

## Physiology and pharmacology of temperature regulation: From basic to applied and across environments

A Call for papers on the theme of Physiology and Pharmacology of Temperature Regulation (PPTR) was announced by Andrej Romanovsky, the Editor-in-Chief of *Temperature* during the virtual PPTR (vPPTR) 2020 conference that was held from Oct 26–29, 2020. During vPPTR 2020 Editor Romanovsky invited each of us as Guest Editors for this initiative and we are pleased to report that the Call received an excellent response, resulting in 13 contributions including 3 Comprehensive Reviews, 3 Priority Reviews, 2 Research Papers, 1 Priority Report, 1 Front Matter comment and 1 Front Matter reply, a Front Matter Discovery piece and the current plus an additional editorial [1] that appear in two special issues of *Temperature*. The Call sought PPTR papers ranging from basic mechanisms of temperature regulation across a variety of species, including humans, to applied temperature regulation in industrial, military, and clinical settings. It has been particularly delightful that there is representation in these special issues of *Temperature* across a diversity of topic areas.

The aim of this editorial is to provide a brief overview of these two special issues and to orient readers to the content of these published papers. To add flavor and to maximize the reader experience, the authors of each paper provided a drink suggestion – beverages with which they suggest to best enjoy reading their work (Table 1). For instance, Andrej Romanovsky's beverage suggestion, following on his fever research theme, reminds us of the original purpose of a gin-tonic – as a prophylactic for malaria and the high fever. For background information on these beverage suggestions, the reader is guided to Simon's [2] tasteful commentary on how temperature influences wine degustation. As discussed below, the papers, together with the corresponding drink suggestions, fall broadly into two categories: Basic and Applied Thermophysiology.

The Basic Thermophysiology section includes a Priority Review by Machado and Saper on genetics and central mechanisms of thermoregulation. This is coupled with Front Matter discussions between Saper and Machado versus Morrison and colleagues on the current state-of-the-art understanding of this topic. It may be there is an analogy between their discussions and beverage suggestions (Table 1). Machado and Saper suggest enjoying the complexities as well as flavory notes of Cachaça that parallels their study of the central thermoregulatory mechanisms in mice. In contrast, Morrison and colleagues recommend an Oregon Pinot Noir that has a different interaction with the palette, supporting thermoregulatory mechanisms in rodents may differ substantively from those in humans and other species. Regardless of your choice of beverage, reading this review and compelling discussions will bring one up to date on the current understanding and remaining enigmas of central mechanisms for thermoregulation.

In addition to this focus on the basics of central thermoregulation, three papers provide detailed information on how humans can all be exposed to the same cold environment with some responding physiologically and perceptually as if they are more cold-exposed than others. Starting with a New England pale ale, Yurkevicius and colleagues in a Comprehensive Review summarize the current understanding of human cold habituation, including the induced general changes in physiology, its timeline, as well as its other modifiers, with attention is given to sources of human inter-individual variability responses to cold. Continuing the theme of integrative thermoregulatory response to cold exposure, Greenfield and colleagues take over the party and give a toast with a Sauvignon Blanc. These authors present a Priority Review of the influences of biological sex and ovarian hormones on physiological responses to body cooling. Continuing this cold exposure theme, Haman and colleagues give a Comprehensive Review on human vulnerability, inter-individual variability in the cold and establishing

**Table 1.** Papers included in the Call and beverage recommendations made by their authors.

Author(s)	Article Title	Category	doi	Beverage Recommendation
Romanovsky	Papers published by the journal <i>Temperature</i> are cited more often than those published by more prestigious journals	Editorial	doi.org/10.1080/23328940.2022.2048549	Gin and (Tree Fever) tonic
Machado and Saper	Genetic identification of preoptic neurons that regulate body temperature in mice	Basic	doi.org/10.1080/23328940.2021.1993734	Cachaça
Morrison, Nakamura and Tupone	Thermoregulation in mice: The road to understanding torpor hypothermia and the shortcomings of a circuit for generating fever	Basic	doi.org/10.1080/23328940.2021.2021059	Estate Winery Oregon Pinot Noir, 2016 or 2019
Saper and Machado	Identifying specific populations of preoptic thermoregulatory neurons: The way forward	Basic	doi.org/10.1080/23328940.2022.2033075	Cachaça
Yurkevicius, Alba, Seeley and Castellani	Human cold habituation: Physiology, timeline, and modifiers	Basic	doi.org/10.1080/23328940.2021.1903145	New England pale ale
Greenfield, Charkoudian and Alba	Influences of ovarian hormones on physiological responses to cold in women	Basic	doi.org/10.1080/23328940.2021.1953688	Sauvignon Blanc
Haman, Souza, Castellani, Dupuis, Fried, Sullivan-Kiwantes, Kingma	Human vulnerability and variability in the cold: Establishing individual risks for cold weather injuries	Basic	doi.org/10.1080/23328940.2022.2044740	Caribou – a legendary Quebec alcoholic drink
Favilla, Horning and Costa	Advances in thermal physiology of diving marine mammals: The dual role of peripheral perfusion	Basic	doi.org/10.1080/23328940.2021.1988817	Chocolate stout
Wright and Sheffield-Moore	Skeletal muscle plasticity and thermogenesis: Insights from sea otters	Basic	doi.org/10.1080/23328940.2021.2004048	Scotch with a bit of smoke, or muscatel Darjeeling black tea during working hours
Ioannou, Foster, Morris, Piil, Havenith, Mekjavic, Kenny, Nybo and Flouris	Occupational heat strain in outdoor workers: A comprehensive review and meta-analysis	Applied	doi.org/10.1080/23328940.2022.2030634	Cyprus Commandaria wine
Ogden, Fallowfield, Child, Davison, Fleming, and Delves	No protective benefits of low dose acute L-glutamine supplementation on small intestinal permeability, epithelial injury and bacterial translocation biomarkers in response to subclinical exertional-heat stress: A randomized cross-over trial	Applied	doi.org/10.1080/23328940.2021.2015227	Protein-rich whey drink
de Korte, Bongers, Catoire, Kingma and Eijvogels	Cooling vests alleviate perceptual heat strain perceived by COVID-19 nurses	Applied	doi.org/10.1080/23328940.2020.1868386	Corona (Cerveza)
Cartwright, Etter, Gnatiuk, Perrotta, Wang and White	Duration limits for exposure for the whole body and extremities with a military extreme cold protection clothing ensemble at an ambient temperature of $-40^{\circ}\text{C}$	Applied	doi.org/10.1080/23328940.2022.2078635	Newfoundland and Labrador “Screech”

individual risk factors for cold weather injuries. This group's drink recommendation of a traditional Quebec "Caribou" might be interpreted to help preserve oneself in the cold.

Switching to comparative studies and getting ready to dive deep into the darkness of a chocolate stout, Favilla and colleagues illustrate in a Comprehensive Review the dual role of peripheral perfusion in the harbor seal and other aquatic mammals. They illustrate how diving seals implement an innate *dive response or dive reflex* with a redistribution of their peripheral perfusion centrally to prolong the possible time for their submersion. This topic is often taught in autonomic/cardiovascular physiology as well as in zoology classes because a reduced version of the reflex exists in humans. Interestingly, the peripheral blood flow control mechanisms during a dive are also important for heat loss in the nose and upper airways when the seal returns to the normobaric pressures at sea level. Also, in the cold maritime environment, Wright and Sheffield-Moore highlight in a Front Matter Discovery paper what we can learn from the sea otter and the importance of skeletal muscle mitochondrial flexibility to maintain body temperature. It is only appropriate that Wright and Sheffield-Moore's drink suggestions that accompany their article are those that warm you from within. Thus, if you are sitting down to read this work with an evening nightcap, their suggestion of Scotch with a bit of smokes, such as that in a Johnny Walker Black Label, should warm you up, as would their second suggestion of a nice cup of muscatel Darjeeling black tea; that is assuming you're still at the office and Scotch isn't an option.

Following these contributions above, on the basic mechanisms central to PPTR, are applied reviews and original contributions that extend the understanding of thermoregulation in extreme environments in clinical settings, in workplaces and during military deployments. Each contribution is central to effective and safe human performance in these settings. During heat exposure, these include topics of monitoring the levels of heat strain in workers/professionals and military service members, reducing heat strain in health care workers in clinical settings and assessing potential methods to improve both hydration and nutrition in troops. Following these contributions relevant to heat exposure is an applied study on technical apparel and personal protective equipment in a simulated extreme cold setting.

Ioannou and colleagues present a Comprehensive Review on occupational heat strain in outdoor workers and show the large reduction in manual labor capacity that is associated with heat exposure. In the European Horizon 2020 HEAT-SHIELD project, they spent an enormous amount of time collecting physiological and labor productivity data, including that from vineyard workers in Cyprus. These workers continue the long tradition of raising ancient Xynisteri and Mavro grape varieties that are sun-dried for production of Commandaria wine in one of the hottest regions in Europe. Commandaria is documented as having existed in Cyprus in 800 BC and has the distinction of being the world's oldest wine that is still in production. To delve deeper into the issues analyzed in their review, they propose readers to enjoy a glass of Commandaria wine, which carries the memories of countless people working in the heat from the beginning of civilization. Ioannou and colleagues stress the importance of complementary measures to protect outdoor workers. Accordingly, in response to subclinical exertional-heat stress, Ogden and colleagues in their Priority Report recommend enjoying a protein-rich whey drink, although they report no protective benefits from low dose acute L-glutamine supplementation on indices of heat strain, including small intestinal permeability, epithelial injury, and bacterial translocation biomarkers.

Continuing the theme of heat stress, de Korte and colleagues present a refreshing original Research Paper on cooling vests for health-care professionals amidst the COVID-19 pandemic. The authors suggest "nursing" a Corona beer while reading their contribution, which should aid in a celebration of the pivotal contributions of these heat-stressed health-care workers during the trying times of the COVID-19 pandemic. The best, however, may be to avoid the heat altogether and to find an extremely cold location since in some respects it may be easier to dress for the cold than for the heat. In a simulated extreme Arctic exposure at an ambient temperature of  $-40^{\circ}\text{C}$ , Cartwright and colleagues give a novel Research Paper on technical apparel for military service members where they highlight the challenge of maintaining temperatures at the extremities when the core remains thermoneutral. For extreme cold, this finding

supports the fact that warming hands and feet is needed, and this might be best obtained with a few shots of Newfoundland and Labrador “Screech” and kissing a codfish from the cold North Atlantic Ocean.


In summary, we are thankful to more than 50 authors and coauthors who shared their wisdom and drink recommendations with us for this Call that is given in these 2 exciting special issues. We are pleased to share these with you as the most up-to-date developments in these basic and applied areas of the physiology and pharmacology of temperature regulation. On the off chance that reading these issues gives one a hangover, one can feel free to blame the authors of these groundbreaking contributions.

## References

- [1] Romanovsky AA. Papers published by the journal *Temperature* are cited more often than those published by more prestigious journals. *Temperature*. 2022;9:1–7. doi:10.1080/23328940.2022.2048549.
- [2] Simons CT. Left out in the cold: Serving wines chilled. *Temperature*. 2019;6:1–3. doi:10.1080/23328940.2018.1563443.

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