Past and Present

Albert Szent-Gyorgyi: The Art in Being Wrong

When Dr. Albert Szent G^rgyi goes fishing in the waters around Woods Hole, Massachusetts, he fixes a gargantuan hook to his line, explaining that "it is far more exciting not to catch a big fish than not to catch a small one."

In a career that has spanned most of the twentieth century, this biochemist, now in his eighty-ninth year, still pursues with the passion of Captain Ahab the grandest and often the most elusive of objectives. Those he has already attained are far more than enough to satisfy most people: those that have escaped him have usually proved to be such beguiling chimeras as to inspire whole generations of researchers.

A brash young man at Cambridge University who once tried to disparage "the Prof," as Szent-Gyorgyi is affectionately known, was gently but firmly put down by the renowned parasitologist David Keilin, who told him, "I much prefer the stimulating ideas of Szent-Gyorgyi, even when he is wrong, to the dull correct ones advanced by most others."

Now somewhat grizzled and craggy as a weather-beaten cliff, Szent-Gyorgyi still drives daily the mile or so from his home to the Marine Biological Laboratories—that workshop, proving ground, and nursery of science on the shore where Cape Cod begins. He gave up his motorcycle when he was 85 and waterskis only occasionally now. It is a sport he took up on his eightieth birthday.

Currently, Szent-Gyorgyi is busily seeking an explanation of cancer in the unexplored world of quantum mechanics and submolecular biology. He is hopeful that his study of the failure of malignant cells to reconstitute healthy submolecular structures will one day throw new light on the nature of the disease. That is the work he projects for his tenth decade.

He operates on insight and on the hunches that come to him as he fingers the instruments in his laboratory. For him, science has always been an art involving the interplay of sensory perceptions, passion, intelligence, and wit. He once described his technique this way:

> I *make* the wildest theories, connecting up the test tube reactions with the broadest philosophical ideas, but I spend most of my time in the laboratory, playing with living matter, keeping my eyes open, observing and pursuing the smallest detail — Usually something crops up. some small discrepancy which, if followed "n, may lead to basic discoveries. The theories serve to satisfy the mind, prepare it for 'an accident' and keep one going. I must admit that most of the new observations I made were based on wrong theories. My theories collapsed, but something was left afterward.

It has been 45 years since Albert Szent-Gyorgyi received a Nobel prize for studies of cellular respiration and for isolating the substance

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Albert Szent-Gyorgyi is perhaps best known for his work on the muscle protein complex, actomyosin. His 1937 Nobel prize was for the discovery of titamin C and for his pioneering explorations of mechanisms of cellular respiration.

that became known as ascorbic acid, vitamin C.

His subsequent work, always characterized by his talent at playing creatively with living matter, led him to discover the proteins of muscle contraction and, for the first time, to demonstrate the interaction of actin and myosin in vitro.

It is the same appetite to understand the cell in a^l its workings that has carried him past the familiar landscape of molecular biology into the submolecular, the electronic. Colleagues, even when they are critical, do not scoff at the possibility that he may be right in maintaining that cancer is not many diseases but one and that it can be understood electronically.

He has been as consistent and as indefatigable in politics as in science. He has used his prestige and his pen to oppose tyranny and war. His battles, whether scientific or political, have always been fought with gusto and sometimes with a disarming directness that his critics have mistaken for naivete.

This life of challenge, adventure, and misadventure began in the peaceful setting of a pedigreed Hungarian family whose title of petty nobility dated to the seventeenth century. It was a family of comfortable respectability, generally well represented on the bench and in the ministries of the Austro-Hungarian Monarchy. Here and there, a maverick spiced the lineage, such as an earlier Szent-Gyorgyi who joined the doomed revolution of 1848.

Into this solid family there was born on September 16. 1893. a boy who was given the ponderous name of Albert Szent-Gyorgyi von Nagyrapolt—the last bit a piece of aristocratic baggage that he dropped very early in life.

He tends to dismiss his father. Nicolaus. as a man totally preoccupied with his role as a semifeudal landholder. The family style was set by the lady of the house, Josefine Lenhossek. Albert Szent-Gyorgyi unhesitatingly credits his mother and her side of the family with inculcating him with a love of science. art, and all things intellectual, to the proud neglect of commercial values. Religion was rarely discussed. Mrs. Szent-Gyorgyi was "an enlightened agnostic," her son recalls, "who would go to church only when her boys were in trouble, so that she could bribe St. Peter with a florin to lobby for her."

The Lenhosseks wove science and music into a family tradition. His mother sang, and his maternal grandfather and great grandfather, who had been professors of anatomy and physiology in Vienna, also played at least one instrument. Albert admits that he must have been a dreadful disappointment. He loved music but showed no aptitude in performance. "I do not have the gift," he says sadly. His older brother, Paul, outshown him scientifically and musically in the early grades. "The fact is," this Nobel laureate confesses, "I must have been a very dull child. Nothing happened to me."

With a little help from tutors, he squeaked by in his examinations, but his record depressed Uncle Michael Lenhossek, who had been something of a child prodigy and was then a celebrated histologist. It was to him and not to her husband that Albert's mother turned for advice on the education of boys. Michael viewed Albert's prospects in science as exceedingly dim.

In early adolescence, however, young Albert's habits took an abrupt turn. Suddenly he showed an omnivorous appetite for books of all sorts and seemed to be developing a late-blooming passion for science. Uncle Michael, not entirely convinced by this sudden change, came to consider a possible career in something elementary, like the concoction of cosmetics. As Albert's record improved. Uncle Michael thought he might aspire to dentistry, and as the boy's high school grades positively soared, he suggested a modest career in medicine—perhaps proctology.

In due course, Albert received the avuncular blessing allowing him to apply for entry into the University of Budapest Medical School. In his freshman year, Albert, ever mindful of Uncle Michael's advice, devoted his first scientific paper to the epithelium of the anus.

In time, his uncle encouraged Albert to rise into the lofty precincts of histology, but by his third year of medical school, Albert became disenchanted with that discipline. Uncle Michael or no. "Morphology told me little about life," he recalled. He was considering a change to physiology, when the Austrian Archduke was shot, throwing Europe into war and Albert into uniform.

He served in the medical corps, and 65 years later still recalls with keen satisfaction that "there was never any need for me to kill." He was sent to the Italian front and then north to the Austrian slice of Poland. He was awarded the Silver Medal for Valor but waves away all questions of how he won it. "Nothing special," he says. As the war dragged on, the slaughter seemed doubly futile with the seeming certainty of defeat. He yearned for a wound that would send him home to his studies. When the enemy failed to oblige, he shot himself in the arm and returned to Budapest. There he finished his medical courses and was awarded his doctoral degree.

With the war still on. he resumed national service in the army's bacteriological laboratories. Almost immediately, he tangled with his superiors over risky experiments of dubious value that were being performed on Italian prisoners of war. His protests won him an assignment to a zone of malarial swamps in northern Italy, from which he was saved, in a matter of weeks, by the collapse of the Central Powers. He returned to Budapest and married Cordelia Demeny, the charming daughter of the Postmaster General, an official whom Albert remembers fondly as a man of "good social feelings" rare in a bureaucrat.

Defeat brought to Hungary six months of a fierce Communist crusade under Bela Kun. For part of that time, the newly licensed Dr. Szent-Gyorgyi was working at a pharmacological laboratory in what

was then the Hungarian city of Pozsony. The map makers of Versailles, however, gave Pozsony to the Czechs, who promptly renamed it Bratislava and assigned border guards to shoot on sight any Hungarian crossing the Danube in either direction.

It was then that Albert Szent-Gyorgyi cultivated a flair for underground maneuvers that was to serve him well in another war. The laboratory had been equipped by young Hungarian scientists, who now plotted to ferry across the Danube whatever instruments were portable or could be dismantled. On one occasion, when Albert took advantage of a surreptitious crossing to visit his mother, he had to stand all night in deep snow to avoid the Czech patrols. He came out of it with a case of pneumonia.

The Bela Kun regime lasted just long enough to ruin the fortunes of the Szent-Gyorgyi family, so that by the time Albert could make it back to Budapest with his wife and their newborn daughter, he faced an uncertain future. He was a man with a family, no money, and few relatives in a position to help him. Searching for a niche in medical research where he could do something useful and even marginally profitable, he traveled to Prague for a stint at electrophysiology with Armin Tschermak, to Berlin for an introduction into physical chemistry, and to Hamburg's Institute for Tropical Hygiene.

The last move was an act of desperation. Very nearly broke, he saw a dubious salvation—but the only one left to him—in some outpost of empire where there might be an opening in a jungle laboratory. Now sitting in his pleasant old house on the Massachusetts shore, with a distinguished career behind him and perhaps ahead of him as well, Szent-Gyorgyi reflects, "In the trop ics I would have been lost forever"

He had already outfitted himself for the jungle when a reprieve arrived. The Dutch Physiological Society was meeting in Hamburg that year. Albert Szent-Gyorgyi attended the sessions and there met a compatriot, Fritz Verzar, who was then returning to Hungary after serving as an associate professor under W. Storm van Leeuwen at the Institute of Pharmacology of the University of Leiden. He suggested that Szent-Gyorgyi take his place in Leiden.

The proposal was accepted, and the Szent-Gyorgyis, in high spirits once again, moved. "I felt I had a future there that did not exist in Hamburg," Albert recalls. Unfortunately, Albert's boss in the laboratory, who had enjoyed a career as a cavalry officer before he took up medicine, began to pay overly cavalier attentions to Mme. Szent-Gyorgyi. He could not be easily discouraged, and the resulting tension sent the Szent-Gyorgyis packing.

Once again, the prospect of a tropical backwater rose like doom before the wandering Szent-Gyorgyis. They stopped at Groningen, where Albert was to prepare for the Dutch licensing examination that would qualify him for a job in the East Indies. He easily passed the first part of the test, becoming a "semi-Arzr (half a doctor), as the Dutch put it. He was running out of money, when a job opened at the laboratory of Dr. H. J. Hamburger at the Physiological Institute in Groningen. The elderly Dr. Hamburger was pursuing an idea that seemed highly improbable to the young Szent-Gyorgyi, but it promised a salary, however minuscule. Dr. Hamburger wanted to implant fistulas in dogs, enabling him to inspect their digestive processes in vivo.

The difficulty was that few dogs survived the surgery long enough to afford Hamburger more than a glimpse. Szent-Gyorgyi, however, achieved a record number of long-term survivors, to Hamburger's delight. In the time he could spare from the operating theater, Szent-Gyorgyi was free to carry out his own ideas. It was in those years, from 1922 to 1926. in Groningen that he hit upon a field of exploration that was to change not only his life but the course of twentieth century physiology.

Otto Warburg and Heinrich Wieland had begun to explore the mechanism of respiration in the living cell by which the energy necessary not only for growth but for the maintenance of cellular structure was derived from foodstuff. Warburg had stressed the activation of oxygen, and Wieland that of hydrogen. Szent-Gyorgyi had a hunch that both were right. He set about proving as much by adding cyanide to minced tissue, thereby eliminating the possibility of oxygen activation. Then he added methylene blue and delightedly observed the action of hydrogen restoring the respiratory process.

He took to working on plant tissue, convinced, as he now puts it, that "there is no basic difference between man and the grass he mows." He had noted that when he added peroxide to a peroxidase and benzidine, the mixture instantly became intensely blue, caused by the oxidation of the benzidine. However, if he worked with the juice of

Otto Warburg's work on cellular respiration was the springboard for Szent-Gyorgyi's own. Both later studied the yellow luminescent protein that came to be known as vitamin B_2, or riboflaiin.

a peroxidase-rich plant—such as the orange or the cabbage—there was a delay before the mixture turned blue. That pause, of no more than a second or two, held a possibly pregnant mystery of the sort that has always attracted Szent-Gyorgyi.

There must be an agent in the plant, he reasoned, that inhibits oxidation of the benzidine. The agent may be present in such minute quantities that its supply is quickly exhausted, he reasoned, after which the oxidation proceeds. Further work suggested that the adrenal cortex might be a more abundant source. (That theory was among those that Szent-Gyorgyi abandoned without a struggle when it was shown that the material was not made but only stored in the adrenal cortex.)

Engrossed in an original project for the first time in his career, Szent-Gyorgyi worked at it relentlessly, pausing only when Dr. Hamburger had another dog waiting for a fistula. He was convinced that he was on the verge of an important insight into the respiratory process. It was not a matter of simple metabolism, it seemed to him, but rather of a catalytic action. He had only the barest suspicion then that this might one day be regarded as a momentous discovery and that the elusive substance he had detected in orange and cabbage juice might affect the nutritional habits of the world and make possible therapies then unimagined.

The work came to an abrupt halt when Dr. Hamburger died. His successor was a young man who was interested only in animal psychology, a field that required no fistulas and no assistant with sufficient surgical talent to install them. When Szent-Gyorgyi sought permission to publish a paper he had prepared on the respiration mechanism in the potato, his new boss suggested that he might toss it into the wastebasket at once, or try to have it published if he cared to make the effort, but that in any case it was totally irrelevant to the laboratory's major concern: canine psychology.

Actually, a small journal did accept the potato paper for publication, but this was minor consolation to Szent-Gyorgyi, who once again was sliding into despair. There seemed no way to do research work and maintain his family in a European city. Sadly, his wife left for her mother's home in Hungary, taking their daughter with her.

Albert prepared for a final fling before the shattering of his young career in science. The International Physiological Congress was scheduled to meet in Stockholm in 1926. It would serve, he thought in a mood of romantic gloom, as the setting for his farewell to science. "Actually," he confesses, "I only wanted a good time."

He listened with only casual interest to the presidential address of Sir Frederick Gowland Hopkins, until, to his astonishment, he heard this reigning celebrity of physiology refer no fewer than three times to a most interesting paper on the potato by Dr. Szent-Gyorgyi. No one else received anything like such attention from Sir Frederick. Elated and bewildered, like a man snatched from the gallows and knighted on the spot, Szent-Gyorgyi introduced himself to the speaker, who took an immediate fancy to him. It was suggested that he come to Cambridge, where Sir Frederick headed the department of physiology.

When Szent-Gyorgyi explained his state of bankruptcy. Sir Frederick reassured him, "Never mind, I will see to it that you get a Rockefeller fellowship." So he did, and Szent-Gyorgyi summoned his family to follow him to Cambridge. To him, Cambridge was then, and remains now, a temple of pure science. With due respect to other institutions that have claimed him, he declares, "Cambridge is my scientific homeland."

Once ensconced at Cambridge, Szent-Gyorgyi saw very little of his sponsor. Sir Frederick rarely spoke in public, and Szent-Gyorgyi cannot remember ever having a private discussion with him on a scientific matter. Actually, it was difficult to talk with him at all. If a knock sounded at the door of his study, Sir Frederick would slip quietly out the back way. Whenever it became urgent to confer with him, Szent-Gyorgyi would knock at the door and then race wildly down the corridor to catch Sir Frederick as he emerged from his escape hatch.

Nevertheless, in ways that to this day Szent-Gyorgyi calls mysterious, Sir Frederick exerted a powerful influence over all those who worked under him, endowing the daily routines of research with the glow of "an intuitive artistic vocation."

In his Cambridge laboratory, Szent-Gyorgyi concentrated on oranges, lemons, cabbages, and adrenal glands, seeking to isolate the ingredient he had noted in Groningen for its ability to momentarily inhibit oxidation. When he finally crystallized the substance, he identified it by the formula $C_HH_8O_B$, but he could not describe it further. In an article prepared for the *Biochemical Journal*, he candidly admitted, even proclaimed, his ignorance by referring to the substance as "Ignose." When the editor found this a trifle flippant, Szent-Gyorgyi suggested an alternative: "Godnose." The editor insisted on a dignified scientific name for the substance, and reluctantly Szent-Gyorgyi agreed to call it "hexuronic acid." It was an absurd misnomer, he points out. since it is not a uronic acid at all. Although Cam bridge University gave him a Ph.D. for the discovery, Szent-Gyorgyi then only dimly saw its potential importance.

He was stymied in his work because of the enormous difficulty in gathering enough hexuronic acid to analyze, much less to "play with," in the laboratory. He could put to gether from the plants available at Cambridge no more than a few milligrams of the stuff at any one time. Adrenal glands yielded more, but it would take massive numbers of them to obtain even a working modicum of the substance. Danish colleagues tried shipping adrenals to supplement the British supply, but the glands did not travel well even by air and proved unusable on arrival.

At that point, another chance encounter pointed Szent-Gyorgyi westward: Edward Calvin Kendall, an American a few years older than Szent-Gyorgyi, who would one day be honored in Stockholm for the isolation of cortisone and was already preoccupied with the products of the adrenal glands. Szent-Gyorgyi's search for an adrenal source of hexuronic acid brought him into a territory they had in common. The American invited his Hungarian colleague to take a leave of absence from Cambridge and spend a year at the Mayo Clinic, where Kendall was then director of the division of biochemistry.

Szent-Gyorgyi had been to the United States once before, briefly but memorably, when he attended an international congress in Boston. He now recalls nothing of that meeting except the lobster that he tasted on a picnic at Woods Hole. He insists that the haunting flavor of that lobster remained with him through all the years of war and poverty and that it eventually served to bring him back to the Massachusetts shore.

He found Minnesota "not especially interesting but the people very nice." His scientific needs were satisfied, not at the Mayo Clinic, but at the stockyards at nearby St. Paul, where adrenal glands were to be had by the carload. At the end of the year, Szent-Gyorgyi returned to Cambridge with 25 grams of his mysterious hexuronic acid painstakingly gathered from tons of adrenal cortical tissue. He gave most of it to Sir Norman Haworth, the renowned investigator of carbohydrates at Birmingham University.

There was little that could entice Szent-Gyorgyi to leave Cambridge for good, but it was impossible to withstand a patriotic appeal from the Hungarian Minister of Education to help restore the scientific community of his native land. Szent-Gyorgyi's prestige had soared with the discovery of hexuronic acid, making him too significant to be left in exile.

The year was 1930. Viewed from cloistered Cambridge, the rise of Hitler was a distant event, but Budapest was within range of the discomforting noises emanating from German beer halls. Hungary was then a kingdom without a king. Admiral Nicholas Horthy, as regent, ruled in the deepening shadow of Hitler. Although hitherto removed from political battles, Szent-Gyorgyi was so outspokenly antifascist that the conservative University of Budapest held him at arm's length. The University of Szeged, however, offered him the chair of medical chemistry. Although a few noisy fascists threatened to disrupt his lectures, Szent-Gyorgyi assembled an enthusiastic corps of students whom he could take along on his explorations into the mysteries of oxidation.

He was struck by a pigment he encountered in his meticulous study of cellular life. He named it "cytoflave" for its "splendid yellow luminescence." Without a spectroscope, Szent-Gyorgyi could not describe it in detail, but it was to prove important in the scheme of cell restoration taking shape in his mind. Later that brilliant yellow protein, studied also by Warburg, came to be called vitamin B_2.

The lack of a spectroscope was only one of the frustrations of work in Szeged. Szent-Gyorgyi still recalls the maddening frustrations he experienced when, seeking to analyze a particular hydrolysate, he found that the bottle of platinic chloride needed to precipitate the substance was empty. Not a drop was to be had in all Hungary, and the hydrolysate withered away.

Szent-Gyorgyi was delightfully surprised one day when an amiable Hungarian-American chemist turned up in the laboratory eager to work. It happened that the newcomer, named Svirbely, had had considerable experience with vitamin C. It was his opinion that there was very little connection between vitamin C and hexuronic acid. Szent-Gyorgyi, who had long held a hunch that the two were identical, turned over his last bit of the acid to Svirbely for testing.

It became clear in less than a month that hexuronic acid very likely was vitamin C. Szent-Gyorgyi was a trifle disappointed because vitamins seemed to him to be "theoretically uninteresting" and tainted by the sensationalism of Sunday supplements. Nevertheless, he accepted the verdict. He and Svirbely tested the antiscorbutic effectiveness of hexuronic acid and found that one milligram of the substance administered daily was enough to protect a guinea pig against scurvy for 56 days.

Szent-Gyorgyi communicated the news to Haworth in Birmingham, and the two of them rechristened the substance "ascorbic acid."

Szent-Gyorgyi did not leap into print with the results but painstakingly set about reworking the experiments. By the time he was ready to write his report, the supply

Sir Frederick Gowland Hopkins recognized the potential of Szent-Gyorgyi's first paper, in an obscure journal, and obtained a fellowship for him at Cambridge, where he did his early work on vitamin C.

Edward Calvin Kendall invited Szent-Gyorgyi to spend a year at the Mayo Clinic. Nearby stockyards proinded tons of adrenal cortical tissue, which yielded 25 grants of hexuronic add.

of the substance, which had been replenished, was again exhausted. The amounts needed for analysis-much less for clinical use—seemed hopelessly beyond reach.

One evening, as he recalls, his wife served a side dish of that mild, slightly sweet red pepper of Hungary called paprika. In no mood for paprika that evening, Szent-Gyorgyi sought a diplomatic way to avoid the vegetable without offending his wife. "I must save this for the laboratory," he told her. "I have tried every other plant I know. Why not paprika?" Once in the laboratory, he felt he had to go through with the tests. By midnight, he found that paprika was "a treasure chest" of ascorbic acid. A gram of paprika yielded at least two milligrams of the vitamin.

By the time the paprika season ended that year, Szent-Gyorgyi had amassed half a kilogram of crystalline ascorbic acid, and in the following year, he produced three kilograms. As quickly as the substance could be prepared, he shipped it out to investigators around the world who might analyze it down to its essentials and reconstitute it in pure form for clinical use.

The little laboratory at Szeged was now working with the intensity and passion of Szent-Gyorgyi's imagination. Reasoning from the demonstrated effectiveness of ascorbic acid against scurvy, associated with subcutaneous bleeding from fragile capillaries, he decided to use it on a colleague who was suffering from Henoch's purpura.

The ascorbic acid derived from raw paprika greatly relieved the stricken man. Later, however, when Szent-Gyorgyi tried the purified crystalline ascorbic acid, he found it useless. There was, then, still another therapeutic ingredient in that sweet Hungarian red pepper.

The active ingredient against purpura turned out to be a flavone. Szent-Gyorgyi called it vitamin P, not for the purpura it helped to cure nor for the paprika that was its source, but for a more whimsical reason. The next unclaimed letter in the alphabetic progression of vitamins was G, but Szent-Gyorgyi was unsure about the qualifications of his substance as a vitamin. If it had to be ousted from that order, he reasoned, it would leave an unfortunate alphabetic gap. By naming it P, he thought to buy time, allowing the credentials of the substance to be validated or rejected before a vitamin O appeared.

However quiet may have been Szent-Gyorgyi's satisfaction at his discovery of ascorbic acid, excitement in the rest of the world was less restrained. He was called away repeatedly to lecture at medical meetings throughout the world. And in 1937, a telegram from Stockholm summoned him to receive the Nobel Prize in Physiology and Medicine.

In presenting the award. Professor E. Hammarsten of the Karolinska Institute cited not only his work in isolating ascorbic acid and doing so much to make it available clinically but his pioneering explorations of cellular respiration. He had proved. Professor Hammarsten said, "that the plant acids were not consumed by combustion, were not ordinary nutrient substances, but were, on the contrary, themselves active groups of catalysts that served to maintain the combustion without themselves suffering any diminution thereby."

The prize money of $8,000—then a very large sum—was a "hot potato" to the impecunious Szent-Gyorgyi. With war apparently inevitable, the new laureate told a broker in London to find an investment that would go up in peace and down in war. In that way, he told the mystified broker, his opposition to war could be unalloyed without any subversive subconscious hope of profit from the coming slaughter. The broker complied, and accordingly, within a few years the Nobel prize money was wiped out. Reflecting on that transaction, Szent-Gyorgyi now says, "I lost my money, but I saved my soul." For this anti-Faustian, it was a fair bargain.

The war did not at once shut down the laboratory at Szeged. The aura of the Nobel prize may have shielded it from the mounting power of the local Nazis. Szent-Gyorgyi was immersed in the chemistry of muscle contraction, which, he considered, might "lead him closer to an understanding of life." With him in the laboratory, in addition to Bruno Staub, was Ilona Banga, a colleague who, he emphasizes, never received adequate credit for the discoveries that flowed from her work.

Szent-Gyorgyi was puzzled—a state of mind he finds conducive to creation—by the failure of myosin to provoke muscle contraction in vitro, even though it was known to be vitally involved in the process in vivo. He and Ilona Banga noted that attached to the rod-shaped particles of myosin was another protein hitherto undescribed. They combined threads of this newly iso lated protein with the myosin in a soup of muscle tissue. Then, in that soup containing the essential adenosine triphosphate (ATP), the experimenters saw the signs of motion. It was a clear contraction of the muscle, down to a tenth of its length, produced for the first time

outside the body. For Szent-Gyorgyi, that astonishing moment remains one of the most thrilling of his life. He called his new protein "actin"; however, the conclusive work on the combination of merged proteins, "actomyosin," would have to wait for a quieter time and place.

The strains of war were beginning to show at the laboratory and at home. They may have been instrumental in the breakup of the Szent-Gyorgyi marriage. By 1941, howeve[r], Albert had recovered from that trauma sufficiently to woo and marry a young scientist, Marta Borbiro, who had worked with him in the laboratory. They were shortly to work together in the war.

A delegation from the underground came to fetch Szent-Gyorgyi, for he was known not only as a scientist but as a man with influential family connections. Hungary had been digesting bits of Slovakia, Transylvania, and the Carpathian Ukraine as crumbs from Hitler's table, but the alliance was nonetheless uneasy. Even high Hungarian officials privately and discreetly chafed at the increasingly odious connection. Count Teleki, the Premier, had been uncomfortable from the start. On the very day he signed his country over to the Axis, he sent telegrams to Berlin and Rome stipulating, as if on second thought, that "on moral grounds" Hungary could not join any military action against Poland. Hitler was so infuriated that the Hungarian ambassador begged him to forget that the Premier's message had ever been sent.

Utilizing his family background, Szent-Gyorgyi cautiously approached the Count to see whether he might be interested in negotiating a way out of the Axis. He was enormously relieved when the Premier did not throw him into jail but, on the contrary, expressed a willingness to talk. Count Teleki had publicly thundered against Jews, but if he behaved any less maniacally, he now pleaded, the Nazis would come in and swiftly wipe out the entire Hungarian-Jewish community. In the end, he gave his blessing to a secret mission to Istanbul, whereby Szent-Gyorgyi would test the waters in that city of spies and counterspies for a Hungarian switch of alliances.

Szent-Gyorgyi went armed with the name of a friendly antifascist journalist who was to pass him on to British diplomats. These, in turn, sent him to British agents. The rest is melodrama, which Szent-Gyorgyi relates with boyish relish. He was directed to arrive at a certain corner in Istanbul precisely at six in the evening. A black car would be waiting. Unhesitatingly, without a word, he was to climb into the backseat.

He followed his instructions to the letter and was driven far out of town to a country house, where two cheery British agents exclaimed, "How wonderful you've come!" Count Teleki had been in touch with them, and they were trying to resolve their doubts concerning him. That very day London had sent a message suggesting that they contact Szent-Gyorgyi. Before they could act, he had arrived.

The British worked out a scheme, according to which Szent-Gyorgyi was to set up a wireless station with the help of an engineer they would assign to the job. The British would then be able to explore matters with Teleki while secretly obtaining verification and advice from Szent-Gyorgyi and others in the underground. Unfortunately, by the time he made his way back to Budapest, his secret had been leaked. First, he was placed under house arrest, but when the Germans occupied Hungary, Szent-Gyorgyi was tipped off, so that he could go into hiding. As he recalls those days, his face takes on a look of pride mingled with a sense of mischief. He glows when he cites reports that Hitler, in a frenzy over the effort at Istanbul, shrieked at his Hungarian *Gauleiter* to "deliver Szent-Gyorgyi."

For years after that, he led the life of one on the run, slipping from one hiding spot to another. His face was too well known to risk appearing in the shelter during air raids. He stayed in his room, pretending to be a dying old man. His wife, acting the part of nurse, assured nosy neighbors and air raid wardens that he could not be moved.

When German agents seemed to

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As Szent-Gyorgyi approaches his eighty-ninth birthday, he works in the laboratory five days a week, searching for submolecnlar clues to cancer.

be closing in at last, the Szent-Gyorgyis fled to the Swedish Embassy. A royal proclamation in Stockholm granted Swedish citizenship to the two of them, but no one expected that such legal niceties would deter the Gestapo.

Before plunging from Szeged into the resistance, Szent-Gyorgyi had taken one precaution, but now that act of foresight was proving disastrous. He had sent a record of his work on muscle contraction to his Swedish friend and colleague Hugo Theorell for publication in a Scandinavian journal.

Still attentive to courtesies that had been obviated by war. Theorell felt he had to acknowledge receipt of the article. Having no other address, he sent a letter to Szent-Gyorgyi in care of the Swedish Embassy in Budapest. The Gestapo arrived not far behind the letter and began to seal off the embassy from the adjoining houses. Word came from friendly contacts in high places that the Germans were about to break in. It was then that the acting head of the embassy. Per Anger, smuggled the Szent-Gyorgyis out in the trunk of his car. Marta went to her parents' house, and Albert went on the run, edging as close as possible to the advancing Russian lines.

When Soviet troops reached Szent-Gyorgyi's street, he came out and followed them until they liberated the area in which his wife and her family lived. Their reunion was interrupted by a Russian officer with a direct order from Molotov to take Szent-Gyorgyi to safety. Marta insisted that she could not leave without her parents, and her parents could not leave without at least 13 other relatives. Most of the family were settled in southern Hungary, already out of hostilities, but the Szent-Gyorgyis were escorted, first, to Soviet headquarters in Budapest and, then, to a posh suite in a Moscow hotel.

They had caviar at lunch and dinner, he recalled, as well as lavish tours through sunny Armenia. Szent-Gyorgyi had shared the

mingled hopes and fears that the Soviet Union inspired among intellectuals in the 1930s, although he had indignantly sent the Finns his Nobel gold medal as a gesture of support when their country was invaded. Despite growing disenchantment concerning the Soviet Union, he thought that some of the evils, at least, could be ascribed to the "excesses of subordinates." He thought, therefore, that it might be useful to inform Stalin directly of the sometimes outrageous behavior of his troops in Hungary.

He was asked to meet first with a man named Decanozov, who, Szent-Gyorgyi notes—with the barest trace of a grin—was subsequently sentenced to be shot. When he described the cruel treatment meted out to Hungarians, even to those who had thrown down their arms rather than fight for Hitler, Decanozov exploded. He was not shocked by the revelations and did not deny the reports, but he shouted that Hungarians had committed atrocities as bad or worse on the eastern front. It was plain that Szent-Gyorgyi could convey no news to the Kremlin.

Without seeing Stalin, he went back to Hungary to help in the re-, construction of the shattered scientific community. Organizing an "Academy of Science" meant not only assembling scientists and equipment but finding a way to feed them. It was not a matter of money but of potatoes. While Albert presided over a laboratory, Marta organized a kitchen to feed the staff.

Despite the off-putting conversation with Decanozov, the Russians cooperated handsomely with Szent-Gyorgyi. Marshal Voroshilov responded to every appeal for transport, then at a premium in Budapest. The academy put the Soviet-supplied trucks to double duty, taking war-weary Budapest neighbors out for a holiday in the countryside, charging them for the ride,* and using the money to bring back fresh food to the laboratory.

Still, although the Szent-Gyorgyis enjoyed a somewhat privileged position, all hope of major scientific work seemed frustrated by economic shortages and political pressures. Szent-Gyorgyi thought the United States—rich, democratic, and scarcely touched by the war that left Europe ravaged—might offer him a bench in a laboratory. He went to Paris to apply for a visa, but the United States was then in the grip of acute Russophobia. The evidence of Soviet favors granted to Szent-Gyorgyi was enough to damn him despite his war record. His visa was therefore denied. In 1947, however, following intervention by U.S. scientists, the authorities granted him the right to enter.

In New York, immigration officials asked only the routine questions. "Do you read and write?" one asked. "I don't read much," said Szent-Gyorgyi, "but I write a lot."

Once in the United States, he was at a loss for a place to settle. Out of his memory there rose the flavor of a lobster, boiled over a beach fire, which he had enjoyed some 20 years earlier. In that fragrant recollection it seemed there had also been a laboratory nearby where a scientist could rent a table and equipment. And so they came to Woods Hole.

The years at Woods Hole have not always been gentle. True, he could take off from the beach at his doorstep and swim far out to sea where men half his age would hesitate to go. He could fish and water-ski and play tennis and chess. He also has found disciples and colleagues who admire him unreservedly.

Szent-Gyorgyi, however, has never been able to work away from the searing political heat of his times, and he has never been discreet about his convictions. He has campaigned against war wherever it has been waged. In a book entitled *The Crazy Ape* written for young people in the 1960s, he thundered:

> Armies are a curse of mankind, a threat to peace, a threat to our very existence, a blot on the face of human culture and intelligence. The greater the army, the greater threat to peace it is__ Who will defend us against the defense departments?

In a letter to the *Bulletin of the Atomic Scientists,* he offered an ironic disarmament proposal. Mindful of the economic dislocations inherent in disarmament, he suggested that military budgets be voted as usual, that firms be given contracts and subcontracts, and that thousands of workers be hired—all provided that they produce absolutely nothing. At no greater expense than usual, the nation would go through the motions of arms production, but no weapons would roll off the assernuiy lines. Industry then could slowly adapt to productive peacetime activity, and the war budget, which would have harmed no one because its stockpiles would have been fictitious, would wither away in the reality of peace.

Such antiestablishment fantasies may have stood in the way of obtaining grants, but Szent-Gyorgyi admits that, in any case, he never had any talent in writing grant applications. "They want to know just what I am going to do," he points out. "If I knew that, there would be no point in my doing it." Grants are not readily given to people who anticipate only the unexpected. Szent-Gyorgyi also fails to impress most givers of grants because he asks for so little. Once, when things were going well, he accumulated a staff of 12 people. "It was the least creative period of my entire life," he recalls. "I spent all my time looking after my staff and correcting their mistakes." He does not want to direct experiments; he wants to experiment—with his hands and eyes as well as his brain.

The 1960s brought him the joy of refining his work on the nature of muscle contraction to an elegant point. He not only demonstrated the presence of actin but was one of those who early showed clearly that myosin was an enzyme with ATPase activity. And previously, he had markedly facilitated the study of ATP and its effect by utilizing extracts of the contractile proteins made by glycerol extraction. His "glycerinated fiber bundle" has become a versatile laboratory concept.

The death of Marta, who had been a colleague as well as a companion, left him bereft and lonely, but that is a condition that has never endured for very long in Szent-Gyorgyi's life. There followed a whirlwind courtship of another woman, a third marriage, and a divorce after a few months. "It was an experiment that failed," he says, "—a catastrophe."

By the mid-1970s, he was "at the end of his tether," as he recalls. His grant applications had fallen through. When he was hospitalized briefly, his wry humor showed through sad reflections. "Every-

Nohel prize winners in 1937 were Walter N. Haworth of England and Paul Karrer of Switzerland, who shared the Pnze in Chemistry, Clinton J. Davisson, American physicist; Szent-Gyorgyi; and French author Roger Martin du Card.

A career that has spanned nearly the entire twentieth century[1] continues. For Szent-Gyorg\i, science has always been an art, often based on insight and hunches.

thing has an end," he told his cousin. Dr. Andrew Szent-Gyorgyi, head of the department of biochemistry at Brandeis University. Then he added: "Except a sausage, which has two... but I am not a sausage."

In 1975, Albert Szent-Gyorgyi, at the age of 82, took off on a new course of life and work. One of his colleagues and enthusiastic admirers. Dr. Benjamin Kaminer, head of the department of physiology at Boston University, gathered a group of distinguished scientists, each with a profound debt to pay to Albert Szent-Gyorgyi. Among them were Fritz Lipmann, Linus Pauling, Hans Krebs, Annemarie Weber, Hugh Huxley, and, of course, Cousin Andrew Szent-Gyorgyi.

It was at that glittering symposium at Boston University that Szent-Gyorgyi announced his departure into the submolecular aspects of biology. In the uncoupling of electrons and in the formation of magnetic fields, he said, he hoped to find the strange anomaly that gives rise to the cancer cell.

.It was also at that meeting that he introduced his colleagues to a young artist, Marcia Houston, who, he declared, had consented to marry him. His world was indeed beginning again. His finances, however, were almost as straitened at the beginning of his fourth marriage as they had been at his first.

That, too, was about to change. The first sign of the reversal seemed no more momentous than a smile from a stranger. Franklin and Tamara Salisbury of New York had heard of Szent-Gyorgyi's plight and had sent off a token of their good wishes: a check for $35. The gesture so touched Szent-Gyorgyi that he responded warmly. The exchange of correspondence led the Salisburys to visit the Szent-Gyorgyis at Woods Hole. The comparatively small sums that he needed and the frigid reception given him by the major organizations funding cancer research moved the Salisburys to embark on a new venture. They formed the National Foundation for Cancer Research, raised the funds he needed, and have gone on to support other scientists as well.

Albert Szent-Gyorgyi goes to his laboratory five days a week. Only when the parking is difficult does Marcia drive. During the winter, he has a devoted and highly competent staff of two. They are all he needs. In the summer, scientists from many parts of the world come to Woods Hole to see how best they can collaborate with him. The foundation meets all his modest requirements. Even in the heyday of grant-giving, he never asked for more than $150,000 a year, and now he gets along on far less.

His work shows enough progress to absorb him for years to come. His home—in the house he has occupied since he came to Woods Hole—is as supremely comfortable as a well-worn slipper There is nothing luxurious in it except the sight and sound of the sea. It has not only a sense of Albert but of Marcia, who delicately and unobtrusively creates a life for herself and the extraordinary man whom she married. "This is," says Albert Szent-Gyorgyi, "an ideal life for a scientist."

Marcia and his home are clearly major components of that quiet ecstasy, but for Albert Szent-Gyorgyi, the essential requirement for life is the freedom to follow a trail of clues, hunches, and insights to some hitherto unglimpsed vista of reality.

He has clearly stated the goal that he still pursues with characteristic panache: "To see what everyone has seen and think what no one has thought."

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