41.8 percent of those withdrawing did so because of reactions; in the fourth project, lack of interest was the prime cause of withdrawal. Between them, these two reasons account for 32 to 50 percent of the withdrawals. Since the reactions are in large measure psychogenic, means for dealing with them may be devised. We have, in fact, shown that an antacid, or even a placebo, pill will relieve up to 90 percent of these reactions (*4, 5*). The lack of interest is due chiefly to lack of motivation among an economically low-level group. The actual rate of withdrawal was highest for the first year of operation of the San Juan project, in which 50 percent of the subjects who started had withdrawn by the end of the year. In contrast, in the Humacao-R project, 11 percent of those who started had withdrawn by the end of the year. We believe these high withdrawal rates for the San Juan project to be due to the following factors: (i) the availability of sterilization for contraception as well as the availability of other means economically practical; (ii) frequency of moving, chiefly to the continental United States; (iii) improvement in economic situation, which makes larger families less undesirable; and (iv) difficulties attendant upon initiating and testing this new method of contraception. Actually, among those starting the second year of medication, the withdrawal rate fell to 30 percent, and in Humacao-R, to less than 1 percent. In the latter project is a stable group of very poor women who are highly motivated, and in this project, begun a year after the one in San Juan, the supervisor had full knowledge of the difficulties encountered during the first year in San Juan. It is perhaps significant that in Haiti, where the population is also quite poor but where it is less stable, the first year's rate of withdrawal for all causes was 34 percent.

Questions and Answers

For the period studied, the foregoing data appear to us to answer the following questions, in the manner indicated: (i) Is the method contraceptively effective? yes; (ii) does it cause any significant abnormalities of the menstrual cycle? no; (iii) does it adversely affect the reproductive tract and adnexae? no; (iv) does it have physiologically adverse effects generally? no; (v) does it affect the sex life of the subjects adversely? no; (vi) does it impair fertility upon cessation? no; (vii) may a low dosage level of the drug be used? yes; (viii) is the method acceptable? yes, but to an extent which varies with motivation, economic situation, and other factors (*7*).

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J. P. Greenstein, Biochemist and Investigator of Cancer

The sudden death of Jesse Philip Greenstein on 12 February 1959 ended a career of outstanding achievement. Dr. Greenstein had achieved eminence in his extensive work on the chemistry of amino acids, peptides, and proteins, and on the biochemistry of cancer.

He was born in New York City on 20 June 1902 and did his undergraduate work at the Polytechnic Institute of Brooklyn, from which he was graduated in 1926 with honors in chemistry. He then went to Brown University, where he worked with C. A. Kraus and P. H. Mitchell. His Ph.D. thesis dealt with electrometric determinations of the dissociation of glycine and certain simple peptides; its character foreshadowed much of his later work. In 1930–31 he was a National Research Council fellow at Harvard, under Edwin J. Cohn, where he continued and extended his studies on the ionization constants of peptides. This was followed by a year's work in Dresden under Max Bergmann, who was just developing the carbobenzoxy method of peptide synthesis. Greenstein's experience in Bergmann's laboratory profoundly influenced his subsequent career. With Bergmann and Zervas he was the first to apply the new methods to the synthesis of lysylglutamic acid and lysylhistidine, and he developed a mastery of both organic and physical chemistry, particularly in relation to the study of peptides and proteins, which was exceptional among the biochemists of his generation.

After a year in Berkeley in the laboratory of C. L. A. Schmidt, he returned to Harvard for six years (1933–39). During this period he was active as a tutor in biochemical sciences at the college and was also research associate at Harvard Medical School, in Cohn's laboratory. His zeal and enthusiasm for both teaching and research, and his extraordinary energy and enthusiasm, were strikingly displayed then as later. As tutor in biochemical sciences he looked after a larger number of students than any other member of the board has ever been responsible for, and served as an inspiring and effective teacher in frequent personal conferences with students. He also served as head assistant to L. J. Henderson in the latter's course in biological chemistry; indeed, as Henderson's major interests were shifting from biochemistry toward sociology, Greenstein for several years was largely responsible for the general management of the course. At the same time he was astonishingly productive in research. He continued to synthesize new peptides and to study their ionization constants and correlate these with their structure, and, in collaboration with J. Wyman and T. L. McMeekin and others, he studied

their dipole moments, solubility, and other physical properties. During these years he began those important studies of the peptides of cystine and cysteine to which he returned, with results of outstanding importance, nearly twenty years later.

Soon he turned also to the study of protein structure and denaturation, making use of porphyrindin, which had recently been synthesized by Richard Kuhn, for the determination of protein sulfhydryl groups, in native and denatured proteins. He discovered the powerful action of guanidinium salts as denaturing agents for proteins and made extensive use of them and of concentrated urea solution.

In 1939 his career entered a new phase when he became a member of the National Cancer Institute at Bethesda. Here again his extraordinary energy and vitality displayed themselves. He threw himself into an extremely active program for the study of the biochemistry of tumors, and in particular set about the determination of the activities of a variety of enzymes—arginase, amylase, catalase, xanthine dehydrogenase, and many others—in normal and cancerous tissue. This long series of studies, which extended over many years and involved numerous collaborators, represents probably the most extensive work of its kind yet carried out on cancer tissue. From this he evolved the concept of the "biochemical uniformity of tumors," the near-uniformity of tumors being due to the loss in a normal tissue, when it becomes malignant, of those specific functional characteristics which distinguish it from other normal tissues. The tumors which so emerge bear little or no physiological resemblance to their normal tissues of origin and appear to converge to a common type of tissue. Thus, normal hepatic and gastric tissues are very distinctly different, but biochemically the hepatoma and the gastric adenocarcinoma are closely similar. These researches were summarized, together with a comprehensive and critical survey of the whole field, in Greenstein's outstanding monograph *Biochemistry of Cancer,* first published in 1947 and extensively revised in a second edition which appeared in 1954.

During his first years in Bethesda he also devoted himself vigorously to the study of nucleoproteins, in normal and cancer tissue, at a time when the importance of these substances was less widely recognized than it is now. His interest in the study of protein denaturation remained unabated, and with Neurath, Putnam, and Erickson he published a review of this subject in 1944 which has become one of the classics in the field.

Jesse Philip Greenstein

In 1946 he was appointed chief of the newly created Laboratory of Biochemistry of the National Cancer Institute, a position which imposed upon him an increasing burden of administrative responsibility. His breadth of vision, his enthusiasm, and his patient good humor and understanding of many diverse types of people were of great importance in the development of the research activities of the institute and in attracting workers to it from all over the United States and from the rest of the world.

These heavy adminstrative responsibilities, however, did not prevent him from continuing with an extraordinarily active program of research; indeed, the last dozen years of his career were probably the most productive of all. He made intensive studies of dehydropeptides and dehydropeptidases, of many cellular peptides, of the enzymatic desulfuration of cystine peptides, of the deamidation of glutamine and asparagine, and of other problems too numerous to mention here.

His outstanding contribution to the chemistry of the amino acids, and thereby to biochemistry and nutrition, lay perhaps in his superb researches on the preparation of optically pure L- and D-amino acids, in which he utilized the asymmetric hydrolytic or oxidative specificity of the amino acid acylases and oxidases to prepare the optical enantiomorphs in better than 99.9-percent purity. These researches have made pure L- and D-amino acids readily available—a matter of great importance for studies of nutrition, for synthesis of pure polypeptides, and for other kinds of biochemical work.

Greenstein also achieved purification of a series of amino acids with two asymmetric centers—threonine, isoleucine, and others. The possible isomers of these amino acids were cleanly separated and characterized, and to a large extent their absolute stereochemical configuration was unraveled.

In the last years of his life he initiated an extensive series of nutritional researches with diets containing mixtures of optically pure amino acids. His work also demonstrated the toxic effect of injecting amino acid mixtures lacking in arginine, and the protective effect of the addition of arginine to these mixtures, which was clearly shown to be due to the function of arginine in the Krebs urea cycle, whereby the toxic ammonia released from other amino acids was rapidly converted to urea.

During these final years he also carried out an important series of further researches on the peptides of cystine. At the time of his death he was engaged, with M. Winitz, in the writing of a comprehensive treatise in three volumes on the chemistry of the amino acids. Fortunately they had completed nearly all of this great work except for the final section of the third volume, which is now being finished by Winitz.

Greenstein was awarded the Neuberg medal in 1950, the Distinguished Service award of the Department of Health, Education, and Welfare in 1952, and the Hillebrand award in 1958. In 1954 he served as chairman of the Division of Biological Chemistry of the American Chemical Society. He was for several years an editor of the *Archives of Biochemistry and Biophysics,* and, with A. Haddow, was editor of *Advances in Cancer Research.* He served as visiting professor of biochemistry at the University of California in 1948, and in 1957 he became a member of the Committee on Biochemistry of the National Research Council and served as the chairman of the Subcommittee on Amino Acids. In 1949 he was a member of the American delegation of the Cancer Colloquium called by Pope Pius XII at the Vatican, and in 1956 he was a visiting lecturer at several Japanese universities and became an honorary member of the

Japanese Chemical Society and the Japanese Foundation for Cancer Research.

He led an arduous life as an investigator, administrator, and writer. During his career he published about 300 scientific papers in addition to the books referred to above. In all of these enterprises he took a constant and active part in every piece of research that was published under his name and was personally responsible for writing all of the papers to which his name was attached. His hours of work were long. After dinner at home he would, several times each week, return to the laboratory quite early in the evening, where he could write or experiment uninterruptedly until one or two o'clock in the morning. Yet with all of this activity he was accessible, friendly, and relaxed when anyone came to see him and talk things over with him. During the last three years of his life he had become a boating enthusiast; starting originally with a small outboard motor, he had purchased in 1958 a 22-foot cabin cruiser and had received several certificates from the Washington Area Power Squadron.

His interests were broad and ranged far beyond the sciences. He was always a prolific reader. In his Harvard days I can remember well his delight in Dickens, and especially in *Pickwick Papers*. He read widely in philosophy, theology, and biography and was something of an expert on the history of the Civil War —its battles, issues, and great men. Undoubtedly the breadth of his reading and his appreciation of literature had much to do with the high quality of his own writings.

Jesse Greenstein was outstanding in scientific skill, learning, energy, and devotion to his work. He inspired numerous young men, who came to work at the National Cancer Institute, with much of his own ardent enthusiasm for science. He was proud to be a servant of the United States Government, in a position of great responsibility, and his service went far beyond the allotted duties of his post. He was a loyal friend, whose wisdom and courage were a source of inspiration to his colleagues. His death leaves a gap that will be difficult to fill.

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News of Science

Views on Secrecy Given by American Nobel Prize Winners

Responding to a letter from Senator Thomas C. Hennings (D-Mo.), chairman of the Senate Constitutional Rights Subcommittee, 17 American Nobel Prize winners from various fields of science have given their views on the effect of security restrictions on the progress of science in the United States. Most of the scientists stated that their work was such that they had had little contact with classified information. With only one exception, however, they agreed that free exchange of information was the lifeblood of scientific progress and that restrictions of this flow were usually either foolish or destructive. A number of the scientists cited the experiences of colleagues to support their views on the security problem. Selman Waksman cited the case of a researcher who did not receive proper credit for his work because other researchers, free of security restrictions, had published before he was allowed to do so. One scientist, Walter H. Brattain, who was a prize winner in 1956, ended his letter with this admonition: "Don't kill the baby just to protect it from the kidnappers." Excerpts from some of the letters follow.

Dickinson W. Richards: "In a broad sense, however, every scientist suffers when there is any restriction, at any level, to the free exchange of knowledge. Except in so far as such restrictions are absolutely required by the exigencies of national defense, we believe that there should be no restrictions. We should like, for example, to have scientists from Russia and from China visit us freely and without hindrance, we should like to discuss with them problems of mutual interest, teach them and learn from them, we should like to have their young men come and live and work with us, and if there should be a sufficient opportunity for our young men to learn, to have them go and work there."

John Bardeen: "Rapid exchange of information has been vital to this progress. What is done in one laboratory today may depend on results obtained in another laboratory in a different part of the world only months before. For example, one of most exciting developments of the past three years was made by a physicist working in an industrial laboratory in Japan. His idea was soon taken up and is now being pursued by several laboratories in this country.

"With its very advanced technology, the United States is able to take best advantage of any new development in the field. The most important thing is to spare no effort so that our country remains in front and does not lag behind. We then have nothing to fear and everything to gain from free exchange of scientific information."

Walter H. Brattain: "Even more fundamental to this matter is the whole philosophy of our political system. It seems to me that it is based primarily on the premise that if our citizens are well informed they will, under our system, take the appropriate political action and come to the right decision. However, we now find ourselves in a very peculiar situation. Because of security restrictions that seemed quite justified in the atomic area, our nation is faced with very momentous decisions and since our citizens do not have access to the essential information, the basis on which our political system operates is undermined. All our citizens can do is to trust that those of our elected officials who do have access to this information will make the right decision. Does anybody want to argue that our founding fathers had any idea that the system they proposed would operate