The hostility to science percolated upwards. Texas and Louisiana threatened to close state borders, and California governor Henry Gage — mindful of his state's annual $25-million fruit harvest and concerned other states would suspect a problem — disparaged "the plague fake" in a letter to US secretary of state John Hay and issued threats to anyone publishing on it. Yet reports reached Washington DC and an independent scientific enquiry was commissioned. Its confirmatory report weeks later did not halt the skulduggery. Gage called the investigation unfair, and organized a state-wide news blackout; Wyman colluded in trying to suppress the report. Yet the news was leaked in early 1901, and both city and state then pledged funding to eradicate the disease and treat patients. Kinyoun, however, was denied vindication. He was dispatched to Michigan and ultimately replaced by the scientifically trained Rupert Blue.

Blue established an office and lab in Chinatown, and worked with Chinese organizations. But infected people were still being hidden by their families, and disputes persisted between state and city health authorities and the federal MHS. Dismayed, Blue requested a transfer, believing that only a widespread epidemic would ever shake San Francisco from its torpor. That happened in 1903.

Immediately recalled, and with new authority and support, Blue set about disinfecting the city. Starting with Chinatown, earthen basements were concreted, concrete ones flooded with carbolic acid, walls washed with lye, streets asphalted, cesspools filled and decrepit dwellings demolished. Infection discovered elsewhere in the city led Blue to ponder modes of transmission. Suspecting flea-infested rats, he initiated a ferocious eradication campaign. In 1905, convinced the city was safe, Blue again left.

He was recalled twice more. San Francisco's magnitude-7.9 earthquake in 1906 destroyed some 80% of the city's infrastructure and left more than 250,000 people homeless, with rats massing over devastated land and open sewers. Blue controlled small outbreaks and left; 16 months later, the disease was back. Returning to the devastated city, Blue — commandeering offices dubbed the Rattery — sent an army of rat catchers into the city, and had hundreds of rodents autopsied daily for signs of plague. To quell complacency, he threatened to quarantine the entire city and prevent the prestigious US Navy battle fleet from docking.

"City officials went to extraordinary lengths to avoid admitting the plague's presence."

San Francisco was finally declared plague-free in November 1908; four years later, Blue became US surgeon-general.

As Blue noted, the disease had crossed into the wild squirrel population. Today, an average of seven people a year, most of them hikers, are infected in the United States and are treated with antibiotics.

Randall's account is pacy and gripping. And his examination of the conflicts, prejudices and priorities involved make for sober reading in a world where Ebola clinics are being torched and anti-vaccination movements threaten a resurgence in diseases such as measles. As most public-health authorities agree, the question we need to ask about the next pandemic is not 'What if?' but 'When?' ■


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Rupert Blue led much of the campaign to eradicate plague in San Francisco.

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BIOTECHNOLOGY

Blood money: Theranos on screen

The company's rise and fall features in a new documentary. **Heidi Ledford** sums up.

It is hard to imagine a Silicon Valley story more riveting than the tale of Theranos, the US$9-billion company founded by a 19-year-old wunderkind who promised to revolutionize medical testing and instead was charged with fraud last year. There is fear and betrayal, money and deception, and perhaps a few lessons about the extension of the technology hype cycle to medicine.

The latest take on this drama — *The Inventor: Out for Blood in Silicon Valley* — is a documentary directed by Alex Gibney. Released in March, it enters a crowded field of analyses centred on the Theranos phenomenon and its founder, Elizabeth Holmes. In January, US television network ABC News and the programme *Nightline* released a compelling six-episode podcast documentary called *The Dropout*, then quickly followed with a video documentary of the same name. Last year, *Wall Street Journal* investigative reporter John Carreyrou, a key player in Theranos's downfall (he broke the story in 2015), published his definitive book, *Bad Blood*. Plans are afoot for a film starring Jennifer Lawrence as Holmes.

The Inventor: Out for Blood in Silicon Valley
Director: Alex Gibney
HBO (2019)

Each treatment so far is a gripping account of how Holmes dropped out of Stanford University in California, and persuaded the glitterati of Silicon Valley and Washington DC to pour money into her vision: technology that could perform hundreds of tests on drops of blood taken from a finger prick. ▶

Holmes pledged that the method would liberate people from the tyranny of venous blood draws, which she likened to medieval torture (*The Inventor* plays on that imagery with unsettling slow-motion close-ups of needles piercing veins).

At its peak in 2013, Theranos had 'testing centres' in more than 40 pharmacies, many of them in Arizona and California. But reporting by Carreyrou revealed that the company could use its machines to perform only a handful of the more than 200 tests on offer, and even then the results were unreliable. The rest of the tests were carried out on standard devices, sometimes used in unproven ways. Worried physicians told Carreyrou of patients with unusual, sometimes alarming, results from Theranos that did not hold up when samples were sent to conventional testing providers.

UNSEEN FOOTAGE

For those versed in the story, *The Inventor* holds few surprises. But a visual medium does offer a few fresh gems. There is priceless, excruciating, footage of Holmes dancing on stage to MC Hammer's 1990 song 'U Can't Touch This'. There is Theranos president Ramesh 'Sunny' Balwani, a tech-industry veteran who favoured Gucci shoes and fast cars but had no experience in medical technology, stepping awkwardly into a bouncy castle at a company party.

As a journalist, I was particularly moved by the documentary's focus on reporter Roger Parloff, author of a glowing 2014 cover story about Theranos for *Fortune* magazine. His face and voice radiate pain, befuddlement and anger — much of the latter directed at himself — at how he was duped into writing an article that boosted the company's profile and probably extended its reach.

The visuals also drive home how young the key whistle-blowers in the case were. Tyler Shultz — grandson of former US secretary of state (and Theranos board member) George Shultz — was 25 when he became one of Carreyrou's key sources in 2015. Erika Cheung was fresh from her undergraduate degree at the University of California, Berkeley. Both worked in Theranos's laboratories and were appalled by their disarray, the alarming results emanating from them, and the potential harm to unsuspecting people using the 'tests'. An e-mail from Cheung prompted the Centers for Medicare and Medicaid Services to inspect a Theranos laboratory in Newark, California, in November 2015. "The deficient practices of the laboratory pose immediate jeopardy to patient health and safety," the inspectors concluded.

"Fear of missing out can lead investors to pile cash into a hot new technology without looking at the mechanics."

In sharp contrast to these two, many of Theranos's backers were veterans of government and venture capitalism who had invested in the company without learning the details of its financials or technology. These investors ranged from assorted billionaires to Henry Kissinger and James Mattis, former US secretaries of state and of defence, respectively.

The fact that these figures succumbed to Holmes's story intrigues me most. Much ink and air time has been spent exploring the young enigma who rarely blinked, and who leveraged family connections and sheer chutzpah to raise hundreds of millions of dollars for technology that did not exist. How did she do it? Why did she do it? Did she even realize what she was doing? *The Dropout*, for example, delves into Holmes's family history and includes interviews with her high-school physics teacher and a childhood friend who talks about Holmes's performance on the running team. Her polo necks, her hair, her unusually deep voice: all have been endlessly discussed.

Often, the conclusion seems to be that charisma was the key to her persuasive ability. Cheung admits to falling for it when she first joined Theranos. Phyllis Gardner, a Stanford pharmacologist with extensive industry experience, did not. Early on, Gardner cautioned Holmes that her technological approach would not work. In *The Inventor*, Gardner notes, with emphasis, that Holmes "aligned herself with very powerful older men who seemed to succumb to a certain charm".

But I wonder whether that is all it takes. *The Inventor* sacrifices precious running time to put Theranos's appeal in context. It highlights several clichés of Silicon Valley culture, where 'fake it till you make it' is all too familiar, and FOMO (fear of missing out) can lead investors to pile cash into a hot new technology without looking into the mechanics.

Theranos took that ethos to a terrifying and unusual extreme. In March 2018, the US Securities and Exchange Commission charged Holmes and Balwani with "massive fraud". Investigators said that the two had raised more than $700 million from investors using false or exaggerated statements. Theranos closed its doors later that year. Holmes settled that case, but has pleaded not guilty to charges of wire fraud brought against her and Balwani by the US Attorney's office in San Francisco, California. That trial is still pending.

Meanwhile, tech fever continues unabated. With some technologies, developers can ship out a hasty, bug-ridden version 1.0 to customers while still working on fixes that can be deployed later. But to take the same approach with health testing risks real harm. As medical technology heats up, will investors make the same mistake again? ■

HBO

Theranos founder Elizabeth Holmes.

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