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Some of the first US children to receive the eagerly awaited Salk polio vaccine in 1955 were in San Diego, California.

Transformations in medical care were never easy or safe

How innovation in drugs and surgery can take a toll on patients and public confidence. By Hannah Wunsch

uthor Paul Offit sits on the US Food and Drug Administration's COVID-19 vaccine advisory panel. An international expert on vaccine development, he co-invented the rotavirus vaccine. He has written many books, some prophetic - such as his 2010 treatise Deadly Choices: How the Anti-Vaccine Movement Threatens Us All – and is an attending physician in the Division of Infectious Diseases at the Children's Hospital of Philadelphia in Pennsylvania.

In short, he thinks a lot about the risks and benefits of medical care.

His latest book - You Bet Your Life - couldn't be more timely. Using the stories of key patients, he weaves a narrative of incredible transformations in medical care that were



You Bet Your Life: From **Blood Transfusions to** Mass Vaccination, the Long and Risky History of Medical Innovation Paul A. Offit Basic (2021)

not easy or safe linear progressions. Charting some of the "greatest advances", Offit focuses on the long history of mistakes, negligence, paternalism, lack of oversight and the many casualties along the way, including individuals and public confidence.

The book breaks down key developments into three parts, traversing a wide range of medical breakthroughs - from heart transplants and anaesthesia ('Risk') to antibiotics and X-rays ('Oversight') and, finally, chemotherapy and gene therapy ('Serendipity').

The stories are riveting and filled with fascinating details, many from the days before

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ethics review boards. Offit writes of slightly crazed doctors and dentists playing with anaesthetics; surgeons putting hearts into people with little ability to stop the organs being rejected; and potentially life-saving treatments gone wrong.

A poignant example is the story of folic acid antagonists in chemotherapy. Paediatric pathologist Sidney Farber (founder of the Dana-Farber Cancer Institute in Boston, Massachusetts) read about work in mice published in 1945 that demonstrated a miraculous reduction in cancer through the use of "folic acid". The words were carefully kept in quotation marks in the early research publications because no one was sure what the extracts being used really contained.

In Farber's rush to help 11 paediatric patients who were terminally ill with acute lymphocytic leukaemia, he treated them with a purified form of folic acid that he thought would be safer. This was before the bench scientists discovered that the extract they had used to treat mice was, in fact, not pure folic acid, but an antagonist that blocks its effects. Farber had inadvertently hastened the deaths of all 11 children.

In 'Risk', Offit describes the desperation of individuals such as Louis Washkansky. Dying of congestive heart failure, Washkansky's only hope was a new heart. But no human had ever received such a transplant. Out of other options, he chose to go ahead with the surgery by Christiaan Barnard in 1967. Washkansky lived for just 18 days. He was at least aware of the experimental nature of the treatment. Others were not, such as Hannah Greener, a girl who died in the 1840s after being given chloroform, an anaesthetic that was only just coming into use.

It is in the section titled 'Oversight' that Offit feels on surest footing, discussing antibiotics and vaccines. In the context of the COVID-19 pandemic, the story of how other vaccines were developed is compelling. Offit centres his narrative around Anne Gottsdanker. In 1955, aged 4, she received the poliovirus vaccine that Jonas Salk had just developed for a world desperate for reprieve from the devastating disease.

In a heartbreaking description, she remembers "lying in the hospital and not being able to move anything". The Salk polio vaccine required the virus to be killed as part of its production. Through a lack of government oversight and sloppy manufacturing as vaccine production was scaled up, Anne was one of 70,000 people inadvertently given live polio virus. The tragedy, called the Cutter incident after the company that made the faulty doses, left 164 people severely paralysed and 10 dead. (Offit wrote a 2005 book on the episode and on how vaccine safety subsequently improved.)

The final section, 'Serendipity', traces work that has led to chemotherapy and gene therapy. Offit is a master at braiding multiple

threads of a story, describing the fits and starts of research and the unexpected findings that lead to new treatments. He describes the first person whose tumour was successfully treated with a folic acid antagonist in 1946–47: Babe Ruth, the US baseball star. Such a footnote is a reminder that new drugs often go to the well-connected (recall the cocktail of drugs Donald Trump received as US president when hospitalized with COVID-19).

In the pursuit of exuberant storytelling, some points get exaggerated, and a few facts and dates are off. For example, Offit calls heart transplants today "as common as bypass surgery", which is far from the case. The choice to provide a bibliography for each chapter without specific referencing makes it challenging to track down and read more about intriguing asides, such as the statement that couples in an unspecified country were barred from marrying if they had different rhesus blood types.

Offit's most important messages are contained in a short epilogue. Here he reflects on the downstream consequences of unanticipated tragedies that can follow new

discoveries. Harm to a few can result in harm to many, if the erosion of trust means that people opt out of preventions or treatments. For example, in 1956 in the United States alone, polio paralysed 15,000 unvaccinated people because of vaccine hesitancy in the wake of the Cutter incident.

Sadly, medical history is repeating itself. As Offit concludes, people are much more fearful of doing something that has a minuscule chance of causing them harm, such as having a COVID-19 vaccine, than they are of not doing something that is likely to result in harm — such as remaining unprotected from a virus that has killed millions of people in less than two years.

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From gold to Bitcoin and beyond

An economist envisions a mostly cashless future, which could make finance more inclusive. By Paola Subacchi

ooking to understand why citizens have taken to the streets over the adoption of Bitcoin as legal tender in El Salvador? Enter economist Eswar Prasad, with his thoroughly researched book *The Future of Money*. Innovations in payment systems and currencies, he explains, reflect both the significant changes in the world economy as it integrates large developing countries, such as China, and the all-encompassing digital transformation. As money has become free to move around the world, Prasad probes how digital innovation is reshaping it as both a tool and a concept.

Two things epitomize the transformation.



The Future of Money: How the Digital Revolution Is Transforming Currencies and Finance Eswar S. Prasad Belknap (2021) The first concerns money as a physical entity. The digitalization of payments challenges the idea of cash as the most definitive form of money. Cashless transactions, however, entail a loss of privacy because they leave electronic traces. This does not seem to be a problem for the majority of people and businesses that make such transactions legally. And requiring digital payments for transactions above a certain amount would help to shrink the offledger economy. In Italy, for instance, where this shadow economy amounts to about 15% of gross domestic product, payments of €2,000 (US\$2,350) or more can no longer be settled in cash.

The governance of data collected through digital transactions remains an open question, one that cannot be dismissed as the product of libertarian paranoia over "harmful or misguided government intrusions", as one commentator puts it. Safeguarding individual liberties and privacy is a legitimate issue in an open, democratic society in which concerns about the use of personal data are addressed in a transparent and accountable way.