Chapter 4: Politics 1962-1966*

HANDLER'S MOMENTUM TOWARD national status in the politics of science began after he became an executive officer of the Biochemical Society and its recommendation of Handler for appointment to the Biochemical Advisory Panel was accepted by the National Institutes of Health. During the next decade, he was a major force behind the maturation of the Society's reputation and the growth of the Institutes' budget and prominence. Handler used the organizations as vehicles to implement his ideas and became a major author of their policies concerning biomedical research. The Society was a loyal and vocal constituency for Handler, and the Institutes provided a level of research funding that enabled him to lift the biochemistry department at Duke University from obscurity to national stature. Handler's achievements led to his national recognition as a manager and organizer and authoritative spokesman for biomedicine and biomedical policy. His celebrity was not like Einstein's as perceived by the public but rather like that of a sciency man as perceived by academic biochemists and congressional budget committees.

Handler was animated by the love of basic biochemical research, an activity he called "pure" because it was done for its own sake rather than some foreseeable useful purpose. He saw basic biochemical research as a magnificent, intellectually stimulating undertaking — the scientific basis of biomedicine in the sense physics was the basis of technology. After Handler recognized that his nutritional research at Duke was only mediocre, and unlikely to ever reach the level of sophistication displayed by top-tier biochemists, he shifted focus from doing pure biochemical research to developing research policies regarding what basic research was, why it should be done, who should do it, and where it should be done. He assumed the research would be paid for by taxpayers because he believed they would be the ultimate beneficiaries. His vision of science became more mystical, what would be called quasi-religious were he not an agnostic.

Handler conceptualized research as an endless frontier where biochemists would discover exhilarating biomedical knowledge if the government provided sufficient funds and allowed biochemists the freedom to pursue their ideas. For years, he campaigned assiduously in congressional testimonies, during personal contacts with congressmen, and in many public speeches seeking to gain governmental recognition that biochemists had a right to do government-supported research without any requirement that it yield a particular societal benefit. The explicitly unfettered federal funds for basic biochemical research he sought never materialized, but the Institutes' budget for applied biochemical research intended to discover cures for diseases spiraled upward. Even so, some basic biochemical research was legitimized in the eyes of the leaders of the Institutes by transparent lies that were routinely accepted by the Institutes' advisory panels — the same rhetorical device that fueled Handler's personal financial success at the Institutes. The device blurred the distinction between applied research and basic research, which the Institutes were legally barred from supporting because, by definition, it served no foreseeable public purpose but rather had as its main goal the personal edification of the investigator. Transparent lies enabled biochemists to undertake any research they desired provided they claimed it was pertinent to a disease — it didn't matter much which disease was

* This is a preprint of a manuscript that will undergo copyediting and review before publication in final form.

invoked because all diseases were styled as biochemical problems. No one could doubt that Handler's historically unprecedented fund-raising advocacy was the single most important factor responsible for annual increases in the Institutes' annual budget and the resulting growth in both applied and faux-applied biochemical research.

University education in biochemistry was strongly affected by Handler's activities. Appearing before congressional budget committees, he successfully invoked the disarmingly simple argument that if some biochemists were good for America, more biochemists would be better. In turn, the resulting annual increase in government funds for prominent universities to produce more PhD biochemists drove up the market for grants to biochemists. Their need for research grants to survive so that they could teach PhD students how to do biochemical research soon exceeded the money appropriated for research. The result was the emergence of "Dr Grant Swinger," an apocryphal archetypal biochemist who used pompous or pretentious biochemical syntax and rhetorical flourishes in the grant applications reviewed by the Biochemical Advisory Panel to outcompete other biochemists. Swinger's application contained language — like "novel," ground-breaking," "unprecedented," unique," and "innovative" — intended to emphasize the importance of preliminary data in a proposal and make it more appealing to the Panel than the applications of other investigators who proposed experiments in the same area.

Another outcome of the PhD glut was the erosion of the previously open and collegial nature of the relationships among biochemists. They became less cooperative and mutually supportive, and more contentious and secretive as they ruthlessly competed for the available federal dollars. When he testified, Handler characterized the problem of cutthroat competition among biochemists for grants as something good because it ensured that the Panel awarded grants only to the best biochemists. He also shifted the basis of his research-funding advocacy from the academic freedom and intellectual satisfaction of biochemists to the benefits he asserted society would reap if biochemists were well funded; he de-emphasized their putative right to perform basic research for personal edification.

Federal research spending was preponderantly purposed for applied research because, with few exceptions, the law required the objective of taxpayer-supported research to be the satisfaction of a particular public need or purpose. Defense-related applied research funded by the military services took place in government laboratories and universities. Nuclear applied research was carried out by the Atomic Energy Commission at government laboratories. Health-related applied research was funded by the Institutes and performed both in Institutes laboratories and under contracts in major universities. And more than two dozen other agencies funded applied research in their own laboratories to support their missions. The plural set of federal agencies that funded applied research sought their funding from a plural set of congressional budget committees where the agencies competed for their share of the federal dollars available for research.

In contrast to the use-inspired objective of applied research, the objective of basic research was the advancement of science itself. The National Science Foundation was a federal agency created soon after the end of the Second World War to manage federal-sponsored basic research in American universities. The Foundation had a microscopic budget and funded research only in physics — the sole science where basic research was conducted. Handler seized on the statutory mission of the Foundation to sponsor university-based basic research and decided the Foundation ought to also support basic research in biochemistry, and he pitched that idea to the Foundation's board of directors. Mindful of Handler's influence with congressional budget committees, the directors received his idea with enthusiasm and agreed that if he helped the them obtain increased funding, at least part of the increase would be used for basic biochemical research. Years later, Handler revealed that the agreement had electrified him because he saw it as a crucial step toward securing congressional recognition that biochemistry was a true basic science, like physics.

In 1962 Handler testified before the congressional committees that decided the Foundation's budget and sought acceptance of the idea that basic biochemical research was part of the Foundation's legal responsibility because biochemistry was a basic science, and also sought a concomitant increase in the Foundation's budget. "Since I am, professionally, a biochemist," he began, "I have a prejudiced and biased view as to what living things are; the view I should like to present is that which may be seen through the spectacles of a biochemist." Handler described vignettes from the history of biochemistry lampshaded to emphasize the importance of biochemical thinking for human progress. He said that what life actually was and how it got started were deep philosophical questions, but not scientific questions because no one could do laboratory experiments to investigate life itself — only the biochemicals extracted from living things could be studied.

Handler tersely explained his concept that a human being was a mixture of about 2000 different biochemicals, almost all of which the body manufactured using the biochemicals and energy in food. The problem, he said, was to understand "the stepwise manner in which we convert the biochemicals which we eat into the biochemicals which we are." The thrust of his testimony was that biochemists could explain how the human worked if they had more money to do basic biochemical research, which he indicated the Foundation would fund if its budget were increased.

Handler told the committees that biochemists had only recently identified the chemical composition of abnormal genes responsible for some hereditary diseases. If sufficiently funded, he said, biochemists might one day be able to show clinicians how to treat heritable diseases by replacing abnormal genes with normal versions. Handler speculated routinely, knowing from experience that speculative testimony about what he thought biochemistry might do to help people had a strong positive effect on congressmen and other laymen, who had no frame of reference to evaluate the speculation. Sometimes he walked back the implications of what he said to avoid sounding like Dr Pangloss — regarding gene replacement, he conceded his idea "has serious moral implications for the future." The consistent thrust of his stories was that, given enough time and money, basic biochemical research could do anything: cure cancer, explain how the brain works, and grow new tissues to replace those that were diseased or damaged, as examples. Privately, he characterized his naïve and unreasonably optimistic fictions as a "minor deception for a major good," by which he meant they often resulted in more money for biochemical research.

Handler wanted money for basic biochemical research, and he wanted the research done at elite universities, which was where the best biochemists worked. He promised the committee members that biochemical research proposals sent to the Foundation would be vetted similarly to the way funding decisions were made by the Biochemical Advisory Panel at the Institutes which, more or less, regarded the elite universities as its main clients and supporters. But the geographic maldistribution of the research funds awarded by the Institutes for applied biochemical research had become politically contentious — either favored or opposed by budget-committee members, depending on whether or not their state had an elite university. During his testimony for the Foundation, Handler was asked whether "we would be better off if we took all of our money and spent it at Duke, Johns Hopkins, Harvard, MIT, and some of the other great universities in the nation." Handler replied that if the amount of money for basic research were unlimited, all biochemists could get some, otherwise "you give it to the very best scientists you have," and he touted the efficiency of Biochemical Advisory Panels for determining who was best. He said the Institutes strictly followed the Panel's advice because it was composed of "biochemists of stature" from the nation's best universities, and that the advisory-panel system was "admirable and served the nation well," and promised that the Foundation would do the same thing.

Handler had a keen appreciation of the of the political considerations involved in funding science. He knew how little politicians understood about science, how much they respected him, and how popular scientific research was with the public. He told good stories and always satisfied the desire of committee members for short, jargon-free answers to their questions. The budget committees accepted his promise that basic research in biochemistry would directly benefit humanity, and increased the Foundation's budget. The amount authorized was relatively small but significant because it effectively raised biochemistry to the intellectual level of physics, at least in the eyes of the Congress. Handler received much credit for his testimony from both biochemists and physicists. Historically, the physicists who supported Handler's appearance before the budget committees acknowledged that they had never sponsored a congressional witness who spoke so persuasively in favor of funding of basic research.

AT THE SAME TIME HANDLER'S STAR waxed nationally, his interest in Duke waned. During his years there, while he was raising millions of dollars from the Institutes and tobacco companies for basic biochemical research, he had also raised money for another long-held goal — a program for training medical students to be biochemists. Handler's basic idea was that a physician who had a PhD in biochemistry was the ideal individual to perform biomedical research and bring clinical medicine into the modern world. At first, every public and private philanthropy from which he sought financial support declined to fund his plan. As Handler's national reputation grew, supporters appeared and he raised the money he needed to implement an academic program he designed whereby Duke medical students who were willing to spend two additional years working in his department could get a PhD in biochemistry as well as an MD degree. Handler secured the support of the chemistry and physics departments, but not the medical-school faculty nor its dean, who strongly opposed the program and called Handler "a political scientist who had doomed practical medical education." He said Handler was someone who "except for training graduate students in biochemistry, had very little contact with medical education, and as far as I can ascertain, that contact has not been beneficial to the medical students." In the end, the administration accepted the money and included the program in Duke's curriculum, but it was just another Pyrrhic victory for Handler — like the outcome of his struggle to create a new Institute dedicated solely to basic biochemical research — and equally disappointing to him. Only a tiny handful of medical students enrolled in the PhD program and his efforts generated considerable long-lasting antagonism; the dean said, "Phil Handler was the worst thing that could have happened to everybody."

As Handler later mused, his career was at a crossroads. The Institutes were well funded by Congress and he had become a permanent part of the upper echelon in the biochemical community. He established pointillism as the basis of Institutes research, effectively making biochemistry the basic science of medicine. His policy of not funding disease-causation studies obviated the possibility of political controversies like those involving tobacco, and his connection with the Institutes facilitated his expansion of the biochemistry department at Duke by twenty times. Despite what he had achieved, the Institutes funded only a minuscule amount of basic biochemical research, and he realized the support for it that he had visualized would never materialize at the Institutes. He decided he could do no more there, or at Duke. He believed he was capable of achieving more in life than just elevating the Institutes and producing PhDs in biochemistry at Duke.

Handler could have become chairman at another elite university, but there was no biochemistry department anywhere that was larger or richer than his. He was offered a deanship at a medical school, but was sufficiently perspicacious to recognize that his chronically disdainful attitude toward physicians would lead to continual conflicts with the faculty. He received job offers from industry, mostly for board membership at companies seeking to benefit from his national stature and connections. He accepted a position as a board member of a drug company, but the responsibilities and remuneration were minor. Some offers were for actual corporate management positions at salaries far higher than his salary from the Institutes, which they paid via grants administered by Duke. However, the jobs were poor fits with his autocratic management style and he decided the financial rewards didn't warrant accepting the uncertainties entailed by a corporate lifestyle.

Unexpectedly, President Kennedy's principal science advisor offered Handler a position on the board of directors of the National Science Foundation. Even though the position was only part-time and unsalaried, it greatly interested Handler because the board made national policy about university-based basic research. The research it funded was chosen by the individual investigators, not the government, which Handler believed was the right and proper attitude of the government toward basic research — that it made no more sense to tell physicists what research to perform than to tell poets what verses to write or artists what paintings to produce. Handler believed the position would make him more effective in securing increased unrestricted federal support for basic science in both physics and biochemistry, but accepting the offer entailed serious financial and health considerations.

Consequent to the ethical slumber of the board of directors of the Institutes regarding conflicts-of-interest, Handler and his department were brimming with financial support. The administration of the Institutes agreed to continue paying Handler's salary via research contracts with Duke, and to allow the contracts to be managed by others at Duke, if Handler agreed to continue testifying for the Institutes as well as the Foundation. The arrangement would effectively cap Handler's income at a relatively low level for a man of his abilities and accomplishment, too low for him to maintain the large house he had built in Durham and also acquire a house in Washington, where most of his professional activity would occur. Accepting the board position at the Foundation therefore require Handler to split his family, with his wife and two sons remaining in Durham while he was in Washington. The stress engendered by the split-living plan was a potential health threat to Handler and his wife because they both had chronic medical problems. Handler was thin as a rail and worked more than twelve hours a day, believing his daily vitamin regimen helped his body extract the necessary energy from food. He smoked heavily, suffered from chronic intermittent and sometimes incapacitating headaches, various allergies, and diabetes. His wife's multiple sclerosis was progressively worsening, with occasional remissions, and she was confined to a wheelchair; she received orthodox medical care, but he self-medicated because he had no confidence in physicians. In the end, Handler decided the rewards of the new position outweighed the associated problems and difficulties, and that the time had come for him to move on. He accepted appointment to the board and adopted a lifestyle of living in an apartment in Washington and continually traveling back and forth to visit his family in Durham.

The first time he testified for the Foundation he said the Foundation's budget the previous year was inadequate, and had forced physicists and biochemists who received Foundation grants to work "on their knees instead of their toes." The size of the increase, Handler said, resulted from a lack of understanding of the Foundation's mission, and he explained why more money was needed:

> Science ultimately produces the jobs which the American people will use to support themselves. Science produces the civilization in which we live. Science expands man's understanding of himself and the universe. The philosophy of the Foundation is that science is in the national interest. I think this is a platform on which one can stand and request more money. While it is quite true that the budget is increasing, the increase is not beyond our national capabilities and not an exorbitant one in any sense.

Handler experienced a push-back from the committee which claimed that the money was being awarded by scientists to other scientists with no effective oversight regarding the wisdom of the studies funded. Handler strongly disagreed:

> The scientists on the panel that authorized Foundation grants were the harshest critics possible of the research proposed by their colleagues and could be trusted to make good decisions, far better than other folk looking in from the outside. We think they spend the money intelligently and well and wisely.

SOON AFTER HANDLER COMPLETED his 1963 annual round of testimony seeking budget increases for the Institutes and the Foundation, President Kennedy was assassinated and authority to determine national science policy passed to President Johnson. He was interested in social programs, especially medical care, and one of his first initiatives was the creation of a Commission to recommend steps to reduce what he called "the burden and incidence" of heart disease, cancer, and stroke. He appointed a heart surgeon as chairman and charged the Commission "to reduce the incidence through new knowledge and more complete utilization of the medical knowledge that we already have." President Johnson envisioned a practical medical approach based on developing new methods of treatment and identification of their causes so that the diseases could be avoided, and he told the chairman to "think big" regarding the cost of the recommendations. His advisors urged him to appoint a biomedical scientist to the Commission so that its recommendations would have the scientific gravitas needed to satisfy the congressional budget committees. When he was interviewed for a position on the Commission, Handler called himself "a biologist who specialized in biomedicine" and emphasized the need for increased university-based basic research into "the biology of disease." He was reluctant to accept another part-time unsalaried job, particularly because he had a low regard for the scientific prowess of the President's choice of chairman of the Commission, who was a surgeon. Handler agreed to serve on the Commission after he was made chairman of its research committee, which effectively was a committee of one, and assured that his recommendations would be included in the final Commission report exactly as he drafted them.

Handler planned to rationalize recommendations for large university-based basic biochemical research that far exceeded the ongoing efforts of the Institutes. Early in the spring of 1964 he was given a suite of offices and a staff to support his efforts, and appointed to the President's Science Advisory Committee — his formal entry into the nation's highest levels of science policy-making. The committee was mostly composed of politically knowledgeable physicists including Frederick Seitz, who was the president of the National Academy of Sciences. About a month later, Handler was appointed to a leadership position on the board of directors of the Foundation and, with Seitz's support, elected to membership in the National Academy of Sciences. Handler was also invited by Seitz to write a chapter in his book about the relation between science and government.

From its inception, the Commission consisted of two incommensurable activities that proceeded independently. The chairman of the Commission concentrated on identifying steps to find the causes of heart disease, cancer, and stroke, and on promoting clinical research aimed at improving diagnosis and treatment of the diseases. Handler's objective, in contrast, was to posture and present as the collective judgment of American biomedical scientists what had long been the objective of his congressional testimonies — unrestricted freedom for biochemists to conduct basic biochemical research. It was Handler's view that improving diagnosis and treatment of heart disease, cancer, and stroke was impossible without first carrying out his research program. The Commission marshalled pertinent clinical information, and Handler directed his effort at compiling numerous supporting opinions from biochemists who shared his views about the best path to accomplish the President's objectives.

Handler sent a form letter to numerous American scientists, all chosen according to his lights, only some whom he identified publicly, and none of whose responses he disclosed. The letter was the antithesis of what could be expected to elicit reliable, coherent, justified scientific information that could justify the multi-billion dollar biochemical research program Handler wanted:

> Dear Dr. ________________
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> In pursuing its task, the Committee on Research of this Commission has deemed it desirable to collect a series of brief but highly authoritative statements or essays summarizing the current status of various segments of the problems before us. On behalf of the Committee therefore, it is my pleasure to ask whether you can prepare such a statement with respect to:
>
> *Topic inserted*
>
> The specific title above is not meant to confine or limit you unduly. Please feel free to alter the title as you see fit and address yourself to such related subject as you may prefer.
>
> It is our hope that this statement might be comprised of four sections. First, we should like you to summarize those cogent facts which, in your view, are of prime significance for understanding and progress within this field. Second, we should like some definition of the current boundary between knowledge and ignorance. Stated otherwise, this would be a delineation of those important problems, which in your view, seriously warrant exploration at this point in time. Third, we would be happy to have a few paragraphs of "blue sky" thinking in which you would be at liberty to discuss possible modes of experimental attack or research ventures, large or small, within this problem area. Fourth, such thoughts as you may wish to express concerning the organization of research in this field, the need for support, the limiting factors, etc., will be extremely welcome.

This essay may be of such length as you find convenient, i.e., from three or four pages to ten times that length should you find this necessary or desirable. It is intended to be your view of the situation at this moment in time, a view which you could substantiate and document in the normal manner under other circumstances, but which, at this time, can probably be prepared “off the top of your head" and with little need for consultation of the prime literature. All such essays will be included in a single volume which will be published as part of the final report of this Commission. Accordingly, it is likely to receive rather wide circulation. And, in turn, this will indicate that the report should not be documented with the usual references. It is not intended for the normal scientific literature but is to be read by both professional and lay personnel. These comments may perhaps also serve as a guide with respect to the language of this report.

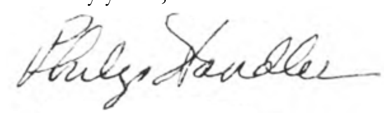
Because of the mandate given to the Commission by President Johnson, I regret that relatively little time can be made available to you for this preparation. It seems imperative that we set as a deadline for receipt, Friday, June 12. Although this seems an outrageously short time, by that very token you will understand that we are not seeking a scholarly effort equivalent to that which is normal to the scientific review literature but rather, as indicated above, a status report of this field as it seems to you from your own personal professional vantage point at this moment.

The Committee joins me in hoping that you will find it possible to accept this invitation.

Enclosed herewith is a notification form which we should like to have at your very earliest convenience.

With all best wishes and kindest regards

Sincerely yours,



Philip Handler
Chairman, Committee on Research

Handler’s rambling set of topics was perhaps fit for a biochemical textbook but essentially irrelevant to the Commission’s objectives:

- Can Hardening of the Arteries Be Prevented by Appropriate Choice of Diet?
- The Role of Electron Microscopy in Cancer Research.
- Significant Features of the Growth of Mammalian Cells in Tissue Culture.
- Endocrine Factors in the Etiology and Pathogenesis of Cancer.
- Endocrine Factors and Neoplastic Growth.
- Ionizing Radiation in the Genesis of Cancerous Change in Cells.
- Etiology and Pathogenesis of Arteriosclerosis.
- Chemical Inhibition of the Growth of Normal and Malignant Cells.
- Hypertension.
- Lipoproteins of Serum and Tissues.
- Permeability and Transport with Particular Reference to Cancer.
- Progress and Prospects of Viral Tumor Genesis.
- Cancer Cells in Light Microscopy.
- Chemical Agents in the Genesis of Cancer.
- The Role of the Thymus in the Reaction of the Host to Cancerous Cells.
- Current Understanding of the Mechanisms of Cellular Differentiation.
- Immunological Defects in the Individual Afflicted With Cancer.
- The Antigenicity of Malignant Tumors.
- Inheritance of the Tendency to Cancer.
- The Kidney in Hypertension.
- Endocrine Factors in the Etiology and Pathogenesis of Cancer.
- Metabolic Abnormalities in the Host:Tumor Relationship.

- Transport Processes in Tumors.
- Summary of Chemical Carcinogenesis.
- Reaction of the Host to Transplantation of Cancer Cells.
- A Biochemical Basis for the Genesis of Cancer.
- Physiology of the Failing Heart.
- Metabolism of Adipose Tissue.
- Chemical Inhibition of the Growth of Normal and Cancerous Cells.
- A New Cause for Stroke.
- Inhibition by Ionizing Radiation of the Growth of Normal and Cancerous Cells.
- Ionizing Radiation in the Genesis of Cancerous Change in Cells.
- Contributions of Electron Microscopy to the Understanding of Brain Tumors.
- Metabolism of Neoplastic Tissues.
- Experimental Cerebral Infarction, Embolism and Hemorrhage.
- Endocrine Factors in the Etiology and Pathogenesis of Cancer.
- Etiology and Pathogenesis of Myocardial Infarction.
- The Metabolism of the Arterial Wall.
- Physiology of the Individual Afflicted With Cancer.

At the end of the process, which took almost a year, Handler wrote “Report to the President.” He said he used the diverse disconnected biochemical comments he had solicited as the basis for his philosophy and recommendations, but the truth was different. The Report contained crystallized characterizations of the philosophical attitudes and beliefs he first acquired as a sixteen-year-old college student when he read *Arrowsmith* and heard his college professor’s lectures, and which he had subsequently promoted during many speeches and congressional testimonies. Whatever information he might have harvested from the scientists he contacted, it had no material effect in shaping the recommendations in his report because they were exactly the same as those he had made many times in the past, with the exception of their vast increase in cost.

In the Report, Handler envisioned a medical utopia in which heart disease, cancer, and stroke would be entirely eliminated from the earth by means of biochemical manipulations, if the government provided the requisite amount of money for basic biochemical research. He made no promises that such a research program would be successful because, he said, scientists never promise they will discover something regardless of how much money they are provided. He wrote, “Promises that the research will certainly lead to a means of prevention or cure are extravagant and irresponsible.” According to him, the money would produce "clues and leads” from pointillist biochemical studies, but that didn’t necessarily mean heart disease, cancer and stroke were “truly susceptible to control, and promises to such effect have no current validity.” He recommended construction of twenty-five institutes devoted to pure biochemical research, thirty institutes devoted to applied research involving heart disease, cancer, and stroke, and changes in the federal contracting rules with universities to award increased funds for research overhead costs. The system Handler proposed differed only in scale from the existing system for supporting research operated by the Institutes and Foundation. Public funds would be administered by private citizens who would control the new institutes which would perform important government functions including the production of scientific knowledge, development of policies for how it should be accomplished, and assessment of its meaning and value for the public.

The work of the administrators of the new institutes would be done in near total secrecy, as if the creators of the system had no faith in the democratic processes. Handler was advised by other Commission members not to submit the recommendations because the cost was prodigious and the likelihood of implementation was nil, and that the President was interested in practical results which led to better utilization of the existing medical knowledge. But Handler had been promised that his proposals would be submitted to the President Consequently, at his insistence, each of his recommendations appeared in the Commission's final report, along with an extended rendition of his opinions and policies regarding why his recommendations should be implemented.

Handler's section of the Commission report was an argument for and a defense of his long-time objectives. The biochemical societies gave their full-throated support, as did some congressmen who seemed to honestly believe in the integrity of Handler's plan. But the president's advisors and many congressmen were stunned by the cost, as was the President; a report appeared that he remarked "When I said think big I didn't mean that big." Contemporaneous news stories described what was called Handler's serious lack of judgement regarding the political circumstances. The President was trying to initiate momentous social changes. He sought and won government financial support for the poor, health care for the elderly, changes in civil rights aimed at ending the social inferiority of blacks in the southern states, and official government warnings that cigarettes cause cancer, all while directing a war in Vietnam. In comparison, Handler's push for basic biochemical research was an insignificant issue.

Handler's recommendations were not seriously considered, and federal support for research that sought cures for heart disease, cancer, and stroke remained centered in the Institutes, which was where the board of the Institutes stoutly maintained the support should remain. He was sorely disappointed but continued to pursue his own objectives and publicize his own policies while remaining a nominal part of the administration and a political supporter of the President. He became chairman of the North Carolina chapter of a group of scientists, engineers, and physicians that supported the President for election to the presidency. According to Handler, the chapter was formed under the assumption that the training in science of those in the group uniquely qualified them to take a public position regarding who would be the better president, and the election of the President's opponent "would be a national catastrophe." Handler's support was recognized by the President who, soon after he was elected, invited Handler and his wife to the White House as guests at a formal State dinner in honor of a visiting head of state.

HANDLER WAS A PRESIDENTIAL science advisor, an officer of the Institutes and the Foundation and the Biochemical Society, and an employee of Duke University. He had opinions about diverse areas of science policy which he propounded in speeches, interviews, congressional testimony, editorials, and public appearances. Typically, however, his science-policy opinions were inscrutably linked to the views of his patrons because he rarely identified whether he represented only himself or also the views one or more of his affiliated organizations. Instead, almost always, like a shell game at a carnival, he invited the listener to imagine which organizations supported the opinions he espoused, and he suggested that one or more of his organizations supported or at least were pleased to hear one or more of his opinions.

Handler continued seeking funds for research on heart disease, cancer and stroke, but without intensity. He thought the public believed the diseases could be cured by drugs, the pursuit of which was an activity suitable for drug companies, not university-based biochemists who worked primarily to elevate biochemistry itself. He shifted the thrust of his fund-raising efforts for basic biochemical research to diseases caused by bad genes, and sought to convince the public and the Congress that discovery of cures for genetic diseases was possible. Such cures, if they were possible, depended entirely on basic biochemical research by university biochemists because only they pursued knowledge irrespective of its potential economic consequences. Handler had always made money for biochemists, and his thrust into genetics was an obvious part of that continuing effort.

Handler also approached his perceived need for biochemical studies of genes from another direction. At a meeting of biochemists, he opined that modern medicine was weakening the human race because it kept alive many persons with congenital defects who would otherwise have died, and that they were "spreading their harmful genes" when they had children. He said persons with congenital defects reproduced at a faster rate than normal humans and therefore, because of society's interference, evolution was favoring the propagation of genetic diseases that could lead to the stagnation of civilization. Basic research in the biochemistry of genes, he claimed, would likely lead to gene-manipulation techniques that allowed clinicians to eliminate defective genes or otherwise offset their consequences.

A desire to elevate his personal status as a biochemist was also a significant part of his motivation to direct national interest toward research involving genes. Famous, even Nobel-prize winning biochemists often sought Handler's help, but because of his connections not his knowledge. He had no illusion that he was a gifted biochemical researcher, but thought his professional reputation would be meaningfully elevated if he made a significant biochemical advance, and he chose evolution as the area in which to make the effort.

The validity of the theory of evolution was generally rejected by physicists, who viewed it as a violation of the thermodynamic law that said nature always moved spontaneously toward disorder, not order. But biologists regarded evolution as a bedrock principle that had importance in biology similar to that of mathematical laws in physics. Handler had an idea and organized a plan to bridge the incommensurability between biology and physics in the understanding of evolution by using the reductive method of physics in biochemical studies to prove its scientific validity. He believed proving a theoretical link between biochemistry and biology would enhance his status in biochemistry as well as the status of biochemistry as a science, and would also rationalize additional congressional support for the Institutes to fund gene-related university research.

Handler sought to show that every living thing on earth evolved from one individual living thing by analyzing proteins in present-day living things. Proteins were known to be the product of genes, and he reasoned that if the same protein occurred in everything that was presently alive, the logical inference would be that everything descended from one thing which was the original source of the gene for the protein. Handler himself had not worked in a laboratory for many years, but he arranged for a series of grants from the Institutes, which he assigned to biochemists in his laboratory at Duke with instructions to search for a protein that was present in every living thing from humans to bacteria and plants. When the biochemists found the same protein in a minuscule fraction of living things randomly chosen from all phyla, Handler declared in a series of speeches and newspaper interviews, and publications that, using only biochemistry, he had proven the validity of evolution. When he thus publicized the results of the research, he did not imply that he also spoke for one of his affiliated organizations, nor could he because the project was ill-conceived and stemmed from faulty reasoning. Indeed, many biochemists were amazed that he was able to obtain the funds to do the research. Handler soon ceased making his outlandish claim; however, at least for a time, he successfully stimulated congressional support for basic biochemical research on genes.

At a meeting of several thousand biochemists early in 1965, he defended the pointillist studies sponsored by the Institutes against objections that, to the average citizen, they seemed irrelevant or even bizarre, and proved nothing. He said criticism regarding the judgment of the administration and Congress, which had approved the use of tax money for the studies, was unwarranted and called the experiments "tools of progress. "Each adds a chink to the structure of scientific knowledge," he said. Advances in biomedical science would be impossible without chink studies and "it would be tragic if Congress or the American people ever were to think that they are trifles." He told the approving audience he hoped that public opinion would understand that biomedical science needed chink studies to "build tomorrow" and that biochemists needed more financial support to accomplish that goal. Handler never explicitly identified his clients, but few in the audience doubted that the Society and the Institutes were pleased with his speech.

Shortly thereafter, at a medical convention, Handler reassured the audience that the law establishing a system of health insurance for the aged would not be a disaster, as they feared. He told the physicians that no member of the federal government "has any desire to alter the traditional relationship between the patient and his physician or the economics of practice." Federal legislation regarding medical practice had not been disastrous in the past and would not be so in the future, he said, strongly implying he spoke on behalf on the administration, although he gave no indication he personally believed what he said. Some who heard the speech gained the impression Handler had no idea whether or not the insurance program would be a disaster and didn't care, and was simply doing his duty for the administration. When Handler spoke for Handler, who he represented was crystal clear.

Handler explicitly represented the Foundation when he testified before congressional committees, seeking to influence their decisions regarding the Foundation budget for basic physics research, which the administration was seeking to reduce. In contrast to biochemical research, which was usually conducted by a single investigator on a relatively small budget, physics research was controlled by large teams of physicists whose universities formed consortia that entered into long-term contracts with the Foundation. The costs were great because of the equipment needed — radio and astronomical telescopes, high-energy particle accelerators, and machinery to obtain samples of the earth's mantle from below the ocean floor. Handler was personally committed to increasing the budget because physicists had become an important part of his constituency. They were a key group that could influence his professional future because, despite the ascendency of biochemists, physicists still held most of the important positions where national science policy was formulated. Handler delivered his support for the big-science physics projects with a level of rhetorical skill never previously displayed by physicists who had appeared before the committees.

Handler conceded that no one could tell in advance what the value to society would be from federal spending in basic research in physics, but asserted that it would open new frontiers for man's imagination and lead to answers to two basic questions, "where we are in the universe and what we are ultimately made of." In support of research by physicists who studied clouds of gas that were billions of light-years away from earth Handler said, "Today no one knows what use humanity might make of the gas clouds, and we can only wonder." He countered congressional concerns that studying the clouds was a waste of money by telling a story about a short-sighted commentator who said it was inconceivable mankind would ever be able to use the energy inside an atomic nucleus and concluded emphatically, "they couldn't have been more wrong."

Handler also testified in favor of funding a long-term project by physicists who tested theories about the parts of the atomic nucleus. Although he personally knew nothing about the subject, his lecture to the members of a budget committee was seemingly erudite:

> Physicists discovered that the neutron and proton that make up the nucleus of the atom are themselves composed of parts, and that the parts differ from one another in baryon number, parity, spin, charge, mass, and strangeness. But the parts displayed no order in the measured values of these parameters. It was utter chaos. Great moments in science come when someone brings order out of chaos. In the last century, Mendeleev created the periodic table of elements and thereby brought order to our understanding of the behavior of chemical elements. With the support of the Foundation, physicists discovered the omega-minus particle, which brought order to our understanding of the subatomic particles. This is one of the great intellectual feats of our time, because it has this hallmark of bringing order out of chaos, and in this case, revealing something of the very most intimate nature of matter, what the stuff is of which everything in the universe is composed.

At that time in history, race riots gripped the nation's big cities, U.S. involvement in the Vietnam War was escalating, there was a civil war in Cyprus and a Marxist revolution in Cuba, and earthquakes occurred in Alaska and Japan. Nevertheless, according to Handler, discovery of a particle that existed for only a millionth of a millionth of a millionth of a second before it disappeared evidenced how basic research in physics benefited humanity and how the Foundation was using taxpayers' money for appropriate social purposes.

A year later, Handler reprised his testimony on behalf of the Foundation, seeking to stem the tide of administration-recommended cuts in the Foundation's budget for big-physics projects in basic research. By the time he joined the board of directors of the Foundation, it had spent several hundred million dollars over a decade while managing a basic research project in physics conducted by the National Academy of Sciences. The project involved drilling core samples of the earth's mantle, and was bungled by the Foundation, which had failed to properly oversee the details of financial decisions made by employees of the Academy, who were building a drilling rig to bore holes in the ocean floor through the earth's crust to study the composition of the earth's mantle. The steep rise in the cost of the project and the nil results it produced reflected adversely on Seitz, the Academy president who had approved the project and used his influence at the Foundation to obtain the necessary funds.

Seitz was a renowned scientist and sole author of the seminal text about the most technically significant branch of physics in the twentieth century. During the Second World War, while Handler was teaching biochemistry to medical students, Seitz was working on radar, explosives, and fundamental problems in the physics of solid materials — work that led to the invention of the transistor. By the early 1960s, he was a physics professor, senior consultant to the President and the Defense Department, and on a part-time basis, president of the Academy. Although less than a decade older than Handler, he was in a powerful position to influence the government's science policies, which he did by means of political activity rather than public speeches and congressional testimony because he lacked Handler's rhetorical skill.

Handler was asked by the Foundation and Seitz to defend the drilling project against sharp congressional criticism. With unprecedented aplomb, he testified that the continuous escalation in costs did not evidence mismanagement but rather indicated the courage of both the Foundation and the Academy which managed the project , neither of whom changed what they were doing even though they knew their actions jeopardized the budgetary acceptability of the program by the Congress. "Unfortunately," he said, "there seems to be no way to avoid such escalations in cost if one is to take bold steps forward in science," and was aggressive in his responses to hostile committee questions. He said the research project was "very exciting because it offers all sorts of possibilities for explorations for many other purposes." When asked, "What are all these other fantastic things you are talking about?" Handler replied, "We might learn what caused waves in the ocean and about how it interacts with the atmosphere." The response prompted a senator to ask, "You are going to run a $45 million platform around the ocean to discover that?" to which Handler replied that the physicists could build several platforms and place them around the world to do "all sorts of useful experiments." When a senator asked what it was intended to accomplish, Handler said, "Science is not predictable. That is the fun of it." "The fun of it?" the senator answered. "It is my belief that we are trying to develop a project here in order to satisfy the curiosity of scientists." Handler responded, "It depends on how you use the word 'curiosity.' The project is an attempt to see the planet on which we live. It has been shown in the past that to do so has great value to society generally." Although Congress cancelled the project, Handler gained enormous respect in the eyes of physicists, especially Seitz, for his efforts to protect it. By stubbornly defended a fatally flawed basic physics research project against near-certain congressional rejection, like Leonidas at Thermopylae, Handler cemented his credibility as a spokesman for basic research.

At the request of the administration, Handler attended an international symposium on the role of science in the twentieth century and delivered a week-long series of lectures he titled the "Frontiers of Science." He offered a litany of opinions about science policy, many of which were far outside what the administration espoused. On the first day, he said:

> I share President Johnson's concern that medical science should move as rapidly as possible toward the alleviation of all major disease. But more basic research must be done first. Basic research will make possible development of new goods and services. But for that to happen, it is imperative we explore the frontiers of physics and biochemistry.

He said that process had already started, but only in the U.S. because it was the only country in the world that entered the scientific revolution, which he explained was the dependency of society on brainpower rather than water, coal, or iron as in the industrial revolution. The greatest consequence of the scientific revolution, he said, was the realization that science was the new frontier for man's imagination. He said:

> Science seeks to answer where we are and what we are, not who we are, which is a question for religion to answer. Religion is an invention to stabilize the status quo whereas science lives to change.

Handler told the audience that the question of where we are was answered by physicists and he explained in detail how the universe had been formed over billions of years. He said that physicists were drilling a hole through the mantle of the earth "to find what is down there."

The next day, Handler said that a search for a universal gene to prove that all living things descended from a common ancestor was ongoing in a multi-million dollar project in his department at Duke. He said life began almost 3 billion years ago in a bacterium and that he had found the proof — a protein that is universally present in living things.

The following day, Handler contrasted the great advances made by science with what he said was the "utter failure" of political, religious and ethical structures. He admitted he was an agnostic and wondered aloud "if there is not some other way to find salvation than through philosophical devices." He said, "There are no aspects of human behavior or identity that cannot be explained in chemical or physical terms. I know this is a terrible thing to say. It removes the mystery from man. But as we look closer into man, we find that the 'soul' spoken of by Socrates is in the brain." Handler also told the conference participants that he believed most of humanity lived in a state just "a little above the animals," and had little time for values and ethics. He said Descartes' "I think, therefore I am" would be better if he had said "I eat, therefore I am" because "hungry people have no thoughts of anything but eating." Handler mocked the claim by some that the recent increase in scientific knowledge had brought more world problems than happiness, saying "I'd rather discuss philosophy on a full stomach," and "if science isn't making man perfect, it is at least making him more comfortable."

In the next lecture, Handler warned that population growth was the most serious problem facing humanity, and that unless the problem was recognized and solved, human degradation and war were inevitable. He said, "If one species begins to outstrip the others, the whole system gets wrecked. And this is what's happening to us. The human population is outstripping the rest of the organisms." "Biochemists and biologists know," Handler said, "that if one kind of animal multiplies to the point of not being able to get enough food, they will invariably fight to fulfill their basic need for food. "It is imperative that people understand the incredible magnitude of the rate of the increase of humanity, and that preventive measures be taken to control population growth if misery and war are to be avoided. Unless this is checked, it really threatens to deprive humanity of the benefits which might have accrued from man's brain power."

In his last lecture, Handler said he believed biochemistry was the ultimate science and will produce the greatest amount of knowledge that is useful for the benefit of man. He listed genetics, the brain, and cellular differentiation as the most important areas of biochemical research and described each area. He said biochemists had made great progress toward understanding genes and were working to gain further knowledge in the hope of one day manipulating them so that hundreds of hereditary diseases could be eliminated. Over a period of several hundred years, he predicted, more intelligent human beings could be produced. Little progress had been made regarding the brain and differentiation, he said, but the situation would improve quickly if the requisite biochemical research were funded. Seemingly knowledgeable, Handler explained what differentiation was and why knowledge about it was important:

> In the period right after human conception, all cells of the embryo are alike. But as the embryo develops, differences in its cells become more and more pronounced until eventually some 100 different cell types can be recognized in a human birth. Some of the cells become brain, others muscle, others liver, others connective tissue or various other parts of the body. Yet all of these cells have exactly the same genetic information in their nuclei, and the question is: how do they come to be different — what mechanism is at play that results in the differential process that finally gets you a human being? A cancer cell Is a cell that has reverted to behaving like the earliest cells of the embryo, before differentiation has taken place. If we knew enough about how cells differentiate, and why the cancer cell reverts, we might be able to devise rational means to control the disease. More understanding of cell differentiation might also explain why a lobster which has a claw torn off can grow another, and thus point the way toward helping a person who has had a limb amputated to grow another in its place.

He said the brain, cells, and life itself would be explained by chemical energy, like it explained genes, when more basic research was done. Handler conceded that, if left alone, many biochemists would ignore the immediate problems of disease and concentrate on the esthetics of biochemistry. These biochemists wanted more money for basic biochemical research and preferred to defer direct attacks on disease to others, but in the long run, he argued, it was the approach that best served the interests of the nation. Modern societies support biochemical research for both purposes, said Handler, allowing some biochemists to amuse themselves in the hope that something good for society will occur, and other biochemists to concentrate on translating the results into something practical. Both kinds of biochemists would educate medical students, thereby producing physicians in sufficient numbers to provide adequate care for all members of society, and would educate new biochemists in the intricacies of basic research, thereby indefinitely ensuring continuation of the upward spiral of theoretical and practical knowledge. The President's other science advisors disagreed with Handler and maintained that regarding the personal preferences of biochemists as sufficient justification for them to be given government research grants was arrogant pretense. The exceptions were several physicists who support Handler's views, but only as applied to basic research in physics — they were as silent as a stone regarding Handler's "New Frontier" approach to funding for biochemical research. Without basic biochemical research, Handler said, our society would "be as primitive and superstitious as the ancient Greeks;" there would be no post-graduate education, hence no basic biochemical research and therefore no new technology

HEALTH OFFICIALS IN THE ADMINISTRATION as well as the cancer society accepted the reliability of epidemiological studies that showed smoking was strongly linked with cancer. However, tobacco was economically significant and socially popular, so smoking was not banned and subsidies to tobacco farmers continued. Handler's attitude about tobacco was initially shaped by his personal addiction to cigarettes, and by the politics in North Carolina which he explained late in his life:

> I was asked to run for Congress but I refused. You can become a Congressman from North Carolina only if, at every opportunity, you vote to support the tobacco industry, which I could not do. You cannot be a Congressman from North Carolina if you do not do that. You can't

> get elected. The tobacco farmers and the industry in North Carolina are in an alliance. It is very much like the old alliance between the Baptist ministers and the bootleggers that kept prohibition in force.

The development of his reductive philosophy of science and his experience at the Institutes completed the shaping process. During the Institutes' early studies of the health consequences of tobacco smoke, no chemical constituent of the smoke was identified as the cancer-causing agent.
Handler argued that the negative results probably meant that there was no toxic chemical in tobacco, and he opposed further research by the Institutes because he viewed avoidance of studies of cancer causation as a politically wise strategy. Handler supported the administration's policy toward tobacco, which was based on politics, because it was the same as his policy, which was based on biochemical dogma as well as politics.

Technological development was occurring rapidly in the U.S. at the time. Commercial production of plastics, pesticides, herbicides, detergents and other synthetic chemicals was continuously increasing, and electromagnetic power was being manufactured at unprecedented levels by nuclear and fossil power plants, transported through a national powerline grid, and radiated by radio and television towers. The numerous chemicals and diverse array of man-made forms of electromagnetic energy ubiquitously present in the environment were absorbed into the bodies of humans and animals. The result was the quintessential health-related problem of modernity, the possibility of side-effects — harm due to unintended consequences caused by legal products. In situations where absorption caused instantaneous harm, as in acute poisoning or electrocution, the government developed labeling instructions and rules to protect the unwary. However, cases occurred in which manifestation of harm was delayed to the point where a cause-effect association wasn't plainly obvious to laymen. The link between cancer and smoking was an initial instance; myriad subsequent cases occurred where the absorption was involuntary. Handler conceptualized such cases as a problem of biochemical toxicology and set a high threshold for their formal recognition by government.

During a speech at a meeting of a medical association, Handler warned the physicians that environmental pollution could cause medical problems in certain limited situations. As an example he pointed to nitrate pollution of rivers caused by nitrate fertilizers and leaching from manure piles on farms. Handler speculated that people living along polluted streams whose skin turned blue might be suffering from low blood oxygen levels caused by nitrate poisoning. He said he chose nitrate poisoning as an example of the health consequences of pollution to emphasize the importance of providing a biochemical nexus between a pollutant and a disease before concluding that pollution was a health hazard.

Handler's ultra-restrictive basis for recognizing health problems related to environmental factors conflicted starkly with a report by the president's other science advisors. They explicitly acknowledged the danger of a deteriorating environment because of pollution of air, soil, and waters. The President announced he was pleased at the thoroughness of the report which would "surely provide the basis for action on many fronts." Handler, in contrast, characterized the warning of the President's other science advisors as a vast overreaction to a problem that could be remedied by developing appropriate technology, which he emphasized would result from basic research.

Handler revealed another facet of his attitude concerning side-effects after he was appointed by the President to head a panel of science advisors on chemicals in the environment. Handler's panel was charged to recommend steps regarding how to make information available concerning the almost one hundred thousand new chemicals that were developed annually so that the public would be guarded against potential hazards. Handler examined the state of information about toxicology and concluded "there exists an urgent need for a computer-based file of toxicological information." The President established a computer system to make freely available the known information about the "poisonous potentialities of all chemicals and drugs used by man." But Handler didn't recommend that all new chemicals be tested on animals for possible side-effects prior to their dispersal in the environment, nor that the chemical companies contribute to the computer system the results of the testing they actually did.

In the area of side-effects from pesticides, especially DDT, Handler opposed the administration's policy. DDT had been used widely, but the possibility of side-effects due to cumulative poisoning from prolonged consumption of DDT residue in food had not been studied prior to marketing. Societal awareness of the existence of side-effects other than from tobacco first developed after the lack of pre-marketing testing of a morning-sickness drug resulted in the birth of thousands of malformed infants. After *Silent Spring* revealed the unintended environmental consequences of DDT, the government adopted rules regarding human exposure to pesticides that were based on a social policy of anticipatory protection of public health against side-effects, similar to the social policy which had been adopted that required pre-marketing testing of drugs before they could be sold for human use. Handler strongly objected to extension of the policy of anticipatory protection to pesticides on the basis that there was no biochemical evidence of the mechanism of action of DDT by which it caused any human disease. At first, he argued that such a link had to be proved in human studies where DDT was administered to the subjects. But he ceased so arguing after an article in a medical journal described numerous examples of unethical human experimentation; the article gained national attention, and made human experimentation politically impossible.

Government regulatory agencies recognized that gaining information about harmful side-effects after ingestion of particular levels of pesticides required the use of animals of as the test subjects. The agencies developed a testing strategy, the gold-standard study, in which laboratory animals served as surrogates for humans and provided scientific data about specific adverse physiological changes in relation to particular levels of the pesticide. Based on the data, agency scientists estimated the potential dangers to human health. Biologists and physicians strongly favored use of the animal surrogate method as the only practical scientific method for deciding what levels of pesticides in human tissues were safe. Handler opposed use of the animal surrogate method because it was non-reductive and had no direct relation to the identification of possible biochemical mechanisms.

Every member of the President's Science Advisory Committee who declared a position, with the sole exception of Handler, concluded that the long-term poisonous nature of DDT had not been adequately assessed prior to marketing, and called for animal research to establish tolerance limits of pesticides for humans in foods. They said the full biological significance of pesticides could have been discovered much sooner if there had been gold-standard studies on animals and recommended they be conducted. The President ordered implementation of the recommendations, which was the first instance of explicit recognition by the government that decisions about potential dangers to human health arising from side-effects of technological advances were fundamentally social rather than scientific judgments, and were to be made for purposes of anticipatory protection of public health not necessarily pursuant to a confirmation of a biochemical mechanism.

Handler's reaction was strongly negative. He viewed the issue of DDT safety as a strictly scientific question and believed the public had no need to know anything about the side-effects DDT might produce because they were only speculative. His advice to the administration, which arrived stillborn, was that university biochemists — not federal agency employees — should be funded secretly to study DDT so as to avoid unduly alarming the public. Prior disclosure of the possibility of harm was undesirable, he said, because it would create fears in the public and disrupt normal economic activities.

Handler became almost apoplectic after the administration banned use of DDT. He called supporters of the ban "dishonest ideologues," and accused them of "the intentional promotion of disease which DDT prevented." It would be "disgraceful and dishonest to deal with DDT that way," he said. Handler accused the supporters of the ban of having a "manifest desire to find society guilty, and particularly to find industry guilty, essentially from ideological convictions." He said the supporters had "a blatant unwillingness to stand up and just be plain honest." He claimed, "There are no charges leveled against DDT which stand up scientifically. None." Nevertheless, the government developed rules regarding pesticide exposure to protect human safety which were based on value judgements of regulators using data from gold-standard studies.

HANDLER DISPLAYED AN INTENSELY laudatory vision of physics, surprising even its most ardent polemicists, when he delivered his full-throated defense of basic physics research during his congressional testimonies. His embrace of physics wasn't the kind that occurs when a student studies its methods, mathematics, and mores over many years, but more like the intense feeling of a teenage girl toward a rock star, and just as real. When he coupled his newly discovered affection for physics with his long-standing views of biochemistry, Handler essentially completed the dimensional growth of his conception of science as an objective, value-free endeavor that yielded permanent knowledge about the world. While Handler was recommending creation of a nirvana for biochemists to perform basic biochemical research to cure disease and pleading for increased support for big-physics projects, Robert Becker, an orthopedic surgeon at a federal hospital for military veterans, was following a non-Handlerian research path in pursuit of answers to central problems in his area of medicine, and developing a small-physics approach toward achieving a solution.

Handler's long-time belief was patients died because physicians were ignorant of biochemical causes of disease, and that more basic biochemical research would ultimately provide the facts physicians needed to cure disease and promote healing. Thus motivated, he secured a stable supply of money at the Institutes for university biochemists, which established biochemistry as the apex biomedical science. Handler never considered the possibility that he himself was partly responsible for the prevalence, incidence, morbidity, and lethality of diseases because his system for biomedical research produced only pointillist information and mis-educated biochemists regarding the nature of biology and clinical medicine. As students , biochemists were indoctrinated with Handler's reductive perspective and programmed to think only at a molecular level, a stratum of human organization where neither life nor growth control nor diseases or their solutions existed. The students learned to regard the intellectual development of biochemistry as the most important object of research, and after receiving a PhD, they were employed by universities but paid by grants from the Institutes, provided their proposed experiments adhered to his orthodoxy, as they had been taught. Any scientist who thought otherwise had a nil possibility of financial support by the Institutes, and could survive professionally only by obtaining support elsewhere — no mean feat because the Institutes dominated the funding marketplace.

Although Handler never imagined that the orthodoxy he created was a big part of the problem faced by physicians and only a relatively small part of the solution, there were scientists who recognized the limitations on progress cause by Handler and the Institutes. I knew some personally but none better than Becker, who sought answers to central biomedical problems in the general domain of orthopedics. Becker's aspiration was knowledge of the scientific principles governing the body's response to trauma and other factors that influenced growth and healing. He perceived the essential features of the process to be its proportionality to the trauma, its harmony between the total organism and the tissue, and its timely cessation when healing when healing was complete. Becker rejected Handler's dictum that direct study of biological processes was un-biochemical and therefore unscientific. Oppositely, Becker decided that the existence of the process of regulated growth and healing entailed the existence of an unknown control system that was discoverable by means of biomedical experimentation — a system that was not purely biochemical in the sense of completely isolatable in a test-tube.

In Becker's experiments, following an amputation, he observed that salamanders naturally regrew a new limb which faithfully reproduced the original even though the anatomical complexity of salamander limbs was the same as that of humans. He recognized that humans retained vestiges of single-tissue regenerative ability in the healing of skin, bone and visceral organ defects, and suspected humans also retained basic elements of the limb-regeneration control system. He theorized that the system had become inadequate in some unidentified aspect, accounting for the lack of limb-regeneration in humans. He believed that knowledge of the details of limb regeneration in the salamander might lead to restoration of a greater measure of this useful disposition in humans, and perhaps even to insights into the negation of hurtful growth processes such as cancer.

Becker conceptually modeled limb regeneration as the result of the operation of an automatic self-organizing control system which differed from the familiar mechanical automata only in complexity and in the modality controlled, and he used concepts from control-system theory to guide his experimental approach. According to Becker, from a control-system viewpoint, continuous information transfer necessarily took place between the growing tissue and the remainder of the organism. The growing tissue was somehow informed of its relationship to the whole organism, so that the system didn't produce a forelimb at a hindlimb location. In turn, the injury site transmitted information to the brain regarding the nature and extent of reparative growth. The difference between the actual and terminal healing state created a difference signal that guided the process until healing was complete.

Based on his observations that amputation produced instantaneous measurable changes in the electromagnetic signal at all points on the skin, he suspected that the systemic-level injury-sensing function was electromagnetic in nature, not biochemical, and that the information contained in the signal was conveyed by the movement of electrons in nerves. He theorized that the spatial pattern of the signal interacted with the local injury-induced signal change, allowing information concerning local injury status to be conveyed to the brain, thereby facilitating control of the regenerative process.

At an international congress in mid-1963, Becker reviewed the results he had published in top science, bioengineering, and medical journals, and described the full dimension of his research regarding the growth-control communication system he believed he had discovered. He said the nerves of animals and humans generated and transmitted electromagnetic energy that was a key part of an analog communication-and-control system by which an organism recognized itself, responded appropriately to trauma, and detected electromagnetic energy in its environment. He told the audience that all living organisms possessed the property of self-repair to one degree or another, and that its fundamental characteristic was its relatedness to the total organism, as shown by the fact that the new tissue was uniquely appropriate to its anatomical location. This meant there was a two-way communication between the new tissue and the organism itself which allowed the new tissue to somehow furnish the organism with information regarding its location and composition, thereby ensuring it fit the organism's requirements. The system necessarily had a monitoring function by which the organism continuously recognized the presence of normalcy, a sensory function by which it determined when and where deviations occurred, an effector function by which it initiated appropriate repairs, and a feedback capability by which the effector function was continuously diminished in proportion to the extent of the repair that had been accomplished.

He went further and described what he thought was the evolutionary provenance of the self-repair system. He said the basic characteristics of living organisms that differentiate them from other complex but non-living entities were self-replication and self-repair. Self-replication had been shown to be mediated by the DNA-RNA coding process, but loss of coding capability is not necessarily fatal to an organism, indicating that self-replication was not an essential characteristic when the transition from non-life to life occurred. In contrast, self-repair probably appeared concurrently with the creation of life because the organism could not otherwise have continued to exist and develop the biochemical machinery of genetics. Becker said the communication system he discovered was primitive by evolutionary standards because it predated the digital communication system that subsequently developed to mediate sensory and motor functions, consciousness and thinking, and that the two systems presently co-existed.

When Becker was asked to explain in a magazine for laymen where he thought biomedical science was headed, he wrote that, in experiments with salamanders and frogs, he had detected and measured electromagnetic energy that flowed from and to the brain along the nerve cells of the nervous system. He said it was the most primitive regulatory system in the human body, the system through which the environment originally instructed mankind's oldest ancestors regarding the behavior necessary to survive on earth. As evolution progressed, and animals grew more sophisticated, the nerve-impulse system gradually took over some control functions, but the older, more basic data transmission system remains active. Becker said his evidence suggested that the ability of nerves to convey sensory and muscle impulses depends on but is distinct from the primordial system. One implication of the work he and his colleagues had published, he said, was that there was a physical basis which could account for the observed correlation between geomagnetic fields and the incidence of psychiatric disturbances.

Handler was also asked by the magazine where he thought the biomedical studies were headed. He mentioned memory and said it must be made of molecules because human beings were made of molecules. Just as DNA molecules are the repository of genetic information and antibodies are the repository of information about prior invasions by infectious microbes, so it must be that molecules are the repository of memory. He conceded, however, that he had no idea what those molecules were or how they created memory.

Becker had presented some indirect evidence for the existence of semiconduction in nerve tissue, but far less than the overwhelmingly convincing proof required to sustain such a marked departure from then current thinking about the nature of propagation of electromagnetic energy in living systems. Physicists claimed their theories showed Becker's idea was impossible and biochemists, in accordance with their dogma, ignored the possibility of any role for electromagnetic energy in living systems, with the trivial exceptions of heat generation and electrical shock. Handler regarded biological electromagnetism as what he called "voodoo science," like that of Mesmer, Perkins, and Abrams. Becker persisted, but his efforts to produce additional experimental evidence supporting semiconduction in nerves foundered because the only extant experimental methods for studying semiconductivity had been developed by solid-state physicists, and their methods were inapplicable to nerves because they were living microscopic cells mostly composed of water, not water-free orderly arrangements of atoms, as were the materials studied by physicists.

The methodological problem stemming from the absence of appropriate experimental methods was only part of the difficulty Becker encountered. He was vexed by the hegemony that Handlerian reductionism exerted over funding for biomedical research by the Institutes and realized it was unlikely to ever fund part of his research if it were perceived to be nonreductive. He was a systems-level biologist by training and temperament, like every practicing physician, and saw humans as organized wholes rather than bags of discrete biochemicals, as did Handler. The path forward Becker saw to pursue studies of the biological role of electromagnetic energy was to utilize the methods of physics as the basis of a reductive approach to explain growth control. To do so, he changed his experimental focus from nerve to bone — a solid material amenable to the use of solid-state methods because it was mostly noncellular and contained relatively little water. Becker developed a reductive model of how electromagnetic energy was a key factor in the control of bone growth that occurred in response to mechanical forces generated by gravity and muscle action.

Orthopedists long recognized that living bone changed its shape in response to mechanical force produced by muscles and gravity, resulting in bone growth in areas subjected to compression, and resorption in areas where the bone was subjected to tension. The overall result of the synchronized processes was a modification in where the bone was in relation to the applied load. The fate of a broken leg that had been set improperly and healed with an angulation exemplified the process; eventually the bone straightened. Becker's novel idea was that electromagnetic signals internal to bone, created as a consequence of the applied forces, altered the activity of the sparse network of cells inside the bone, directing them to change the shape of the bone to best resist the forces.

Using animal and human bones that he dried and cut to produce suitable specimens, Becker applied tensile, compressive, bending, and shear forces and discovered that the specimens displayed electromagnetic signals that were caused by the forces. The phenomenon whereby mechanical force was transduced into electromagnetic energy, called "piezoelectricity," historically was known to occur only in mineral crystals. Becker believed force-induced electromagnetic energy occurring in living bone could account for the clinical observation that living bone grew in areas subjected to compression and resorbed in areas that experienced tension. According to his theory, the relative handful of cells housed in matrix lacunae inside bone deposited or resorbed bone depending on the local electromagnetic signal, which was determined by the type of local force, and coordination of the processes resulted in the changed three-dimensional shape of the bone.

He evaluated where the electromagnetic signal came from by chemically dissolving the calcium mineral of bone, and observing that the matrix alone produced an electromagnetic signal when subjected to force. After he dissolved the matrix, the resulting bone mineral was too fragile to sustain forces, preventing him from making similar observations, but he observed that each bone component alone conducted applied electromagnetic energy by means of electrons, and more so at higher temperatures, indicating that they both were semiconductors. He interpreted his results to indicate that the matrix and the mineral crystals were each semiconductors and that that their association in bone produced a diode, a specific semiconducting device that allows electrons to flow in only one direction, a condition needed for an electromagnetic circuit to exist. In this view, the microstructure of bone produced the one-way flow of electromagnetic energy needed to transfer information — the requirement met in neural semiconduction by the anatomical arrangement of the sensory and motor fibers. Becker adopted the interpretation the same year solid-state physicists had reported the discovery that man-made diodes were capable of transforming mechanical force into the flow of electromagnetic energy. The discovery provided Becker with another reductive mechanism — a force-sensitive junction — in addition to piezoelectricity that could account for the production of the electromagnetic signal. In a series of publications, he provided experimental evidence for both mechanisms by demonstrating that bone specimens had the reductive solid-state properties expected for a diode and semiconduction including rectification, photoconductivity, photovoltaic responses, and electronic action spectra. Additionally, using the technique of electron paramagnetic resonance, which had only recently been developed by physicists for detection of electrons like those in semiconductors, Becker demonstrated free electron resonances in both matrix and mineral.

Becker's reductive model and application of solid-state measurement methods to bone received a powerful boost after he and his colleagues published a report showing that man-made electromagnetic energy applied by means of implanted battery-powered circuits could make bone grow in dogs. Specific control over a growth process by means of human intervention had never previously been demonstrated. In effect, the mechanical force that produced the electromagnetic signal which was the signal that triggered cellular activity was eliminated in favor of a directly application of a primitive version of the signal. The result was that the leg bones in living dogs responded by exhibiting new bone growth as though force were applied. The experiment also revealed that dissolved ions and water molecules bound to bone by physical forces materially affected the path of the applied electromagnetic signal. The observations led Becker to consider physics-type measurements of bone's dielectric constant and the extent of its bound water compartment — methods for measuring the parameters. Becker was advised to begin using the discovery clinically to treat nonunions — the failure of fractured bones to heal — but he declined because of the lack of knowledge of the role of the ions and the bound water in the response manifested by the dogs, and because the possibility of side-effects of applied electromagnetic energy had not been studied.

I first learned about Becker in 1964, when I was at the point in my first year of graduate study leading to a PhD in physics where I had to choose my field of specialization. The traditional options like nuclear physics, relativity, and semiconductors did not interest me but biophysics did, even though it was the least prestigious subspecialty in my department. Becker was expanding his laboratory to include further measurements on bone and my mentor, who was a consultant to Becker in matters related to physics, recommended me along with other students in his laboratory. Becker interviewed each of us, seeking someone who was interested in performing doctoral dissertation research on bone in his laboratory. He told me about his work and I saw immediately what I thought was greatness in his ideas. When he asked, "Do you want the job?" I accepted even before the air molecules that carried "job" to my ears had stopped vibrating. Working full-time in his laboratory for four years, I obtained bone from the operating room, dried it, treated it with chemicals to remove the fat, cut it into cubes, and made measurements of its dielectric constant, electrical conductivity, piezoelectric constant, and electron resonance properties, and the size of its bound water compartment, and earned my degree. I remained in his laboratory for thirteen more years.

Becker believed science benefited humanity greatly, even though unwise use of technology sometimes had unhealthy consequences. He was certain that further improvement in the destiny of mankind depended upon the continued growth of science, particularly human biology and medical science. Nevertheless he saw troubling developments in the American system for biomedical research regarding its purpose, process, and ethical foundations. To a meaningful extent, he believed those involved in biomedical research, from the physician engaged in clinical research to the biochemist who studied the intricacies of chemical reactions, had become players in a gigantic system he called "how to succeed in science by publishing papers." He said the system "is monstrously expensive, terribly complex and exceedingly dangerous to the future of mankind." The system began as a shining vision for the future but "had devolved into a kind of game that produces artificial and shoddy research which yields a plethora of publications that do not serve biomedical science or the public."

Financial support for the research was furnished by public funds and "the public was entitled to expect not only that each project be pursued with devotion but also that the results be disseminated to ensure their incorporation into the body of knowledge where they may assist in the general growth of biomedicine." However, "too often, the publications amount to pedestrian strolls through vague or obscure objectives in already well-cultivated areas by investigators playing the academic game of publish-and-seek-more-grants." The publications too often had misleading titles which bore little relationship to the contents, "similar to the cover of a paperback book — promising much but delivering little." Published results of research were frequently fragmented, apparently to produce as many papers as possible from one study and to denote priority for purposes of personal prestige. A common unethical practice by politically powerful investigators such as department chairmen was their addition of their names to the works of their junior faculty, which fraudulently "allowed credit for research to be gifted for purposes of enhancing status and obtaining grants." "The number of people who played the game have increased greatly — a growth in the John-Doe rather than Alexander-Fleming populations of biomedical scientists." This unlimited, uncontrolled increase in papers, "much of which contained valueless information," had made it extremely difficult for bona fide investigators to detect the information that was of value, and made interdisciplinary communication among the members of the Balkanized super-specialized biochemical societies practically impossible. The journals they sponsored insinuated that the fundamental problems in biomedicine could be solved only by means of the knowledge possessed by their members-subscribers. The upshot was that the growth of biomedical research "became more like the growth of a tumor that has exceeded its circulatory supply and begun to develop areas of necrosis that were detrimental to biomedicine's further growth and development." The young investigators who played the publish-or-perish game were forced to also play the don't-rock-the-boat game, which consisted of staying within the presently defined safe boundaries, not doing anything really new, and often citing the papers of the established scientists who sat on the advisory boards. "Eventually they acquire status and join the establishment, losing, along the way, their illusions and ideals." Their work inevitably "showed a lacked creativity and they, in turn, did their best to discourage it among their colleagues."

The National Institutes of Health was the major driving force behind the system that awarded public money to private investigators. It "functions as an unwelcome return to the days of the so-called invisible colleges in seventeenth-century England where scientific research was carried out in secret." According to rules the Institutes birthed and nurtured, a good scientist was someone who published numerous papers, conformed to orthodox theories, and was well liked by those on the advisory panels, which was institutionally biased against liberalized modes of thinking. "The system is like a black box where the input is public money and the output is the distribution of federal dollars according to criteria wholly determined by the possessor of the box." The system discriminated against scientists who, while better motivated and more insightful and productive of meaningful results, lacked a reductive focus and personal connections with the advisory panels.

The criteria for funding by the Institutes should have been "the explanatory value and clarifying power of the program — the degree to which its results seem likely to resolve what previously was unresolved or perplexing." The personal characteristics of the program director were also pertinent considerations. "Courage, insight, and experience in the area of the proposed work are relevant, and allowances should be made for the unique hurdles faced by such an investigator." An innovator who displayed purposeful intellectual curiosity, a desire to find the answers to problems, and who sought the satisfaction of having engaged nature in combat in an area that mattered significantly to the taxpayers who paid for the research and had won, should be encouraged. "Someone who chose to work in a field of research that was little explored with no noble predecessors who set down guidelines, and where one cannot predict with any degree of confidence that publishable data will be obtained, should be afforded more freedom in planning future research, compared with a plodder who turns over the same ground again."

Handler's notion of permanent biomedical knowledge was rejected outright by Becker, who regarded all scientific knowledge as subject to challenge by succeeding generations of scientists. "While no one can dispute the value of a paper that explains what was previously unexplainable, what about the reverse situation? I believe that a paper presenting data that renders unexplainable what was previously satisfactorily explained is equally valuable. Such destruction of cherished dogma formed the basis for modern science, and we must always have a place for it — even today."

Becker discovered that animals and humans generated steady patterns of electromagnetic signals that were detectable everywhere on the intact skin, mirroring the anatomic organization of nerves. The signals were transported by electrons and changed during healing, anesthesia, and the presence of external electromagnetic energy. His acute cognizance of the financial hegemony Handlerian reductionism exerted over biomedical research led him to pursue his interest in the study of growth control and the role of electromagnetic energy in biomedicine by developing a reductive biological model for what was inherently an integrative biological question — a new research strategy. In keeping with what he saw as the unity of nature, Becker postulated that bone should have a similar electronic control system governing its growth, but that the entire system should reside in the bone itself and be relatively independent of the central nervous system. He utilized the methods of physics, which recognized the existence of electromagnetic energy, as opposed to biochemistry which did not, as the basis of his reductive approach. He shifted his research focus from nerve to bone because physicists had developed methods for studying materials like bone but not nerve. Using a range of physical methods, he found supporting evidence for his thesis that bone was composed of components that were semiconductors, and that their intimate anatomical association gave rise to the electromagnetic signal that was observed when bone was subjected to mechanical forces. Becker believed that force-generated electromagnetic signals regulated bone growth by means of a direct effect on bone cells, a model that linked control-system theory and solid-state theory to provide a mechanism for controlling bone architecture and growth. Based on the theory, a measure of control over bone growth in animals was obtained by injecting electromagnetic energy into animals. Becker's work and that of all others who studied the role of natural and man-made electromagnetic energy in biology and medicine was an area of research purposefully ignored nearly completely by the Institutes for the simple reason that the work was electromagnetic and not solely chemical. He laid the groundwork for a novel approach to basic problems in biology and medicine that included but were far from limited to the healing process. His new biological philosophy required a fundamental conceptual change. The cell and its internal structures were no longer considered an amorphous fluid system in which biochemical processes proceeded in solution as in a test-tube, but rather in a highly structured solid-state system with many important processes occurring through electron-transfer mechanisms. It was impossible to imagine a philosophy and approach to the study of human biology that differed more from those of Handler. He saw work like Becker's as beneath the level of a true scientist and fit for engineers working in industry, not scientists funded by the government. His views had already tainted the blood of the Institutes by the time Becker first applied for research support. But his proposed reductive model and use of physical methods, coupled with Handler's departure from the Institutes probably accounted for Becker's success in the mid 1960s, when he received two grants from the Institutes for the work.

HANDLER'S FORAY INTO Washington politics as a science advisor, science manager, and science-policy maven did not go as well as he hoped. He continued to testify at congressional budget hearings, but the halcyon days when he was warmly welcomed by budget-committee chairmen were over — familiarity no longer worked in his favor. He was probably the least influential science advisor within the administration because he couldn't be trusted to put its interests above his; he remarked that his invitations from officials and politicians to lunch and dinner at the Cosmos Club decreased. He was the most eloquent speaker and decisive policy manager in the Foundation's history, but success in gaining approval of big-physics projects continued to elude him and his original ambition of gaining Foundation support for basic biochemical research was never fulfilled.

Handler disagreed with those who blamed the increasing financial burden of the Vietnam War for the tightening research budgets; he blamed the lack of will within the government and said the U.S. was rich enough to afford both the war and research. Some people criticized him because he talked too much about too many things, too stridently, in areas where he had too few qualifications to opine; he rejected the criticism the same way he offered opinions, without analysis or explanation. His opinions on many issues were not only inconsistent with the values and objectives of the administration he nominally served, they often didn't match the official views of any of his affiliated originations. More than once he explained that he spoke as he did because he thought science was too important to be left to politicians. Handler couldn't be fired or otherwise prevented from saying whatever he thought because he had never actually been hired in the sense of being paid a salary by the administration to perform specific tasks — he wasn't answerable to anyone.

Handler experienced financial and personal problems trying to manage his life in Washington while his family lived in Durham. His sons were graduating from college, his and his wife's medical conditions continued to worsen, but he was more or less trapped in Washington. He continued to draw his salary from Duke, but functioning in the Washington political scene while supporting a family in Durham on a professor's salary was not easy. Progressively fewer officials at the Institutes had first-hand knowledge of the influence Handler commanded when he served there, a development that jeopardized continuation of his long-standing grants. Any diminution of the federal money Handler brought in to Duke would likely empower his enemies there, of which he always had more than a few. Handler's acceptance of a position on the board of a drug company only partially relieved his financial difficulties.

Handler's deepest problem was finding a home where he could pursue a goal that stemmed from the evolution of his view of science. He had developed a religious-like belief in science itself as a basic ordering principle in society and mankind's salvation. His conversion occurred while his dissatisfaction with his functionary role for the administration was peaking, and led him to question whether there was a place for him where he might be able to help elevate the status of science in society. Under the guidance of Seitz, who more or less served like a Professor Higgins to Handler, he became increasing familiar with the procedural and political machinery of the National Academy of Sciences, any the possibility occurred to him that the Academy was just such a place.