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Letter

In Fairness to Mosquitoes

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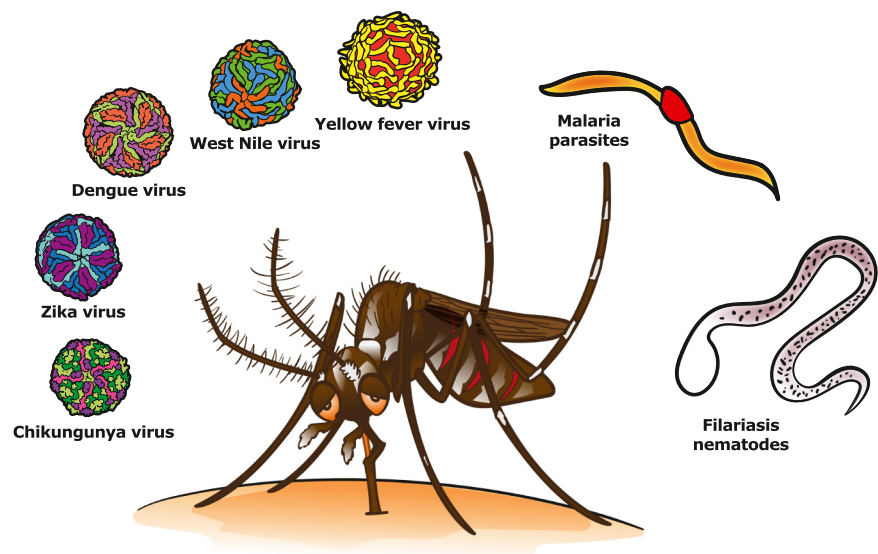
Search 'world's deadliest animals' in Google and you will get thousands of hits that take you to various lists of animals, ranked by how many people they are estimated to kill every year. Sharks, lions, snakes, and humans, among other animals, commonly feature in these rankings. But invariably, it is mosquitoes that make the top of the list as the practically undisputed biggest killers of all [1,2]ⁱ⁻ⁱⁱⁱ. This is perhaps not surprising if one bears in mind the number of deaths caused by mosquito-transmitted diseases. It is also, however, technically wrong.

Mosquitoes are responsible for the transmission of the pathogens that cause multiple diseases in humans, including viruses such as Zika virus, yellow fever virus, chikungunya virus, dengue virus, and West Nile virus, filariasis-causing nematodes, and *Plasmodium* parasites, the causative agents of malaria that is, by far, the deadliest mosquito-borne disease [3]^{iv,v}. Malaria alone is estimated to kill more than 400 000 people every year, mostly children under the age of 5, a number that remains unacceptably high in today's world [4]. Since *Plasmodium* parasites are transmitted from one human host to another via the bites of *Anopheles* mosquitoes, the latter are commonly referred to as the vector of malaria. As it happens, this is technically not correct, as the fact that the sexual phase of the *Plasmodium* life cycle occurs in the mosquito makes this insect the parasite's definitive or primary host, and humans its vector [5]. But one way or the other, the fact remains that mosquitoes are indeed responsible for the transmission of this and other devastating diseases (Figure 1).

Unquestionable as this may be, it is equally undisputable that it is not the mosquitoes *per se* that kill people. Animals typically kill humans when they feel threatened, to protect their young, or to meet their feeding necessities. In other words, animals kill to survive, and human deaths occur as a direct result of those animals' intent to attack and, often, kill. Female mosquitoes need to feed on the blood of humans and other mammals in order to be fertile. When such a mosquito happens to be carrying a human-infective pathogen, transmission of the latter to humans can occur as a by-product of that blood meal, but it is certainly not its main purpose. We are all too familiar with the symptoms that may ensue following the bite of a mosquito. They include pain, itching, and discomfort, caused by an allergic reaction to substances present in the mosquito's saliva, but no deaths have been reported as a result of anaphylactic shock caused by a mosquito bite [6]. Mosquito bites are a real nuisance, as we all know, but their direct impact on human health is hardly

equivalent to being devoured by a hungry lion or stamped upon by an elephant, trying to protect its newborn, who may deliberately kill to satisfy their nutritional needs or to eliminate what is perceived as a threat.

While it is tempting to designate mosquitoes as the biggest killers on Earth, this does not appear to be absolutely accurate. To ascribe the deaths caused by malaria and other mosquito-borne diseases to mosquitoes would be equivalent to allocating to humans the deaths caused by tuberculosis, AIDS, coronavirus disease 2019 (COVID-19), and other infectious diseases that are directly transmitted from one human to another. Humans already do feature on all the lists of the 'world's deadliest animals' on account of their heinous actions, including homicides and wars. If we were to add to that number the deaths caused by human-to-human transmission of deadly pathogens there would be one undisputed leader in any list of killers, and that would be us.



Trends in Parasitology

Figure 1. The Microorganisms, Responsible for Several Infectious Diseases, That May Be Transmitted to Humans during a Blood Meal by a Female Mosquito. *Aedes* mosquitoes can transmit Zika, yellow fever, chikungunya, and dengue viruses; *Culex* mosquitoes can transmit the West Nile virus; *Anopheles* mosquitoes can transmit *Plasmodium* parasites that cause malaria. *Aedes*, *Culex*, and *Anopheles* mosquitoes can transmit nematodes that cause filariasis. Image by Simone Capasso.

Mosquitoes do play an important role in many ecosystems, as crucial pollinators for many plants and food for a range of species [7]. However, they also constitute a threat to a large percentage of the world's population, and it has been convincingly argued that the benefits of their extinction would vastly outweigh the ecological scars they would leave behind [8]. The burden of the diseases caused by mosquito-borne pathogens undoubtedly justifies all efforts to understand the complex biology and ecology of mosquitoes [1] as well as to constantly improve and implement mosquito-control programs [9]. It certainly warrants the firm warning made by Bill Gates – one of the people who has done the most for the fight against malaria and other neglected tropical diseases [10] – about the danger that these small creatures represent^{vi}. Nevertheless, from a strictly technical point of view, mosquitoes cannot be accused of murder any more than any person unwillingly and unwittingly transmitting *Mycobacterium tuberculosis*, HIV, or severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to another could be subjected to a similar accusation. Thus, while placing mosquitoes at the top of the 'most-wanted' list may seem understandable in view of the suffering they indirectly cause, one can hardly fail to question whether their reputation as the world's deadliest animals is entirely fair.

Resources

ⁱwww.sciencealert.com/what-are-the-worlds-15-deadliest-animals

ⁱⁱhttps://en.wikipedia.org/wiki/List_of_deadliest_animals_to_humans

ⁱⁱⁱwww.cnet.com/pictures/the-24-deadliest-animals-on-earth-ranked/24/

^{iv}www.cdc.gov/niosh/topics/outdoor/mosquito-borne/default.html

^vwww.who.int/neglected_diseases/vector_ecology/mosquito-borne-diseases/en/

^{vi}www.gatesnotes.com/health/most-lethal-animal-mosquito-week

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<https://doi.org/10.1016/j.pt.2020.08.003>

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Forum

Yes, Irradiated Sterile Male Mosquitoes Can Be Sexually Competitive!

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Adequate sexual competitiveness of sterile males is a prerequisite for genetic control methods, including the sterile insect technique. During the past decade several semi-field and open-field trials demonstrated that irradiated male mosquitoes can be competitive.

Although the biological quality or competitiveness (Box 1) of released sterile male

insects is essential to ensure success in genetic insect pest-control programmes, in most cases this is rarely assessed [1]. Entomological effectiveness in all male release programmes – including irradiated, *Wolbachia*-infected, and transgenic males – that use colonized insects can only be proven by calculating the competitiveness of the released males. Here, we argue that a reduction in quality of the produced sterile male insects is mostly related to the mass-rearing, handling, marking, and release processes, rather than radiation per se. As an example, in the sterile insect technique (SIT) programmes against tsetse flies, it was demonstrated that chilling and transport of sterile male pupae were the main factors impacting their quality [2].

The competitiveness C of a sterile male is the odds of a wild female being mated with a sterile male compared with a wild male when exposed to both in equal numbers. A C value of 1 indicates that sterile and wild males are equally competitive. A C value of 0.5 indicates that females are two times more likely to be mated with wild males. The SIT is a genetic control tactic used for the management of selective insect pests and relies on the release of mass-produced male insects that are sterilized by ionizing radiation. The mating of a wild female insect with a sterile male will result in no offspring. Insemination of the oocyte with sperm that contains numerous dominant lethal mutations will cause embryonic arrest and death. In the case of SIT, an appropriate irradiation dose must be selected that ensures adequate sterility without impairing C .

Insights from Semi-field Trials

Eleven studies with four mosquito species (*Aedes aegypti*, *Ae. albopictus*, *Anopheles arabiensis*, and *An. coluzzii*) were analysed, and in most cases the irradiation treatment was given during the pupal stage (see Table S1 in the supplemental information