entered their host’s cell can their genetic material be reproduced with new viruses ready to infect more cells.\textsuperscript{11}

The true revolution that boosted the growth of virology came in the late 1940s with the development of cell culture techniques by the American scientist John Enders. Animal or human cells could now be grown in laboratory flasks and would indicate, through a change in the appearance of the cells, the presence of a harmful virus. Before that time, researchers had to resort to live animals or chopped up animal organs in order to detect and identify viruses. Not surprisingly, only eight viruses dangerous to man had been found in the first half of the twentieth century and nobody was able to coax them to reproduce inside a test tube.\textsuperscript{12} With the new techniques, a torrent of human disease-causing viruses could be isolated and the science of virology progressed exponentially.\textsuperscript{13}
Chapter I
Leuven: a hotbed for antiviral research

*A true fundamental researcher is an introvert who takes pleasure in looking for answers to questions that nobody asked.*

— Piet De Somer

**The cross-fertilization between academia and pharma**

In the early years of World War II, the small university town of Leuven was suffering badly from the Nazi occupation. The Germans had again ransacked its world-famous library, which had been devastated during the First World War. In a drafty old building, a young researcher named Piet De Somer and his boss were studying the behavior of a strain of penicillium they had smuggled from the Netherlands.¹ They were fascinated by reports that it could produce a new infection-fighting drug.

British war broadcasts and Swiss medical journals had revealed that American companies were producing a miracle drug based on a discovery by the Pathology School of Oxford University.² Unlike their British counterparts, the Americans had sensed the strategic importance of this discovery and alerted the Roosevelt Administration. In 1941, the production of penicillin became part of an urgent government-industry venture with the sole purpose of making the drug available to the troops so that soldiers would not perish from infectious diseases.

Producing penicillin seemed simple enough; it required cultivating an omnipresent penicillin mold similar to the one that had accidentally contaminated Alexander Fleming’s bacterial culture.³ The British discovery as such was not patented. The technical protocol on how to mass-produce and extract the penicillin from the culture fluid, however, was guardedly protected by the American pharmaceutical industry. Secrecy surrounded
Cold War Triangle

the penicillin production even after the war was over. Hospitals and doctors in the rest of the world literally begged the Americans to obtain a few ounces of penicillin. Producing this drug on Belgian soil would become a matter of national pride.4

Piet De Somer’s boss and two fellow professors at the Catholic University were eager to take up the challenge. They were partners in a small company, Soprolac, an offshoot of a cheese company that doubled up as a pharmaceutical business. The byproduct of the cheese-making was used to produce Panferma, a medicinal water to treat all kinds of aches and pains. After Soprolac was purchased by a young Belgian industrialist active in the paper industry, the academic co-owners suddenly became partners in a much larger enterprise named rIT (Recherches et Industries Thérapeutiques).5 Piet De Somer was entrusted with their goal to produce penicillin. But he had one problem. His knowledge of chemistry was modest and purifying the product after he had cultured the mold was a complicated process.

That is when his legendary charm came to the rescue. He befriended a fellow medical student, Christian de Duve, who was working on a Master’s degree in chemistry and needed a topic for his thesis. At that time, there were shortages in the lab, so they took discarded milk bottles from the former Soprolac plant to culture molds.6 De Somer and de Duve shuttled daily between Leuven and Genval to monitor their cultures. Communication and travelling were still very restrained in those days, but their trips were quite flamboyant. De Somer drove an Amilcar 1928, a racecar which had neither roof nor battery and needed a roller bearing crankshaft to jumpstart the car. Wherever they went, they were greeted with roaring laughter.7 De Duve succeeded with the purification and thus the first milligrams of penicillin were produced on Belgian soil. He eventually moved on to other research projects and later won the Nobel Prize in 1974, but he always kept fond memories of those wild times.

The rIT co-owners realized that in order to produce larger yields of penicillin a “deep fermentation” method would be needed instead of the artisanal “surface culturing.” The American companies were not sharing information. However, the professors found a way to circumvent them. They had excellent contacts with the Director of Connaught Medical Research Laboratories in Toronto who had just started his own production
of penicillin. In 1946, they dispatched Piet De Somer to Toronto where he was introduced to in-depth culture production of penicillin. He returned to Belgium a few months later and set up a small fermentation plant for rIT. Together with his co-workers, he spent the next few years working intensively on improving the mass-scale production of penicillin. Not encumbered by any license, it became a huge financial success and gave De Somer the incentive to look for other antibiotics.

Penicillin proved very effective against some bacterial infections such as those that caused blood poisoning. But it was useless against other bacteria that caused such mortal illnesses as tuberculosis, cholera, or urinary and intestinal infections. Tuberculosis, a scourge known throughout history as the White Plague, had been contained in recent years mainly thanks to better sanitation but it remained a major public health issue due to its contagious nature.

While stories about another miracle drug, streptomycin, coming from Selman Waksman’s lab at Rutgers University spread like wildfire, research with streptomyces molds in the antiquated Leuven laboratory had been less than successful. rIT, however, was eager to acquire streptomycin to fight tuberculosis and a host of other bacteria. It was left to Piet De Somer to negotiate with Waksman and purchase a production license. He also acquired the license for the production of aureomycin. This helped to transform the small rIT facility into a well-oiled manufacturing plant that reaped huge financial successes.

The time had come to create a modern research facility in Leuven. An agreement was reached whereby the university would provide the land and Piet De Somer’s industrial partner would erect the research building. The company’s research laboratories would become part of a new Institute. Its structure, bridging sections from two rival university faculties, medicine and pharmacy, required uncommon skills. De Somer, Head of the Institute and at the same time Director of the university department of microbiology, possessed the charm and wiles of a Florentine prince.

The Director of the university hospital was given the privilege to name the institute. The choice was Rega after Hendrik Joseph Rega, a renowned scholar of the 1700s and author of several medicinal treatises in Latin. The name Rega was an auspicious omen for close cooperation.
between academia and industry, which was an entirely new phenomenon in Europe in 1954. It would also marry medicinal chemistry with microbiology, a new virology branch that was an extravagant novelty for the University of Leuven at the time.17

When the new Institute opened its doors, virology would become the heart of its work. Piet De Somer sent his assistants to other virology laboratories in Europe where they studied the equipment and copied protocols necessary to tackle this new science in Leuven.18 He closely followed all these exciting developments, especially the cell culture techniques and sensed the imminent explosion in vaccine research. He wanted his group to become the first and the best in the field.19

**Vaccines and celebrity scientists**

In the Fifties, commotion over paralytic polio engulfed the United States. Despite health statistics in the years after World War II concluding that children were three times more likely to die of cancer and ten times more likely to be killed in car accidents than by polio infections, polio kicked up a media storm and gained special status as a public scourge that required urgent treatment. This was due in large part to the efforts of the National Foundation for Infantile Paralysis, which employed the latest techniques in advertising, fund raising, and motivational research to transform a relatively uncommon disease into the most feared affliction of its time.

The media hype spread to Belgium and other countries across Europe.20 Polio was not the deadliest of viruses, but it was an insidious one. Less than one in a hundred of those infected showed symptoms of paralysis.21 It was precisely those infected who did not show any symptoms that caused the virus to spread. Those who were struck by paralysis were handicapped for life.

In the United States, panic often escalated into mass hysteria. Every time a polio wave emerged, usually during the summer months, swimming pools and movie theaters would close, beaches and streets were deserted and spraying of DDT or other insecticides was used on a massive scale to sanitize cities, and sometimes even the interiors of houses.22 Nobody knew then that the disease was actually an outgrowth of improved sanitation and that those who lived in cleaner, more comfortable
homes were at greater risk. Much later it became clear that young children who lived in crowded and unsanitary conditions, such as households without indoor plumbing or toilets, had developed resistance by exposure to the poliovirus at a young age when they still benefited from their mother’s antibodies. The virus had already been isolated in 1908, but it took almost half a century before a preventive remedy was introduced, a vaccine based on the killed virus.

The inventor and savior, Jonas Salk, was born and raised in New York City. He had discovered that there were three different polio strains and that antibodies against one did not offer protection against infection from another. Salk grew the viruses in cell cultures following the new discoveries of John Enders and subsequently killed the viruses without destroying their immunizing power. His killed-virus vaccine could trick the immune system into believing that the body was under attack and needed to react with an increase in protective antibodies. On 12 April 1955, Jonas Salk’s polio vaccine had formally been declared safe, effective and potent. He was hailed a hero. To many in the US, April 12 resembled another V-Day, the end of a war. People huddled around radios to hear the news, some wept openly with relief, outside one could hear car horns honking and church bells chiming in celebration. President Eisenhower declared Salk a benefactor of mankind and honored him with a Rose Garden ceremony.

Piet De Somer met Jonas Salk during a conference in Stockholm and began corresponding extensively with the celebrity scientist to discuss better ways to deactivate and filter the virus. He convinced the Board of Directors of the rit company to start development of the polio vaccine. Production was to be launched in the Rega Institute in 1955, the year that De Somer was appointed as a full-fledged Professor in the medical faculty. A whole colony of monkeys was promptly housed on the top floor of one of the Rega buildings, as monkey kidney cells were needed to culture the poliovirus.

In those days, as recounted by one of De Somer’s assistants, culture media had to be “homemade.” Growth-promoting serum had to be obtained through the centrifugation of blood collected from horses or calves in local slaughterhouses. Personnel were still inexperienced and not yet accustomed to antiseptic techniques. It was a constant struggle to
combat impurities in cultured cells. Moreover, the process involved the complicated acquisition of the three types of virulent polio strains. The new Institute overcame all these hurdles.

The polio strains purchased from the Institut Pasteur arrived in Leuven in November 1955. A few months later, the vaccines were ready. They were first administered in the Rega Institute, starting, as dictated by tradition, with Piet De Somer and his children. Unhindered by rules and regulations, the vaccine was distributed in some schools later that year. Soon, the polio vaccine operation was moved to the RIT company facility in Genval-Rixensart for large-scale production. To aid the testing of RIT production, one of De Somer’s newly hired assistants was sent to Pittsburgh to work in Salk’s lab as a visiting scientist. The Dutch and German governments were among the first international buyers of RIT vaccines. The Swedes, Danes and French had all been involved in vaccine production several years before the first cell cultures were established in Leuven. However, in less than 24 months, Rega and RIT had caught up with their competition in Europe.

In 1958, at the height of the media frenzy around polio, the first post-war World Fair was held in Brussels. For Piet De Somer, it was a unique opportunity to showcase Belgium as one of the first countries outside the US that could produce its own polio vaccines. De Somer’s reputation as a scientist-entrepreneur achieved iconic status.

Meanwhile Salk’s rivals were working on an innovative live virus vaccine. Instead of killing a virulent virus, they used a living virus that is non-virulent to begin with and weakened it in animal cells. Piet De Somer kept a close eye on his competitors and especially on Albert Sabin, who was conducting the largest trials in medical history for his vaccine in the Soviet Union.

His assistant met with Albert Sabin during a conference in Tokyo in September 1961 and a few months later, the live attenuated virus vaccine was manufactured by RIT in Belgium. The speed with which the Rega Institute and RIT went into production astonished everyone. Only a few months after Albert Sabin’s oral vaccine replaced Salk’s injectable vaccine in the USA in 1962, it was introduced in Belgium. By 1967, Belgium would become one of the first polio-free countries.