Books & arts

LEWIS KHAN

Catherine Green (left) and Sarah Gilbert developed a COVID-19 vaccine.

The COVID vaccine makers tell all

Behind the scenes as the Oxford–AstraZeneca team and others race to vaccinate the world. **By Heidi Ledford**

Last August, biologist Catherine Green was camping with her daughter in Wales when a chance conversation at the pizza van turned to a familiar topic: COVID-19. "We don't know what they put in these vaccines," a fellow camper told her. "I don't trust them. They don't tell us the truth."

Green was uniquely placed to know. She runs a clinical biomanufacturing facility at the University of Oxford, UK, and is part of a team that had developed a COVID-19 vaccine that was in clinical trials at the time. Pharmaceutical company AstraZeneca of Cambridge, UK, aims to produce three billion doses of this vaccine for distribution around the world by the end of 2021, significantly protecting people from severe disease and death. Yet, nearly a year after Green's encounter, conspiracy theories continue to stymie take-up of COVID-19 vaccines, risking lives both in regions where doses are abundant, and in those where there are precious few. In April, the non-profit Kaiser Family Foundation, based in San Francisco, California, found that 54% of US adults either believe common misinformation about COVID-19 vaccines or think that it might be true (see go.nature.com/3fyfaoi).

It was with the epidemic of misinformation in mind, Green says, that she and Oxford vaccinologist Sarah Gilbert decided to write *Vaxxers*, a behind-the-scenes story that attempts to humanize vaccine-making in the hope of boosting trust. The book, along with *The Vaccine* — a documentary commissioned by the BBC and CNN Films — offers a welcome glimpse inside the race to develop COVID-19 vaccines in the middle of a raging pandemic.

Vaxxers: The Inside Story of the Oxford AstraZeneca Vaccine and the Race Against the Virus
Sarah Gilbert & Catherine Green
Hodder & Stoughton (2021)

The Vaccine
Directors: Catherine Gale & Caleb Hellerman
Wingspan (2021)

The book and documentary are a useful pairing. The film follows five research groups as they forgo sleep and family time to develop vaccines using approaches ranging from tried-and-true inactivated viruses to cutting-edge messenger RNA techniques. The book is a deep dive with one team as it juggles funding stress, press interviews and domestic responsibilities. All the groups painstakingly balance the need to be careful and methodical with the pressure to create and test a vaccine faster than ever before. They carry the hopes of the world — and they know it.

The film's images reveal the toll of relentless stress. At the University of Queensland in Brisbane, Australia, virologist Keith Chappell's eyes grow progressively redder and his clothing more dishevelled. The slump in his shoulders after he learns in December that his protein vaccine must be abandoned is heartbreaking. Wu Guizhen, a biosafety specialist at the Chinese Center for Disease Control and Prevention in Beijing, describes her coping mechanisms: "When it feels like you're too tired to go forward," she says, "my solution is to sleep for a bit while standing."

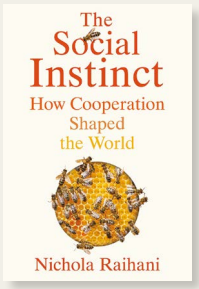
The documentary occasionally slips into a prominent narrative of the time: the idea of a race between the groups to build a vaccine first. Media stories sometimes framed this as a quest for profit, but the real race, Green and Gilbert repeatedly emphasize, was always against the virus and its mounting death toll, not the other groups.

The Oxford–AstraZeneca story begins around 2014, as Gilbert hops between grants and contracts at Oxford, scraping together laboratory funds. They look for ways first to develop an Ebola vaccine and then to prepare for a future epidemic "Disease X". The identity of this illness was uncertain, but its eventual arrival was never in doubt.

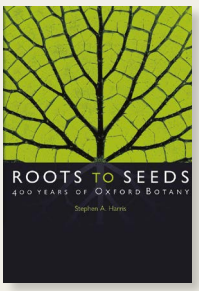
Soon after news of SARS-CoV-2 arrives in early January 2020, Gilbert and Green decide that COVID-19 could be Disease X. They risk their reputations and a substantial amount of Oxford's money to prepare a vaccine, even before the need becomes clear. Although I have reported on many aspects of COVID-19 vaccine development over the past year, I was surprised to learn the extent to which they had to gamble in those early days, without knowing if funding would come through — and that the vials of vaccine used in the first clinical trials were filled by hand at Oxford's facility.

From April, a collaboration with AstraZeneca boosts their manufacturing capabilities. But it

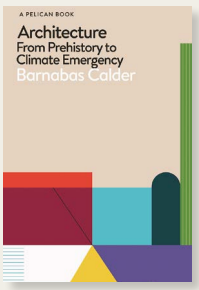
Books in brief



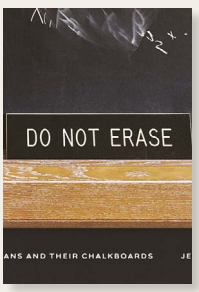
The Social Instinct
Nichola Raihani *Jonathan Cape* (2021)
Cooperation is a double-edged sword. Within totalitarian nations and between democratic ones, it dominated the Second World War. But working together also created a post-war consensus that paved the way for the UK National Health Service and gender equality. If used well, cooperation delivers riches, but "in the wrong hands or used in the wrong ways", it brings ruin, observes psychologist Nichola Raihani. Her rewarding analysis ranges from genetics to politics, and from the individual to the international, including the COVID-19 pandemic.



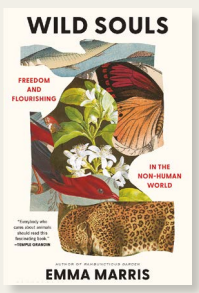
Roots to Seeds
Stephen A. Harris *Bodleian Library Publishing* (2021)
The University of Oxford's botanical garden was founded in 1621 as the Physic Garden, to support medical training. Early plants included the mandrake, with a homunculus-like root thought to emit a lethal shriek if pulled up, notes plant scientist Stephen Harris. His history of the garden, accompanying a Bodleian Library exhibition, displays diverse illustrations and portraits. Authoritative and gorgeous, it is also honest: "Oxford's success at both the generation of botanical knowledge and its dispersal over four centuries has been very patchy."



Architecture
Barnabas Calder *Pelican* (2021)
Constructing and running buildings produces 39% of global human greenhouse-gas emissions, notes historian Barnabas Calder in his powerful, disturbing account of architecture and energy since ancient times. Construction of Egypt's Great Pyramid of Giza used less energy than is consumed over the lifetimes of seven average modern US residents; stone has a strength-to-carbon-footprint ratio 25 times better than concrete's. Calder argues that architecture must end its reliance on fossil fuels by learning from the past, including ancient Rome.



Do Not Erase
Jessica Wynne *Princeton Univ. Press* (2021)
A blackboard filled with mathematics by Albert Einstein takes pride of place in a museum in Oxford, UK. Ironically, Einstein opposed its preservation — unlike 111 mathematicians whose hugely varying chalkboards feature in photographs by Jessica Wynne. The simplest, by Tadashi Tokieda, shows a white circle outlined against black, labelled 'WHITE'; a second circle, filled with white, is labelled 'BLACK'. Tokieda compares watching a board being chalked with listening to music "note by note". This is an original, elegant, if baffling book.



Wild Souls
Emma Marris *Bloomsbury* (2021)
Environment writer Emma Marris begins her colourful study of wild animal–human interactions with a helicopter ride to a sanctuary in Hawaii. There, conservationists are trying to save eight bird species threatened by human influences, including mosquito-borne viruses brought in by ship in 1826. She also considers Australian bilbies, Peruvian monkeys and wolves reintroduced to Oregon. "Ecosystems are built on death", she muses, so which 'wild' animals should be preserved, and which allowed to die? **Andrew Robinson**

comes with a dash of culture clash between the small, nimble academic lab and the corporate behemoth. This collaboration, as well as one with the Serum Institute of India in Pune, and an early insistence on minimizing the price and making the vaccine available to the world, have helped to ensure that Gilbert and Green's early gambles have global impact.

There are details about some of the more frustrating moments in the Oxford–AstraZeneca vaccine's development. This includes an explanation of why some clinical-trial participants received different amounts of vaccine, and waited for different lengths of time between doses. Both of these incidents complicated interpretation of study results.

Other key moments get less attention. There is no reference to South Africa's February decision not to use its doses of the Oxford–AstraZeneca vaccine, because the jab failed to prevent infections with the Beta variant of SARS-CoV-2 sweeping the region. And safety concerns over an extremely rare but potentially deadly blood-clotting disorder that might be associated with the vaccine are mentioned only briefly. Yet the resulting fears and roll-out pauses threw a huge spanner in the works.

Hidden heroes

Still, the book highlights the under-sung research behind vaccines, and the need to promote it. The authors repeatedly emphasize how development was accelerated not by skipping safety steps, but by taking financial risks, such as running various testing stages concurrently. Developers must usually ensure that one step is successful before moving to the next.

Throughout, food metaphors make the people and science relatable. The first viral cultures are like a sourdough starter; the conventional process of getting a lab result, then applying for funding for the next step, is like having to make a separate run to the shops for each ingredient in a roast dinner. The biggest mystery, ultimately, is how the authors found time to write the book in the middle of it all.

Although the chronology of events and science sometimes get jumbled — readers are given a detailed explanation of the chewy "replication-deficient recombinant simian adenoviral-vectored vaccine" well before they are introduced to the basics of how vaccines work — Green and Gilbert lay everything out clearly, from molecular biology to clinical-trial design. There is even a handy appendix listing the ingredients of the vaccine and what each does.

It would be wonderful if that were enough to quell the sort of concerns Green heard at the campsite. Sadly, it is hard to imagine that even her down-to-earth charm can compete with the flood of anti-vaccine propaganda that fills social-media feeds. Even so, it is worth a try.

Heidi Ledford is a senior reporter for *Nature* in London.