Meetings

Seventh Meeting of Nobel Prize Winners in Lindau

In July of 1957, the winners of the Nobel prize in medicine met in Lindau, Germany, for the third time. Among the participants were the following Nobel prizewinners: K. Alder (Cologne), M. Born (Bad Pyrmont), and O. Hahn (Göttingen).

Uses of Cortisone

In 1950, Philip S. Hench (Mayo Clinic, Rochester, Minn., U.S.A.) was awarded the Nobel prize, together with Kendall and Reichstein, for the discovery of treating rheumatic diseases with cortisone. Unfortunately, this treatment entailed some side effects, which are now subject to further medical research. In his address at Lindau, Hench considered this question.

It has been known since 1948 that cortisone and ACTH can suppress certain inflammations (rheumatic and gouty arthritis, rheumatic fever, and certain other diseases). Although numerous inflammations are modified by the use of cortisone, this drug cannot be rated as a specific for inflammations. During prolonged use of cortisone in the treatment of a disease like rheumatic arthritis, a number of undesirable reactions might occur: activation of internal conditions (either microbial or nonmicrobial) such as tuberculosis or gastric ulcers; increase in susceptibility to an epidemic disease such as influenza; or flare-up of the inflammation which is under hormone treatment. In order to find out more about the development of certain rheumatic and nonrheumatic inflammations, Hench concentrated on cases of relapses in connection with hormone and nonhormone therapy in surgical cases (for example, pregnancy and trauma). Reaction to the withdrawal of any kind of cortisone (in some cases this applies also to ACTH) includes effects connected with the remedy and others connected with the nature of the disease under treatment. Quite often, in cases of rapid change from spontaneous or stimulated overdoses of cortisone in the blood (hypercortisonism) to subnormal amounts of cortisone in the blood (hypocortisonism), certain reactions may occur in susceptible persons. Those are two factors that have to be considered: the sensitivity of the patient and an abrupt hypercortisone transfer.

The factors that provoke reactions need some special consideration, since they are often related to prolonged therapy. Thus, patients, who are susceptible to those factors may be unknowingly exposed and several ordinary diseases might be activated. The most important point in this connection is the fact that not only can these factors produce a reoccurrence and spread of a disease but they can also produce first attacks of these latent diseases. The period of greatest danger for susceptible patients seems to be shortly after the appearance of the first symptoms of rheumatic disease and the intensification of the hypercortisonism. The results may include different kinds of inflammation of the joints as well as of eye, skin, and blood vessel components.

The conclusions drawn by Hench show that patients with gout, rheumatic fever, rheumatic arthritis, psoriasis, and lupus erythematodes seem to react normally to the biochemical stress of abnormally high levels of cortisone in the blood stream. Symptoms in the joints, if not already present, do not appear. If present, they are suppressed as long as the biochemical stress is maintained, either in a natural or a therapeutical way. As soon as the hypercortisone phase decreases and terminates, an acute or subacute joint- or skin inflammation breaks out. This kind of patient seems to adjust very well to the biochemical stress; however, it is extremely difficult to bring him back to his normal status.

Lung Angiography and Catheterization of the Heart

Twenty-eight years ago, Werner Forssmann (Bad Kreuznach), the second speaker of the first evening, performed on himself the first probing of the heart. He started his experiments shortly after receiving his M.D. degree at the University of Berlin. He introduced a catheter 65 centimeters in length through the vein of the elbow into the ventricle of the heart and thus demonstrated the possibility of examining the heart in a relatively safe way. In his address, Forssmann only casually mentioned his experiment, but the significance of selective lung angiography and of catheterization of the heart for clinics of heart and lung diseases was obvious.

We all know that there is a close relationship between respiration and the circulation of the blood, and we realize that every disease provokes a disturbance of the metabolism, a change in the circulation of the blood and of the respiration. This fact was discovered more than three hundred years ago by William Harvey, who described "the great circulation of the blood," in his book *De Motu Cordis et Sanguinis,* in 1628. There was a long and difficult road ahead through the centuries. In 1710, for the first time, exact research was carried out on the circulation of the blood, and the volume passed per minute was determined. Two centuries later measurements of the arterial blood pressure followed. These experiments and similar ones, performed on animals, enabled research workers to measure the blood pressure and metabolism by exposing the vein of the neck and inserting a tube from there to the right side of the heart.

In 1929, with Forssmann's experiment on himself, a catheter was introduced into the human heart for the first time. However, this method of examination was not given much consideration at first, and it was only in 1941 that Cournand came back to it. He succeeded in passing the catheter through the right side of the heart to the periphery and measured the pressure of the artery of the lung.

A surgeon must have an exact x-ray picture in order to diagnose and plan a successful operation. As early as 1930 good x-ray photographs were obtained in dogs who had been given intravenous injections of contrast media which filled the small blood vessels. Only much later, after a series of difficult experiments, was this method (called angiocardiography) adapted for man. By means of a catheter which is introduced all the way to the heart or to the lung and through which a relatively small amount of a contrast medium (8 to 11 milliliters) is injected into the area which is to be photographed, it was possible to obtain good x-ray pictures, which could be used by the surgeon. Today we are in a position to make x-ray pictures of these organs and to use them for purposes of research, thanks to selective lung angiography. With a small amount of contrast compound it is possible to show, by means of this kind of x-ray technique, the fine structure of the vessels with their ramifications. This method made it possible to introduce the von Euler-Cournand effect into the clinic in 1953. This effect proves that bad circulation within the lung causes a throttling of the connecting vessels. This permits certain conclusions about the healing of

tuberculosis through the pneumothorax method, which is based on the theory that a lung which is at rest or whose volume is diminished is better nourished than another, and that healing is thus accelerated in tuberculosis. On the basis of the von Euler-Cournand effect we are forced to admit that those conclusions are not relevant and thus that the use of the pneumothorax method should be considerably reduced in favor of other treatments. One can summarize the argument in the following way: owing to the disease of the lung parenchyma, less ventilation of the lung takes place. Thus the vessels are narrowed, and this leads to an increase of resistance to the flow of blood. This increase in resistance results in an increase in pressure in the artery of the lung, and this must be transferred to the right side of the heart. Naturally, this increased burden cannot be handled for a long time by the right side of the heart and will gradually result in insufficiency of the heart. This shows clearly the functional and pathological unity of the lung, the blood circulation, and the heart, and one realizes that the selective angiography of the vessels of the lung should not be considered as an isolated topic.

What does the selective angiography mean in cases of heart disease? In the case of mitral stenosis (narrowing of the mitral valve between the left auricle and the left ventricle of the heart) we have a clinical model which shows us what can be accomplished by heart surgery in case of a valve rupture. It is well known that in the case of a stenosis of the mitral valve, the pressure is increased within the lesser circulation; use of the catheter makes this evident. But how shall we know whether this increase in pressure is the result of a functional, reversible narrowing (regulatory adaptation) or whether it is due to a permanent, irreversible narrowing? In the latter case more harm would be done by a valve rupture. This is where the selective angiogram gives the correct picture and shows the prevailing situation to the heart surgeon. This example shows us that, since the introduction of the angiogram into the clinic, it has been possible to determine the need for surgery at a stage when there is the greatest possibility of its being successful, before organic changes have occurred which cannot be treated by means of surgery. As Forssmann expressed it: "These methods brought us a deep insight into the physiological sides of the problem, which up to now were ignored and which will help us considerably in curing human beings. We actually entered an era of studying circulation. The greater circulation has been subject to research for a long time, whereas the lesser circulation has been more or less neglected. One-sided research in medicine can never bring progress, but only retrogression. Only if everything is included do we get the picture as a whole. Medicine, which all of us revere, seems to me like an unexplored work of art which can be seen in different lights and from different angles. Always one can find new beauty in it, and yet it is always the same. Medicine constantly opens up new insights into life and so, sooner or later, this circulatory concept will be replaced by something new, as earlier ideas have been replaced and yet have never become obsolete."

New Insights in Cancer Research

Wendell M. Stanley (Berkeley, California) discussed in a very broad manner the possible relations between viruses and cancer. The discovery, around the turn of the century, of the first viruses—the tobacco mosaic, the foot-and-mouth, and the yellow-fever viruses—did not stir up too much excitement, and the knowledge in this field did not rouse very much interest in the 1920's. By about 1930 it was possible to determine, with some accuracy, the size of certain viruses (they were found to be smaller than some protein molecules). In 1935 the tobacco-mosaic virus was isolated in crystal form and recognized as a nucleoprotein. It was discovered that this nucleoprotein molecule has a diameter of 15 mμ and a length of 300 mμ and that it possesses the extremely high molecular weight of 50 million. Thus, it is larger than any molecule ever described before, but it was also discovered that it possesses all the qualities of the larger protein molecules which are related to this kind of protein molecule. The same material could be extracted from plants which had the mosaic disease, and thus was discovered a molecule which was able to reproduce itself and to have mutations. It seemed that the difference between living and lifeless substance was not very sharp any more, and this was the beginning of a complete revolution in the ordinary concepts in this field.

Today we know that the gap between 20 and 200 mμ—that is, between the molecules of the chemist and the organisms of the biologist—is closed by the viruses. Some of the larger viruses are larger than several of the known living organisms, whereas other smaller viruses are actually smaller than certain albumin molecules.

For a long time it was believed that animal and human viruses are fundamentally different, since all crytalline viruses that had been discovered were plant viruses. This belief, however, became obsolete when the two Americans, Schwerdt and Schaffer, discovered poliomyelitis viruses, which represent a typical animal or human virus, in *crystalline* form. Since then, at least one more animal or human virus has been observed to be crystalline; this was the Coxsackie virus, which was discovered by the American Mattern. Hundreds of viruses are known, and yet only about one dozen could be isolated in pure form. Stanley thinks it is justifiable to assume that viruses cover the range from small crystallized animal, human, or plant viruses, through intermediate structures consisting of nucleoproteins, lipoids, and hydrocarbons, to those viruses which have the same morphology and composition as the organisms which consist of cells. All these structures are somehow related to each other by their own characteristic property, and they are all able to reproduce themselves.

In 1903 Borell thought that cancer could be the result of the living and reproductive forces established in the virus. In the meantime several laboratories have found evidence of the virus etiology of cancer, and thus it may be expected that viruses will be found to be responsible for most kinds of cancer. Cancer is a problem of growth ("cancer is life against itself," as F. Deich has pointedly said). The fact that, up to now, only two kinds of little-studied, benign tumors in human beings are known to be caused by viruses, and that it has not been seriously assumed that excitants are present in human cancer, does not mean that these are nonexistent and that they are of no etiological significance. It only means that, up to now, efforts to prove the existence of a virus as a causative factor in cancer have been (for one reason or another) without success. The assumption, as a working hypothesis, of a viral etiology in human cancer will cause a significant change in the attitude of many researchers. This is a necessity, if a correct approach and correct experimental planning are to result.

There is no proof that human cancer is infectious, but it is known that viruses that cause tumors can be both filtrable and infectious at times and, at other times, nonfiltrable and noninfectious. Apparently this is connected with the fact that the viruses are very specific and that a certain virus only infects a certain type of cell. Thus, under different conditions it does not appear to be infectious. This explains the difficulty in demonstrating the existence of virus in human cancer. The breeding of normal and malignant cells offers a good approach. Experiments of this kind are carried out in the laboratories at the University of California, Berkeley. The fact that many different kinds of human viruses have been found leads to the conclusion that there must be still undiscovered viruses in a supposedly healthy human being. It is significant that the infection of cancer cells of a certain type with certain viruses causes the destruction of the cancer cells. Due to the mutability of the viruses, it should be pos-

sible, with the help of already known passage techniques, to develop viruses which have no effect on normal cells but which have a special specificity for the destruction of cancer cells. Various laboratories are now working on these problems.

The fact that viruses are able to remain in cells for generations makes a relationship between virus and gene probable. Genes and viruses are carried over from one generation of cells to another. It was found, for example, that genetic factors of one type of *Salmonella* cells can be transmitted through bacteriological viruses to another. Thus it has been supposed that, under certain circumstances, genes act like viruses and vice versa, that viruses can cause cancer, and that they are forms of the transition zone of life, carrying both life and molecular characteristics.

A discovery which was recently made in the laboratories of Stanley by Fraenkel-Conrat changed the situation considerably. It can now definitely be assumed that nucleic acid is the dominating factor in these considerations. Fraenkel-Conrat and, a short time later, the Germans Gierer and Schramm, discovered that after the tobacco mosaic virus is treated in a special way, a specific nucleic acid is found which possesses the characteristics of viruses. It seems to be a fact that a nucleic acid entity of molecular weight about 300,000 contains, within its approximately 1000 nucleotides, the information to allow the production of the same nucleic acid within its host cell, and apparently it is also able to perform the synthesis of its own characteristic and specific protein, by which it is surrounded. These experiments give beautiful proof of a direct relationship between specific nucleic acid and specific protein synthesis, and they make it possible to consider the activity of the virus and gene, including their temporary connection with cancer, in the form of nucleic acid and not as a nucleoprotein. The finding that viruses, genes, and cancer are all directly dependent upon the structure of nucleic acid is considered extremely important. In Stanley's words, "These and similar studies lead you directly to the heart of the whole cancer problem and should be able to bring a solution in this field, which today is quite confused."

Georg von Hevesy (Stockholm), who almost every year gives an outstanding report on his research, talked about cancer anemia. In recent years many scientists have worked on the concentration of hemoglobin in the blood of persons stricken with cancer. Determinations of concentration showed that the hemoglobin concentration in most people with cancer is 20 percent or more below the concentration in healthy people. This phenomenon, however, very often finds compensation in an increase in volume of blood in people stricken with cancer, and thus the total number of red blood corpuscles of patients with cancer equals that of healthy people. The concentration of hemoglobin in the blood depends on the decay and production, per unit of time, of hemoglobin molecules. It is also determined by the number of red blood corpuscles (which contain the hemoglobin) which decay and originate in this same time interval. These quantities can be determined through radioactive labeling of the iron, one of the main constituents of the hemoglobin.

W. M. Stanley, M. Born, W. Forssmann, S. A. Waksman, O. Hahn, K. Alder, G. von Hevesy, P. H. Muller, P. S. Hench, G. Domagk.

Dal Santo, a colleague of von Hevesy, made some experiments in Stockholm on patients suffering from cancer of the uterus. He found that, quite often, red blood corpuscles have a shorter lifetime in a cancer-stricken organism than in a healthy one but that the shorter lifetime is usually compensated for by a faster new growth of red blood corpuscles.

Similar results were obtained in the United States and by Kiderlein in the clinic in Freiburg im Breisgau, with patients who had cancer in other organs. The shortening of the lifetime of the red blood corpuscles in a cancerous organism is due to the presence of one of these attacking agents in the blood and is also due to the beginning of the growth of abnormal red blood corpuscles in the cancer. This can clearly be seen in experiments with animals, performed in Stockholm by von Ehrenstein. He labeled the red corpuscles of several hundred mice with radioactive glycine. The disappearance of the radioactivity from the blood shows the rate of decay of the red corpuscles. If, after the labeling of blood corpuscles, cancer cells were injected into the animals and tumors resulted, it was found that the radioactivity disappeared twice as fast from the blood of these animals as from that of healthy animals. But the cancerous animals had the same amount of hemoglobin as the healthy ones, since the rapid decay of the blood corpuscles was compensated for by a more rapid formation of new cells. This could also be proved by the fact that the marking of the red blood corpuscles occurred only after the formation of a tumor—that is to say, not in a healthy but in a cancerous animal. Four times as much radioactive hemoglobin was formed in the red blood corpuscles of a diseased animal as in those of a healthy animal. This result very clearly shows the rapid formation of red blood corpuscles in cancerous animals. With this kind of experimentation the way is paved for drawing conclusions, from investigation of the blood, about the existent cancer cells and their activity.

Gerhard Domagk (Wuppertal-Elberfeld), who introduced the sulfonamides into medicine, talked about the chemotherapeutical side of the malignant tumor. The first inhibitor of cell growth (cytostaticum) found, by Otto Warburg, urethane, arrests mitosis in cell tissues. Later on it was observed that urethane not only is cytostatic but also can produce cancer. Other groups, amongst them benzpyrene, were only of passing interest. The cytostatica developed by Domagk brought great relief in the treatment of polycythemia but, on the other hand, also the danger of the formation of new bone tumors. In this ambiguous therapy it is up to the physician to decide whether the patient can be helped

or not by the taking of this medicine. In the 1920's, while doing research on cancerous cells, Warburg found a reduced cellular metabolism, with intensified fermentation. For a long time it was not possible to repeat these experiments in other laboratories, because of the extreme difficulty of the measuring technique, but, through the use of isotopes, these results have been confirmed and carried further. Today we consider tumorous cells to be deteriorated cells, marked by certain morphological structures, and we notice a loss of the mitochondria. This degeneration can also be noticed in the metabolism of these cells through the loss of certain enzyme systems, like respiration ferments. This can be caused through the inhalation of destructive matter or through wrong nutrition during part of the lifetime of an organism, or as a result of other, not yet defined, injuries.

In the last few years it has been possible to combine many single results, and in this way it was found, for instance, that the activity of the cytochrome oxidase and the oxysuccinic acid in sarcomas are only one-fifth those in normal liver cells. A reduction of the catalase content was also noted. The effect of effective cytostatica, like triosephosphate dehydrogenase, for instance, today can be seen in these enzyme systems. Lewisite compounds not only made tumors disappear but also caused tumors, and thus could only be used within limitations. Arsenic and heavy metals (such as lead and gold) are not in great use any more today. But great interest was aroused in the group of the antimetabolites, which include the cytostatica. These were able to prolong the life of leukemia-stricken children by years. Specific and nonspecific albumin therapy in the meantime also brought some success. Cortisone alone or in combination with mercaptopurine showed certain results. Further research is in progress on ways to increase the prophylactic forces in the organism by extracting preparations from tissues immune to tumors. These substances, however, cannot be considered as real cytostatica. The treatment with heterosexual hormones brought good results with carcinoma of the prostate, but there is the fundamental question whether the majority of these tumors can still be considered as genuine cancer. Overdoses, which are quite often given, result in an inverse effect (mammary gland carcinoma). Among the antibiotics there can also be found cytostatic substances, such as actinomycin C and D, which show success with lymphogranulomatosis and Hodgkin's disease. In the meantime new actinomycins have been found, but they have not yet been used in clinics. "That there really are chemotherapeutical drugs to cure cancer has never been stated in any scientific publication, nor has it ever been mentioned in any lecture, only in noncritical newspapers and magazines," stated Domagk.

We can talk about a supplementary chemotherapy of cancer, and in this connection the so-called ethylene iminochinones are of special interest. These substances, belonging to the groups of the cytostatica, not only retard the growth of tumors but also inhibit the growth of normal human, animal, and plant cells. With these substances, the germination of wheat can be stopped. Therefore care must be exercised in administering these drugs in people who are capable of procreation, since these substances are able to change the genes, just like x-rays and other radioactive rays.

These cytostatica can be used only on patients with tumors on which it is too late to operate, and we should be grateful that in this way we are able to prolong the life of the patient under tolerable circumstances. E 39, in the form that is soluble in water, promises a better method of application, as has already been observed on animals which were under constant control for 45 days. It could be confirmed by microscopic examination that tumors of the size of walnuts had decreased considerably. But

one should not be misled by these experiments, since some animals, when under treatment, refuse all food. But during the experiments described above the animals gained weight, which means that E 39 has a "tumor specific" effect.

With surgery we try to eliminate the tumorous cells as completely as possible, but success is very rare, especially when one considers the metastases. Good results are also obtained by means of radiation therapy, but in this treatment one must consider that radiation therapy also destroys the natural prophylactic forces of the body. Therefore the smallest dose possible is applied in therapy for malignant tumors, and one has to be extremely careful to hit the tumorous cells only. By now it is very well known which tumors are best removed through surgery and which ones should be exposed to radiation therapy. Chemotherapy is applied only to tumors which can neither be removed through surgery nor treated with irradiation, and so the chemotherapy has by far the most difficult task to accomplish. It therefore cannot be expected that all treatments of malignant tumors by chemotherapy can be successful. Lately, intravenous injections of ethylenimine compounds have been rather successful. Whether the climate of the North Sea has something to do with the success of these treatments is hard to determine. Research is being done on these questions at the University Clinic for Throat, Nose, and Ear in Münster in Westfalen, Germany.

It must be understood that a body stricken with cancer generally is a weakened organism, a fact which is also to be taken into account in regular treatments. The individual thus stricken should seek rest and a suitable climate for the chemotherapeutical, surgical, and radiation treatments. These requirements are even more important for the cancer patient than they are for the tuberculosis patient. We know from experience that in a case of oxygen deficiency—that is to say, in a poorly aired room—animal tumors grow faster than in the climate of the North Sea. The living conditions of people in big cities become more and more unnatural as a result of exhaust fumes, dust, and so forth, and thus the number of cases of cancer will steadily increase. To quote Domagk: "In therapy we will have to be satisfied, for the present at least, with a certain equilibrium between body cell and tumorous cell, even if the tumor cannot be completely eliminated. We will be satisfied if we can slow down its growth, in order to preserve the life of the patient longer and under bearable conditions. In this case too, we have to learn to think more physiologically and less naively. The chemotherapy of cancer still is in its very beginning and will have to be further extended. The observations we have collected to the present day show that not only leukemia but also carcinomas and sarcomas can be influenced through cytostatica. This seems to be the most important result for the further development of the therapy. The results of these experiments can be related to the treatment of different malignant tumors in man, at least in principle, and this is decisive for further experiments."

Antibiotics

"The influence of antibiotics on human society has been so tremendous that one was almost tempted to call the present era the age of the antibiotics instead of the atomic age." With these words, Selman A. Waksman (New Brunswick, N.J., U.S.A.), started his talk on the social significance of the antibiotics. This scientist, who was awarded the Nobel prize for physiology and medicine in 1952, is the discoverer of streptomycin, which has shown good results in the treatment of tuberculosis in particular.

Through the progress of practical medicine and public health efforts, the life expectancy of man, which was about 30 years in the 18th century, has been increased to about 70 years. If medicine continues to develop at the

same pace, the life expectancy should reach almost 100 years by the end of this century. These prolongations of the life span can be explained through the fact that diseases, particularly in infancy, are much better controlled than they used to be. Although tuberculosis could be controlled to a certain extent one hundred years ago, nevertheless 500 out of every 100,000 persons died (this includes deaths in all countries of the world). Last year the mortality in the United States and in some European countries was down to about 10 per 100,000. Streptomycin, the first of the drugs used in the medical treatment of tuberculosis, was soon followed by others, such as para-aminosalicylic acid. Lately it has been discovered that isonicotinic acid hydrazide has healing effects in tuberculosis. Since 1940, the year of the discovery of the first antibiotic, many epidemics and infectious diseases have been treated with great success—diesases such as pneumonia, syphilis, typhoid fever, typhus, tularemia, undulant fever, plague, and cholera.

The amazing success of the application of antibiotics also caused great social changes, which I will discuss shortly. The almost complete abolition of diseases of childhood as a result of the use of antibiotics can be shown best in the figures on tubercular meningitis. Until 1946, with no chemotherapy available for this disease, the mortality was 100 percent. In 1947, with the introduction of streptomycin, the mortality was 80 percent. In 1950, with para-aminosalicylic acid therapy also in use, the mortality was 50 percent. And in 1953, with isonicotinic acid hydrazide complementing the other two drugs, mortality was down to 15 percent. Countries which previously had a great mortality among infants, which served as a brake on the constant rise of the population, now are facing serious problems in the fields of economics and population policy, such as birth control.

The prolongation of the life span of the average human being poses the problem of finding ways to look after older people and of finding work for them. Countries which are already overpopulated and have a steadily increasing number of jobless people face a serious social problem. A slow decrease in the number of hospitals and sanatoria can be predicted. Just consider the formerly prolonged treatment of tuberculosis. The increased tendency toward ambulatory treatment of patients should not be overlooked, either. In the future, a short period in the hospital will be followed by treatment on the outside by the family physician. Greater safety in the use of vaccine preparations has been made particularly evident with the development of vaccines against virus infections such as poliomyelitis. An increase in the production of food has been

made possible through elimination of various infectious diseases in plants and animals and, moreover, improvements in food preservation have been made by adding antibiotics to food products. Another tremendous area of progress is that of the psychological attitude toward disease. There need be, in the future, no more panic and fear of epidemics and diseases which used to decimate the human race. The fact that venereal diseases can be controlled harbors also a great danger and may lead to an unimaginable degree of carelessness concerning mental and physical hygiene. The appearance of certain new diseases needs definite attention. This fact is connected with the reduction of natural resistance. Nevertheless, one should not overemphasize this problem.

The situation of the physicians has changed too. They have at their disposal a great many antibiotics which they can use, but they have to judge in each case whether, by killing the primary cause of the disease, they may not activate a secondary disease germ. No physician should allow himself to let antibiotics replace his reasoning.

The extensive use of antibiotics is another social aspect. In the first place, there exists the tendency toward self-treatment. Then there is the patient's expectation of a rapid cure, and if it is not forthcoming, he blames the physician or the antibiotic. As Waksman remarked, "In the case of severe chronic diseases or diseases of unknown etiology, such as cancer, many have come to expect miracles from newly discovered antibiotics and other drugs. Excessive promises have been made, even to the effect that 'cures' will be forthcoming after so much money has been spent for research."

Paul Hermann Müller (Basel, Switzerland), who was awarded the Nobel prize in 1948 for his discovery of DDT as a contact poison, talked about the further development of the antibiotics and application in agriculture. Ever since 1942, the so-called "antibiotics era," more than 3500 different substances with antibiotic effect have been discovered, but only 17 preparations have been made available commercially. It is surprising to see their fast spread and increased use in many fields. Since 1950, the production of these extremely helpful chemicals has tripled.

New applications for the protection of staple goods and plants, and in agriculture, are constantly found. In the use of antibiotics for plant protection, the most limited range of action is against fungi; yet the fungus diseases are more important than the bacteria against which the antibiotics have a relatively broad range of action.

One of the few antbiotics with a definite fungicide effect is cycloheximid or actidion, which is a by-product in the production of streptomycin. Actidion is effective against mildew and mint rust and is also used against the disease of cherry trees (Schrotschuss) caused by *Clasteroporium carpophilum* AD. In contradistinction to inorganic fungicides it can be used on fruit-bearing trees. For the protection of stored food, and in animal breeding, antibiotics are used more and more. In 1954 about 250 tons were added to animal food, as a growth stimulant. The cause of this effect, however, could not be explained definitely. Thus it is understandable that a certain skepticism still prevails.

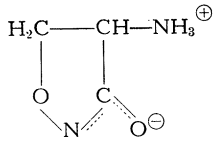
New experiments, carried on mostly in Germany, show that effects similar to those produced by antibiotics can be obtained with ordinary substances (for example, nasturtium or horseradish) without side effects (for example, change in the intestinal flora).

The addition of antibiotics to easily perishable foods also presents a certain danger, which should not be overlooked; it creates the possibility that human beings may be constantly given small, uncontrolled amounts of antibiotics. As a result, there is the possibility of a gradual development of resistance by important pathogenic bacteria. Besides this, a change in the intestinal flora may

also appear. In view of these reasons, it is forbidden in the United States to add antibiotics to uncooked food.

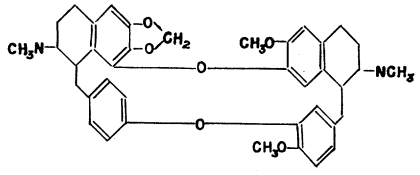
In the last three years, more antibiotics have been introduced; these I will mention briefly:

Cycloserine: This has a very broad range of action on Gram-positive and Gram-negative bacteria and against strains of *Mycobacterium tuberculosis.* It is a 4-amino-3-isoxazolidon with a relatively good stability in an alkaline environment, and has the following structure:



Gonyleptidin: This antibiotic was isolated from the glands of a South African spider of the Gonyleptidae family, and is effective against 18 kinds of bacteria. It consists of a mixture of various benzochinones in which 2,3-dimethyl-, 2,5-dimethyl-, and 2,3,5-trimethyl benzochinone predominate.

Cefaranthin: This is an alkaloid and antibiotic, isolated from the roots of the *Stephania cepharantha* Hayata. It is effective as a preventive for tuberculosis, leprosy, and whooping cough, and inactivates snake poison and toxine of tetanus. It has the following structure:



In this connection, gibberellic acid should also be mentioned. This is not a real antibiotic but, in very small amounts, has physiological effects. The active material, which is extracted from the mushroom *Gibberella fujkuroi,* strongly influences the growth of plants. In this way the growth of geraniums, roses, sunflowers, beans, pepper, corn, and so on, can be tripled after 4 weeks of treatment. But for application on a large scale in agriculture, more practical experience with this new product is needed.

H. ROTTA

Stuttgart, Germany

We are indebted to Mrs. Heidi Steffen of Purdue University for translating this report from the German.

Forthcoming Events

November

12–15. Society of Naval Architects and Marine Engineers, 66th annual, New York, N.Y. (W. N. Landers, SNAME, 74 Trinity Pl., New York 6.)

16–21. Radiological Soc. of North

America, Chicago, Ill. (D. S. Childs, 713 E. Genesee St., Syracuse, N.Y.)

16–23. Scientific Information, intern. conf., Washington, D.C. (Mrs. M. Sheppard, Intern. Conf. on Scientific Information, Natl. Acad. of Sciences–Natl. Research Council, 2101 Constitution Ave., Washington 25.)

17–19. Association of Military Surgeons of the U.S., Washington, D.C. (R. E. Bitner, Suite 718, New Medical Bldg., 1726 Eye St., NW, Washington 6.)

17–20. Conference on Magnetism and Magnetic Materials, Philadelphia, Pa. (H. B. Callen, Dept. of Physics, Univ. of Pennsylvania, Philadelphia.)

17–22. Radiological Soc. of North America, Chicago, Ill. (D. S. Childs, Sr., 713 E. Genesee St., Syracuse 2, N.Y.)

18–20. Air Pollution, 1st natl. conf., Washington, D.C. (Dept. of Health, Education, and Welfare, U.S. Public Health Service, Washington 25.)

18–20. Standards, 9th natl. conf., New York, N.Y. (American Standards Assoc., 70 E. 45 St., New York, N.Y.)

18–21. Weather Radar Conf., 7th, Miami Beach, Fla. (K. C. Spengler, American Meterological Soc., 3 Joy St., Boston 8, Mass.)

18–22. Pan-American Dental Cong., Mexico City, Mexico. (Association Dental Mexicana, Sinaloa 9, Mexico 7, DF, Mexico.)

19–21. Electrical Techniques in Medicine and Biology, 11th annual conf., Minneapolis, Minn. (O. H. Schmitt, Univ. of Minnesota, Minneapolis.)

20–22. Acoustical Soc. of America, 56th meeting, Chicago, Ill. (K. Kramer, 3839 Grand Ave., Western Springs, Ill.)

20–22. American College of Cardiology, New Orleans, La. (P. Reichert, Empire State Bldg., New York 1.)

20–22. International Symp. on Tuberculosis, Philadelphia, Pa. (M. J. Schwartz, Deborah Sanatorium & Hospital, 642 Widener Bldg., Philadelphia 7.)

20–23. American Anthropological Assoc., Washington, D.C. (W. S. Godfrey, Jr., APA Logan Museum, Beloit College, Beloit, Wisc.)

20–23. European Confederation of Agriculture, Vienna, Austria. (M. H. Abegg, Confédération Européenne Agriculture, Brougg (Argovie), Switzerland.)

21–22. American Soc. of Animal Production, annual, Chicago, Ill. (H. H. Stonaker, Animal Husbandry Dept., Colorado State Univ., Fort Collins, Col.)

24–26. Fluid Dynamics, division of American Physical Soc., San Diego, Calif. (R. J. Emrich, Dept. of Physics, Lehigh Univ., Bethlehem, Pa.)

24–26. Mechanisation of Thought Processes, symp., Teddington, Middlesex, England. (The Secretary, Natl. Physical Lab., Teddington, Middlesex.)

24–6. Plant Specialists, 4th Latin American conf., Santiago, Chile. (R. Cortazar, Departmento de Investigaciones Agricolas, Ministerio de Agricultura Casilla 4088, Santiago, Chile.)

27-29. Central Assoc. of Science and Mathematics Teachers, 58th annual, Indianapolis, Ind. (N. G. Sprague, Indianapolis Public Schools, 1644 Roosevelt Ave., Indianapolis 18.)

28–6. International Conf. of Social Work, 9th intern., Tokyo, Japan. (J. R. Hoffer, Intern. Conf. of Social Work, 345 East 46 St., New York 17, N.Y.)

30–5. American Soc. of Mechanical Engineers, 79th annual, New York, N.Y. (O. B. Schier, ASME, 29 W. 39 St., New York 18.)

December

1–3. American Soc. of Refrigerating Engineers, New Orleans, La. (R. C. Cross, ASRE, 234 Fifth Ave., New York 1.)

1–4. Entomological Soc. of America, Salt Lake City, Utah. (R. H. Nelson, 1530 P St., NW, Washington, D.C.)

1–5. American Rocket Soc., 13th annual, New York, N.Y. (A. F. Denham, 925 Book Bldg., Detroit 26, Mich.)

2. Scientific Study of Glass, 11th technical meeting of the European Union, Paris, France. (Société française de céramique, 44, rue Copernic, Paris 16e.)

2–4. Electric Steel Furnace Conf., 17th, Cleveland, Ohio. (E. O. Kirkendall, AIME, 29 W. 39 St., New York 18.)

2–5. American Medical Assoc., clinical meeting, Minneapolis, Minn. (G. F. Lull, 535 N. Dearborn St., Chicago, Ill.)

3. Animal Care Panel, 9th annual, Chicago, Ill. (R. J. Flynn, Argonne Natl. Laboratory, Lemont, Ill.)

3–5. American Inst. of Electrical Engineers, St. Petersburg, Fla. (N. S. Hibsham, AIEE, 33 W. 39 St., New York 18.)

3–5. Eastern Joint Computers Conf., Philadelphia, Pa. (G. W. Bailey, IRE, 1 E. 79 St., New York 21.)

3–5. Global Communications, 2nd natl. symp., St. Petersburg Beach, Fla. (M. R. Donaldson, 1501 72 St. N., St. Petersburg.)

4–5. Vehicular Communications, annual, Chicago, Ill. (G. W. Bailey, IRE, 1 E. 79 St., New York 21.)

5–7. American Psychoanalytic Assoc., New York, N.Y. (J. N. McVeigh, APA, 36 W. 44 St., New York 36.)

6. American Rheumatism Assoc., Rochester, Minn. (E. F. Hartung, ARA, 580 Park Ave., New York, N.Y.)

6–11. American Acad. of Dermatology and Syphilology, Chicago, Ill. (R. R. Kierland, Mayo Clinic, Rochester, Minn.)

7–10. American Inst. of Chemical Engineers, annual, Cincinnati, Ohio. (F. J. Van Antwerpen, 25 W. 45 St., New York, N.Y.)

8–10. American Nuclear Soc., winter, Detroit, Mich. (ANS, P.O. Box 963, Oak Ridge, Tenn.)

9–10. Conference on Learning Effectiveness, Univ. of Pennsylvania, Philadelphia, Pa. (Air Force Office of Scientific Research, Air Research and Development Command, U.S. Air Force, Washington 25.)

10–16. American Acad. of Optometry, annual, Boston, Mass. (C. C. Koch, 1502 Foshay Tower, Minneapolis, Minn.)

12–13. Association for Research in Nervous and Mental Disease, annual, New York, N.Y. (R. J. Masselink, 700 W. 168 St., New York 32.)

15–17. American Soc. of Agricultural Engineers, winter, Chicago, Ill. (J. L. Butt, American Soc. of Agricultural Engineers, St. Joseph, Mich.)

15–19. Radiation Biology, 2nd Australian conf., Melbourne, Australia. (J. H. Martin, Physics Dept., Cancer Inst. Board, 483 St. Lonsdale St., Melbourne, Victoria.)

17. Institute of Aeronautical Sciences, Washington, D.C. (R. R. Dexter, IAS, 2 E. 64 St., New York 21.)

18–20. American Physical Soc., Los Angeles, Calif. (K. K. Darrow, APS, Columbia Univ., New York 27.)

26–31. American Assoc. for the Advancement of Science, annual, Washington, D.C. (R. L. Taylor, AAAS, 1515 Massachusetts Ave., NW, Washington 5, D.C.)

The following 47 meetings are being held in conjunction with the AAAS annual meeting.

AAAS Committee on the Social Aspects of Science (C. D. Leake, Ohio State Univ. College of Medicine, Columbus, Ohio). 27 Dec.

AAAS Cooperative Committee on the Teaching of Science and Mathematics (J. W. Buchta, Univ. of Minnesota, Minneapolis, Minn.). 28 Dec.

Academy Conf. (J. A. Yarbrough, Meredith College, Raleigh, N.C.). 27–28 Dec.

Alpha Epsilon Delta (M. L. Moore, 7 Brookside Circle, Bronxville, N.Y.). 27 Dec.

American Assoc. of Clinical Chemists (Miss E. G. Frame, Clinical Center, Natl. Institutes of Health, Bethesda 14, Md.). 29–30 Dec.

American Assoc. of Scientific Workers (R. J. Rutman, 6331 Ross St., Philadelphia 44, Pa.).

American Astronautical Soc. (R. Fleisig, 58 Kilburn Rd., Garden City, N.Y.). 27–30 Dec.

American Geophysical Union (W. E. Smith, AGU, 1515 Massachusetts Ave., NW, Washington 5).

American Meteorological Soc. (K. Spengler, 3 Joy St., Boston, Mass.).

American Nature Soc. (S. Mulaik, Biology Dept., Univ. of Utah, Salt Lake City). 26–30 Dec.

American Physiological Soc. (F. A. Hitchcock, Ohio State Univ., Columbus).

American Political Science Assoc. (E. M. Kirkpatrick, APSA, 1726 Massachusetts Ave., NW, Washington, D.C.). 27 Dec.

American Psychiatric Assoc. (L. J. West, Univ. of Oklahoma School of Medicine, Oklahoma City 4). 27–28 Dec.

American Soc. of Criminology (D. E. J. MacNamara, Dean, New York Inst. of Criminology, Inc., 40 E. 40 St., New York 16). 27–28 Dec.

American Soc. of Naturalists (J. Schultz, Inst. for Cancer Research, Philadelphia, Pa.).

American Soc. of Photogrammetry (R. G. Ray, U.S. Geological Survey, Washington 25). 29 Dec.

American Soc. of Zoologists (G. Moment, Dept. of Biology, Goucher College, Towson, Baltimore 4, Md.). 27–29 Dec.

American Sociological Soc. (K. Davis, Inst. of International Studies, Univ. of California, Berkeley 4). 29 Dec.

Association of American Geographers, Middle Atlantic Div. (J. E. Guernsey,

9707 Parkwood Dr., Bethesda, Md.). 29 Dec.

Association for Computing Machinery (J. Douglas, Mathematics Dept., Rice Inst., Houston, Tex.).

Astronomical League (Miss G. C. Scholz, 410 Mason Hall Apts., Alexandria, Va.). 26 Dec.

Biometric Soc. (J. Cornfield, Johns Hopkins Univ., Baltimore, Md.). 30 Dec.

American Statistical Assoc. (E. Glazer, 305 George Mason Dr., Falls Church, Va.). 30 Dec.

Conference on Scientific Communication Problems (G. L. Seeilstad, Technical Reports Group, Applied Physics Lab., Johns Hopkins Univ., Silver Spring, Md.). 28–30 Dec.

Conference on Scientific Manpower (T. J. Mills, National Science Foundation, Washington 25). 30 Dec.

Ecological Soc. of America (D. E. Davis, Johns Hopkins Univ., School of Hygiene, Baltimore, Md.).

History of Science Soc. (M. C. Leikind, 1334 Aspen St., NW, Washington 12). 29 Dec.

Instrument Soc. of America (O. L. Linebrink, Battelle Memorial Inst., Columbus, Ohio). 30 Dec.

International Geophysical Year (H. Odishaw, National Acad. of Sciences, Washington 25). 29–30 Dec.

Junior Scientists Assembly (K. C. Johnson, Supervising Director of Science, District of Columbia Public Schools, Woodrow Wilson High School, Washington 16). 27–28 Dec.

Metric Assoc. (J. T. Johnson, 694 W. 11 St., Claremont, Calif.).

National Acad. of Economics and Political Science (D. P. Ray, Hall of Government, George Washington Univ., Washington, D.C.). 27 Dec.

National Assoc. of Biology Teachers (P. Klinge, Jordan Bldg., Indiana Univ., Bloomington). 26–30 Dec.

National Assoc. for Research in Science Teaching (E. S. Obourn, U.S. Office of Education, Washington 25). 26–30 Dec.

National Assoc. of Science Writers (J. Billard, U.S. News and World Report, Washington, D.C.).

National Geographic Soc. (W. R. Gray, NGS, 16 and M Sts., NW, Washington 6). 30 Dec.

National Science Teachers Assoc. (W. A. Kilgore, District of Columbia Teachers College, Washington 9). 26–30 Dec.

National Speleological Soc. (W. E. Davies, 125 Greenway Blvd., Falls Church, Va.). 28–29 Dec.

Philosophy of Science Assoc. (C. W. Churchman, Case Inst. of Technology, Cleveland, Ohio).

Pi Gamma Mu (Mrs. Effie B. Urqhart, Winfield, Kan.).

Scientific Research Soc. of America (D. B. Prentice, 56 Hillhouse Ave., New Haven 11, Conn.).

Sigma Delta Epsilon (Mrs. V. L. Blackford, 2630 Adams Mill Rd., NW, Washington 10). 26–30 Dec.

Society for General Systems Research (R. L. Meier, Mental Health Research Inst., Univ. of Michigan, Ann Arbor). 29 Dec.

Society for Industrial Microbiology, Washington section (W. N. Ezekiel, Bur. of Mines, Washington 25). 27–28 Dec.

Society of the Sigma Xi (T. T. Holme, 56 Hillhouse Ave., New Haven 11, Conn.). 29 Dec.

Society of Systematic Zoology (G. W. Wharton, Dept. of Zoology, Univ. of Maryland, College Park).26–30 Dec.

United Chapters of Phi Beta Kappa (C. Billman, 1811 Q St., NW, Washington, D.C.). 27 Dec.

Washington Acad. of Sciences (G. W. Irving, ARS, U.S. Dept. of Agriculture, Washington 25).

27–29. American Economic Assoc., Chicago, Ill. (J. W. Bell, AEA, Northwestern Univ., Evanston, Ill.)

27–29. Econometric Soc., Chicago, Ill. (R. Ruggles, Box 1264 Yale Station, Yale Univ., New Haven, Conn.)

27–30. American Folklore Soc., New York, N.Y. (MacE. Leach, AFS, Univ. of Pennsylvania, Philadelphia, Pa.)

28–30. Archaeological Inst. of America, Cincinnati, Ohio. (L. A. Campbell, AIA, Dept. of Classics, Brooklyn College, Brooklyn, N.Y.)

29–30. National Council of Teachers of Mathematics, New York, N.Y. (M. H. Ahrendt, NCTM, 1201 16 St., NW, Washington 6.)

28–30. Western Soc. of Naturalists, Seattle, Wash. (J. P. Harville, San Jose State College, San Jose 14.)