

AROUND THE WORLD IN 80 DOCTORS



No. 22:

This is the twenty-second feature article on physicians in various parts of the world, picturing their endeavors and their achievements. In each case the physician is interviewed by a member of MD's editorial staff.

Photography by Terence Le Goubin

Dr. Ulf von Euler of Stockholm



MD

Vol. 13, no. 7

July, 1969

P. 173

MOST MORNINGS at eight Professor Ulf von Euler leaves his apartment on Karlavagn in central Stockholm and drives to the northeastern outskirts of the beautiful city in his small white Volvo. At a cluster of low red brick buildings he turns into a driveway that passes a bed of roses, a bust of Alfred Nobel and a head of the great chemist Jöns Jakob Berzelius.

From afar, the simple three-story structures surrounded by lawns and trees look like college dormitories but they house one of the world's greatest research centers and medical schools, the Karolinska Institutet. There in his laboratory and office on the second floor of the physiology building Dr. von Euler leads a multifaceted life.

Besides teaching medical and graduate students he is a member of the state medical board, vice-chairman of the board of defense medicine, vice-president of the International Union for Physiological Sciences, and chairman of the Nobel Foundation. For many years he has served on the committee that selects Nobel laureates, and his own studies include a number of milestones in medical research.

Ever since his birth in Stockholm on February 7, 1905, Ulf Svante Hansson von Euler has been closely associated with scientists. His father Hans von Euler-Chelpin* whose family in the 18th century was related to mathematician Leonhard Euler, shared the 1929 Nobel Prize for his studies of the coenzymes in sugar fermentation, and his godfather Svante Arrhenius won the 1903 Nobel award for his theory of electrolytic dissociation. His mother Astrid Cleve von Euler, a chemist, botanist and geologist, was the daughter of Professor Per Teodor Cleve who discovered the rare earths holmium and thulium and chaired the committee which selected Nobel Prize laureates in chemistry for a number of years.

There is a legend that Hans von Euler planned to be an artist and studied chemistry to learn about pigments, but Dr. von Euler says his father became a scientist because of a bet. He wagered a wealthy friend that he could get a doctorate in two years, won the degree, a large sum of money and went to Stockholm as Arrhenius' assistant. In 1902 he married, had five children, was divorced from his wife after ten years, remarried and had three more sons.† Among hundreds of works published by Hans von Euler are a classic text on enzymes, studies of vitamins, an early report on streptomycin resistance in *Escherichia coli* and a dissertation on cancer chemotherapy that appeared two years before he died in 1964 at the age of 91.

When the parents separated Ulf and his one older and three younger siblings remained with their mother in the family's suburban home. While the children were growing up Astrid Cleve von Euler taught chemistry, joined a hydrographic commission and became interested in the study of plankton.

As a boy Ulf von Euler attended the local public

*Dr. von Euler rarely uses the hyphenated name.

†Sten his oldest son is a retired minister of foreign affairs; Curt L., a son by his second marriage, is a neurophysiologist at the Karolinska Institutet.

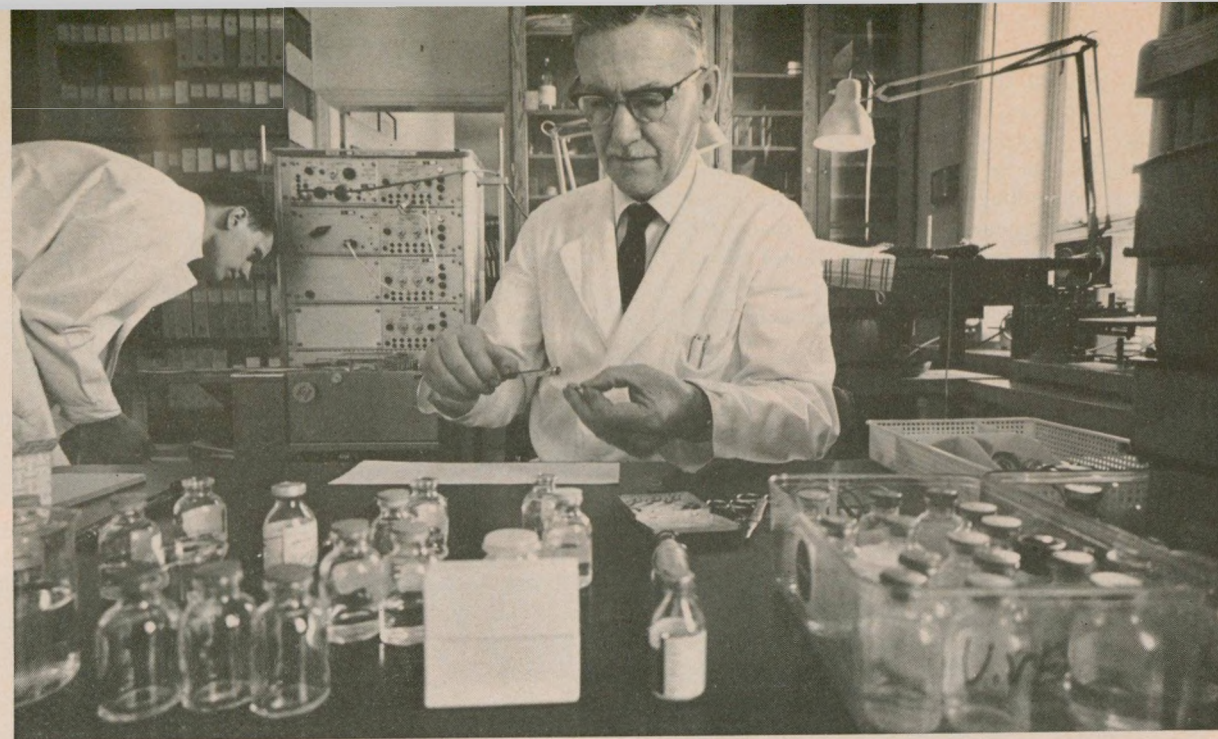
school where his first teacher also served as the church cantor, compiler of records and the health officer who gave the children their vaccinations. At 17 the youth received his baccalaureate, co-authored a chemistry paper with his father, and began his medical studies at Karolinska.

The government-sponsored Karolinska Institutet was established by royal decree in 1810 to train military surgeons after many Swedish soldiers died of infectious disease during the war with Russia. For many years its development was impeded by the rivalry of older schools at Uppsala and Lund but after Alfred Nobel gave it the privilege of awarding his prizes in medicine or physiology it became famous for its research and teaching.

The 89 permanent members of its faculty, which is twice the size of other Swedish medical schools, annually graduate about 200 students who have completed the seven-year course, including a rotating internship. The curriculum includes special courses in child psychiatry, social and war medicine, extensive clinical training at the adjacent 2500-bed Karolinska Sjukhuset and other hospitals in town. The school includes research units in bacteriologic bioengineering, aviation and naval medicine and associated with it are institutes of theoretic alcohol research, radiophysics, radiation protection. Among the illustrious faculty members are biochemist Hugo Theorell who won the 1955 Nobel Prize for his work on the enzymes of cell respiration, and Torbjörn Caspersson, head of the department of cell research and genetics.

Among Dr. von Euler's teachers were Hans Christian Jacobaeus, who worked out a method of crushing adhesions of the chest wall in the treatment of tuberculosis, and Johan Johansson who had collaborated with Nobel on blood transfusion experiments and apparently persuaded his friend to offer a prize in physiology or medicine. He spent some time in Otto Warburg's laboratory learning the German physiologist's technique for measuring tissue respiration, and in Stockholm he studied with Robin Fahraeus who developed the sedimentation rate test. Of about 12 papers that he published as a student one on the increased production of adrenaline during fever won the Swedish medical society's Alvarenga Prize in 1927.

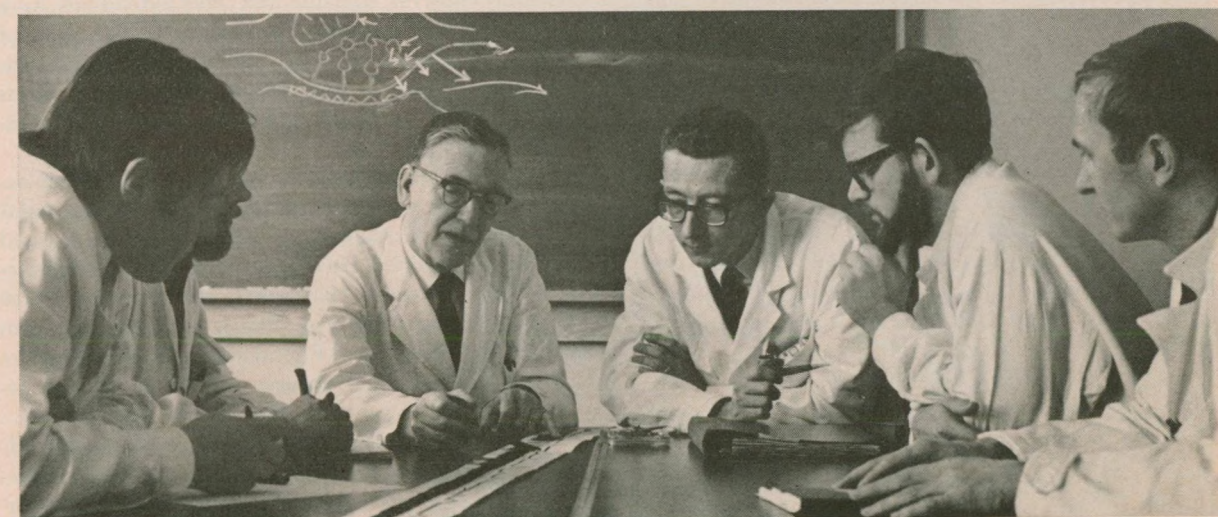
By the time he received his M.D. in 1930 Dr. von Euler had decided to concentrate on research. He won a Rockefeller fellowship and went to London to work in the late Sir Henry Dale's laboratory. At that time since chemical neurotransmission was one of the great frontiers in physiology, Sir Henry told his new researcher to try to demonstrate the presence of acetylcholine in the intestine. Dr. von Euler made a tissue extract that stimulated the rabbit's intestine but since its effect was not counteracted by atropine he knew that it was not acetylcholine or histamine. When he refers to these early experiments he says: "Being young and enthusiastic I was sure I had discovered a new substance. Sir Henry who was older and wiser was not as certain. He assigned me to work with John H. Gaddum." They found it was something new: substance P, a polypeptide related to bradykinin that is found in intestines, nerves, brain.



In his laboratory at the Karolinska Institutet Dr. von Euler prepares an experiment. His work includes research in the granules of adrenergic nerves. When not busy with meetings of school committees or the Nobel Foundation he usually spends afternoons in his laboratory. At right, a photograph of the Institutet which is sponsored by the Swedish government.



At the Institutet Dr. von Euler confers with young assistants he refers to as his "think tank." From left, Dr. Lagercrantz, Dr. Sjostrand, Dr. von Euler, Dr. Hedquist, Dr. Swedin and Mr. J. Lishajko, who is Dr. von Euler's personal technical assistant.



From London Dr. von Euler went to Birmingham to work with Ivan De Burgh Daly on the functional activity of pulmonary vasomotor nerves. His next stop was Ghent where he worked on the effect of chemical stimuli in controlling blood pressure and respiration with Corneille Heymans who credited their collaborative efforts when he received the Nobel award. Returning to London he studied factors influencing heat production in muscles with Nobel laureate Archibald Vivian Hill.

Back in Stockholm Dr. von Euler was looking for substance P in various tissues in 1934 when he discovered that an extract of the prostate exerted an unusually strong stimulating effect on smooth muscle.* He identified the potent substance as a lipid soluble acid, tested its physiologic effects and named it prostaglandin. At Dr. von Euler's suggestion biochemist Sune Bergström began an extensive study that showed that there were at least 13 prostaglandins. These new hormones which are most concentrated in human seminal fluid but also occur in the lung, pancreas, kidney, iris, menstrual fluid, brain and probably other tissues, lower blood pressure, inhibit uterine movement, lipolysis and gastric secretion. They counteract the effects of adrenaline and noradrenaline and when injected into the ventricles of the brain produce sedation. Many investigators think they may eventually be important as therapeutic agents.

Dr. von Euler, who was appointed full professor of physiology at Karolinska Institutet when he was only 34, became interested in aviation medicine during the war. He helped create what is now the board of defense medicine for Sweden which has not had a war for 155 years but maintains compulsory military service for men between 18 and 47.

In the late 1930s he continued research on the carotid sinus receptors, studied pressor substances in organ extracts and the effect of excitation on nerve permeability. He and Göran Liljestrand showed that breathing low concentrations of oxygen increased pulmonary arterial pressure; when André Cournand received a Nobel Prize for his work in cardiac catheterization he said this demonstration had stimulated his interest in hypoxia. While Dr. von Euler was working in Nobel laureate Bernardo Houssay's laboratory in Buenos Aires in 1947 he and Eduardo Braun-Menendez demonstrated the hypertensive effect of bilateral nephrectomy in parabiotic rats.

For many years physiologists had tried to identify the transmitter substance in sympathetic nerves: some suspected that it was adrenaline but a number of Dr. von Euler's experiments in the 1940s proved that it was noradrenaline. This important discovery stimulated a tremendous amount of research and introduced the use of less toxic noradrenaline for shock. Dr. von Euler says he was able to find the active substance because he had become "quite adept at making the tissue extracts that chemists call 'soups.'"

Some years later he and Nils Hillarp demonstrated the presence of tiny peas in the soup: granules about

0.05 of a micron in diameter in the terminal ends of sympathetic nerves. Remembering the way he had seen sugar cane pressed in Brazil Dr. von Euler squeezed cattle splanchnic nerves with an ironing machine, spun the juice in a high speed centrifuge and obtained a concentrate of the granules. He discovered that these minute bodies, visible by electron microscopy, take up or release noradrenaline depending on its concentration in the medium. Since the exchange takes place at a rapid rate the transmitter substance is always present and is never exhausted even after intense and continued stimulation of the nerve, owing to rapid resynthesis. Adrenergic blocking agents seem to have a common effect: they interfere with the uptake of noradrenaline by the granules.

The big question is what mediates this moving belt system, inasmuch as it cannot be a simple diffusion. It is known that adenosine triphosphate is involved, but a complete understanding of the process might explain other important transport mechanisms in the body.

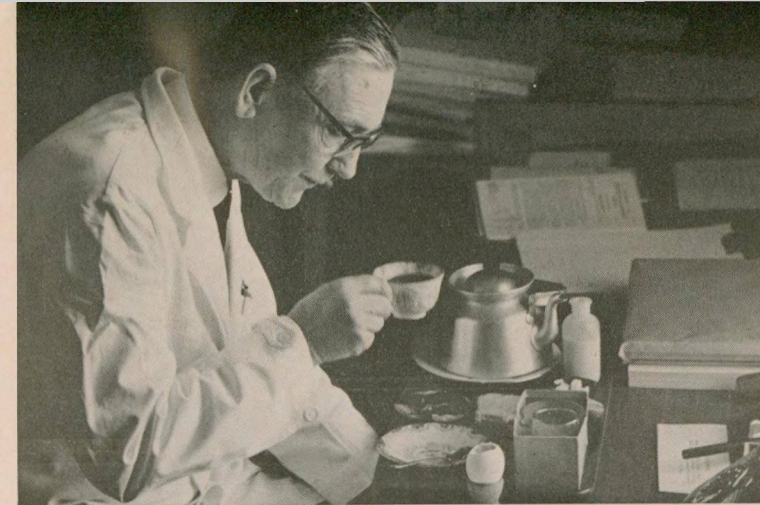
Among the many contributions from Dr. von Euler's extensive research are colorimetric and fluorometric techniques which he and co-workers developed for assaying noradrenaline and adrenaline in urine. He and Dr. Arthur Engel found that a marked increase in the excretion of these catecholamines was diagnostic of pheochromocytoma, a vascular tumor of chromaffin cells in the adrenal which is accompanied by palpitation, headache, visual disturbances.

With Rolf Luft he showed that standing increases the nervous release of noradrenaline which contracts blood vessels, thereby preventing blood from rushing to the legs. Other studies showed that physical work increases the output of noradrenaline which tends to be associated with aggressive reactions (fight) while emotional stress raises the level of adrenaline which is more closely related to anxiety or flight. When Dr. von Euler suggested testing the catecholamines excreted by astronauts it was found that Alan Shepard's output of adrenaline was high for four days before his flight and dropped six hours after he landed.

A study of paratroop trainees indicated that "oppositional, extrapunitive and maladjusted individuals have high noradrenaline and low adrenaline levels, whereas cheerful, sociable and vital individuals have low levels, and anxious individuals have high levels of both catecholamines." This suggested that vital individuals may not excrete noradrenaline under stress because they need not mobilize emergency mechanisms.

Nobel Prize. In addition to his own numerous experiments Dr. von Euler for many years had to evaluate the work of other researchers who were proposed for the Nobel Prize. He became a member of the selection committee in 1952, was chairman for three years, secretary for five. Since 1965 he has been chairman of the Nobel Foundation which administers the prize fund and supports several of its own research institutes.

While Dr. von Euler has several fine economic advisers, his work with the foundation involves numerous meetings. The selection committee's task con-



To have time for reading scientific literature and correspondence he lunches in his office on a sandwich, sometimes of smoked reindeer, and a boiled egg that he brings from home. Coffee is made in the laboratory.



As chairman of the Nobel Foundation since 1965 he presides over the ceremonies in which the Nobel prizes are awarded. Seated behind him at the 1966 ceremony are laureates Alfred Kastler (physics), Robert Mulliken (chemistry), Francis Rous and Charles Huggins (medicine and physiology), S.Y. Agnon and Nellie Sachs (literature). At right, he meets with the Nobel selection committee, of which he has been a member for 17 years.



*New York gynecologists Raphael Kurzrok and Charles C. Lieb in 1930 had reported that fresh human semen produced strong contractions or relaxation of the uterus.

tinues throughout most of the year. In September as many as 1000 scientists, physicians, former laureates and faculties of Swedish medical schools are invited to make nominations which the committee begins to review in February. By spring, when the field has been narrowed to the most serious contenders, various experts are asked to submit detailed reports of each candidate's research. Dr. von Euler spent a large part of last summer studying all the work of one man. In the fall after examining the experts' reports the committee submits its recommendations to the Karolinska faculty which makes the final decision. When the committee decides unanimously on one candidate the faculty's approval is usually a matter of form. At one time winners were informed in October and requested to keep the secret until the award ceremonies; now the Karolinska Institutet announces its decision to the press when it sends congratulatory cables to laureates.

On December 10, the anniversary of Alfred Nobel's death, the king of Sweden awards the prizes in an impressive ceremony witnessed by about 2000 guests in Stockholm's Concert Hall. With an interesting reversal of protocol the royal family in the first row of the audience remains standing until the laureates are seated on the platform. Then as each prizewinner is announced he descends a short flight of stairs to receive his medal, check and leather bound citation and walks up the steps to the platform without turning his back on the king.

After the presentations Dr. von Euler is host to about 750 guests at a banquet in the sparkling Golden Room of the Town Hall. Last year's laureates dined on smoked salmon, artichoke hearts, wild duck, salad and were toasted in Pommery & Greno brut champagne.

Some scientists think that were it not for his long association with the Nobel committee Dr. von Euler would have himself received the prize. He holds honorary degrees from the universities of Rio de Janeiro, Ghent, Tübingen, Dijon, Umea, Brazil's Cruzeiro do Sul and Sweden's Order of the North Star. He won the Carl Ludwig Medal, the Gairdner Foundation's award for medical research, Norwegian shipowner Anders Jahre's prize for outstanding research in Nordic medicine, and in Cleveland he shared the Stouffer Prize in 1967 for contributions to the understanding of hypertension and arteriosclerosis.

Dr. von Euler's working day begins at home where he attends to some of his voluminous mail before leaving for the office. At the institute he spends the mornings lecturing to medical students or conferring on the experiments of the day with his coworkers: currently he has 12 of them and thinks it would be difficult to supervise more.

To gain time for correspondence and reading the literature Dr. von Euler brings a sandwich from home, makes coffee in the laboratory and lunches in his office, a bright airy room filled with books, neat piles of journals and papers, photographs of colleagues and teachers. On afternoons that are not crowded with committee meetings at school or the Nobel Foundation in town he works in his laboratory. He says he is still "playing" with the interesting granules in adren-

ergic nerves and is grateful for a high speed centrifuge provided by the United States' National Institutes of Health.

At six he leaves the office and dines at home with his wife, the former Dagmar Cronstedt whom he married in 1958. When there are not evening meetings of the faculty, physiology or endocrinology societies his work begins again at seven; because of the many interruptions at the office he does his writing at home. He has published more than 375 papers and books including *The Physiology of Man*, *How the Human Body Functions*; *Noradrenaline* appeared in English, Swedish and was translated into Japanese. He co-edited a two volume *Comparative Endocrinology* and currently is the editor of *Acta Physiologica Scandinavica*. His most recent book, with R. Eliasson, is *Prostaglandins* (1968). His wife also does editing, and at ten o'clock they meet for tea.

Some evenings the von Eulers attend or give the elegant formal dinners for which Sweden is famous. Entertaining foreign guests is no problem as Dr. von Euler speaks German, English, modestly says he makes himself understood in French and Spanish; he has no problem with Danish or Norwegian which are similar to Swedish.

For summer holidays and winter weekends he and his wife take a 40-minute drive to the archipelago where they have a cottage near the seaside town of Vaxholm. Dr. von Euler likes to do gardening and chop logs in the surrounding woods.

His philosophy is that science needs three types of researchers: conscientious hardworking investigators who use standard methods; "unconventional, untidy, sometimes lazy" fellows who approach problems in a different way without caring about recognition; the organizers with many secretaries, several telephones and dozens of coworkers to handle systematically planned experiments. He cautions scientists to avoid banalities and says: "We must always guard the liberties of the mind and remember that some degree of heresy is often a sign of health in spiritual life."

Last year Dr. von Euler left Sweden at least ten times: he is peripatetic not by choice but because he finds it difficult to say no to the many requests he receives to attend international symposia or to lecture. He went to England for a study group that the Ciba Foundation arranged in his honor, to Italy, Yugoslavia, Mexico, Belgium, the United States and Australia where he visited his youngest daughter's family. He has four children by his first marriage: Leo, 38, is a physician with the National Institutes of Health in Bethesda; Christopher, 36, is a Stockholm anesthetist; Ursula who was born in 1941 is married to an official of Stockholm's National Art Gallery; Marie is the wife of an Australian engineer. With gentle humor Dr. von Euler says of visits to his grandchildren: "One has to go around inspecting them every now and then."

In 1968 Dr. von Euler wrote about a stimulating physiologist with imaginative ideas who "had a delightfully simple manner with young and old abhorring any form of conceit and pompousness." It was a tribute to his teacher and collaborator Göran Liljestrand but it could also describe Dr. Ulf von Euler.



In a rare moment of relaxation Dr. von Euler strolls with his grandchildren Louisa, his daughter Ursula's child, Fredrik and Gabriel, sons of his son Christopher. When he is not entertaining or being entertained, he does his writing at home in the evening, above, after dinner with his wife Dagmar, editor of a scientific journal whom he married in 1958. After writing for three hours, Dr. von Euler ends his working day by joining his wife at tea at ten o'clock in their graciously appointed living room.

