change.* Cambridge University Press, Cambridge, United Kingdom and New
1214 York, NY, USA, pp. 271-359.
1215 Shariff, M., Richards, R.H. and Sommerville, C. (1980) The histopathology of acute and
1216 chronic infections of rainbow trout *Salmo gairdneri* Richardson with eye flukes,
1217 *Diplostomum* spp. *Journal of Fish Diseases,* 3, 455-465. doi:10.1111/j.1365-
1218 2761.1980.tb00432.x.
1219 Sitjá-Bobadilla, A. (2008) Living off a fish: A trade-off between parasites and the immune
1220 system. *Fish & Shellfish Immunology,* 25, 358-372. doi:10.1016/j.fsi.2008.03.018.

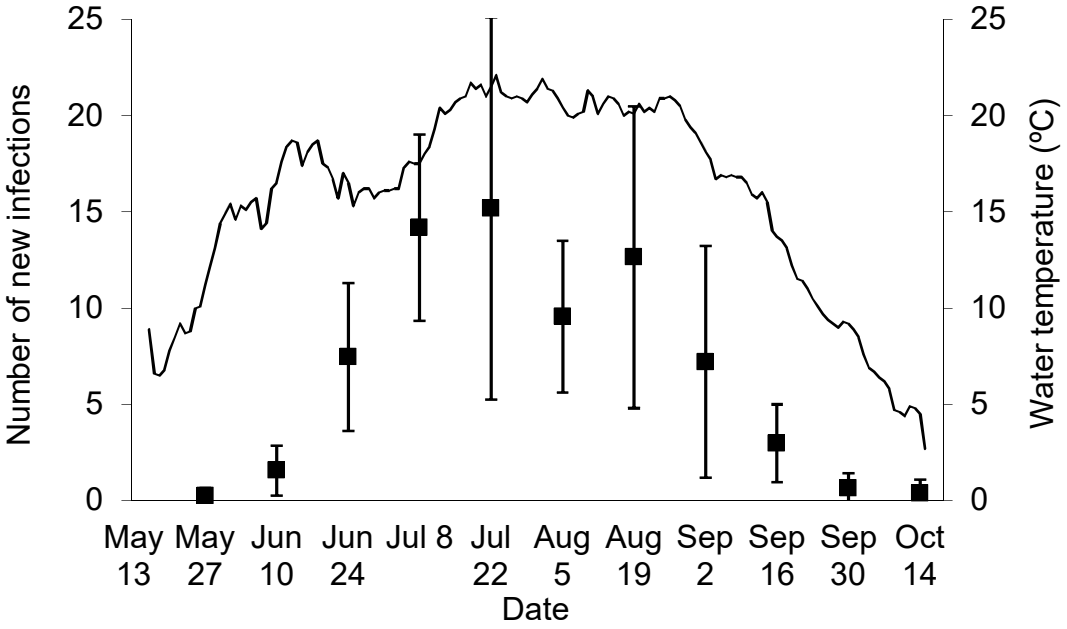
1221 Sous, S.M. (1992) Influence of abiotic factors on emission and survival of *Diplostomum*
1222 *chromatophorum* (Brown,1931) (Trematoda, Diplostomatidae). *Ecological*
1223 *Parasitology,* 1, 154-159.
1224 Stables, J.N. and Chappell, L.H. (1986a) Putative immune response of rainbow trout, *Salmo*
1225 *gairdneri*, to *Diplostomum spathaceum* infections. *Journal of fish biology,* 29, 115-
1226 122. doi:10.1111/j.1095-8649.1986.tb04931.x.
1227 Stables, J.N. and Chappell, L.H. (1986b) *Diplostomum spathaceum* (Rud 1819) - effects of
1228 physical factors on the infection of rainbow trout (*Salmo gairdneri*) by cercariae.
1229 *Parasitology,* 93, 71-79. doi:10.1017/s0031182000049830.
1230 Stables, J.N. and Chappell, L.H. (1986c) The epidemiology of diplostomiasis in farmed
1231 rainbow trout from north-east Scotland. *Parasitology,* 92, 699-710.
1232 Stahl, R.G., Hooper, M.J., Balbus, J.M., Clements, W., Fritz, A., Gouin, T., Helm, R.,
1233 Hickey, C., Landis, W. and Moe, S.J. (2013) The influence of global climate change
1234 on the scientific foundations and applications of Environmental Toxicology and
1235 Chemistry: Introduction to a SETAC international workshop. *Environmental*
1236 *Toxicology and Chemistry,* 32, 13-19. doi:10.1002/etc.2037.
1237 Studer, A. and Poulin, R. (2014) Analysis of trait mean and variability versus temperature in
1238 trematode cercariae: is there scope for adaptation to global warming? *International*
1239 *Journal for Parasitology,* 44, 403-413. doi:10.1016/j.ijpara.2014.02.006.
1240 Sweeting, R.A. (1974) Investigations into natural and experimental infections of freshwater
1241 fish by common eye-fluke *Diplostomum spathaceum* Rud. *Parasitology,* 69, 291-300.
1242 Tort, L., Balasch, J.C. and Mackenzie, S. (2003) Fish immune system. A crossroads between
1243 innate and adaptive responses. *Inmunologia,* 22, 277-286.
1244 Tully, K., Gedan, K., Epanchin-Niell, R., Strong, A., Bernhardt, E.S., Bendor, T., Mitchell,
1245 M., Kominoski, J., Jordan, T.E., Neubauer, S.C.*, et al.* (2019) The invisible flood: The
1246 chemistry, ecology, and social implications of coastal saltwater intrusion. *Bioscience,*
1247 69, 368-378. doi:10.1093/biosci/biz027.
1248 Uribe, C., Folch, H., Enriquez, R. and Moran, G. (2011) Innate and adaptive immunity in
1249 teleost fish: a review. *Veterinarni Medicina,* 56, 486-503.
1250 Waadu, G.D.B. and Chappell, L.H. (1991) Effect of water temperature on the ability of
1251 *Diplostomum spathaceum* miracidia to establish in lymnaeid snails. *Journal of*
1252 *Helminthology,* 65, 179-185. doi:10.1017/s0022149x00010671.

1253 Valtonen, E.T. and Gibson, D.I. (1997) Aspects of the biology of diplostomid metacercarial
1254 (Digenea) populations occurring in fishes in different localities of northern Finland.
1255 *Annales Zoologici Fennici,* 34, 47-59.
1256 Valtonen, E.T., Holmes, J.C. and Koskivaara, M. (1997) Eutrophication, pollution, and
1257 fragmentation: Effects on parasite communities in roach (*Rutilus rutilus*) and perch
1258 (*Perca fluviatilis*) in four lakes in central Finland. *Canadian Journal of Fisheries and*
1259 *Aquatic Sciences,* 54, 572-585.
1260 Wegner, K.M., Kalbe, M., Milinski, M. and Reusch, T.B.H. (2008) Mortality selection during
1261 the 2003 European heat wave in three-spined sticklebacks: effects of parasites and
1262 MHC genotype. *BMC Evolutionary Biology,* 8. doi:10.1186/1471-2148-8-124.
1263 Verma, A.K., Pal, A.K., Manush, S.M., Das, T., Dalvi, R.S., Chandrachoodan, P.P., Ravi,
1264 P.M. and Apte, S.K. (2007) Persistent sub-lethal chlorine exposure augments
1265 temperature induced immunosuppression in *Cyprinus carpio* advanced fingerlings.
1266 *Fish & Shellfish Immunology,* 22, 547-555. doi:10.1016/j.fsi.2006.08.001.
1267 Whyte, S.K., Chappell, L.H. and Secombes, C.J. (1988) In vitro transformation of
1268 *Diplostomum spathaceum* (Digenea) cercariae and short-term maintenance of post-
1269 penetration larvae in vitro. *Journal of Helminthology,* 62, 293-302.
1270 doi:10.1017/s0022149x0001169x.
1271 Whyte, S.K., Chappell, L.H. and Secombes, C.J. (1989) Cytotoxic reactions of rainbow trout,
1272 *Salmo gairdneri* Richardson, macrophages for larvae of the eye fluke *Diplostomum*
1273 *spathaceum* (Digenea). *Journal of Fish Biology,* 35, 333-345. doi:10.1111/j.1095-
1274 8649.1989.tb02986.x.
1275 Whyte, S.K., Chappell, L.H. and Secombes, C.J. (1990) Protection of rainbow trout,
1276 *Oncorhynchus mykiss* (Richardson), against *Diplostomum spathaceum* (Digenea) - the
1277 role of specific antibody and activated macrophages. *Journal of Fish Diseases,* 13,
1278 281-291. doi:10.1111/j.1365-2761.1990.tb00784.x.
1279 Whyte, S.K., Secombes, C.J. and Chappell, L.H. (1991) Studies on the infectivity of
1280 *Diplostomum spathaceum* in rainbow trout (*Oncorhynchus mykiss*). *Journal of*
1281 *Helminthology,* 65, 169-178. doi:10.1017/s0022149x0001066x.
1282


SN
1
2
3
4
5
6




Number of parasites in the eye lenses
90
80
70
60
50
40
30
20
10
10
20
30
40
50
60
70
80
90
100
110
Mean cataract coverage of lens area (%)


25
20
15
10
5
0
Number of new infections
Water temperature (°C)
May 13
May 27
Jun 10
Jun 24
Jul 8
Jul 22
Aug 5
Aug 19
Sep 2
Sep 16
Sep 30
Oct 14
Date