



Invited Review

# Sex Ratios in a Warming World: Thermal Effects on Sex-Biased Survival, Sex Determination, and Sex Reversal

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## Abstract

Rising global temperatures threaten to disrupt population sex ratios, which can in turn cause mate shortages, reduce population growth and adaptive potential, and increase extinction risk, particularly when ratios are male biased. Sex ratio distortion can then have cascading effects across other species and even ecosystems. Our understanding of the problem is limited by how often studies measure temperature effects in both sexes. To address this, the current review surveyed 194 published studies of heat tolerance, finding that the majority did not even mention the sex of the individuals used, with <10% reporting results for males and females separately. Although the data are incomplete, this review assessed phylogenetic patterns of thermally induced sex ratio bias for 3 different mechanisms: sex-biased heat tolerance, temperature-dependent sex determination (TSD), and temperature-induced sex reversal. For sex-biased heat tolerance, documented examples span a large taxonomic range including arthropods, chordates, protists, and plants. Here, superior heat tolerance is more common in females than males, but the direction of tolerance appears to be phylogenetically fluid, perhaps due to the large number of contributing factors. For TSD, well-documented examples are limited to reptiles, where high temperature usually favors females, and fishes, where high temperature consistently favors males. For temperature-induced sex reversal, unambiguous cases are again limited to vertebrates, and high temperature usually favors males in fishes and amphibians, with mixed effects in reptiles. There is urgent need for further work on the full taxonomic extent of temperature-induced sex ratio distortion, including joint effects of the multiple contributing mechanisms.

**Subject area:** Genotype to phenotype

**Key words:** global warming, phylogeny, sex conversion, temperature-dependent sex determination

Global warming can affect sex ratios through a range of mechanisms. Distorted sex ratios can then increase mate shortages, sexual aggression, and breakdown in parental cooperation (Le Galliard et al. 2005; Eberhart-Phillips et al. 2018). Distortion is also expected to alter effective population size, limit sexual selection and adaptive potential, and increase extinction risk (Wedekind 2002; Godwin et al. 2020). Biased sex ratios may be particularly common at the end of species ranges. This is expected to

reduce a species' ability to track shifting climate envelopes if distortion is male biased, but can enhance it if distortion is female biased (Miller and Inouye 2013; Boyle, Hone, et al. 2014; Boyle, Schwanz, et al. 2014; Boyle et al. 2016). Because males and females are not always ecologically equivalent, sex ratio distortion can also have cascading effects on other species and even ecosystems. For example, female-biased populations of mosquitofish induce stronger trophic cascades than male-biased populations,

including effects on primary productivity, zooplankton abundance, pH, and temperature (Fryxell et al. 2015). Similarly, in dioecious plants, skewed sex ratios can alter ecosystem function through impacts on community structure, photosynthesis, water use, and nutrient cycling (Munné-Bosch 2015; Hultine et al. 2016, 2018; Olano et al. 2017; Zhang et al. 2018). Importantly, male- and female-biased sex ratios are expected to have different consequences, with male bias expected to be more detrimental to population growth and viability, as both are often constrained by female fecundity (e.g., Wedekind 2002).

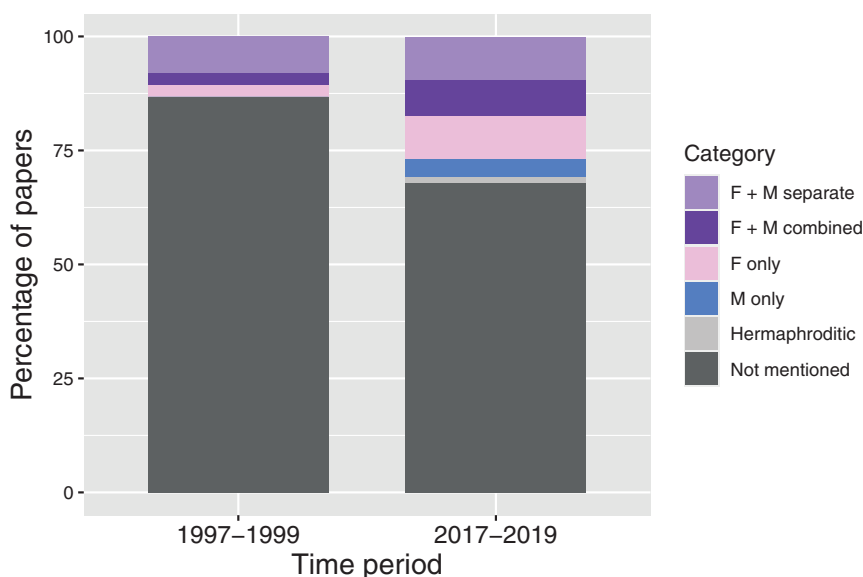
This review focuses specifically on how high temperature affects sex ratio. Although a few examples have received considerable attention (e.g., warming-induced feminization of turtle populations), the full extent of the problem across different taxa and mechanisms has not been well documented. There are 3 main mechanisms through which high temperature can distort sex ratios. One mechanism is sex-biased heat tolerance, which refers to sex differences in the ability to survive high-temperature exposure. A second mechanism is temperature-dependent sex determination (TSD), meaning cases in which sex is not determined genetically, and is instead controlled by the environmental temperature experienced during development. A third mechanism is temperature-induced sex reversal, which refers to cases in which sex is initially determined genetically, but is then altered by environmental temperature. It is important to consider these mechanisms jointly because they can interact. That is, temperature-dependent sex determination can be either relieved or aggravated by sex-biased thermal tolerance (Geffroy and Wedekind 2020). This review is the first to assess broad phylogenetic patterns for all 3 contributing mechanisms. The review begins with a survey of the frequency that both sexes are considered in publications on heat tolerance. For each of the 3 mechanisms, I then review existing information on taxonomic and evolutionary patterns, with examples plotted onto phylogenetic trees. This allows assessment of data gaps and evolutionary lability for different mechanisms of warming-induced sex ratio distortion.

## Sex-Biased Heat Tolerance

### Survey of the Treatment of Sex Differences

In biomedicine, sex differences were understudied for decades, with a preponderance of work focusing only on males to reduce variation from hormonal cycles, standardize the study population, and/or protect females of reproductive age (e.g., Beery and Zucker 2011). The problems with this approach and the practice of extrapolating results from males to females have since been realized, and the biomedical community is making considerable effort to study both sexes. For example, research funded by the United States National Institutes of Health (NIH) is now required to account for sex as a biological variable (Clayton 2016; Woitowich and Woodruff 2019; Woitowich et al. 2020).

Although biomedical research is beginning to address the importance of studying both sexes, the study of sex differences in physiological tolerance across taxa lags far behind, albeit for different reasons. Here I focus specifically on heat tolerance, which is estimated by survival-related metrics (e.g., Bennett et al. 2018; Kingsolver and Umbanhowar 2018) including critical thermal maximum (the upper temperature causing physiological failure), median lethal temperature (the temperature resulting in death of 50% of exposed individuals), and upper lethal temperature (the upper temperature causing death of a specified fraction of exposed individuals). To gauge the level of attention given to sex differences in studies of heat tolerance, I surveyed ISI Web of Science (Thompson Scientific) for publications in 2 time periods (1997–1999 and 2017–2019) using search terms “critical thermal maxim\*,” “median lethal temperature,” or “upper lethal temperature.” Search results were further refined to include only those with original data on heat tolerance. Publications were then examined to determine the sex of the experimental subjects (search terms “sex,” “gender,” “male,” “female,” hermaphrodite”), as well as their life stage (search terms “egg,” “embryo,” “larva,” “juvenile,” “adult”). A total of 38 publications were retained for 1997–1999 and 156 for 2017–2019 (Figure 1, Supplementary Appendix 1), suggesting increased recent interest in heat tolerance. However, attention to sex differences in heat tolerance shows only a modest



**Figure 1.** Survey of the treatment of sex in papers on heat tolerance published during 2 time periods: 1997–1999 (38 papers) and 2017–2019 (156 papers). F, females; M, males.

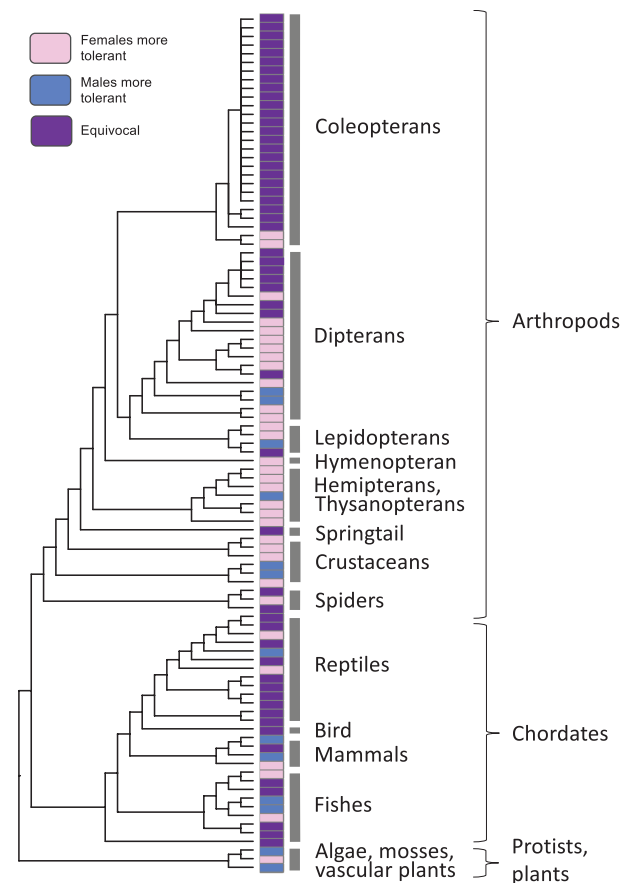
increase, with the majority of studies in both time periods not mentioning the sex of their subjects (86.8% in 1997–1999, 67.9% in 2017–2019) and less than 10% reporting results for males and females separately (7.9% in 1997–1999, 9.6% in 2017–2019).

Why do so few studies address sex differences in thermal tolerance? Of the 176 studies that did not assess sex differences, only 14 offered explanations. These explanations included the species being hermaphroditic, one sex being more common in collections, the desire to eliminate confounding effects of sex or reproductive status, concern that sex identification would require excessive manipulation of samples, research questions focused on only one sex, and previous work that did not find a statistical difference between sexes. However, for another 63 studies the tested organisms were in early-life stages (eggs, embryos, larvae, juveniles) that were presumably too young to be sexed, although this was not discussed. Many studies of stress tolerance focus on early-life stages because they are expected to be more sensitive, although there are certainly cases where this assumption is not valid (e.g., Rodnick et al. 2004; Tangwancharoen and Burton 2014; Clark et al. 2017; Vidal et al. 2017). Although this approach focusing on early-life stages may aim to identify the “weakest links” in climate response (Pandori and Sorte 2019), if sex identification is not feasible or not undertaken for the studied organisms, it may have the unintended consequence of obscuring our understanding of the sex-biased results of rising temperatures.

### Taxonomic and Evolutionary Patterns

Global warming may alter sex ratios due to sex-biased tolerance of factors such as water deficiency and high temperature. In dioecious plants, males are quite often more drought tolerant, in part due to lower reproductive investment, and drought-induced masculinization of plant populations can have cascading effects on soil carbon flux, nutrient transformation rates, photosynthesis, and community composition (Munné-Bosch 2015; Hultine et al. 2016, 2018; Olano et al. 2018; Zhang et al. 2018). Here I instead focus on sex differences in high-temperature tolerance. Such differences have been reported to cause severe sex ratio distortion in some natural populations, such as in tropical black flying foxes where 84% of adults killed by an extreme high-temperature event were females (Welbergen et al. 2008). This review is the first to compile studies of sex-biased heat tolerance across a broad range of taxa. Publications were surveyed on ISI Web of Science (Thompson Scientific) using search terms “sex” and (“thermal tolerance” or “temperature tolerance” or “thermal performance” or “heat tolerance” or “critical thermal maximum” or “CTmax” or “upper lethal temperature” or “median lethal temperature” or “LT50”). A total of 73 publications were found with original data on sex-biased heat tolerance, spanning 99 different species (Supplementary Appendix 2). Sex-biased tolerance for a species was scored as “Equivocal” if no significant sex differences were found within a publication or if conflicting conclusions were found in different publications.

Phylogenetic relationships among the 99 species were reconstructed using the “rotl” package, v3.0.10 (Michonneau et al. 2016) interfaced to the “Open Tree of Life” or OTL (Hinchliff et al. 2015), using R v3.6.0 (R Core Team 2019). Species names were matched to those in the OTL database using the Taxonomic Name Resolution Service (TNRS). The resultant tree was redrawn using ggtree v1.16.1 (Yu et al. 2017), and sex differences in high temperature tolerance were then mapped onto the tree (Figure 2). Results show that data on sex-biased heat tolerance spans a diversity of taxa (arthropods,



**Figure 2.** Phylogeny of 99 species tested for sex-specific heat tolerance.

chordates, protists, plants) but is dominated by arthropod species, which are popular subjects for experimental assessment of heat tolerance. When sex differences were found, higher tolerance was more common in females (32/99) than in males (13/99); however, results were equivocal for the majority of species (54/99). The general trend toward greater tolerance in females is the relatively less problematic direction in terms of population viability. Across the tree, the direction of sex-biased tolerance appears highly labile, with both higher-female and higher-male tolerance found within many taxonomic groups, including dipterans, lepidopterans, hemipterans, crustaceans, reptiles, mammals, and fishes.

The phylogenetic fluidity of sex-biased heat tolerance seen in Figure 2 may reflect the large number of variables contributing to this trait. One factor that might be expected to make a major contribution is sex chromosomes. The expectation here is that the heterogametic sex (males in an XY system and females in a ZW system) will be more vulnerable due to the unmasking of deleterious recessives on their unprotected sex chromosomes (e.g., Trivers 1985; Pipoly et al. 2015). Contrary to this prediction, frequencies of sex-biased heat tolerance in the current dataset (Supplementary Appendix 2) do not differ between species known to have male heterogamety (13 females more tolerant:5 males more tolerant:14 equivocal) and those known to have female heterogamety (3 females more tolerant:1 males more tolerant:5 equivocal) (Fisher’s exact test,  $N = 41$ ,  $P = 0.88$ ). Although there is strong evidence that the sex with heterogametic sex chromosomes is more likely to die earlier (Xiracostas et al. 2020), it is not clear from this limited dataset that the heterogametic sex exhibits lower heat tolerance.

Another factor that may contribute to sex differences in heat tolerance is body size, although effects may go in either direction. In some cases, smaller organisms may be more heat tolerant, due to factors such as greater surface to volume ratios allowing better heat dissipation in endotherms (e.g., Gardner et al. 2011) or greater oxygen dissolution in ectotherms (e.g., Atkinson 1994). In other cases, smaller organisms may be less tolerant due to greater vulnerability to dehydration and overheating during acute exposure to extremely high temperature (McKechnie and Wolf 2010). It has therefore been predicted that gradual warming may favor smaller size, whereas extreme high-temperature spikes may favor larger body size (Gardner et al. 2011). In the current dataset (Supplementary Appendix 2), body size is mentioned as a possible factor affecting sex-biased heat tolerance in 4 species where the larger sex was more tolerant (all ectotherms) and 3 species where the smaller sex was more tolerant (2 ectotherms, 1 endotherm).

Many other factors may contribute to sex differences in heat tolerance. The sex with higher metabolic rate and/or activity level can be expected to exhibit lower tolerance, assuming that oxygen is limiting (Pörtner 2010). Hormones are another factor in sex-biased heat tolerance, with estrogen generally being beneficial (Tower et al. 2020), whereas cortisol (Jeffries et al. 2012) and testosterone (Chen and Yu 2018) are generally detrimental. Heat tolerance may also trade off with sex-biased investments in growth, mating, reproduction and offspring care (Marshall and Sinclair 2010; Roze et al. 2013).

## Temperature-Dependent Sex Determination

TSD is a subset of environmental sex determination (ESD) in which sex is determined after conception by the environmental temperature experienced during embryogenesis (Charnier 1966; Bull 1983; Valenzuela 2004). The possibility that global climate change will wreak havoc with sex ratios in TSD species has long been recognized. It has even been suggested that sex determination in dinosaurs may have been temperature dependent and that warming-induced sex ratio distortion may have played a significant role in their extinction (Miller et al. 2004). Recent data suggest climate change can result in extreme sex ratio distortion for TSD species. For example, loggerhead sea turtle populations in warmer areas are reported to be up to 99% female (Jensen et al. 2018), and single-sex populations are projected for the near future in other TSD reptiles including lizards, crocodylians, and tuatara (Valenzuela et al. 2019).

Environmental sex determination has been suggested in a range of taxa including invertebrates (Bull 1983), but unambiguous cases of TSD are so far limited to vertebrates, specifically reptiles and fish (Ashman et al. 2014). After vigorous debate, there is no clear conclusion as to whether TSD or genotypic sex determination (GSD) is the ancestral state in vertebrates, as both appear to have evolved multiple times (Bull 1983; Janzen and Paukstis 1988; Pokorná and Kratochvíl 2014). The exact molecular mechanisms underlying TSD have long remained elusive. Recently, it has been proposed that cellular calcium and redox status acts as a conserved sensor of environmental conditions mediating vertebrate ESD (Castelli et al. 2020). In the case of red-eared slider turtles (*Trachemys scripta*), it has been shown that temperature-dependent calcium signaling regulates a transcription factor (STAT3) controlling *Kdm6b*, which in turn effects methylation at the promoter to the male sex-determining gene *Dmrt1* (Ge et al. 2017, 2018; Weber et al. 2020).

True cases of TSD do not include examples of genotypic sex determination with temperature effects (GSD + TE). For a species

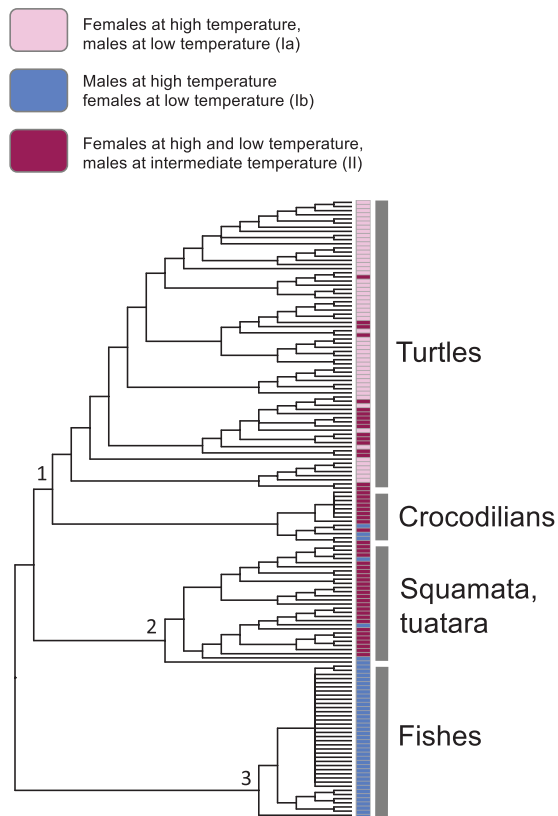
to be unambiguously identified as having TSD, it should (1) not have sex chromosomes and (2) exhibit sex ratio shifts in response to temperature fluctuations within the “range of natural temperature” (Valenzuela et al. 2003; Conover 2004; Ospina-Álvarez and Piferrer 2018). For reptiles, cases of TSD have been further subdivided into 1 of 3 patterns (Ewert and Nelson 1991). In TSD Ia, low temperature produces males and high temperature produces females (MF). In TSD Ib, low temperature produces females and high temperature produces males (FM). In TSD II, both low and high temperatures produce females, whereas intermediate-temperature produces males (FMF). Fish with TSD have traditionally been grouped into patterns equivalent to Ia and Ib, as well as an additional pattern (MFm) wherein males are produced at both low and high temperatures, whereas females are produced at intermediate temperatures (Conover 2004). However, more recent examination of the data showed that all unambiguous cases of TSD in fish fall into the FM pattern (Ospina-Álvarez and Piferrer 2008). Although there is no explicit support, it has been proposed that the FMF pattern is the underlying pattern for all TSD species and that the FM and MF patterns are a byproduct of the limited temperature range over which developing animals are viable (Webb and Smith 1984).

To assess the evolutionary lability of TSD patterns, I mapped examples onto a phylogenetic tree. The dataset includes TSD species with information on TSD pattern in the vertebrate Tree of Sex database (Ashman et al. 2014), excluding cases listed as “equivocal,” “tentative,” or “questionable.” This dataset was extended and modified with additional information on TSD patterns in fish from Ospina-Álvarez and Piferrer (2008) and in reptiles from Godfrey et al. (2003), Gamble (2010), Charruau (2012), and González et al. (2019). The 3 reptile TSD labels (Ia, Ib, and II) were used to categorize all taxa in the dataset. This yielded a total of 149 TSD species with information on TSD pattern (Supplementary Appendix 3). A phylogenetic tree was generated using the same methods described for Figure 2, and TSD patterns for each species were mapped onto this tree (Figure 3).

Figure 3 shows that all 70 turtle species with TSD produce females at higher temperatures (patterns MF and FMF). In crocodylians, high temperature favors females in 10 species (pattern FMF) and males in 3 species (FM). In clade 2 (Squamata, tuatara), high temperature favors females (pattern FMF) in the majority of species, with 4 exceptions: for 3 species in the order Squamata and the single tuatara species (order Rhynchocephalia), males are favored at high temperature (pattern FM). And finally, for all 37 fish species (clade 3) high temperature favors males (pattern FM). Based on this analysis, crocodylians and squamates show the greatest evolutionary lability in high-temperature effects, and thus the greatest hope for escaping deadly effects of climate warming through evolution of a different TSD pattern. Alternatively, TSD species may be able to avoid warming-induced sex ratio distortion through the evolution of sex chromosomes (e.g., Grossen et al. 2010).

The adaptive significance of ESD (including TSD) continues to be debated. With sexual reproduction, population sex ratios are generally expected to be 1:1, as individuals of the rarer sex should have an advantage until an equilibrium is reached (Darwin 1871; Düsing 1884a, 1884b; Fisher 1930; Edwards 2000). In GSD species, 1:1 sex ratios are also enforced by random meiotic segregation of the primary sex-determining element (Williams 1979; Charnov 1982). However, when sex is determined environmentally, sex ratios can be highly skewed, a pattern that can theoretically be explained by environmental effects on fitness (Bull 1981; Freedberg et al. 2001). The most widely accepted evolutionary explanation for ESD remains





**Figure 3.** Phylogeny of 149 vertebrate species known to have temperature-dependent sex determination. Numbers indicate clades 1–3.

the Charnov–Bull model (Charnov and Bull 1977; with subsequent variants reviewed in Schwanz et al. 2016), which posits that selection favors ESD when the fitness of individuals depends on the environment in a sex-biased manner. For example, in the painted turtle *Chrysemys picta*, one of many MF species in clade 1 of Figure 3, the sex determination system may be adaptive in that it allows embryos to develop into the sex best suited to its environment due to sex-biased overwintering physiology (Spencer and Janzen 2014). The concern is that with rapid global warming, distorted sex ratios in TSD species may lead to demographic collapse. Indeed, extreme sex ratio distortion has been reported recently for all 3 TSD patterns, reaching up to 75% males in FM fish species (Ospina-Álvarez and Piferrer 2018), up to 89% females in FMF species like *Crocodylus niloticus* (Bókony et al. 2019), and up to 99% females in MF species like the green sea turtle, *Chelonia mydas* (Jensen et al. 2018).

### Temperature-Induced Sex Reversal

Although the potential effects of climate change on sex ratios of TSD species are well established, less attention has been given to how climate change may alter sex ratio in GSD species exhibiting environmentally induced sex reversal. In these taxa, sex is determined genetically at fertilization, but can be overridden during a critical period of ontogeny by environmental factors including pH, photoperiod, density, water availability, endocrine disrupting chemicals, and, especially, temperature (Quinn et al. 2009; Bhandari et al. 2015; Baroiller and D’Cotta 2016; Flament 2016; Holleley et al. 2016; Li et al. 2016; Weber and Capel 2018). This leads to a mismatch between genetic sex and phenotypic sex. Documented cases of sex

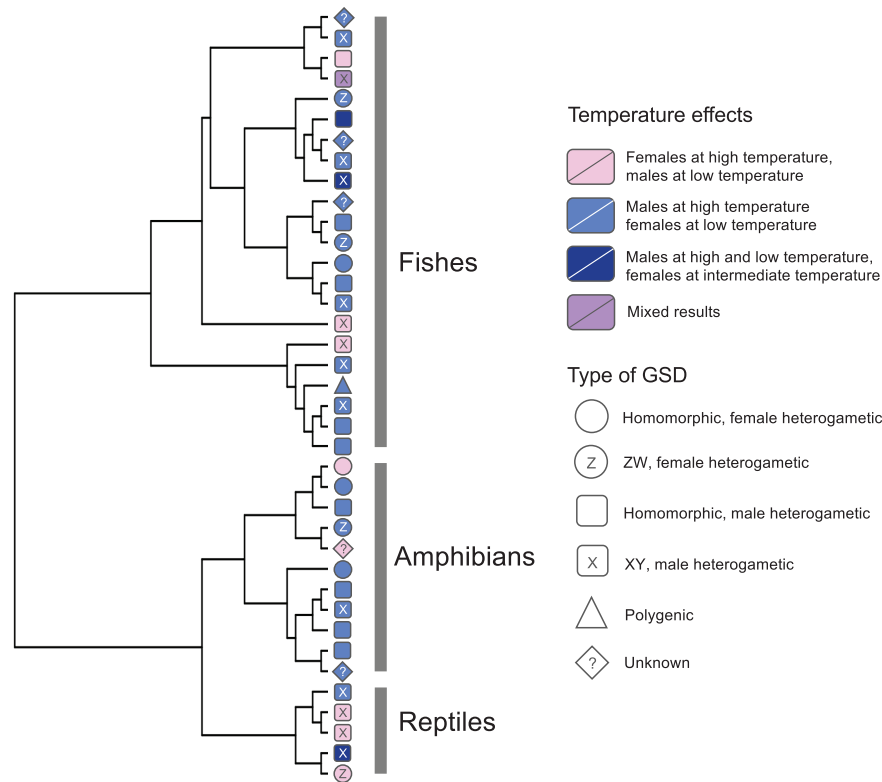
reversal are likely to increase as we continue to develop sex-linked molecular markers that can reveal these genetic/phenotypic mismatches. In fact, it has been estimated that one third of the fish species thought to have TSD actually exhibit GSD + TE (Ospina-Álvarez and Piferrer 2008). Although the data for natural populations are still sparse, environmentally induced sex reversal has been shown to cause extreme sex ratio distortion in some cases. For example, in the flounder *Paralichthys lethostigma*, where warm temperatures masculinize genetic females, sex ratios have been found to reach as high as 94% male in some southern populations (Honeycutt et al. 2019).

Global warming can induce sex reversal through both temperature effects and water restriction. For example, in 2 reptile species, water restriction promotes conversion to males (Baroiller and D’Cotta 2016; Dupoué et al. 2019). Here I focus specifically on temperature-induced sex reversal, termed GSD + TE. The mechanism(s) underlying temperature-induced sex reversal remain an area of active research, with key factors including levels of cortisol and aromatase (Uchida et al. 2004; Ferdinando et al. 2013; Holleley et al. 2016; Castañeda Cortés et al. 2019), with cellular calcium and redox status proposed as a sensor of environmental signals (Castelli et al. 2020). In several cases, epigenetic control of promotion/inhibition has been demonstrated (Baroiller and D’Cotta 2016; Ma et al. 2016; Zhou et al. 2019). Behavior may also play an important role, as sex reversal has been shown to be impacted by individual temperature preferences of sexually undifferentiated juveniles (Nivelle et al. 2019).

Because thermal sex reversal is easily manipulated, it is frequently used to alter sex ratios in managed populations. In many fish species, one sex grows faster than the other so aquaculturists often use thermal sex reversal (as well as hormone-induced reversal) to create cost-effective monosex populations (Baroiller and D’Cotta 2016; Cui et al. 2018; Zhou et al. 2019). Thermal sex reversal can also be manipulated for pest management. For example, fruit flies have been genetically engineered to produce sterile male populations at high temperature (Li and Handler 2017).

Well-documented natural cases of GSD + TE are largely limited to vertebrates, specifically poikilotherms. Here I focus on 38 vertebrate species found to exhibit thermal sex reversal under natural conditions, including 22 fish, 11 amphibians, and 5 reptiles (Figure 4, Supplementary Appendix 4). Phylogenetic relationships among these taxa were reconstructed using the same procedure used for Figure 2. Type of temperature effect and GSD for each species was then mapped onto the tree (Figure 4).

The most common pattern of thermal sex reversal in vertebrates is a masculinizing effect of high temperature, which is found in 76% of the species shown in Figure 4. Masculinization at high temperature was found to predominate in fishes and amphibians, but not in reptiles. An excess of males is, unfortunately, the more problematic direction of sex ratio distortion in terms of population viability. Male-biased sex ratios may become particularly common in fishes (Geffroy and Wedekind 2020), where high temperature favors males in cases of TSD (Figure 3) as well as GSD + TE (Figure 4). For cases of sex reversal, the demographic consequences will also depend on the underlying form of GSD (Bókony et al. 2017). When high temperature masculinization is combined with male-heterogametic sex chromosomes (47% of the species in Figure 4), homogametic pseudo-males (“XX”) mating with homogametic females (“XX”) will produce 100% genetically female (“XX”) offspring, thereby countering the masculinizing distortion. Greater distortion is expected when high temperature masculinization is combined with female heterogamety (16% of the species in Figure 4). Here, heterogametic



**Figure 4.** Phylogeny of 38 vertebrate species known to exhibit temperature-induced sex reversal (GSD + TE). Type of temperature effect (TE) shown by color and type of GSD (genetic sex determination) shown by shape.

(“ZW”) pseudo-males mating with heterogametic (“ZW”) females should produce a ratio of 1 “ZZ”:2 “ZW”:1 “WW,” resulting in 25% “ZZ” males or 33% “ZZ” males if the “WW” female genotype is not viable. The actual phenotypic sex ratio consequences of such a cross are more difficult to predict. For example, in tongue sole (*Cynoglossus semilaevis*), most ZW females from this type of cross develop into ZW pseudo-males even without temperature induction (Chen et al. 2014; Cui et al. 2018). Under these scenarios, high-temperature masculinization causes greater excess of males when females are heterogametic. Alternatively, if the WW genotype is resistant to masculinization, the female-heterogametic system can maintain balanced sex ratios by evolving male heterogamety (Nemesházi et al. 2021). High-temperature feminization is considerably less common (21% of the species in Figure 4), but its effect on sex ratio is also expected to depend on the type of GSD. Here, greater excess of females is expected when males are heterogametic. Based on empirical data for amphibians over the past 60 years (Bókonyi et al. 2017), adult sex ratios shifted toward males in ZZ/ZW species but did not change significantly in XX/XY species.

Temperature-induced sex reversal may also have important consequences over evolutionary time scales. One major outcome may be accelerated transitions between sex determination systems, eventually leading to elimination of sex chromosomes (Holleley et al. 2016; Schwanz et al. 2020). For example, frequent crosses between ZZ males and ZZ pseudo-females could lead to loss of the W chromosome. Modeling work (Schwanz et al. 2020) shows that such sex chromosome loss is buffered by immigration, heritable variation for thermal sensitivity, and reduced reproductive fitness in sex-reversed individuals. The actual fitness effects of sex reversal are incompletely known. There are cases where sex-reversed individuals have been

found to have reduced fitness, such as in the frog *Rana dalmatina* (Nemesházi et al. 2020). In contrast, in the case of the bearded lizard *Pogona vitticeps*, ZZ pseudo-females have novel, male-like behaviors that can increase reproductive fitness relative to genetic (ZW) females, potentially favoring replacement of the old GSD + TE system with pure TSD (Li et al. 2016). Between these 2 extremes, a systematic survey of fishes found little evidence for fitness differences between sex-reversed and wild-type individuals (Senior et al. 2016).

A second major evolutionary consequence of sex reversal is the potential for rejuvenating degenerating sex chromosomes. According to the “fountain of youth” hypothesis (Perrin 2009), XY or ZW recombination in sex-reversed individuals can block the decay of Z and W chromosomes, thereby keeping the sex chromosomes homomorphic. This may help explain the high frequency of homomorphic sex chromosomes in Figure 4 (14 of 38 species) and in amphibians and fish in general, where sex reversal is relatively common. This recombination may also help explain the high lability of sex determination systems among ectothermic vertebrates.

### The Future of Sex Ratios on a Warming Planet

There are already examples of severely distorted sex ratios in natural populations caused by each of the 3 mechanisms discussed above (e.g., Welbergen et al. 2008; Jensen et al. 2018; Honeycutt et al. 2019), and such examples are likely to become more common. Can we expect species to adjust their sex ratios in response to warming temperatures? In some cases, species will be able to shift their geographic or elevational distribution (e.g., Lenoir and Svenning 2015; Sunday et al. 2017). Other taxa will stay in place but buffer sex ratio distortion through changes in

behavior. For TSD species like turtles, there is evidence of adjustment of primary sex ratio by choosing cooler locations or seasons for nesting (Mainwaring et al. 2017; Patrício et al. 2017) and by embryos moving within the egg to select specific thermal regimes (Ye et al. 2019). Similarly, GSD + TE species such as Nile tilapia have been shown to induce sex reversal through their temperature preference during the juvenile phase (Nivelle et al. 2019). Fish have also been shown to mitigate sex ratio distortion in their offspring through nonbehavioral maternal effects (Donelson and Munday 2015).

Thermal disruption of sex ratio may also be ameliorated by microevolutionary change, particularly in taxa with short generation times. Evolutionary adjustments for sex-biased mortality are expected to be constrained by Fisherian sex ratio selection, which predicts equal investment in male and female offspring, even if males and females have very different chances of surviving to adulthood (Fisher 1930; Székely et al. 2014). For GSD species, balanced sex ratios are also imposed by meiotic segregation of sex chromosomes or other sex-determining elements (Williams 1979; Charnov 1982). For TSD species, however, we might predict evolutionary changes in factors such as the pivotal temperature of sex determination, or maternal choice of nesting site or season (Refsnider and Janzen 2016; Blechschmidt et al. 2020). Similarly, for GSD + TE species, evolution might adjust sex ratios through genetic changes underlying thermal sensitivity of sex reversal (Grossen et al. 2010) or preference for normal versus sex-reversed mates (Nemesházi et al. 2021).

If sex ratio adjustments do not occur naturally, human intervention may be justified, particularly for small and declining populations. The goal here could be either to balance sex ratios to maximize effective population size and adaptive potential or to create female-biased ratios, at least temporarily, to increase population growth (Wedekind 2002). For TSD species like some reptiles and fishes, this could be done by manipulating the thermal environment during critical developmental stages (Wedekind 2002; Esteban et al. 2018; Jensen et al. 2018). Environmental sex reversal, found in amphibians, fishes, and reptiles, can also be manipulated by altering temperature or other extrinsic factors (Baroiller and D'Cotta 2016; Cui et al. 2018; Zhou et al. 2019). Sex ratio manipulation in cases where sex determination is strictly genetic will require different approaches, such as supplementation with individuals of the desired sex from captive breeding programs (Lenz et al. 2007). All of these strategies for sex ratio manipulation are temporary solutions, which are likely to fall short if underlying threats to population viability are not addressed.

## Conclusions

Our understanding of sex-biased consequences of temperature is obscured by the widespread practice of “sex-blind” physiological tolerance assays, as illustrated by the above survey of literature on heat tolerance, in which less than 10% of studies reported results for males and females separately. The situation could be improved if studies of thermal biology begin seriously addressing sex as a biological variable, an approach that is now mandated for biomedical research funded by the NIH. Although the data are far from complete, this review assessed phylogenetic patterns of thermal effects on sex ratio for 3 separate mechanisms: sex-biased heat tolerance, TSD, and temperature-induced sex reversal

(GSD + TE). Studies of sex-biased heat tolerance are dominated by arthropods, with additional examples in chordates, protists, and plants. When sexes differ in high-temperature tolerance, high female tolerance is more common. However, the direction of sex-biased tolerance appears to be phylogenetically fluid, perhaps due to the variety of contributing factors including sex chromosomes, body size, metabolism, hormones, and life-history traits. Examples of TSD are limited to cases where genetic sex determination can be definitively ruled out, and are currently restricted to vertebrates. Effects are fairly phylogenetically constrained, with high temperature usually feminizing reptiles and always masculinizing fishes. Definitive examples of GSD + TE are also currently limited to vertebrates. In these examples, high-temperature sex reversal usually masculinizes fishes and amphibians, with more mixed effects in reptiles. The type of GSD is important here, as temperature-induced sex reversal is expected to have very different consequences in male-heterogametic systems versus female-heterogametic systems. Overall, the potential for warming-induced sex ratio distortion appears to be an understudied yet taxonomically widespread problem. Risks are particularly large when high temperature favors males, as is found across multiple mechanisms in fishes (Geffroy and Wedekind 2020), for example. Avoiding population collapse due to warming-induced sex ratio bias will require much greater attention to the taxonomic extent of sex-biased thermal effects, as well as management strategies for cases that have already reached the emergency level.

## Supplementary Material

Supplementary data are available at *Journal of Heredity* online.

**Supplementary Appendix 1.** Survey of publications on heat tolerance during two time periods: 1997–1999 and 2017–2019.

**Supplementary Appendix 2.** Information on species included in Figure 2, showing the phylogeny of species tested for sex-biased heat tolerance. Species are listed by rank order in the tree, from top to bottom, with information on sex determination when available. For each publication on a particular species, the entry includes citation for heat tolerance, metric of heat tolerance, sex with higher tolerance (Female, Male or Equivocal; including consensus for species with multiple publications) and comments.

**Supplementary Appendix 3.** Species included in the phylogeny of temperature-dependent sex determination (TSD) in Figure 3, listed in order from top to bottom. Ia = females at high temperature, males at low temperature; Ib = males at high temperature, females at low temperature; II = females at high and low temperature, males at intermediate temperature.

**Supplementary Appendix 4.** Information on species included in Figure 4, showing the phylogeny of species with genetic sex determination (GSD) with temperature effects (TE). Species are listed by rank order in the tree, from top to bottom. GSD + TE types: M = males favored at high temperature; M2 = males favored at low and high temperature; F = females favored at high temperature; Mixed = mixed results.

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## Data Availability

All data generated in this study have been reported within the main text or in the supplementary files.

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