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Introduction

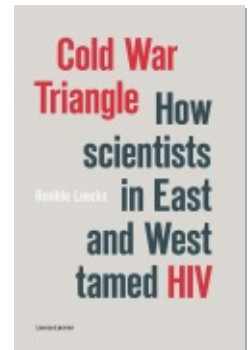
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Introduction

Excellence is rarely found, more rarely valued.

— Johann Wolfgang von Goethe

“Cold War Triangle” is about the human face of science, how scientists from three different cultures collaborated to create the complex drugs that saved millions of lives. Who were the mentors that influenced them and their careers? How did they intersect with one another? What traits in their unique backgrounds and disparate journeys led them toward the making of key discoveries in modern medicine? This book recounts an inspiring story of the groundbreaking cooperation between East and West during the darkest days of the Cold War. How did scientists behind the Iron Curtain overcome authoritarian rule, cross hostile borders and ultimately collaborate with colleagues in the West? Who would have thought then that their cooperative spirit would culminate in a vital weapon to inhibit HIV and thwart an epidemic?

Preventing the onslaught of infectious disease has been an innate human concern since the dawn of time. The discovery of antibiotics to combat bacteria laid the groundwork for a new medical field, virology, which focused on the tiniest of microbes. The development of vaccines to prevent debilitating diseases and save lives brought relief to mankind. The search for antiviral drugs was initially considered extraneous. Unaware of a looming epidemic, some scientists were already starting to put the tools in place to combat a retrovirus.

HIV is a slow-moving retrovirus but contrary to all other viruses-causing infectious disease, it has proven to be one of the deadliest forms that humanity has ever encountered. If not treated, this virus kills almost all without fail. When HIV came into the limelight in the 1980s, people became painfully aware that there were hardly any antiviral drugs in existence. None of them could inhibit HIV. Even the entire arsenal of antibiotics, one of the biggest triumphs of medicine, proved useless against viruses.

AZT, the first drug to treat AIDS, became available in 1987. However, it gave only a short reprieve as it proved too toxic for long-term treatment. Death continued to lurk at the doorstep of those infected with HIV. When science could not produce a real life-saving treatment, disillusion turned into anger. The streets exploded with demonstrations by gay protesters, besieging large pharmaceutical companies. As the AIDS epidemic expanded and more lives were lost, the media and public demanded to know why modern science could not find an effective treatment.

It took almost ten more years until a new generation of drugs hit the market. Patients struggled to keep pace with their therapy; the mix of medications involved taking more than twenty pills at six different times of the day and still had plenty of side effects. It kept people alive but in a miserable way.³

A triangular partnership, formed during the Cold War between Belgian, Czech and American scientific teams, led the way to the most effective treatment in the world today that features a one-a-day pill with few side effects. The protagonists—Erik De Clercq, a Belgian scientist from the University of Leuven, and his Czech colleague, Antonín Holý, from the Academy of Sciences in Prague—first met in West Germany in 1976. Their work yielded splendid discoveries that were licensed to an American company before the fall of the Berlin Wall. Holý and De Clercq had single-handedly created a whole class of molecules out of which *Tenofovir* emerged. The conviction of one man, John Martin, was the driving force behind his team at Gilead Sciences to develop this compound. Tenofovir has since evolved into several drugs that allow HIV-infected people to lead a normal life. One of them, Truvada, has also been approved for the prevention of HIV, which could put an end to the epidemic if enough people could take it. The Gilead drugs became the gold standard for HIV treatment in the West. John Martin played a pivotal role in bringing these twenty-first century drugs to Africa and the rest of the developing world.

A brief excursion into the history of virology and vaccines

The power of a microbe is a baffling phenomenon. It can unseat empires and shape history. The end of the Roman Empire was connected to a steep demographic decline caused by smallpox epidemics, which

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had been spread throughout the Mediterranean by Roman soldiers. The bacteria causing Black Death (*Yersinia pestis*), which originated in China, was carried on the backs of Mongolian hordes to a major Genoese trading port on the Black Sea. The bacteria travelled on black rats in cargo destined for Europe.⁴ The Black Death that swept the continent in the fourteenth century unseated the dominance of Christianity and sparked the Renaissance.

In 1492, Christopher Columbus's ships introduced a host of new microbes to the New World, which unleashed diseases onto the Native American population. A combination of smallpox and measles caused a devastating drop in population. After those diseases weakened the Aztec capital in 1519, it allowed for a small Spanish army to build alliances and conquer the empire. Twenty years later, an epidemic, most probably smallpox, similarly aided the Spanish troops when they invaded the Inca Empire.

People believed these diseases were caused by the rare conjunction of planets, miasmatic vapours or the wrath of the gods. They did not realize that tiny microbes were in fact the culprits.

Microbiology emerged in the 19th century, when French wine and beer chemist, Louis Pasteur, disproved the spontaneous generation of living things. By using filters to exclude dust particles, he could prevent mould from growing in boiled broth. Pasteur was the one who alerted the world to the deadly power of microbes. He knew that some of these germs could be useful in wine and beer making but he had also observed how physicians knew less about antiseptic methods than vintners or brewers did. He accused medical doctors of causing the death of women during childbirth as they transmitted and infected them with microbes from other patients.⁵

His rival in Berlin, Robert Koch, established strict criteria, now known as the Koch postulates, for linking a microbe to a disease. In the 1870s, any infectious invader, bacterial or otherwise, was considered a virus, derived from the Latin word for poison. Only the larger microbes like bacteria could be seen under microscopes.⁶ The tiniest among the microbes, the viruses, remained invisible and their existence could only be surmised.

Louis Pasteur became famous for treating the deadly rabies virus after noticing there was an infectious substance so small it could pass through his filters but could not be seen under a microscope.⁷ He devised a

vaccine by growing microbes in living animals and using them as a weapon against their own kind. His injections saved a boy bitten by a rabid dog. They won the race against the slow-moving but deadly virus before it had completed its incubation time. He singlehandedly put an end to the savage killings of humans from packs of rabid dogs that used to roam the French countryside.

This was not mankind's first vaccine. Throughout medical history there was an intuitive knowledge that survivors of some infections like smallpox became immune to the disease. Calculated exposure to infectious disease in order to stimulate immunity was known in many parts of the world.⁸

Vaccines were first discovered in the late eighteenth century after country doctors in rural England noticed that dairymaids with small lesions had become infected by the harmless cowpox and yet were fully protected against smallpox. One of these doctors, Edward Jenner, tried to use that cowpox, much weaker than the virulent smallpox virus, for inoculations in humans, and discovered he could protect people from the dangerous disease. He proved that a foreign substance similar to but not as dangerous as the one that causes disease could trick the body into believing it was under attack and stimulate it into making antibodies. The *vaccinia virus*, the Latin name for cowpox virus, became the operative word in "vaccination."⁹

It took almost eighty-five years from Jenner's time until Pasteur developed mankind's second vaccine. Pasteur realized that the body's memory of its encounters with microbes was key to its defense. It led to the building of antibodies and resistance to prevent re-infection by the same microbe. At the turn of the century, Paul Ehrlich studied this phenomenon more closely and called it "immunity." During the first half of the twentieth century, scientists added five more vaccines to save mankind from crippling and deadly diseases. The vaccines against diphtheria, tetanus, and whooping cough were cultured out of bacteria mixed with chemicals.¹⁰

Knowledge about viruses remained in the dark for a long time. Even once the electron microscope was invented in the 1930s, viruses were often disregarded as chemical elements, not living organisms. It was not until the late 1940s that the modern concept of a virus emerged. Viruses resemble seeds; they can only spring to life when they find the right soil. They must find a cell to infect in order to survive. Only when they have