Natural and other experiments: the secret history of the war on cancer

Esperimenti naturali ed altri: la storia segreta della guerra contro il cancro

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Summary

In 1936, the world's leading cancer scientists gathered in Brussels for the Second International Congress of the Scientific and Social Campaign Against Cancer, exchanging information on the capacity of benzene, radiation, hydrocarbons, synthetic hormones and sunlight to induce cancer experimentally and in humans. The nature of evidence on environmental causes of cancer considered at that gathering ranged from experimental studies to observations that "uniovular" (monozygotic) twins did not develop the same cancer much of the time. As the world turned to war-time footing, concerns about the long-term consequences for health of workplace and other exposures were eclipsed by immediate threats – a condition that haunts thinking about cancer to this day. The sowing of doubt regarding the relevance of experimental science to explaining the hazards of tobacco provided a model that was easily extended to many other modern health dangers, including those of the workplace and general environment. Eur. J. Oncol., 13 (2), 77-85, 2008

Key words: **cancer history, cancer prevention**

Riassunto

Nel 1936, i principali ricercatori al mondo esperti di cancro si riunirono a Bruxelles in occasione del Secondo Congresso Internazionale della Campagna Sociale e Scientifica Contro il Cancro, scambiandosi informazioni sulla potenzialità del benzene, delle radiazioni, degli idrocarburi, degli ormoni sintetici e della luce solare di indurre sperimentalmente il cancro nell'uomo. La fonte delle prove delle cause ambientali di cancro riportate a tale assemblea spaziava dagli studi sperimentali all'osservazione che i gemelli "monovulari" (monozigoti) molte volte non sviluppano il medesimo cancro. Quando il mondo si trovò in un contesto bellico, gli interessi per le conseguenze a lungo termine per la salute negli ambienti di lavoro e in altri luoghi di esposizione furono messi in ombra da minacce immediate, una condizione che ossessiona tutt'oggi l'opinione sul cancro. Il diffondersi del dubbio circa la rilevanza della scienza sperimentale finalizzata a chiarire i rischi del tabacco fornì un modello che venne facilmente esteso a molti altri fattori contemporanei di rischio per la salute, inclusi quelli presenti nel luogo di lavoro e nell'ambiente in generale. Eur. J. Oncol., 13 (2), 77-85, 2008

Parole chiave: **storia del cancro, prevenzione del cancro**

Received/Pervenuto 14.3.2008 - Accepted/Accettato 2.4.2008
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Adapted from The Secret History of the War on Cancer, Basic Books, 2007, with permission of the author

In the summer of 1936, over two hundred of the world's top cancer scientists convened in Brussels to attend the second international congress of the Scientific and Social Campaign Against Cancer. The meeting had the makings of a veritable Manhattan Project on cancer, as the best minds available met to create something astonishing and new. The great experimentalist Isaac Berenblum later remembered it as *"the most momentous cancer congress ever held"*[1]. The scientists sailed from Latin America, North America or Japan, a journey that could have taken close to two weeks, or took trains from Russia and Europe. With the world clearly on the brink of world war, such a trip required considerable courage as well as a strong stomach. At least one of the participants, Wilhelm Hueper, had survived poison gas attacks in the Great War; no doubt several others had had similar experiences. They kept no secrets – government or industrial – but ironically this historic gathering itself remained nearly secret for more than seventy years. Many of your late relatives and mine might still be with us if the things these eminent women and men of science knew about the causes of cancer in 1936 had entered mainstream medical practice.

But they didn't. Something mysterious happened over the course of the twentieth century. At that meeting in Brussels the accomplishments of several centuries of cancer research flashed onto the scene, ready to coalesce into a substantial and coherent body of scientific understanding about the environmental causes of cancer. Instead, many of these accomplishments were forgotten, their message ignored. Much knowledge that really mattered ended up in that dusty section of the library reserved for books that are never read and papers that are never cited. Today, we're locked in ferocious debates about matters that scientists thought they had solved more than three generations ago. What kinds of evidence tell us the causes of cancer that we can do something about? What passes for scientific proof, while ultimately founded in methods and measures, is not immune to changing political and economic forces?

Many of the texts of this extraordinary report were written in several languages, English, Spanish, French, and German, all presumed to be understood by the multilingual scientific crowd. One speaker, Clarence C. Little, then famous for creating ways to study the inheritance of cancer in mice, argued on the basis of animal studies that most cancer arises from inherited defects, an opinion then shared by some scientists throughout the world. But at this conference, the view that cancer dictated by our genes was in the clear minority.

William Cramer of London's Imperial Cancer Research Fund carefully examined patterns of cancer in people over about a century. He was able to do this because the British had been keeping records of deaths and illnesses for more than three hundred years. Cramer noted that much of the recorded increase in cancer was nothing other than better record keeping and people living longer lives. He went on to present techniques for evaluating these patterns that took these facts into account. The numbers of cancer cases had almost doubled since the turn of the century. Taking into account the fact the more people were alive and older, cancer was about one-third more common than that at the beginning of the twentieth Century[2].

Cramer also pointed to other proof of the modern growth in cancer, noting a profoundly simple and important observation that has been repeatedly confirmed. He looked at what happens in what he called "uniovular" twins (more commonly known as identical twins these arise when a single fertilized egg splits into two developing embryos). By 1936 he had already determined that in most of these genetically identical pairs, if one develops cancer, the other does not. Cramer concluded that *"cancer as a disease is not inherited"*. He urged that patterns of cancer – especially those of the workplace – should be tracked in order to learn how to control and reduce the disease[2].

Cramer understood that human patterns were the result of past exposures. If one wanted to make progress against cancer it would be important to rely on experimental research with animals. Animal tests provide an important way to learn whether chemical and physical agents which produce cancer in animals also produce cancer in man. Cramer noted that cancer often develops in both rodents and humans in the same tissues. The time between exposure to a chemical and the time when a tumour shows up varies greatly, occurring within a year in rodents and after decades in humans. Yet this period of latency is remarkably similar if expressed in fractions of the usual span of life in each case. Cramer argued that there are few diseases in which the experimental production in animals so closely simulates the disease in man as in cancer. He allowed that cancer in man may, in fact, be considered as an experiment carried out on man by Nature, or by himself, an experiment, however, in which only the end results are known[2].

The three volumes from this congress included surprisingly comprehensive laboratory and clinical reports showing that many widely used agents at that time were known to be cancerous for humans, including ionizing and solar radiation, arsenic, benzene, asbestos, synthetic dyes and hormones. Angel Honorio Roffo, the founding director of the Institute of Experimental Medicine in Buenos Aires, Argentina, described experiments showing that both invisible forms of radiation – ultraviolet and X-ray – could produce cancers in animals. He was one of several experts at the time to show that these tumours can be removed from one animal and made to grow in another, a method of tumour transplantation still in use today. Roffo's work referenced earlier experiments by Andre Clunet, who had produced sarcomas in rats in 1910, and clinical reports by Bruno Bloch from 1923 finding that radiation induced cancer in animals and in workers exposed on the job.

Roffo's studies of workers showed that those who spent the most time outdoors had the greatest vulnerability to skin cancer. His paper was accompanied by exquisitely detailed drawings of tumours growing from the heads, eyes, ears and thyroid glands of rats following months of solar or X-ray treatment[3]. He also reported that combining some hydrocarbons with either sunlight or radiation produced worse cancer damage than any one of these exposure alone. He advised avoiding radiation and sunlight, and reducing exposure to hydrocarbons. These are observations the modern world did not begin to take seriously until the 1980s.

Roffo was one of many experts to issue a strong statement against the fashionable view that a tanned skin signals good health. At a time when suntanned movie stars and cowboys were seen as glamour figures, he concluded by *"protesting strongly against excessive sunbathing which exposes the skin to intensive irradiations from the sun, placing individuals victims of a ridiculous fashion, into a particularly dangerous state of receptivity to the development of skin cancer"*[3].

Noted researchers J.W. Cook and E.L. Kennaway and others with London's Royal Cancer Hospital reported that more than thirty different studies had found that regular exposure to the hormone oestrogen produced mammary (breast) tumours in male rodents. The National Toxicology Program of the US government did not formally list both oestrogen and ultraviolet (sun) light as definite causes of human cancer until 2002[4].

How did these scientists decide what was a cause of cancer in 1936? They combined autopsies with medical, personal and workplace histories of people with cancer. They reasoned that if they found tar and soot in the lungs of those who had worked in mining, and showed that these same things caused tumours when placed on the skin or in the lungs of animals, that was sufficient to deem these gooey residues a cause of cancer that should be controlled. Their work with animals extended from complex laboratory studies of rats, mice, rabbits, monkeys, dogs and cats to various physical and chemical agents that left clear marks of cancer. They also established new approaches for looking at patterns of cancer in groups of workers, adjusting their analysis for the ages of those being studied and the fact that more older people would mean more cancer.

Before the twentieth century, physicians and scientists had an expansive view of what it took to be able to say that anything could be considered a cause for cancer. A broad range of natural experiments, some carried out by researchers on themselves, repeatedly showed one simple thing: our health reflects the sum of our life experiences. Most cancer arises not because of who our parents were but because of what happens to us after we are born. Where and how we live and work, what we eat, how we spend our private time, how we move about: all these things affect the kind of health we will have. Heat, cold, dust, dirt, radiation, soot, fumes and myriad natural and synthetic agents combine to affect the chances that anyone will get any disease. Cancer develops not because of one unique circumstance, whether hereditary or environmental, but out of the sum total of the goods and bads of our lives.

Hippocrates was not the first of the ancients to be fascinated with the uncommon and monstrous growth of cancer, nor was he the earliest to describe a sprawling crab-like tumor of the breast, called *Karkinoma*. Nearly four centuries earlier, around 900 B.C., one of the first depictions of the disease is found in a collection written on pressed papyrus reeds from Egypt – the world's first preserved paper. The Edwin Smith Papyrus, named for the English surgeon and Egyptologist who translated it in the nineteenth century, describes eight cases of breast tumours or ulcers in startlingly modern terms. The author of the papyrus reports only one treatment for these ancient tumours: repeated use of a "fire drill" to burn out the growths that had broken through the skin.

Cancers that could be seen were sometimes removed successfully during the Middle Ages. Even then a healthy life was considered to lessen the chance the disease would occur. The twelfth-century Jewish polymath Moses Maimonides, who served as chief rabbi of Cairo as well as chief physician to the sultan of Egypt, carefully explained how to excise a cancer and uproot all surrounding tissue. But he warned that this would not work *"if the tumor contains large vessels & [or] the tumor happens to be situated in close proximity to any major organ"*[5]. To prevent the disease, he counseled staying away from dusty cities and dirty air, eating chicken soup and garlic, and getting regular exercise.

In the mid-sixteenth century, the geologist and physician Georgius Agricola spent years preparing a massive report on mining that included detailed information on the cancerous ailments of miners. He did not just rely on what others told him. Agricola went underground into the Erz Mountains of Central Europe to watch boys and men extracting, preparing and processing ore. He was struck by the number of young miners with tumors in their chests.

Agricola's magnum opus, *"De re metallica"*[6], appeared in 1556, one year after the author's death, and included some of the earliest reports on the chronic ailments of underground work. Those who entered the mines the youngest, if they did not perish in gruesome accidents, fared the worst and eventually died from lung diseases and tumours. Agricola's work was printed with 289 remarkable woodcuts (fig. 1) portraying the brutal work of mining both above and below ground.

Sometimes important news takes a few centuries to make the rounds. In 1912 Herbert Hoover, then

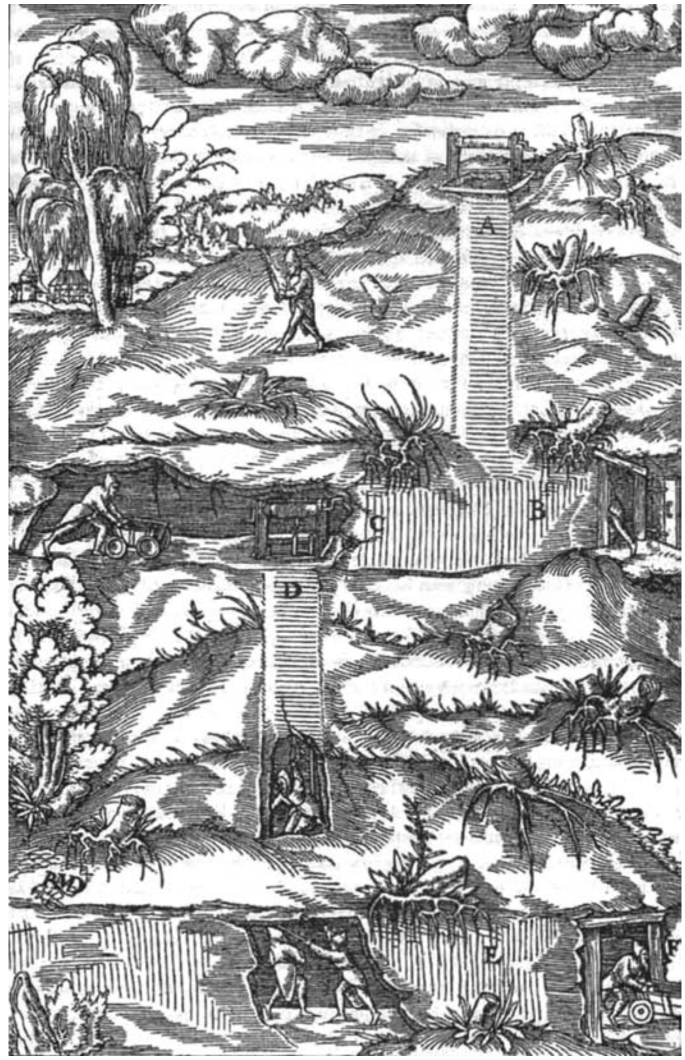

Fig. 1. A sixteenth-century woodcut by geologist and physician Agricola depicting the hazards of underground mining, reproduced in an English translation of his book *De Re Metallica* (On Metals) by Lou and Herbert Hoover in 1912[6]

one of America's top mining engineers, and his wife, Lou, a Latin scholar, published the first English translation of Agricola's work in "Mining" magazine with the four century old woodcuts[7]. In their introductory comments, they explained that they made the translation because this sixteenth-century work remained relevant to the lives and deaths of twentieth-century miners – something we are reminded of today by occasional reports of mining disasters in Russia, China and West Virginia. The Hoovers admitted that harms to workers were regrettable, although the ways they could be avoided were less apparent than the profitability of the materials.

By the turn of the eighteenth century, the pathbreaking Italian physician Bernardino Ramazzini had documented more than three dozen different cancer-prone professions, including mining of coal, lead, arsenic, and iron. At that time the disease was still uncommon and usually lethal. Ramazzini could not tell you which specific part of the job caused which maladies, but he knew that people in many different jobs were subject to risk, including metal gilders, chemists, potters, tinsmiths, glassmakers, painters, tobacco workers, lime workers, tanners, weavers, coppersmiths, mirror makers, painters, sulphur workers, blacksmiths, apothecaries, cleaners of privies and cesspits, farmers, fishermen, soldiers, printers, confectioners, carpenters, midwives, wet-nurses, and corpse carriers. For each of these trades, he explained what particular agents or conditions he thought gave rise to certain classes of illness. Those who worked with dust and fire, like miners, blacksmiths, glass workers, printers, bakers and smelters, tended to suffer from weakened lungs, incurable cough and occasionally suffocating tumours of the lung.

When he reached his late sixties (an achievement at the time), Ramazzini published his major work, *"De morbis artificum diatriba"* (Diseases of workers)[8], which showed that what men and women did at work played a major rôle in determining what ailments they developed. This book laid the foundations of occupational medicine.

Ramazzini died at eighty-one in 1714, in an era when most workingmen did not reach forty years of age. In addition to being adventurous, he was an observant doctor with a penchant for record keeping. He noted that nuns tended to be free of cervical cancer, then one of the most common fatal tumours of women. Those who lived celibate lives, however, were more often struck by breast cancer than other women. Ramazzini speculated that both of these anomalies could be related to the same cause: nuns did not bear children but experienced a lifetime of menstrual cycles uninterrupted by pregnancy or nursing. His theory that something associated with the failure to bear children affects cancer risk remains a central tenet of cancer research today.

One other thing distinguished Ramazzini's work. He believed that those who learned of workplace hazards had a simple moral duty to warn workers about the risks and urge them to lower those risks for themselves, their families and their towns. He offered this modification of Hippocrates' ancient advice: *"When a doctor visits a working-class home he should be content to sit on a three-legged stool, if there is not a gilded chair, and he should take time for his examination; and to the questions recommended by Hippocrates, he should add one more: What is your occupation?"*[9] Ramazzini based this advice on his own practice. *"I for my part have done what I could and have not thought it unbecoming to make my way into the lowliest workshops and study the mysteries of the mechanical arts"*[9].

Among the many facts about that remarkable cancer congress of 1936 that are not well known (or hardly known at all) is that most of the assessments regarding carcinogenic effects from hormones, arsenic, sunlight, radiation, benzene and other chlorinated hydrocarbons were accepted by official industrial sources at that time. Ten years earlier, the American National Safety Council had issued a final report on the hazards of benzol, the German term used to describe benzene, their document noted the doses at which it induced narcosis and severe weight loss in animals, and included 125 different references. Highly exposed workers became anemic and sometimes died when overcome by fumes they encountered when cleaning out deep tanks. Those without lethal exposures had a range of blood problems that were well studied.

Out of a total of eighty-one workers studied in all plants, the council reported, *"26 gave a blood picture characteristic of benzol* [benzene] *poisoning; and this ratio of about one man in three affected was maintained even in those workrooms with efficient local ventilation. … We were therefore forced to conclude that … the use of benzol (except in enclosed mechanical systems) even when the workers are protected by the most complete and effective systems of exhaust ventilation … involves a substantial hazard"*[10].

In response to these reports of serious health problems in men working with benzene, a series of studies were conducted in cats, dogs, rabbits, guinea pigs and rats. These studies, like many carried out in toxicology at that time, chiefly asked how much benzene was needed to anesthetize or kill the animal and how quickly this happened. Animals were observed for minutes, hours or days to see when they developed jerky tremors, weakness and muscle contraction, and at what point they dropped dead. Their blood was examined after death for evidence of what benzene did. Animals that recovered from these exposures looked normal within days. But one study that injected much smaller amounts of benzene in rats found that it induced an array of symptoms, including loss of appetite, reduction in infection-fighting cells of the blood and tremors[10].

Based on this work, the safety council decided that benzene was a highly problematic material in the industrial workforce: *"We are forced to conclude that the control of the benzol hazard (except where the substance is used in completely closed systems) is exceedingly difficult; that in practice, systems of exhaust ventilation capable of keeping the concentration of benzol in the atmosphere below 100 parts per million are extremely rare; and that, even when this is accomplished, there remains a decreased, but substantial hazard of benzol poisoning"*[10].

Echoing this work nearly two decades later, the American Petroleum Institute in 1948 conceded that *"it is generally considered that the only safe concentration for benzene is zero". "Skin contact should be avoided. Acute poisoning by benzene should be considered as an acute emergency. … Chronic benzene poisoning is refractory to treatment. Practically all therapeutic measures attempted have failed"*[11]. The American Petroleum Institute today takes a radically different position on benzene, actively working to fund research that it expects will overturn national standards in many countries.

In 1949 a report in "Scientific American" by Groff Conklin featured a graphic display of *"carcinogens known to be present in human environment"*[12]. Asbestos was described, along with solar and ionizing radiation, chromates, tar, synthetic dyes, and arsenic, as causing cancer by physically damaging the body or chemically inducing malignant growth. The article offered a clear statement: *"Scientific and technological progress has exposed man to new physical and chemical agents. Some are believed associated with the rise of cancer as a cause of death"*. It is worth quoting Conklin's half-century-old views at length because the ideas are remarkably contemporary.

"The growth in the relative importance of cancer as a cause of death is one of the outstanding medical facts of the past fifty years. The disease has moved from eighth to second place in the United States since 1900, and today only heart ailments surpass it. The reasons customarily given for this change – improved diagnosis and an aging population – do not entirely explain it. They provide no satisfactory answer to the fact that 7.5 percent of the known cancer deaths in 1944 occurred in age-groups under forty. There is evidence, moreover, that the disease is not an inevitable consequence of bodily degeneration due to age, although the changes of senescence under certain conditions may be contributing factors. A net increase in true cancer deaths seems almost certain, if only because fewer people die from other diseases than in the past.

An explanation for this increase and for the causes of the disease is therefore being sought in the environment, so much more complex than it was in 1900. The investigation is focused on carcinogenic agents (the substances that produce cancer) and on the general question of the extent to which the increase in cancer may be caused by agents in the environment that have hitherto been considered relatively harmless.

It has been established that certain agents to which people are exposed through industrial occupations cause cancer if the exposure is sufficiently intense and prolonged. As an example, over 75 percent of the miners in the Schneeberg cobalt–uranium mines of Germany die of lung cancer; more than 50 percent of those in Joachimsthal uranium mines across the border in Czechoslovakia die of the same cause. In the eighteenth century it was learned that among chimney sweeps exposed to intense concentrations of soot, deaths from cancer were between three and four times as high as those in the general population. It is known also that certain common substances in concentrated doses can produce cancer; for example, mouth cancers are frequent in some people in India who smoke cigars with the lighted end in the mouth. Consequently they suffer frequent burns and receive a concentrated dosage of tobacco tars.

These cases of intense exposure arouse speculation as to whether relatively mild but sustained exposure to new substances in a contaminated atmosphere, in processed foods, in cosmetics and in other elements of our environment may be a contributory cause of cancer. We have as yet no conclusive *evidence for or against this possibility. We have no accurate estimate of how many of the artificial substances common to our industrial civilization may be carcinogenic under special circumstances, nor how many seemingly harmless substances, interacting with others that appear to be equally innocuous, may produce carcinogenic results.*

Generally speaking, however, employers are no more responsible for the lack of information about industrial cancer than are the many thousands of physicians who have cancer patients in industrial areas or who actually are associated with factories. An appreciable number of occupational cancers slip through the hands of doctors unidentified, due in a great degree to a general ignorance of the occupational aspects of cancer. Physicians have never been adequately informed of the basic symptomatic and sociological factors involved in identifying occupational carcinogenesis.

The medical profession should be better educated about the need for exhaustive case histories which carry the individual's jobs record in detail back as far as twenty-five years, about the urgency of checking medical suspicions of industrial cancer hazards against careful epidemiological studies of all workers in a plant, and about the paramount importance of impressing plant management with the seriousness of the problem.

The standard protective and hygienic measures currently used in industry to combat industrial poisons and other health hazards are not always adequate for the control of occupational cancer. The following case history is a compelling illustration. Some thirty years ago workers in one of the newer metal industries began to develop lung cancers. At that time the cancers were found to remain latent from ten to fifteen years. The incidence was unusually high when the carcinogenic substance was present in particularly high concentration as an airborne dust. An effort was made to safeguard these operations. Up-to-date equipment for removing dust and fumes was installed, and a standard industrial hygiene program was inaugurated, including protective clothing. But the outcome was exactly the opposite of what had been expected. The incidence of lung cancer did not diminish, and cancer began to appear among workers who had been exposed for less than six years, a much shorter period than had been previously observed. At the time when the protective measures were adopted, the factory had also begun to use a more finely ground material to improve production. The finer dust, though present in a much lower concentration than the original material, penetrated farther into the bronchial tubes. Thus despite the latest in protective devices and procedures, the cancer hazard was actually increased.

It is obvious, therefore, that the control of occupational carcinogenesis – and even to a great extent of cancers stemming from indefinite environmental agents, if and when they are discovered – is a public health problem of considerable magnitude. This is made even more apparent by the scope of a control program that has been proposed by Dr. Wilhelm C. Hueper, head of the new environmental cancer section of the National Cancer Institute. Hueper, one of the world's leading experts on occupational cancer, has studied the problem in the United States and elsewhere for many years. Several of the elements of his program have already been put into effect in European countries. The program proposes eliminating carcinogenic agents from industrial military and civilian use as much as possible and practical; enclosing manufacturing processes that use such materials; protecting the community by preventing the discharge of carcinogenic wastes; requiring the licensure and inspection of factories; providing workers with protective clothing, equipment and medical supervision, including frequent and thorough physical examinations"[13].

Four centuries ago some observant physicians laid down the basic foundations of public health research. By the 1950s, some scientists had developed a programme aimed at training physicians to recognize and reduce risks from workplace and environmental hazards. How do scientists today determine the health hazards at work or in the world around us? We do pretty much what Agricola, Ramazzini, Pott and Roffo did. We look around. We visit and talk to people who are going through natural experiments of their own sort to learn about the goods and bads in their life histories that could account for their health. In classic scientific experiments, results are contrasted between two groups that ideally differ in only one way. In public health research, we rely on our ability to compare groups that may differ in many ways, in order to conclude whether or not some of those differences account for why some are healthier or sicker than others. For workplace hazards, such as those that first fascinated Ramazzini, we compare various measures of wellbeing of those in some jobs with those in others. We ask and count what types and amounts of illness arise in those who work directly with certain agents. Where we can, we measure residues in air and water, blood and urine. We then contrast this information with what happens to those who lack such experiences.

We are left to wonder, if the top scientists from Italy, France, Germany, Argentina, America, England, Japan and Russia understood in 1936 that much cancer came from workplace, nutrition, hormones, sunlight, radiation and other external sources, and if the US National Cancer Institute had begun a programme to train doctors to look out for signs of these health risks and to promote their reduction by 1949, why were these efforts stymied? What happened to derail programmes to reduce the burden of cancer? Why have we spent so much effort treating cancer and so little understanding how to keep the disease from happening?

In the run-up to World War II as well as in its aftermath, science could not remain an abstract matter carried out because of the inherent curiosity of lone geniuses. Instead, scientific investigations became part and parcel of vital national efforts to conduct and carry out warfare. During the various early-nineteenth-century French revolutions, the philosophes had boasted – at least until some of them were beheaded for doing so – of the value of pursuing cross-national exchanges.

For humanity, the spectre of death and national conflict that began to course around the world in the second quarter of the twentieth century concentrated the imagination wonderfully. But it seldom did this in a way that inspired clear thinking about the future. The future got shorted by those who looked solely at the present.

As we have come to know, the mid–1930s, when the august cancer congress was held in Brussels, was an era of mounting hostility and widespread militarization of the most common aspects of life. As a committed Unitarian, the biologist Walter B. Cannon saw international scientific collaboration as a moral duty. He resisted nationalistic impulses to pull back from working and meeting with scientists from other nations. He journeyed to Leningrad, Russia – then in the grip of its own revolutionary violence – to meet his colleague Ivan Pavlov, the pioneering behavioral psychologist, in 1935. His address to this congress foretold the lapse of long-term interest in scientific matters, including the ability of chemicals and radiation to damage human life:

"During the last few years how profoundly and unexpectedly the world has changed. Nationalism has become violently intensified until it is tainted with bitter feeling. The world-wide economic depression has greatly reduced the material support for scholarly efforts. What is the social value of the physiologist or biochemist?"[14]

Cannon is known today for coining the term "fight or flight" to describe the physical response of living beings to life-threatening terrors. A chance finding of what made cats get their backs up under duress led him to a lifework examining the complex physical ways that bodies deal with danger, collaborating across oceans and national borders to do so[14]. When facing danger, the body mobilizes. A surge of hormones turns on the ability to fight or run harder, faster, longer. The heart beats more powerfully, energy surges throughout the body and the hair stands on end; every organ system is marshalled in defence against the perceived threat.

Nations do much the same. The prospect of massive, unrestrained global conflict fundamentally changed public priorities and altered the way science was supported and used by those who underwrite its efforts. The immediate need to defend against threats of Axis conquest trumped consideration of the longer-term results of leading crisis-driven lives. To be concerned with preventing cancer requires planning for and thinking about what will happen in a few decades. A world facing highly uncertain, potentially cataclysmic, prospects was not inclined to ponder the future.

Once the war was over (and a slower, colder war took its place), the old knowledge about cancer hazards fell victim to enthusiasm for modern industrial advances and the social and economic forces that lay behind them. A combination of optimism about the industrial future, *bona fide* improvements in the ability to see and grasp the basic biology of disease, and darker forces fuelling that optimism guaranteed that the burden of proving any modern activity caused cancer would become impossibly heavy. The search for more scientific information easily morphed into a reason to reject what had once been known. The sowing of doubt regarding the relevance of experimental science to explaining the hazards of tobacco provided a model that was easily extended to many other modern health dangers, including those of the workplace and general environment[15].

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