D. LEFRANC/GAMMA-RAPHO/GETTY

Despite threats such as the 2001 US anthrax attacks, vaccine innovation has slowed in the past 40 years.

PUBLIC HEALTH

Biodefence built on teamwork

The golden era of US vaccine research holds beneficial lessons for today, finds **John Grabenstein**.

Biomedical researchers who are familiar with the US National Institutes of Health as a funding body and agenda-setter might be surprised by *Long Shot*. Science historian Kendall Hoyt shows that there was once a different way to drive medical progress. In the 1940s and 1950s, focused expertise and goal-oriented collaboration between the military, academia and industry yielded key vaccine innovations that bolstered national security, yet had benefits for civilians. That era of medical discovery stands in marked contrast to today's patent constraints, regulatory hurdles and disjointed efforts.

The book is timely, with the United States and other countries continuing to search for pharmacological defences against unforeseen biological threats such as the 2001 US anthrax attacks, which killed 5 people and infected 17. The current US biodefence effort has been expensive — less so when compared with the cost of certain military aircraft — yet it has not focused adequately on developing products that are usable. Recalling a time when introducing vaccines seemed easier could provide salutary lessons for today.

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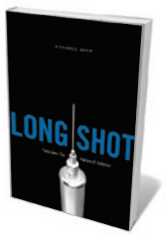
Hoyt begins her deft treatment by describing the threats from pathogens and how she measures vaccine innovation, then reviews vaccine research during and after the Second World War. She also discusses recent factors that have disrupted vaccine-producing government–industrial networks and led to contemporary frustrations.

In the 1940s, vital research aiming to create practical products for protecting soldiers and nations overwhelmed theoretical studies. Most developments were not a response to enemy bioweapons, but rather to viral and bacterial pathogens in countries where troops were based, or to diseases linked to crowding or poor hygiene. For example, influenza A and B vaccine was developed in response to the 1918–19 pandemic that killed tens of millions of people; pneumococcal polysaccharide vaccine came about because of the crowded conditions in barracks that often led to pneumonia; and typhus and tetanus vaccines were produced to combat two common diseases faced by troops throughout history.

As Hoyt shows, the urgent need to find vaccine solutions drove highly effective collaborations between various military, academic and industrial research bodies. But that urgency led to stumbles too. When production of yellow-fever vaccine was scaled up to enable vaccination of US Army troops in the 1940s, the vaccine was stabilized with human serum that was unknowingly contaminated with hepatitis B virus, leading to almost 50,000 hospital cases. Formulation changes later allowed the vaccine to be used to prevent yellow fever across broad swathes of the globe.

The book's narrative is enriched by a description of how the US Office of Scientific Research and Development, the Office of the US Army Surgeon General and the War Research Service conducted vaccine-research planning and operations during the war. With peace in 1945, wartime scientific relationships continued to bear fruit, such as vaccines against adenovirus and meningococcal infections. She lauds collaborations throughout the 1960s between the Walter Reed Army Institute of Research in Silver Spring, Maryland, and vaccine firm Merck, Sharp and Dohme in West Point, Pennsylvania. She describes them as science integrators that brought together experts from disciplines including medicine, immunology and virology, all focused on common goals. Much of their success, she says, is due to that focus and to teamwork that avoided over-specialization.

To measure vaccine innovation between 1900 and 1999, Hoyt reconstructs historical records of annual US vaccine introductions. This was a challenge: responsibility for vaccine registration (or licensing) was transferred from bureau to bureau. Between the establishment of the US Hygienic Laboratory in 1902 to that of the Center for Biologics Evaluation and Research in 1987, there were seven institutional transitions, and multiple variations in record-keeping.



Long Shot: Vaccines for National Defense
KENDALL HOYT
Harvard University Press: 2012. 320 pp. $29.95, £22.95

According to Hoyt, vaccine innovation activity peaked in the 1940s at 50 innovative licences per decade, remained at

35–40 licences per decade through the 1960s, and declined steadily to 12 per decade in the 1990s. The numbers reflect all vaccines developed for endemic and exotic pathogens. She convincingly contests similar analyses.

Today's biological revolution cuts both ways, offering great advances in medicine while providing new means of attack for terrorist groups. It is thus short-sighted that US biodefence funding is largely overseen by congressional committees that are oriented towards health rather than national security.

If the 1940–69 model was a worthy paradigm, why did we migrate away from it? Hoyt attributes the change to several factors. Government contracting and licensing became mired in bureaucracy, and concerns over intellectual property curtailed collaborations. Oversight of vaccine development across a number of bodies became inadequate. The political constituency for biodefence issues weakened and funding for products suffered. Arguably, the lack of US government prioritization of vaccines was the most damaging factor. The result is that now, the time it takes to develop a vaccine is increasing. A better balance of basic and applied research could restore a product-oriented focus.

Government-sponsored research of bioweapon countermeasures has generated knowledge and publications, but faltered in delivering practical results. Biodefences cannot be put in place solely by accepting or dismissing research hypotheses; they require safe and effective pharmaceutical products. We need the biological equivalent of the defences that now protect Hawaii's Pearl Harbor.

So what should society and governments do next? At this point, the book's contributions fade. Hoyt dismisses most vaccine stockpiles as unresponsive to today's threats, yet doesn't indicate any need for quick-acting antibody formulations or therapeutics. Instead, she advocates an emphasis on multipurpose technologies and 'platforms', many of which are hypothetical. How can we measure success using a platform approach? How quickly could platforms be transformed into defences against bioweapons?

Perhaps Hoyt's idea is the right interim solution for today's nadir in national will. Perhaps later, if and when it returns, the well-coordinated, product-centric development of vaccines can resume. History offers us lessons in how to do so. ■

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FICTION

Cosmic creation

Pedro Ferreira explores Alan Lightman's latest novel — a magical-reality take on the origins of the Universe.

When a physics heavyweight is mentioned in the same breath as Salman Rushdie and Italo Calvino, it is tough for a reviewer. Few venture into air that rarefied and make it out alive. But when the book is *Mr g*, a creation myth by physicist Alan Lightman, it is worth the risk.

In *Mr g*, Lightman has taken the core of what we know about the origins of the Universe from physics, chemistry and biology and wrapped a few characters around it. The protagonist is the narrator: god, dubbed Mr g. Mr g lives in a timeless Void with his Aunt Penelope and Uncle Deva, playing out skits that could have been lifted from a Woody Allen film — but with the humour on mute. One day, Mr g wakes up from a nap, decides to create a Universe called "Aalam-104729", and from then on marvels at his creation as it evolves and becomes more complex — from the beginning of space and time, to the emergence of fundamental laws, particles, forces, stars, galaxies, planets and, ultimately, life itself.

Mr g: A Novel About the Creation
ALAN LIGHTMAN
Pantheon/Corsair: 2012. 224 pp. $24.95/£9.99

As sentient beings finally emerge out of the cosmic mess, Mr g is torn: should he intervene or let them go their own way? Throughout, he is taunted by the creepy Belhor, a devilish character (a fine role for Al Pacino if this were ever made into a film) and Belhor's annoying daemons, the Baphomet siblings. Belhor pushes Mr g to allow his creations to do their own thing, and watches with glee as evil and unhappiness begin to emerge — leaving Mr g to observe as, for instance,