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Drain the Swamps
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The Mosquito: A Human History of Our Deadliest Predator
by Timothy Winegard.
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It starts with bone-shivering chills, which give way to a high fever. The attacks last between six and twelve hours, and end in profuse sweating. When the chills and fever subside, they leave behind an enveloping fatigue. But the relief may not last long. The symptoms can cycle back again, sometimes returning like clockwork every day, and sometimes every second or third day. If you're unfortunate, there are also headaches and muscle aches; vomiting and diarrhoea; weight loss; jaundice and, eventually, pallor; enlargement of the spleen and liver; and that all-consuming lethargy. In many cases, these cyclical attacks, having eventually faded away, will reappear months or even many years later. And if you are very unlucky, the original episodes will be followed by bleeding from the nose and gums, convulsions, impaired vision, a variety of neurological disturbances, coma. In attacks of the less serious sort, you may wish you were dead; in the worst cases, you will be.

What is afflicting you and what is its cause? In early modern England, you would have understood yourself to be suffering from an ague – an acute (or sharp) fever. Agues were part of popular consciousness; you didn't have to be a doctor to know about them. They appeared in certain environments, at certain times, and had certain symptomatic patterns and outcomes. Shakespeare and his audiences were familiar with agues. Julius Caesar greets one of the plotters with the assurance that he was 'ne're so much your enemy/As that ague which hath made you lean', and Caliban, shaking and shivering, is thought to be 'some monster of the isle with four legs, who hath got, as I take it, an ague'. From antiquity until the 19th century, particular attention was paid to the species of ague. Quotidian agues (or fevers) recurred every day, tertian agues every second day, and quartans every third or fourth day. Agues had their seasons: late summer and early autumn were the worst, death coming in with the harvest; spring agues, while unpleasant, were less fearful. The order in which symptoms appeared was also common knowledge: the Restoration poet Samuel Butler compared love to 'an ague that's reversed,/Whose hot fit takes the patient first'. Fever infected early modern culture as much as it afflicted the early modern body. It was dreaded as a portal to death the way we now fear cancer or heart attacks. An 18th-century Dutch doctor judged that 'no person can live without a fever, and few have died without it.'

According to traditional medical knowledge, 'intermittent' agues had several types of cause. First, the appearance of different agues in different sorts of people pointed to the role of temperament (or humoral constitution): melancholics were afflicted by certain types of ague, phlegmatics by others. Second, the seasonality of agues was customarily taken as evidence that the environment was involved, that there must be a putrefaction or corruption in the atmosphere. Their tendency to cluster in certain sorts of environment – especially fens and marshy places – seemed to support the theory that disease was caused by the vapours or 'miasmas' arising from stagnant and foul-smelling waters. In *The Tempest,* again, Caliban curses his master: 'All the infections that the sun sucks up/From bogs, fens, flats, on Prosper fall and make him/By inch-meal a disease!' 'Marsh fever' came to designate a species of the recurrent chill-fever-sweat genus. Third, your way of life laid you open to specific sorts of ailment. There was speculation about dietary causes or dispositions. Robert Burton's early 17th-century *Anatomy of Melancholy*, for instance, reckoned that a quartan ague might be brought on by eating too much pork.

The category of intermittent fevers remained current in the 19th century, but one much discussed, much feared type came to be seen as discrete. If you were suffering from recurrent cycles of shivers, fever, sweats and lethargy, you would now know that you had 'malaria'. The word entered English usage in the middle of the 18th century: in 1740 Horace Walpole wrote from Rome of 'a horrid thing called malaria that comes to Rome every summer'. In Italian, *malaria* meant 'bad air', so that its original English usage designated either unwholesome atmospheric conditions – characteristic, for example, of those notorious Roman summers – or the fevers supposed to be caused by foul air. The 17th and 18th-century category of intermittent fever may have included several different conditions known to modern medicine, including typhus and influenza. But when, by the early 19th century, the new designation caught on, English doctors recognised the malaria of Italy as a member of the class of intermittent fevers that was kin to – and perhaps the same as – the agues known to afflict the inhabitants of the Fenlands and the coastal and estuarine marshes of Kent and Essex.

There were all sorts of creeping, crawling, flying and buzzing insects in marshes and swamps, but it was the airs and waters of malarial places that drew attention when people came to think about the causes of disease. 'Mosquito' was, like malaria, a loan word, coming into English from Spanish (the diminutive for *mosca*, 'fly') in the late 16th century. English natural histories largely assimilated this newly named annoyance to an existing insect category: an early 17th-century bestiary noted that what in English we call a 'gnat' or 'midge' was 'in Spanish Moxquite & mosquito, whence our seamen call it a Muschite'. Explorers and colonists reported from the New World and the East that they were 'pestered with Musketoes, flyes and other vermine'. By 1800, the association of such irksome insects with standing water was widely observed: 'In the less populous and cultivated regions of America, where the climate is warm, and the waters occasionally stagnate,' one Scottish naturalist wrote, 'mosquitoes are the instruments of incessant annoyance to every thing that breathes.' The mosquito was sometimes lumped together with the fire ant in the category of insects considered to be venomous or vexing: 'The mosquito prevails in overwhelming proportions upon the sea coast, and in the vicinity of lagoons, low woods and swamps,' the English surgeon William Lempriere said in his *Popular Lectures* of 1830, 'and prove an unfailing source of discomfiture, pain and disfigurement.' They bit and they bothered, but they didn't factor in thinking about the causes of agues and fevers or any other human disease.

It wasn't until the end of the 19th century that the modern story about malaria emerged. 'You can have mosquitoes without malaria,' the English-born American physician Albert King wrote in 1882, 'but you cannot have malaria without mosquitoes.' Malaria was one of the first documented 'zoonotic' diseases, transmitted to human beings from animals. Mosquitoes were eventually recognised as a vector in a variety of human diseases: yellow fever, dengue, Zika, West Nile fever, filariasis (or elephantiasis), chikungunya and several sorts of encephalitis. All of these take a toll, but malaria is, and has long been, the great scourge.

Work in the last decades of the 19th century by Italian zoologists and British physicians in the Indian Medical Service established that species in the *Anopheles* genus of mosquito were the vector for malaria. Only the females bite, and their bite transmits a protozoan parasite called *Plasmodium*. (Mosquito-borne yellow fever, dengue and Zika are caused by viruses.) Human volunteers placed in a malarial environment, but protected from mosquitoes, did not develop the disease, while unprotected subjects almost all did. Later malariologists worked out the intricate details of the *Plasmodium* life-cycle as it passes from mosquito to human and back to mosquito. A spore-like form of the parasite lurks in the mosquito's salivary glands and is injected through the bite into the victim's bloodstream. It then migrates to the liver, where it undergoes further developmental transformations. Many times multiplied, the transformed parasite is released into the bloodstream, where it invades red blood cells and reproduces. It's the blood-stage parasite, and the inflammatory protein it releases, that is responsible for the clinical symptoms of malaria; the cyclical symptomatic stages correspond to the synchronised bursting of the victim's infected blood cells. When another *Anopheles* bites an infected person, the parasite is passed on to the mosquito, and the process is repeated.

Different species of *Plasmodium* have different careers in the human host, which account for the observed variation in lethality and the stages of recurrence. The most deadly species is *Plasmodium falciparum*, implicated in the Roman malaria of the past and in the great majority of present-day malaria deaths. The other *Plasmodium* species that infect humans – *P. vivax, P. ovale* and *P. malariae* – were probably responsible for many of the intermittent fevers described in early modern England, though there is evidence that *falciparum* may also have been present. Developmental forms of *Plasmodium* species other than *falciparum* are especially likely to lie dormant in the liver for a long time after the initial infection and, roused into activity months or years later, prompt a repeat of the chill-fever-sweat cycle.

In 2018, there were 228 million new cases of malaria; more than 400,000 people died, two-thirds of them children under the age of five. In past centuries, malaria was widely distributed: it was present in Italy, England, America and Asia, but also in Scandinavia, sub-Arctic Russia and Scotland as far north as Inverness. Historical epidemiology is a shaky science – there can be no definitive count of the malarial dead of past centuries – but the toll might be in the tens of billions. Today, both the incidence of the disease and the deaths from it are overwhelmingly concentrated in sub-Saharan Africa (more than 90 per cent of cases), with smaller, but significant, presences in India, South-East Asia and Papua New Guinea. Malaria damages when it does not kill: of 11 million infected pregnant women in sub-Saharan Africa, 872,000 delivered low-birth-weight babies, and of 24 million infected children, 1.8 million suffer debilitating anaemia. Malaria is a major obstacle to economic development: the cost to Africa is estimated at more than $12 billion a year; 25 per cent of household income is lost to the disease; and economists reckon that countries where malaria is endemic pay an 'economic growth penalty' of as much as 1.3 per cent a year.

There's a pub quiz question: 'What's the deadliest animal?' Lots of people guess sharks (just four deaths a year), lions (a hundred), or crocodiles (a thousand). The animal that causes the second highest number of human deaths is other humans (475,000), but the answer is the mosquito, at 750,000 deaths, many of them caused by diseases other than malaria. That's the statistic behind Timothy Winegard's *The Mosquito: A Human History of Our Deadliest Predator*. In Winegard's punchy presentation, humankind has long been locked in deadly conflict with the bug – 'We are at war with the mosquito'; 'Our war with the mosquito is the war of our world'; the mosquito is 'the destroyer of worlds' – and the course of global history has been determined by it. 'The biting truth', Winegard claims, is that 'the mosquito, as our deadliest predator, drove the events of human history to create our present reality.' There are better books on malaria – notably, Sonia Shah's *The Fever* from 2010 – but Winegard's peppy style, and some aggressive marketing, have made his a bestseller.

Winegard is a Canadian-American military historian: the notion of mosquitoes as an enemy army comes naturally. So too do the passages of history he selects to illustrate the role of mosquito-borne disease in shaping world history. 'General Anopheles,' he writes, 'razed armies and decided the outcome of countless course-altering wars.' The Persian Wars were decided by malaria; malaria put an end to Alexander's eastern conquests and to Alexander himself; Hannibal's advance on Rome was halted by the malarial Pontine Marshes south-east of the city; the Romans' attempt to subdue Caledonia was thwarted by a malarial assault which killed half the legions; the outcome of the Crusades was settled by malaria. British troops dispatched to the Caribbean in the 1790s to seize Haiti were eventually sent packing by malaria and yellow fever, and General Henry Clinton's 'southern strategy' in the War of American Independence met with disaster: two-thirds of the British forces in the Carolinas were laid low by the 'fevers and agues' – malaria and yellow fever in particular – transmitted by mosquitoes.

In the Second World War, there were 725,000 cases of mosquito-borne disease among American troops; General MacArthur assumed that for every operational division he had there was a second in hospital with malaria and one more recuperating from its effects. The mosquito doesn't take sides: sometimes it's on the side of defenders and sometimes it's with the attackers, especially when they have some adaptation to malaria and the defenders have none. And sometimes, even when all participants are afflicted, one side has better ways of coping. Christianity won against paganism, Winegard suggests, because it offered comfort to the 'quaking malarial masses' of the Roman Empire: 'The bane of malaria would have reinforced the shortfalls of traditional Roman spirituality, medicine and mythology. Amulets, abracadabra and offerings to [the god] Febris failed in the face of this newfound hope offered by therapeutic Christian rituals and philanthropic nursing practices.'

In the 20th century, the mosquito was weaponised. Armed with modern scientific knowledge, governments mobilised the mosquito in service of state policy and military tactics. Drawing on the expertise of Italian malariologists, Mussolini powered up an array of public works projects, with the goal of eliminating the malaria of the Pontine Marshes. The wetlands in which *Anopheles* swarmed were pumped out and the fertile agricultural land settled with a view to breeding a fascist super-race fit for a new Roman Empire. It was a project managed on military lines – 'the battle of the swamps' – and it was successful, practically ridding the marshes of malaria.

The subsequent destruction of the Pontine hydraulic works was also an act of war. On the advice of German malariologists, the Wehrmacht, retreating from southern Italy in the winter of 1943-44, flooded the Pontine Marshes with seawater to bring back mosquitoes – and malaria – as an obstacle to the Allied forces who were landing at Anzio, south of Rome, as well as to punish the Italians, who had just switched sides. The outcome of the Battle of Anzio wasn't much affected by the Nazis' act of biological warfare – both sides suffered – but it had a marked effect on Italian civilians: in 1939, there were 614 cases of malaria in the area; in 1944, there were 54,929.

There have always been defences against the mosquito and against the symptoms of mosquito-borne disease. One sort of human defence is physiological and evolutionary. The *Aedes aegypti* mosquito, which bears the yellow fever virus, and the *falciparum* parasite both seem to have come to the New World via the slave trade's Middle Passage; the *vivax* form was probably introduced by Europeans. African populations have evolved an adaptation to one of the genes that codes for haemoglobin. When someone inherits this adapted gene from both parents, they will have the seriously life-shortening sickle-cell disease. But if they inherit the gene from only one parent – sickle-cell trait – and survive the genetic handicap, they will have a substantial resistance to *falciparum* malaria. Many African slaves could therefore function with greater efficiency in New World conditions than European indentured servants and Native Americans, who were more seriously afflicted by malaria. New arrivals in affected environments could expect to contract a fever but, if they survived the initial infection by malaria or yellow fever, they would acquire a degree of immunity, or experience less severe symptoms in later infections: they were said to be 'seasoned'. The military used seasoning as a tactic, sometimes leaving forces onboard ship in malarial areas until they had suffered a bout of fever.

Before the mosquito was recognised as a vector of disease, fits of marsh fever were customarily countered by diet and drugs: some physicians advised pottage made with herbs, beets and oranges; others recommended cider or coffee; Robert Boyle (who had himself been afflicted) passed on a recipe involving powdered human kneebone. Some recommended horse riding, and Descartes thought that fevers, like hiccups, might be remedied by a good fright. Opium was very popular both as a cure and to relieve symptoms, especially when taken with wine or brandy. But the appearance in the 17th century of a miracle drug from the New World had a phenomenal and long-lasting effect on malaria treatment. The bark of the *Cinchona* tree – variously known as Peruvian bark, Jesuit's bark or Fever Tree bark – is a specific therapy for malaria: its remarkable effectiveness against certain types of intermittent fever is what makes historians so confident that the condition it was used to treat in previous centuries was, indeed, malaria.

By the 1870s, the bark had become so valuable that huge cinchona plantations were established in British India. The medically active ingredient in the bark – an alkaloid called quinine – had been extracted by French chemists in 1820, but there was no total laboratory synthesis until American chemists completed one in 1944, spurred on by Japanese control of what were then the world's largest cinchona plantations in Indonesia. Despite this, the cinchona tree remains the major economic source of quinine.

The taste of empire was bitter: gin and tonic was formulated in an attempt to make quinine more palatable; and Barolo Chinato of Piedmont, as well as many other Italian *amari* formulated in the 19th century, was marketed not just as a *digestivo* but as anti-malarial medicine. In the 1930s, chloroquine was developed as an improved medication. (Hydroxychloroquine, Trump's 'game-changer' Covid-19 wonder drug, was invented during the Second World War as an alternative with fewer toxic side-effects.) Primaquine came into use a few years later, then the atovaquone-proguanil combination. In the 1970s, artemisinin was isolated from a botanical used in Chinese traditional medicine and became a potent standard treatment for *falciparum* malaria.

The mosquito and its parasite fought back. Quinine and its successor drugs became less effective as the parasite's resistance increased. Resistance to artemisinin has emerged in South-East Asia and there are anxieties that it will develop too in sub-Saharan Africa, where *falciparum* malaria takes its greatest toll. A yellow fever vaccine was created in the 1930s: it is cheap, safe and effective. But the search for a malaria vaccine isn't going well. The current *falciparum* vaccine, developed by GlaxoSmithKline with support from NGOs, international bodies and foundations, requires four injections – which is not ideal in underdeveloped countries. The evidence suggests it provides only 40 per cent protection, and that its efficacy drops over time. Alternative paths to a vaccine are being explored, but no one knows how long it will take.

The development of anti-malaria drugs has often taken a back seat to efforts to kill the mosquitoes themselves or limit their access to humans. The copper-arsenic compound Paris Green, used as a larvicide even before the connection between mosquitoes and malaria was established, was taken up in the great Italian anti-malaria campaigns. DDT was originally developed in the 1870s, but its insecticidal properties weren't discovered until 1939, after which it was soon being treated as the magic bullet for killing mosquitoes and putting an end to mosquito-borne disease. Vast amounts were produced by the American military during the Second World War: it was sprayed on standing water to kill mosquito larvae, and on the inside and outside of houses; clouds of the stuff was sprayed on people.

DDT worked very well, and there was a period after the war when international bodies thought that by killing mosquitoes they might be able to eliminate malaria. In 1962, when Rachel Carson's *Silent Spring* put DDT in the worst odour, organic compounds called pyrethroids – generally harmless to people – started to be used as an indoor insecticide and as a coating for mosquito nets. Again, the mosquito fought back, becoming resistant first to DDT and then, from the 1990s, to pyrethroids. While public-private partnerships search for new insecticides, India continues to use tons of DDT, and other countries have started using it again since the emergence of resistance to pyrethroids.

In the face of these disappointments, new genetic technologies are increasingly regarded as the best hope for a final solution to the mosquito problem. CRISPR-Cas9 gene-editing technology is recruited in 'gene drives' that aim to push changes in mosquitoes' DNA through entire populations. You could, in principle, introduce a gene making mosquitoes resistant to the parasite; or you could make all offspring male, and drive the *Anopheles* to extinction. Of course, there are regulatory issues involved in deciding to exterminate a species, and some uneasiness has been caused by the interest taken in gene-drive technologies by Darpa, the Pentagon's research and development arm.

The incidence of malaria was, however, being reduced long before the mosquito was identified as its vector and, for the most part, without any intention to prevent the disease. At one time endemic in the fens and marshes of England, malaria had substantially disappeared there by the late 19th century. Between the late 1940s and the 1970s, many countries where malaria had once been present were declared free of indigenously caused disease – including the United States, the United Kingdom and Italy. Sri Lanka joined the club in 2016; last year so did Algeria and Argentina. Marshes were drained because they offended the nose and because of the desire for more, and more profitable, agricultural land. An increase in the planting of root crops made for an expanded cattle population, which gave mosquitoes something else to bite, and over time farm animals were more effectively separated from human habitation. Houses were better constructed; there were new building materials, window screens, and improved physical barriers between inside and outside. With increasing urbanisation, and the mechanisation of farm work, rural populations declined: there were fewer country people for *Anopheles* mosquitoes to bite – and also, in a virtuous circle, fewer people with malaria to infect mosquitoes. And there was better medical care. Cheaper cinchona meant that protection from malaria was no longer a luxury afforded only to the rich. (Quinine attacks the parasite, so that when mosquitoes do bite, they are less likely to suck in *Plasmodium*. From the mosquito's point of view, human beings are a vector; you can have anopheline mosquitoes without malaria.) There is some anxiety that global warming will bring malaria back to temperate environments, but it may not be justified: much of the decline in malaria in England occurred as the Little Ice Age of the 16th and 17th centuries gave way to warmer temperatures.

Winegard isn't wrong to see the mosquito as an actor in military history, but there's a case for thinking about it in the context of environmental history and political history too. Long ago, human beings shaped the environment by domesticating animals and living among them, by cutting down trees, cultivating the land, making waterways and (unintentionally) making more puddles for mosquitoes to breed in. Malaria was a disease of civilisation. More recently, civilisation took a different turn, towards the drying out and cleaning up of our immediate environment. We drained many of the wet places; we began to sweep away the rubbish that cluttered the ground and the waterways; and we were annoyed by the insects that swarmed in such places and did what we could to swat them, spray them, keep them out of our houses and off our skin. And some well-off parts of human society had access to medicines that made them feel better when agues were upon them, and to substances that seemed to prevent affliction.

These developments – some of them intentional, many unintentional – changed the distribution of malaria and other mosquito-borne diseases. They remain diseases of civilisation, but in a different way. Malaria is now a disease of our political and economic order, a disease of poverty. The wretched of the earth suffer from underdevelopment, which is both a cause of their malarial afflictions and an effect of malaria. And they suffer from political indifference, as the jobs of prevention and cure have increasingly been off-loaded onto charitable foundations: the Rockefeller Foundation in the early part of the 20th century, then the Gates Foundation, which now spends more on global health than the World Health

Organisation. Bill Gates has pointed out repeatedly that more money goes into curing male baldness than into research on the prevention and cure of malaria. Capitalism is 'flawed', he says, and the persistence of malaria is a failure of the marketplace.

Malaria is a disease of indifference and inequality. For the rich world, malaria is a disease that happens elsewhere, and the buzzing mosquito is easily configured as the enemy because it is an irritant – and, unlike *Plasmodium* or inequality, it is visible. Killing mosquitoes, even driving them to extinction, seems an attractive course of action. High-tech solutions are more exciting than low-tech ones: an effective vaccine would be unambiguously wonderful, while the CRISPR gene drives are worrying. State of the art biomedical science appeals to the vanity of the rich world, while long established, effective measures get less respect: economic development, better housing, insecticide-impregnated bed-nets, the supply of effective drugs, clearing the vegetation around houses, filling in potholes, cleaning up the used drinks containers and tyres in which mosquitoes breed, unblocking drains. The political swamp breeds the inequality and poverty on which malaria thrives; the physical swamp breeds its insect vector. Drain the swamps.

Letters

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Steven Shapin writes that 'it wasn't until the end of the 19th century that the modern story about malaria emerged' (*LRB*, 4 June). That may be when it became widely understood that mosquitoes rather than nebulous miasmas were the active agent in many illnesses, but some individuals had made the connection much earlier. In 1853, Louis Daniel Beauperthuy, a French-trained doctor and naturalist working in Cumana, Venezuela, witnessed a severe earthquake and tsunami, followed by outbreaks of cholera and yellow fever. Beauperthuy identified 'a striped-legged mosquito' (now *Aedes aegypti*) as the likeliest vector for his patients' yellow fever. He went on to link *paludisme*, or malaria, to a different species of mosquito. Elephantiasis (filariasis) was common around the local marshes too, but he wasn't certain which biting insect might be responsible.

Beauperthuy's findings were recorded in journals, but never widely publicised. However, his work did have an impact locally. When Cumana was rebuilt after the earthquake, it proved difficult to drain the swamps, both the physical and the political kind. Beauperthuy instead recommended the widespread use of mosquito nets.

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