tenure. Noting that there was considerable difference of opinion at various review levels and that Burns had reversed his own decision, Dumke said that "any serious doubts in a tenure decision must be resolved in favor of the institution." Kurzweil has again appealed—this time to a statewide faculty panel—but his opponents have been changing the rules of the game faster than he can win appeals. Previously the statewide panel had had final authority over grievance cases, but last month the state college trustees made the panel purely advisory to the chancellor.

Ultimately, Kurzweil expects to have to argue his case in the courts. If litigation takes place, it will presumably reveal whether there is any merit at all in the case against Kurzweil or whether the attempt to denigrate his professional competence has been as trumped-up as it looks. In the opinion of Burns, who was replaced as top administrator at San Jose in August:

"The overriding fact in the entire situation is that Dr. Kurzweil has violated no law of the State, no regulation of the Trustees, no executive order of the Chancellor, no directive of the President, no policy or procedure of the College. He is innocent of any wrong-doing. He is academically competent. He has earned tenure."

—PHILIP M. BOFFEY

Nobel Prize: Three Share 1970 Award for Medical Research

The 1970 Nobel prize for medicine or physiology was announced last week. Following are appreciations by researchers familiar with the recipients and their work.

1. Von Euler and Axelrod

Ulf von Euler and Julius Axelrod made their notable contributions in the area of the sympathetic nervous system. Research in this field has led to an understanding of the actions of many drugs in cardiology, psychiatry, and neurology. The introduction of α-methyldopa (α-methyldihydroxyphenylalanine) for the treatment of hypertension and more recently of L-dopa for the treatment of Parkinson's disease are direct outgrowths of basic research on the sympathetic nervous system. I am sure that the Nobel committee was aware that many individuals have made important contributions to this field. However, in selecting Ulf von Euler and Julius Axelrod they have shown excellent judgment. Before referring to their scientific contributions, it would be of interest to give something of their backgrounds, which happen to be in sharp contrast. Ulf von Euler was born in Stockholm in 1905. His father, Hans von Euler, who received the Nobel prize in chemistry (1929) was, at the time, director of the Chemical Institute at the University of Stockholm. His mother, Astrid Cleve, was also a prominent scientist. After a false start in engineering, he obtained an M.D. degree at the Karolinska Institute in 1930. His interests turned to physiology and were directed to humoral transmitters as a result of collaborations with Sir Henry Dale, Sir John Gaddum, and Corneille Heymans. Much later he was to be influenced by Bernardo Houssay. By 1939, von Euler had become professor and director of physiology at the Karolinska Institute, a position he has held since then. Over the years he received many notable awards and honors and served on many committees around the world. At present he is president of the Nobel Foundation, which, I gather, is more of a handicap than an asset in this instance. Von Euler lives with his wife, Dagmar, in an apartment in Stockholm. He has four grown children by a previous marriage.

Ulf von Euler

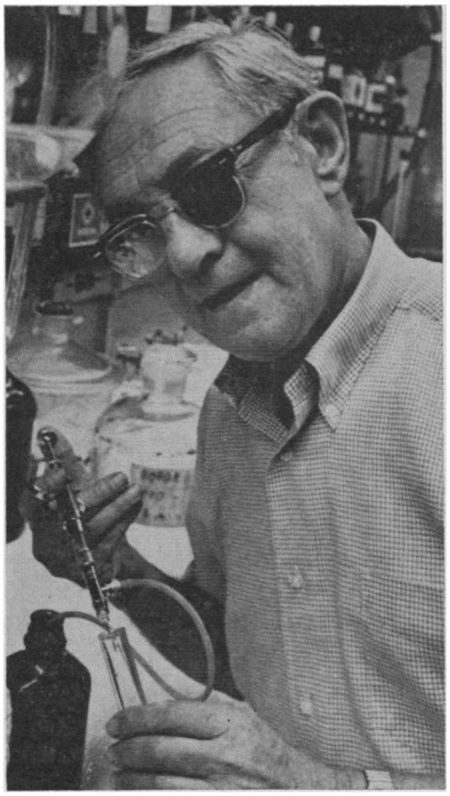
Julius Axelrod's background is quite different. He was born in New York City in 1912. His parents were of modest means, and he attended the free College of the City of New York where he obtained the B.S. degree in 1933. In the United States, the 1930's was hardly the time for a young man without money to begin a scientific career. As a result, Axelrod had to work at many menial and irrelevant jobs to earn a living. After 8 additional years he managed to obtain an M.S. at New York University in 1941. This led to a job as a technician with the Laboratory of Industrial Hygiene. Fate led this organization to seek the help of Bernard B. Brodie in some problem, and as a result the two were brought together. They were to remain together for about 9 years, first at the New York University Research Service located at Goldwater Memorial Hospital in New York and later at the National Heart Institute in Bethesda, Maryland.

During this time Brodie was developing his new concepts of drug metabolism which later revolutionized modern pharmacology. These influences rubbed off on Axelrod, who, by the early 1950's, had himself become an authority in drug metabolism. At this time he still had no doctorate, although he had by then produced the equivalent of several Ph.D. theses. The late Paul K. Smith, professor of pharmacology at George Washington University, was instrumental in arranging for Axelrod to obtain the Ph.D. degree. He was awarded the doctorate in 1955 at the age of 43. Shortly before this, Seymour Kety managed to lure Axelrod to the National Institute of Mental Health, where he has been ever since and is now chief of the section of pharmacology of the Laboratory of Clinical Sciences. Axelrod too has received many honors, awards, and honorary degrees. He and his wife Sally live in an apartment close to the National Institutes of Health. They have two grown sons.

The contributions made by these two scientists comprise a large portion of our current knowledge concerning humoral transmitters in sympathetic nerves. In 1940, von Euler isolated and identified norepinephrine as the transmitter substance in the sympathetic nervous system. He then played an important part in demonstrating the role of norepinephrine in shock and other conditions of stress. As a result he became interested in aviation medicine and developed into such an authority in this field that his consultation has been sought by many governmental agencies throughout the world. In 1955 he demonstrated that stimulation of the nerve to the adrenal gland leads to increased synthesis of adrenal epinephrine, revealing an important regulatory process. More recently he isolated and characterized the norepinephrine storage granules in nerves and demonstrated how the transmitter was stored, taken up, and released by them. It should be noted that very early in his scientific career (1934) he discovered prostaglandin and subsequently laid the groundwork for one of his colleagues, Sume Bergstrom, to carry the studies to their present exciting state of development. The prostaglandin story is itself worthy of a Nobel prize.

Axelrod's earliest contributions to the field of humoral transmitters were with tritium-labeled epinephrine and norepinephrine of very high specific activity. He showed that traces of the synthetic transmitters, when administered, equilibrated with the pools of transmitters in the nerve terminals. He was then able to show directly that many drugs acted by modifying the storage of neurotransmitters in one way or another. These included cocaine, tyramine, reserpine, chlorpromazine, bretyllium, and many other drugs. Uptake by the nerve terminals also proved to be an important mechanism for inactivating the transmitter.

In 1957, after Marvin Armstrong had demonstrated the presence of vanillyl mandelic acid (VMA) in urine, Axelrod began his studies which led to the elucidation of the enzymes



Julius Axelrod

and intermediates involved in the major route of norepinephrine metabolism. His interests in methylation led him to investigate the biosynthesis of melatonin and its relationship to the physiology of the pineal gland and to diurnal rhythms. These same interests led him to the enzyme involved in converting norepinephrine to epinephrine in the adrenal gland and to the demonstration that this reaction is controlled by steroid hormones. Most recently his group demonstrated an induction of norepinephrine-synthesizing enzymes in response to severe demands on the sympathetic nervous system.

It should be noted that over the years both men had many collaborators. A large number of these are now distinguished scientists each in his own right. Although space does not permit listing them, it is readily apparent to those working in this field how much these younger people have gained from their associations with the two Nobel laureates. Both their laboratories are still important training centers.

Julius Axelrod and Ulf von Euler are both extremely hard-working scientists. They are modest and reserved and are not in the habit of wasting words in the laboratory or at scientific gatherings. Axelrod's furious pace in the laboratory is well known. In the middle of an experiment he does not stop for anything. There is a story that his colleagues, to test his powers of concentration, once moved a large centrifuge into the aisle near his lab bench so that it blocked his way. Axelrod never stopped his experiments but continued at the same pace even though he had to squeeze through the very narrow opening between the bench and the centrifuge over and over again during the day. In the case of von Euler his distaste for small talk is best brought out by his refusal to give the usual humorous, chatty after-dinner speech at a banquet given in his honor at the Second Catecholamine Symposium in 1959. He gave, instead, a lecture with slides concerning his current experiments on the nerve storage granules.

The recognition bestowed upon von Euler and Axelrod by the Nobel committee is not only for their own studies but also for the leadership they have provided over the years. Their concepts and laboratory techniques have provided a continuing impetus for all of us engaged in research on the sympathetic nervous system. We are delighted that they have received this great honor.

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2. Katz

Bernard Katz shares this year's Nobel prize because of his contributions to our knowledge of the mechanisms involved in the release of transmitter substances from nerve terminals. His work in this area began in 1941 and still continues. His most outstanding contributions have been the discovery of the "miniature end-plate potential" in 1950, in collaboration with Paul Fatt, and of the subsequent formulation, with Jose Delcastillo, of the "quantum hypothesis" of transmitter release.

Bernard Katz was born in Leipzig in 1911. He received his medical education there, graduating in 1934. During this period he was particularly influenced by the physiologist Gildemeister and became interested in neurophysiology. After graduation he went to England, where he worked on nerve excitation in the laboratory of A. V. Hill. Hill was very influential in shaping the young scientist's development; their relationship is described concisely by Katz's dedication of his 1966 book, *Nerve, Muscle and Synapse*, "To my friend and teacher, A. V. Hill." In 1939 Katz left England for Australia, where he joined J. C. Eccles and Stephen Kuffler at the Kanematsu Memorial Institute of Pathology in Sydney and began work on neuromuscular transmission. His research was interrupted by service with the Royal Australian Air Force, where he served as a radar operator in the Pacific from 1942 to 1945. After the war he returned to Hill's laboratory in London and resumed work on nerve excitation and conduction and the electrical properties of excitable membranes. At this time he also collaborated with A. L. Hodgkin and A. F. Huxley on the initial studies of the ionic basis of the action potential in the giant axon of the squid at the Marine Biological Laboratory in Plymouth. After an elegant study of the initiation of impulses in the muscle spindle, he redirected his attention to the neuromuscular junction and, in collaboration with Paul Fatt, used the technique of intracellular recording with glass micropipettes to describe in detail the nature of the end-plate potential. In 1952 he became head of the department of biophysics at University College London and, in the same year, was made a fellow of the Royal Society. He is widely known as an excellent speaker and has given lectures in many parts of the world, including, in this country, the Merter Lectures at Johns Hopkins in 1958 and the Dunham Lectures at Harvard in 1961. He received the Royal Society's Copley Medal in 1967 and was knighted in January 1969. He is currently biological secretary of the Royal Society.

Bernard Katz

During their studies of the end-plate potential, Fatt and Katz noticed small deflections on the oscilloscope trace of about 0.5 mv amplitude, occurring at apparently random intervals. The inevitable rumor is that these were at first ignored as being some kind of annoying instrument noise, until the investigators realized that the "noise" was present only when the micropipette was in the muscle fiber at the end-plate region. In any case they soon determined that the potentials were abolished by curare and enhanced by neostigmine, and postulated that the deflections were "miniature end-plate potentials" produced by the spontaneous release of packages, or "quanta," of acetylcholine. They proposed further that the normal end-plate potential, produced by nerve stimulation, was the result of the synchronous release of a large number of such quanta. In subsequent experiments in which transmitter release was reduced by bathing the preparation in low calcium and high magnesium solutions, Fatt and Katz and Delcastillo and Katz obtained evidence that transmitter release was, indeed, quantal. Under these conditions the end-plate potential fluctuated in a stepwise manner, indicating the release of 0, 1, 2, or more quanta during successive stimulation. The smallest step was identical in size and shape with the spontaneous miniature potentials.

In order to explain the fluctuations from trial to trial, Delcastillo and Katz proposed the "quantum hypothesis" of transmitter release. This states simply that there is a large number of quanta stored in the nerve terminal, each with a finite probability of being released on arrival of an action potential. The hypothesis was immediately testable, since it implied that, if the mean number of quanta released during a series of trials were known, then the total number of failures, single quantal releases, doubles, and so on, should be predictable. Their experiments bore out these predictions in detail, and the hypothesis was subsequently shown by others to be valid at a wide variety of synapses in both the peripheral and central nervous systems of many species. These experiments provided important information about the release process. First, transmitters are inevitably released in quantal units, regardless of whether the transmitter is acetylcholine, as at the neuromuscular junction, or some other substance. Second, transmitter release is a statistical process involving interaction of the quantal unit with the nerve terminal membrane. In 1956, Delcastillo and Katz proposed that the transmitter at the neuromuscular junction might be contained in synaptic vesicles and that the release process might involve interaction between the vesicular membrane and the nerve terminal membrane. They estimated that each quantum might correspond to about 104 molecules of acetylcholine. Another important observation of this period was that facilitation and depression of the end-plate potential were due to changes in the number of quanta released from the nerve terminal, information that is now an inevitable part of any model proposed for plastic changes in synaptic transmission in the nervous system.

Katz's contributions to our knowledge of the transmitter release process did not end with the formulation of the quantum hypothesis. He has continued to push microtechniques to their limit to obtain further information about the properties of the nerve terminal and the release process itself, particularly in collaboration with Ricardo Miledi. They have obtained important evidence that the initiating event for transmitter release is the influx of calcium across the nerve terminal membrane in response to depolarization and have shown that the synaptic delay is largely in the release process itself; that is, after calcium entry there is a latent period of a few tenths of a millisecond before the first quanta are released. These and many other observations on the neuromuscular junction and the giant synapse of the squid have brought us closer to understanding the process of synaptic transmission.

Those who have had the good fortune to work in Bernard Katz's laboratory have come away with great admiration and respect for his abilities as a scientist and with gratitude for his unfailing interest in our own scientific development. He is, to all of us, a friend and teacher.

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