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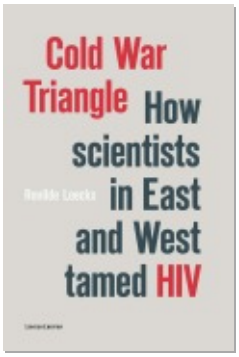
III. Strange bedfellows: a Czech chemist and a Flemish virologist



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[148.135.83.86] Project MUSE (2025-02-16 13:15 GMT)

some barn.[287] The following year, Milan Hašek signed a petition against a dogmatic article propagating the Lysenkoist doctrine in a leading Czech newspaper. He did not know he would later have to pay a heavy price. Those were still the happy days before the Soviet Invasion.[298]

One of Šorm's more famous visitors was Carl Djerassi, an American with Bulgarian and Viennese roots who felt perfectly at home in Prague. Djerassi recounts his invitation to give a lecture in the mid-Fifties just after the Budapest uprising. He remembered Šorm as a dutiful communist technocrat with a large Stalin picture hanging behind his desk, "his cunning eyes seemed to follow me whichever way I sat during our conversation."

By the early sixties, after Šorm had become President of the Academy, the picture had disappeared. Carl Djerassi, father of the first oral contraceptive, combined his position as a company Research Director of Syntex with a professorship at Wayne University in Detroit.[29] When Djerassi became the Head of Stanford's chemistry department in 1960, he intensified his contacts with the Academy in Prague and welcomed quite a few postdoctoral fellows from Šorm's stable into his laboratories. Like his friend Djerassi, Šorm became an active Pugwashite and hosted in 1964 a Pugwash conference in the Czech spa town, Karlovy Vary.[30] The town was a playground for the communist elite, but would also become a temporary venue for concerned scientists wanting to bridge the gap between East and West.

František Šorm used this forum to openly argue that a small country needed access to Western technology in order to participate in the scientific-technological revolution. It was a radical change for Czechoslovakia. Until then, it had been the Soviet Union's most loyal ally; but the Czechoslovak economy, that once ranked among the ten most industrialized countries before the war, had become a disaster. The only path to salvation was cooperation with the West. Despite its misgivings, the communist party establishment acquiesced once it realized that the country desperately needed to catch up economically.

Trade and exchanges with the West were also a boon for the Academy since its goal was to combine research with industrial applications. Despite patenting just about every research result, the Institute had only concluded license agreements with companies within the Socialist bloc. Šorm believed that agreements with the West would bring in hard

[148.135.83.86] Project MUSE (2025-02-16 13:15 GMT)

currency and allow the institutes to equip themselves with valuable new devices. In 1965, Czechoslovakia made arguably the most successful transfer of technology from East to West when the Academy sold the license to produce Otto Wichterle's soft lens to an American company.[311] Ironically, the invention made by a "socialist scientist" sparked interest into hydrophilic materials in the West and created a new field of study.

Another "first" was the agreement Šorm and Djerassi signed. The father of the pill had become interested in birth control for insects. Djerassi's pill had been instrumental in unleashing the sexual revolution of the 1960s and now he wanted to control the insect population. His new company Zoecon, with Syntex as its largest shareholder, convinced a whole group of researchers in Prague to work on insect growth regulators.[332] It was the first collaboration agreement between the Institute and an American company. Another scientist who began his career at Syntex, John Martin, became the driving force behind a major agreement that consolidated a critical triangular relationship between IOCB, the Rega Institute and Gilead Sciences, an upstart American biotechnology company two decades later.[343]

Chapter III
Strange bedfellows: a Czech chemist and a Flemish virologist

Poets and prose writers are like amphoras waiting to be filled with wine or water. Scientists do not wait for their amphoras to be filled; they search for faucets producing spurts of liquid. Only the passage of time tells whether ambrosia or vinegar has issued. The search for the faucet is what counts.

— Carl Djerassi

Auspicious omens

Antonín Holý felt lucky. After his graduation from Charles University and military service, he was able to pursue his passion for chemistry, which he had nurtured since his youth. A book on chemistry for children, which he stumbled upon in his parents' attic, had ignited his fascination. His mother, who possessed a phenomenal memory for numbers, and his father, an artisan who made beautiful locks and other tools, stimulated his calling. They built a miniature laboratory for him in a corner of the garden shed. With a burning interest in his father's instruments and machinery, he developed uncanny skills during the 1940s.

Since his father was a craftsman and not associated with capitalist intellectuals, Antonín Holý was never branded as a bourgeois element. In high school he often substituted for his chemistry teacher who regularly abandoned the classroom. The teacher, as a fervent music lover, preferred to attend choir rehearsals instead.

Life in the family village near Prague was simple. His childhood friend, Ludmila, became the love of his life. She would have liked to become a biologist but the communists considered it unproductive and allowed only very few students into this field. She had no choice but to reorient her

[148.135.83.86] Project MUSE (2025-02-16 13:15 GMT)

studies and focus on chemistry for the food industry instead. Antonín and Ludmila married, had two little daughters and formed a close-knit family. They shuttled between their modest home in the village near Prague and a *chalupa*, a country house where they grew vegetables to feed the household when shelves in the shops were depleted and distribution of goods in the communist economy was lacking.

His brilliant studies in organic chemistry at Charles University brought him to the attention of František Šorm, who snapped him up to work on a doctorate in the IOCB.[1] Chemistry was considered apolitical and its students were not as closely supervised as in other faculties. Organic chemistry, the chemistry of substances found in living matter, was so dear to his heart that it was quite a shock and disappointment to be assigned to an oligonucleotide chemistry group. Holý described his feelings in one of his essays, "My life with nucleic acids":

> When I joined the oligonucleotide chemistry group in IOCB I knew nothing about nucleic acids at all. I was not particularly fond of biochemistry lessons during the happy days at the faculty and there was nothing to improve this affinity during the days of my PhD study in synthetic organic chemistry.[2]

Things changed once he was hired as a full time employee and paired with an ingenious laboratory assistant. A statuesque woman, authoritative and gentle at the same time, taught him everything in biochemistry as well as the synthesis of the building blocks of heredity.[3]

His supervisor, Jiri Smrt, had a name with only consonants—*Smrt* literally meaning "death" in Czech. A pun was never far behind especially when he made one of his frequent visits to the lab of Sir Alexander Todd in Cambridge. Jiri's co-workers pronounced it *Tod*, also meaning "death" in German.[4] Holý absorbed every new technique or procedure his supervisor had picked up in Cambridge as if by osmosis.

The IOCB in Prague became in the early sixties one of the three or four renowned places in the world where nucleotide synthesis was cultivated.[5] This attracted many researchers at the Institute. Among them was Marc Van Montagu, a doctoral fellow from the Ghent University in Belgium. He was encouraged to go to Prague by his university's president, who did

not hide his communist sympathies and had befriended many intellectuals and institutions behind the Iron Curtain.

Van Montagu would later become one of the first plant geneticists, a pioneer in engineering transgenic plants resistant to insects. He also happened to be the first foreign scientist Holý had ever met. They quickly became friends. During the three months spent in the IOCB in 1963, Van Montagu regaled him with stories of famous Belgian scientists. His favorite story was about Jean Brachet, considered by many as the father of RNA. He had found a method to show that this kind of nucleic acids is present in all cells whether they belong to plants, animals or human beings.[6] Brachet also indicated exactly where in the cell RNA is localized and pointed out its ability to transform genetic material into proteins.[7] Brachet, as so many academics in his time, defended communism as a reaction to the xenophobic and authoritarian governments that held Europe in its sway before the war.[8]

After the war, Brachet's communist friends forced him to endure their own form of harassment. He was required to write an article in support of Lysenko for the local communist newspaper. When he objected, he was then invited or rather summoned to Moscow to personally meet Lysenko. Brachet was so appalled by his absurd theories and the pressure he was put under to subscribe to them, that he abruptly quit the communist party upon his return to Belgium. Leaving politics aside, Jean Brachet and his work with nucleic acids inspired a whole group of bright scientists. Among them was Marc Van Montagu.[9]

Later, Tony Holý would write that their happy acquaintance was an auspicious omen that foreshadowed what would become his lifelong friendship and scientific partnership with another Belgian, Erik De Clercq. Holý's postdoctoral stay in 1964 in Göttingen, West Germany provided another lucky break that introduced him to the West. By the time he was invited to come to the Max Planck Institute, Czechoslovakia's former number one enemy, West Germany, was becoming its most significant partner in trade and in science cooperation.[10] The growing importance of international scientific exchanges was a troubling paradox for Czechoslovak hardline communist authorities. They disdained the way that West Germany would attract Czechoslovak scientists with money and research possibilities but they also realized that the knowledge

[148.135.83.86] Project MUSE (2025-02-16 13:15 GMT)

gained in these exchanges was invaluable for their country's progress.

Holý was one of the beneficiaries. Aside from Russian and English, he spoke fluent German and thus was regularly invited to visit the Max Planck Institutes in Göttingen, an important site of pilgrimage for nucleic acid chemists in Europe. Holý became close to Fritz Eckstein, one of the brightest chemists in Germany at that time, who ten years later introduced him to his future science partner, Erik De Clercq. Holý's time in Göttingen was a productive phase in his career. His friendships brought him back to Germany almost every year, or whenever the Czechoslovak authorities allowed him to leave the country.

His friends in Göttingen gave him an endearing souvenir to take home: a handful of cactus seeds. The seeds grew into a most unusual cactus collection that he treasured with great care for the rest of his life. His German friends also helped him squirrel away a little money in a foreign savings account. His earnings in four months were about as much as he could earn during four years of work in Czechoslovakia, thus allowing him to buy a breath of freedom that came in the form of a small Italian car.

While Czechs and Slovaks were enjoying the loosening grip of the authorities and "socialism with a human face" was taking shape, Tony and his wife could travel abroad provided they left enough money in a communist-controlled bank account. They travelled with their little car to the Polar Circle in Norway and to the Low countries near the North Sea, the Netherlands and Belgium, where they visited his old friend Van Montagu. In Brussels, they were eager to visit the grounds where the World Fair of 1958 took place, a mythical place for Czechs of their generation. For the first time since the communist coup, the talents and creativity of Czech artists had been showcased in such a masterly way that Czechoslovakia won the prize for the most beautiful pavilion of the World Fair. Czech style and swanky furniture were admired by the whole world. Those were the happy days before August 1968.

A young prodigy's path to science

Did Erik De Clercq ever want to become a scientist? The thought probably never crossed his mind as a child. Erik was born during the first years of World War II and lived on his grandparents' farm until the war was

over. He was raised in Hamme, a village bordering the river Scheldt, in Northern Belgium. Erik's parents owned one of the biggest plots of land in the middle of the village, which they transformed into a garden of wild flowers interlaced with vegetable patches and orchards. As an only child, he was doted on by both parents. His father worked as an employee in a fertilizer plant and regularly took young Erik to visit his lab[11]. They often went on Sundays when nobody was present so he could see "the chambers where sulfuric acid was produced." In Erik's mind, the whole lab belonged to his father; the smell of sulfuric acid and mysterious canisters discovered on those Sunday outings triggered his lifelong passion for chemistry.[12]

His mother had her own tailoring workshop on the ground floor of the house where she trained several assistants in the art of dressmaking. Young Erik loved to entertain them with his encyclopedic knowledge of world geography. They called him their "geography tutor." His mother, the dominant force in the family, decided very early on that her son should become a medical doctor and often prevented him from playing with other children. It was the time of the polio scares and isolation seemed the only way to avoid contagion, but in Erik's case staying indoors meant being locked up in his room to study. He lived in a world of his own, as he did not have many friends. For a while, his main interests were plants and animals. He first admired Carolus Linnaeus, the great Swedish botanist, but then shifted his curiosity to the animal kingdom and to lions in particular.

Academic discipline, inculcated by his mother, led Erik to achieve strong results in school. With his excellent grades in Latin and Greek, his teachers suggested he become a priest. Religion was far from his mind when he graduated from Dendermonde high school with the highest marks as a *primus perpetuus*. Art history, and the renaissance painter Rafael in particular, was much closer to his heart. He had no idea what university studies to pursue since nobody in his family had ever gone to university. One day, a longtime friend who had just started his studies in medicine dropped by their house and complained about the heavy load of chemistry lessons. As soon as he uttered these words, Erik's choice was sealed. He joined the medical faculty at the Catholic University of Leuven and it became his new home. There, he could pursue his passion

in chemistry and at the same time fulfill his mother's dream of becoming a small town physician.

Leuven was a whole new universe, a city filled with students and tradition dating back to the 1400s when the university was founded by papal decree. Erik took to it like a duck to water, thoroughly enjoying his introduction to the microbial world in the university lab. Erik De Clercq, however, was not yet interested in virology; he was preoccupied with lectures on chemistry and assisting his fellow students. He became known as the "chemistry tutor," always eager to guide his fellow students stopping by his door with their questions. There was no textbook to accompany the lessons of their biochemistry professor, so Erik's notes were in high demand. Publishing his notes made him very popular and turned into a lucrative venture for the student in charge of the sales, who later bought a new car with the proceeds.

In the third year of the medical studies, only a handful of students could gain experience in a private laboratory. Professors would ask their brightest students during the oral exams to join their research projects. Erik received such an offer from Piet De Somer, a remarkably talented professor who was to become the president of the university. Inexplicably, Erik refused his offer. Yet in order to work in a prestigious lab, a student had to have solid introductions, which were hard to come by. One had to set in motion a whole network of relatives and friends. A cousin of Erik's father, who was a prominent school inspector, enlisted the help of her colleague to arrange an introduction with a professor from the Brussels University.

He suggested Erik, then 19 years old, join the laboratory of Christian de Duve, who had discovered lysosomes.[13] It implied studying cell fractionation, but this did not appeal to an innate stubborn young man. De Clercq had molecules in mind, not cells. After having snubbed De Somer, he declined to work with Christian de Duve, a future Nobel Prize winner. Instead, Erik ended up in 1962 in the obscure Laboratoire de Chimie Hormonologique.[14] He was not allowed to work with steroid hormones like cortisone and estrogens, which were his favorite, but was assigned catecholamines instead[15]. Alas, his duties consisted of diagnostic testing rather than hormonal protein chemistry. It didn't help that Erik disliked the spectrophotometer[16]. Clearly research in a laboratory seemed to be the wrong track for him. Seeing how he languished for more than two