"If I could offer you only one tip for the future, sunscreen would be it"

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With global warming being a "hot topic", the lyrics of Baz Luhrmann's song (Everybody's free to wear sunscreen) are pertinent. Climatic change will have a deleterious effect on humans as a consequence of increased prevalence of natural disasters, famine and heat waves. Currently, nearly one third of the World's population is regularly exposed to climatic conditions of elevated surface air temperature and/or humidity that exceed human thermoregulatory capacity, a trend that is set to increase (Mora *et al.*, 2017). Elderly individuals are at greatest risk for mortality and morbidity during heat waves partly due to their reduced vasodilatory and sweating capacity in response to heating. One of the other potential consequences of climatic change is an increased exposure to solar radiation. Stratospheric ozone decreases the amount of ultra-violet radiation (UVR) reaching the Earth and thus depletion of the ozone potentially increases exposure to UVR. Exposure to UVR is also dependant on human behaviour. One of the behavioural thermoregulatory responses to heat is a reduction the amount of clothing worn to enhance evaporative and convective heat loss from the skin. In addition, an increase in leisure time combined with the promotion of regular exercise in green environments to improve physical and mental health may all result in an increased exposure of the skin to UVR.

UVR exposure can cause skin reddening (erythema), cutaneous vasodilatation, immunosuppression, oxidative stress, photo-aging and skin cancer which can be attenuated by the use of sunscreen. Conversely, UVR is important for vitamin D synthesis and exposure to UVA radiation can decrease diastolic blood pressure (Liu *et al.*, 2014). Indeed, the seasonal changes in blood pressure and cardiovascular mortality at latitudes between 40° and 60° correlate with the seasonal variation in UVA exposure (Liu *et al.*, 2014).

In this issue of *Experimental Physiology*, Wolf and colleagues (Wolf *et al.*, 2019) report the time course of skin erythema and increased cutaneous blood flow in response to UVR exposure, and the effect of sunscreen. Erythema occurred before an increase in skin blood flow, but both were prevented by application of sunscreen. This temporal distinction between the two responses, the lack of relationship between them and the presence of vasodilatation to sub-erythema doses of UVR suggests that there are different underlying mechanisms, with the increase in blood flow taking longer to develop, possibly as a result of a more complex pathway involving inducible nitric oxide synthase and cyclooxygenase. In addition, although sweating and salt water (similar in composition to the Dead Sea) on the skin has been found to augment UVR-induced erythema (Moehrle *et al.* 2000); Wolf *et al.* (2019) found simulated sweat prevented the UVR-induced reduction in nitric oxide (NO)-mediated vasodilation. This again points towards a different mechanism of action for the erythema and vasodilatation caused by UVR. However, methodological differences cannot be discounted since hydration of the skin through topical application of simulated sweat and sweat produced physiologically may differ.

Focussing on the vasodilatory effect of UVR, Wolf *et al.* (2019) examined the effect of sub-erythema doses of UVR on endothelial function. The cutaneous heating protocol they employed is well-established, with the initial transient vasodilatory peak being due to a sensory nerve reflex and the sustained plateau being mediated by NO and endothelium-derived hyperpolarising factor. UVR exposure had no effect on the magnitude of this response but did appear to alter the mechanism through which the increase in blood flow was achieved. UVR reduced the contribution of NO to the vasodilatory response to local heating which was prevented by the application of sunscreen or the presence of simulated sweat. In light of their previous findings, the authors suggest that the

reduction in NO-dependant vasodilation is a result of UV-B producing reactive oxygen species (ROS) which reduce 5-methyltetrahydrofolate (5MTHF) bioavailability. 5MTHF plays an important role in NO availability by increasing tetrahydrobiopterin (which is an essential cofactor of endothelial NO synthase), and by acting as a ROS scavenger.

Wolf *et al.* (2019) demonstrated that sunscreen can protect against the damaging effects of UVR in the conditions of their study. How these findings translate to the real world scenario where individuals typically apply sun protection factor (SPF) 15 sunscreen at a thickness of only 0.79 $mg.cm^{-2}$ (thus lowering the effective protection to SPF 3), and only after they have been exposed to UVR (Petersen *et al.*, 2013), requires further investigation. Wolf *et al.* (2019) also reported sunscreen enhanced NO-mediated vasodilation in UVR exposed skin compared to control sites. They speculated that the absorption of UVR by the sunscreen may have reduced ROS production and increased vitamin D synthesis which augments endothelial NO synthase expression. The blood pressure lowering effect of UVA exposure has been attributed to an increase in cutaneous vasodilatation through photolytic release of NO from cutaneous NO stores into the vasculature (Liu *et al.*, 2014). This raises the possibility that controlled UVR exposure with appropriate coverage of sunscreen could be used as a treatment in populations with endothelial dysfunction such as the elderly or hypertensives. Similarly, heat therapy using warm baths or saunas improves vascular health; UVR could represent an alternative "means" to the same "end". Conversely, it also raises the potential increased risk that individuals with compromised endothelial function may experience if exposed to UVR without sunscreen. The health risk is even greater when the UVR exposure is concomitant with heat stress in individuals such as the elderly who have impaired thermoregulatory function.

Wolf *et al*. (2019) present an intriguing paper that raises many questions, for example: does sunscreen hold the key to tipping the effects of UVR exposure from endothelial impairment, erythema and skin cancer to the beneficial production of vitamin D and enhanced NO availability leading to decreased blood pressure? Are these findings applicable to the wider population (with different skin pigmentation) and in more ecologically valid scenarios of UVR exposure of dorsal skin surfaces in the combined presence of sweat and sunscreen? Importantly, does the UVR-induced reduction in NO-dependent dilation further decrease vasodilatory capacity in the elderly where there is already compromised endothelial function, or is there enough redundancy within the control of cutaneous blood flow to cope with the extra demands of global warming? As is so often the case, more research is required.

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