Contributions of Biological Sciences to Victory

Genetics and the Integration of Biological Sciences

BIOLOGY COLLOQUIUM
1943 and 1944

OREGON STATE CHAPTER OF PHI KAPPA PHI
OREGON STATE COLLEGE  ∙ CORVALLIS  ∙ 1945
Sixth Annual Biology Colloquium
Saturday, April 22, 1944

Genetics and the Integration of Biological Sciences
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FOREWORD

INFORMAL DISCUSSION OF BIOLOGY

The Biology Colloquium is conducted in a spirit of informal discussion and provides opportunity for participation from the floor. The colloquium is sponsored by the Oregon State Chapter of Phi Kappa Phi with the collaboration of Sigma Xi, Phi Sigma, and Omicron Nu. Sigma Xi assumes special responsibility for the colloquium luncheon. Phi Sigma and Omicron Nu provide afternoon tea. The College Library arranges special displays of the writings of colloquium leaders and notable works on the colloquium theme. Grateful acknowledgment is made of the cooperation and interest of the several faculties of Oregon State College that are concerned with biology, of those biologists contributing to the program, of Chancellor F. M. Hunter, President A. L. Strand, and other executives of Oregon State College.

The first Biology Colloquium was held March 4, 1939, with Dr. Charles Atwood Kofoid of the University of California as leader, on the theme "Recent Advances in Biological Science." Leaders and themes of succeeding colloquia have been: 1940, Dr. Homer LeRoy Shantz, chief of the Division of Wildlife Management of the United States Forest Service, theme "Ecology"; 1941, Dr. Cornelius Bernardus van Niel, Professor of Microbiology, Hopkins Marine Station, Stanford University, in collaboration with Dr. Henrik Dam, Biochemical Institute, University of Copenhagen, theme "Growth and Metabolism"; 1942, Dr. William Brodbeck Herm, Professor of Parasitology and Head of the Division of Entomology and Parasitology, University of California, theme "The Biologist in a World at War."

WARTIME ORIENTATION IN BIOLOGY

In the face of the disturbances and demands of wartime it was felt that the 1943 Biology Colloquium could make perhaps its best contribution by providing orientation for people working in the field of biological science. The theme "Contributions of Biological Sciences to Victory" was selected with the realization that some of the most timely biological knowledge was at the moment confidential information. Some of the papers read at the colloquium had been officially censored. Parts of the discussions were "off the record." The discussions of the day nevertheless helped to clarify some of the important aspects of the relation of the biological sciences to the winning of the war.

The 1944 Biology Colloquium had as its theme "Genetics and the Integration of Biological Sciences." Happy in both theme and leader, the colloquium reviewed some of the newer knowledge in biology and conveyed something of the spirit of creative scholarship in its task of advancing biological science.

THE COLLOQUIUM LEADERS

Dr. August Leroy Strand became ninth President of Oregon State College in October 1942. In recognition of his eighteen years' service as a biologist he was invited to be the leader of the fifth annual Biology Colloquium. Dr. Strand is a graduate of Montana State College with his master's and Ph.D. degrees from Minnesota. In the first world war he served as an ensign in the U. S. Naval Air Force. He has been assistant state entomologist in Montana; assistant extension entomologist at Pennsylvania State College; research assistant, instructor, and assistant professor of entomology and economic zoology at the University of Minnesota; and professor, head of the department of entomology, experiment station entomologist, and state entomologist at Montana State College. He became President of Montana State College in 1937.

Dr. George Wells Beadle, leader of the sixth annual Biology Colloquium, is professor of biology at Stanford University. Graduate of Nebraska and Cornell universities, he has been National Research Council fellow at California Institute of Technology, genetics professor at Harvard University, and guest instructor at the Institut de Biologie Physio-chimique, Paris. His reputation as biologist and man was well sustained in his dynamic leadership of the Colloquium.
August Leroy Strand, Ph.D.
Leader of Fifth Annual Biology Colloquium
Fifth Annual Biology Colloquium

Theme: Contributions of Biological Sciences to Victory
Leader: AUGUST LEROY STRAND, Ph.D., Biologist and President of Oregon State College

Discussion Leaders:
- ROBERT L. BENSON, M.D.
  Assistant Clinical Professor of Internal Medicine, University of Oregon Medical School.
- CAPTAIN JOE K. ELLSWORTH, Ph.D.
  Sanitary Corps, U. S. Army; Medical Inspector, Camp Adair.
- FRANCIS ARCHIBALD GILFILLAN, Ph.D.
  Dean and Director of Science, Oregon State System of Higher Education; Dean of the School of Science, Oregon State College.
- HENRY HARTMAN, M.S.
  Head of the Department of Horticulture, Oregon State College.
- JOSEPH ELLSWORTH SIMMONS, M.S.
  Professor of Bacteriology, Oregon State College.

Chairmen of Sessions:
- NATHAN FASTEN, Ph.D.
  Head of the Department of Zoology, Oregon State College (morning session, luncheon session).
- CHARLES ELMER OWENS, Ph.D.
  Head of the Department of Botany, Oregon State College (first afternoon session).
- CLAIR VAN NORMAN LANGTON, D.P.H., Ed.D.
  Director of the Division of Physical Education; Professor of Hygiene, Oregon State College (second afternoon session).
- DELMER MORRISON GOODE, M.A.
  Editor of Publications, Oregon State College (dinner session, representing John C. Burtner, president of Phi Kappa Phi).

OPENING OF THE COLLOQUIUM

Welcome by President of Phi Kappa Phi,
Mr. John C. Burtner

Visitors, Faculty Members, and Students: It is a pleasure for me to extend this greeting on behalf of the Oregon State Chapter of Phi Kappa Phi. I trust that you who are attending this fifth annual Biology Colloquium will derive benefit and pleasure from it equal to that which we have experienced in sponsoring this event.

When the time came some months ago to decide between continuing the Colloquium and abandoning it for the duration, we were impressed by the almost unanimous opinion that it should be continued. This expression came not only from our own campus but from a number who had participated in other years and felt that it would be a loss to interrupt the series.

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Naturally we were gratified at this widespread approval of this admittedly unusual event with its equally unusual name. We of Phi Kappa Phi see in this annual occasion an exemplification of one of the foundation principles of this society. Phi Kappa Phi recognizes the unity of education and scholarship. All branches of learning are considered worthy of equal esteem.

This Biology Colloquium, while emphasizing one field of science, is not intended as an occasion merely for the exchange of technical knowledge among professional biologists, valuable as that may be. Rather it is a place for biologists to share their findings with those in other fields of science and with those whose primary training and interest are quite apart from science. Thus we see in the Colloquium a broadening and unifying influence that will increase the understanding and, therefore, the respect among the several fields of learning.

It has been a bit more difficult to arrange a challenging Colloquium under present wartime conditions, but thanks to the excellent work of those on the committee, whose names you will find on the printed folders, and to the cooperation of other societies on the campus, a program has been prepared which I am sure you will enjoy.

Welcome on Behalf of the Sciences,
Dean F. A. Gilfillan

Dr. Fasten, Biologists, both professional and amateur: Throughout all of northern Europe there exists a wild story, or numerous wild stories, concerning the migration of those peculiar little rodents, the lemmings. There are millions of people in northern Europe who firmly believe that at rather irregular periods these lemmings rush down to the mountains, destroying everything in their way, and drown themselves in the sea. The explanation is offered that many years ago there was no Baltic Sea there—it was land—and these lemmings were rushing down to find food since the food in the mountains had played out. And by instinct they still rush down to where these fertile valleys used to be—involuntary mass suicide. Biologists, of course, have exploded a great deal of this (although the migrations of the lemmings are still something wonderful to see) and now give credit to the lemmings for more sense than that.
Nevertheless, every twenty-five years or so a certain people in northern Europe start out on a similar migration, intent on destroying everything in their way, and bringing considerable destruction to themselves, also. This meeting is called in order that we might consider as biologists what we can do about stopping this particular migration. The theme of this Colloquium is, "Contributions of Biological Sciences to Victory." Now we are more and more focusing our attention on what the biologists can do in ending the present conflict.

On behalf of the biologists in Corvallis, both in the School of Science and in the schools of Agriculture, Forestry, and other professional schools based on science, I want to take this opportunity to welcome to Corvallis and to the campus other biologists from over the state of Oregon and elsewhere. We hope that through your contacts here you, as well as we, may see more clearly what each of us may do to fit into the war program. We hope that your stay will be both pleasant and profitable.

Opening of the Colloquium by the Colloquium Leader, Dr. A. L. Strand

As indicated by the chairman, not only the word "colloquium" is rather new to me but the method of procedure in this rather enticing event on this campus. I presume that I, as leader of this colloquium, should serve as an enzyme or activator and have very little to say other than to poke up discussions or maybe to raise objections that will excite discussions. I should like to take about the same length of time as Dr. Fasten did in introducing me, though, in making a few remarks.

I don't have a great deal of time for reading, but there is seldom a week when I feel I can afford to pass up some quick going over of the first article in Science. I seldom miss a first article in Science. A couple of months ago there was an article by Dr. Gustav Egloff entitled "Peacetime Values from a War Technology" that fits into this colloquium rather well in part. Egloff is an industrial chemist. At present he is president of the American Institute of Chemists. I should like to read a couple of paragraphs from under what he calls "Health Engineering" that I believe cover about what I could say in much longer time:

... Health Engineering. Man's struggle to survive is ever present. He has either vanquished or domesticated large animal life. Our present battle is to overcome the ravages of rats, insect life and bacteria; it would seem that the smaller the scale of life the more difficult is the problem of its extermination or control. Even the very nature of some of the smallest forms has presented man with some of his greatest difficulties of discovery and eradication by chemical or physical means. Great strides in this direction have been made, but the ultimate solution is still far off. Increased tempo in research and experimentation along many fronts will ultimately present the remedy, but with the vastly improved tools man is constantly providing for himself, the end is certain to be on the favorable side for mankind.

That seems to me a bit optimistic. Biologists as a rule cringe before the words "eradication" and "extermination."

From the necessities that war has forced upon man have grown the scientific principles of health engineering so vitally necessary to man's well-being as a fighting force. Accurate knowledge of vast areas hitherto seldom visited by dwellers in temperate regions have been the motive force behind a medical exploration of tropical territories that may well be carried over in the future development of our own hemisphere.

When it became necessary to provide troops with anaphylactic measures against tropical and sub tropical diseases, it was the problem of the medical force [and biology*] to provide accurate knowledge of the type of health dangers encountered and to provide prevention and cure of malaria, cholera, typhus, hookworm, bubonic plague, sleeping sickness, dysentery and typhoid. Mosquitoes, rats, leeches, fleas, flies, bats and a host of other disease-bearing or spreading agents had to be studied and their control and extermination planned.

Drugs of all types had to be ready for disease combat and the checking of infection. In the Far Eastern and African campaigns insects and infections have beset our armies. Our men went down with malaria and other diseases. Among these are dengue fever, dysentery, tropical ulcers and sores, as well as the bites of malarial mosquitoes and tropical spiders, some as large as crabs. There is a drainage of the soldier's vigor in this pestilential atmosphere wherein he fights, eats and sleeps but a few hundred miles from the Equator.

What has research done to modify this type of torture and death to which our fighting forces are subjected? The methods of attack are chemical, physical, medical and engineering.

An indispensable tool in the study of man's health for many years has been the microscope, discovered over three hundred years ago. Slow improvements had been made in this instrument until a few years ago when a revolutionary principle was discovered through the use of the electron. This made possible a magnification of over 200,000 times compared to the 3,000 from the best previous microscope.

Anti-insect sprays, delousing, swamp drainage, felling of certain trees, sanitation, oil and chemical dust spreading and other methods are used to keep our troops in fighting condition and will have great value industrially and agriculturally during peace.

A number of synthetic chemicals, such as the sulfa drugs, synthetic quinine and synthetic vitamins are finding

* Words added by Dr. Strand.
amazing uses on the fighting fronts. Where the World War I record was four deaths out of five due to germ infection of abdominal wounds, the present record is one out of five. Quoting Howard Blakeslee (New York Times, January 10, 1943):

"On the 2,000-mile front, in all the war, only 1.5 per cent of the Russian wounded have died. That is slightly higher than the remarkable recovery rate at Pearl Harbor, 96 out of each 100. The report says the Russian recovery rate is 98.5 per cent of all wounded. The Russian rate is one-half of 1 per cent worse than the Guadalcanal miracle of 1 per cent of wounded dying . . ."

"The Russians claim some new medical advances of their own. When plasma is made in America, the red blood cells are thrown away. The Russians report that they have made a process to use these cells to manufacture blood. Nerve sections taken from the dead have been successfully grafted into the wounded. The peritonea of animals, the inner linings of visceral cavities, have been used as living bandages for gaping wounds. It is claimed that cure is facilitated and that the scars are not so heavy . . ."

"A compound that is not a vitamin, yet has the bloodclotting effects of Vitamin K, is in use. The Russians say they have found a method to obtain thrombin in thousands of quarts volume. Thrombin is a natural clotting substance in blood."

The latest sulfa drugs which are working wonders against infection and disease are sulfathiazole, sulfapyridine, sulfaguanidine and succinyl sulfathiazole which have been synthesized for specific diseases. Each soldier's kit contains first aid doses of sulfanilamide for combating infection and far less toxic. Pentothal, which is injected intravenously, is one of the very best of the newer anesthetics, having no explosive hazards such as ether and the hydrocarbon gases. In addition, the equipment necessary for its administration is simple. A shot in the arm is all it takes to put one asleep.

Bacteria, soil molds and molds found in the intestines of animals or insects create chemicals that are highly useful in destroying infection. Penicillin, a new drug produced in soil mold, is about 100 times as effective as sulfanilamide for combating infection and far less toxic. Gramaticin from soil bacteria has been found to be a powerful germicide for both pneumococci and streptococci, two extremely dangerous germs to man.

The rest of his article is well worth reading, but I won't take up your time on that. It seems to me that from a biological way, from a medical way, the United States is in about the same condition as we have been for a generation from the standpoint of international politics and government. We have been too much on an isolationist policy, and we feel now the lack of knowledge regarding the world and what our men will find when they get to various parts of it where competition with the forces of nature is almost as severe as the struggle against the enemy. A few places in America, though, have been internationally minded in regard to biology. I was struck the other day in reading something that I had written myself. Actually. Because I saw something else in it. About ten or twelve years ago I wrote a sort of a quick chronological history of the investigations of Rocky Mountain spotted fever, and in part of that I listed all the organizations which had contributed to the investigations on spotted fever since 1902—a rather unusual list, private individuals, counties (that is, county governments), the state government of Montana, and some others. But there were five educational institutions represented. One was Montana State College. That was to be expected, but there were four others, and what were they? The University of Paris. Imagine the University of Paris being interested enough in an obscure disease way over in a little old mountain valley in Montana. There's a thought in that. Dr. Brumpt had a wide vision. Another was Harvard University, one of the places now where you can get and get information on some of the things we need to know. The other two were the University of Chicago and the University of Minnesota. All four of those interested in a little obscure but rather complicated biological and medical problem way out somewhere in the West in the Bitter Root Valley that no one had ever heard of. They were interested because of the prospect originally of the disease being transmitted by ticks. They were interested in the complicated associations between the tick and its host. The cause of the disease was finally discovered by Ricketts of Chicago to be one of the rickettsiae organisms, and that organism brought to Montana the brains of internationally minded institutions. We'll have to be a bit broader in our biological interests to keep up with the needs of our modern world. I think it is an appropriate topic selected for this particular colloquium, the biologist and the war.

In behalf of my part, in behalf of this colloquium, I might say, I welcome you here. In behalf of Oregon State College, we are very happy to have you on the campus. I know this colloquium will be a success. I know that there are men present who, though not on the program, can contribute much by the interjection of their ideas in the discussions that follow papers. I'd even suggest that it is all right to interrupt speakers at any time if you have something to ask or if you have a thought that contributes to the theme under way.

The leader will try to be as quiet as possible. We are glad you are here. Thank you.
THE BASIS OF MODERN CAMOUFLAGE

HENRY HARTMAN

Because of the heterogeneous nature of camouflage it is difficult to define the term in a specific manner. Major Breckenridge speaks of it as any and every means of hiding or disguising a target from the enemy, and misleading and confusing him as to its character, strength, or purpose. The French word "camoufler" in a literal sense means "to blind or veil." An important phase of camouflage has to do with deception, wherein the intent is to deceive rather than merely to conceal.

Although the term camouflage is of comparatively recent coinage, the use of camouflage probably antedates recorded history. The Greeks' famous wooden horse, the use of clouds of dust by the Thebans in their movements against the Spartans, the use of leaves and twigs in their caps by the hordes of Genghis Khan, and the moving forest in Shakespeare's Macbeth are examples. War paint as used by American Indian tribes is now known to have been in some cases a camouflage device.

The modern era of camouflage originated, as did its name, during World War I. It was widely used by both sides, although it was not until nearly the end of the war that it began to assume definite form. For the most part, the use of camouflage during this period was confined to forward areas and consisted chiefly of nets and draperies placed over field pieces, machine gun nests, and observation or sniper posts. Dummies and decoys were used to a certain extent, and the zigzag or "dazzle" painting of ships.

World War II has witnessed the use of camouflage on an unprecedented scale. Its use now is no longer confined to military installations but has found wide application in the protection of civilian objectives.

Aside from the matter of actual protection, camouflage is an aid to morale. Troops under camouflage are more at ease and are in a better frame of mind to perform their duties. The same is true of workers in plants situated in combat zones. Reports from Europe emphasize this point.

Although modern camouflage is based upon much scientific knowledge and makes use of many scientific principles, it is nevertheless an art and not a science. This is true not only because camouflage is still more or less in the creative stage, but because of the very nature of its subject matter. Camouflage is largely concerned with human reactions both physical and emotional. For this reason its precepts can hardly be reduced to laws and theorems as in science.

Like some other forms of art, camouflage cannot be static. To serve its purpose it must be ever-changing. The camoufluer and the bombardier are engaged in a game of hide-and-seek. Deception that may be effective today may not be effective tomorrow. New ruses must be evolved constantly if the game is to continue on even terms.

No two problems of camouflage are ever exactly alike, and camouflage does not lend itself to mass production methods. Each problem must have its own theme and its own solution. No one can become proficient as a camoufluer by merely learning, in a routine way, the various methods and techniques of camouflage. Originality, ingenuity, and imagination are essential.

Camouflage Objectives

Some of the popular literature has tended to create the impression that camouflage is superficial in character. To many the camoufluer is merely a person who covers objects with "phony" or fantastic pictures. To others, he is a pseudo-magician who performs certain feats of magic. These concepts, however, are entirely erroneous. Camouflage is not superficial and it is not mysterious. The camoufluer may be a P. T. Barnum, but he is never a Houdini.

Camouflage properly conceived is based upon common sense and extends into many fields. It goes to the very roots of engineering, architecture, landscape architecture, and art itself. It invades the precincts of physics, chemistry, biology, ecology, psychology, geology, and even agriculture, for some of it is plain dirt farming.

Civilian camouflage in the United States aims to protect vital installations against possible aerial attack, and more particularly against the type of aerial attack known as precision bombing. In the opinion of authorities the enemy, for the present at least, is not likely to resort to area or saturation bombing. He is more likely to direct his attacks to specific targets, which he considers important to our war effort.

The task of the camoufluer, therefore, is to protect by all means at his disposal those plants...
and installations that play a vital role in our war activities or in our domestic economy. Any device of camouflage that causes the bombardier to miss the important targets is considered successful, even though bombs may be dropped and may do damage to other installations in the vicinity.

Camouflage need not be armored against detection through the agency of photography. It is true that photography will reveal practically all types of camouflage and it is also true that reconnaissance photography may aid the bombardier in locating the position of his target. The bombardier, however, has to rely almost entirely on his own eyes for actual target recognition, and photographic records previously made are of minor value to him at the moment he must release his bombs.

The precision bombardier encounters definite handicaps in the accomplishment of his mission and it is around these that camouflage must be built. To begin with, the bombardier must recognize his targets from great heights and great distances. We are told that the most precision bombing is done at altitudes ranging between 10,000 and 30,000 feet. Viewed from these heights even comparatively large objects appear small.

Precision bombing is also limited by adverse atmospheric conditions. Obstacles such as clouds, natural haze, industrial haze, fog, and nightfall itself can either make precision bombing impossible or materially impair its accuracy.

Then, too, the period of time available to the bombardier for target recognition is exceedingly short. Bombing planes travel at great speed and only a few seconds elapse between the time the target first comes into view and the time the bombs must be released. The target must also be picked up at a difficult oblique angle.

At great heights, color as a definite entity largely disappears, and the eye is conscious only of tone values. The element of third dimension, also, disappears to a considerable extent. Objects are always merged against a background. They never appear in silhouette form. These are definite obstacles to the bombardier but they are valuable assets to the camoufleur.

Psychology plays an important part in camouflage. The role of psychology, however, is difficult to appraise, since it is associated so much with subconscious mental activity. Nevertheless, the bombardier as well as the camoufleur may be influenced by it.

The eye is a remarkable apparatus, but as a precision instrument it is far from being perfect. Architects are well aware of the force of optical illusions, yet optical illusions are due entirely to imperfections of the vision process. The phenomenon of fusion which plays no minor part in camouflage is, likewise, due to defects of sight.

Psychologists tell us that what we see is influenced to a considerable degree by our past experiences, by our desires, and by our imagination. Expressions in common usage bear testimony to this fact. "We see what we want to see." Conversely, we don't see what we don't want to see. Naturally, the camoufleur wants his installations to be invisible and because of this desire, there is a chance that he may "squint" his eyes a little too much when he views his handiwork, or he may resort to the use of his "haze box" a little too frequently. In his appraisal of the bombardier's limitations, the camoufleur can easily underestimate the bombadier's ability to pick out targets.

Camouflage Tools and Methods

The present-day camoufleur has a large kit of tools at his disposal. These, however, are not generally of the pick-and-shovel variety. Rather they belong to spheres that are more elusive, and that, at first, are more difficult to recognize. Modern camouflage makes extensive use of simulation, disruption, and confusion. The elusive phenomenon of fusion, also, has its place in camouflage, as well as the more obvious elements of dispersion, randomization, concealment, and obscurcation. Objects as seen from the air are identified largely by their shape, size, color, and shadow patterns. Any device, therefore, that tends to hide or alter these features is camouflage.

The specific methods of camouflage cover a wide field. The modern camoufleur, for example, makes extensive use of paint. Paint techniques usually include toning down, disruptive painting, simulation painting, pattern painting, dazzle painting, and counter-shading. Another method of camouflage makes extensive use of plant materials for both concealment and shadow disruption. Flat tops and garnished nets play an important part in camouflage. Dummies and decoys have their place as well as blackouts and dimouts. Smoke and artificial fog, while still somewhat in the experimental stage, are already being used and offer possibilities for the future. The glare barrage and pattern lighting are used to a considerable extent in Europe and are now receiving attention in this country.

Nature is the great teacher of camouflage and from her we can learn some of our soundest and most practical lessons. In the struggle between
species, survival is not confined to the physically strong. Creatures poorly equipped for physical combat maintain themselves among powerful enemies, and often their chief weapon is camouflage. Wild animals in their native haunts display camouflage of a high order, involving both concealment and deception. Protective coloration is common to the animal kingdom, and from this we obtain our best designs of countershading and pattern painting. Some harmless reptiles imitate our best designs of countershading and pattern and deception. Protective coloration is camouflage of a high order, involving both concealment and deception.

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Given time, nature will camouflage practically any material object that man can build. For example, we make a clearing in the woods, and, if left alone, nature will close up the open space in a short time. We work diligently to polish a piece of marble but as soon as we are through nature begins to etch the surface and to cover it with grime, so that in time the general aspect is again that of an ordinary piece of stone. We make a scar in the earth, but soon nature will heal it by covering it with vegetation. We labor to put a high polish on our automobile but as soon as we drive it on the roads nature begins to cover it with dust and mud, so that it more nearly blends with the surroundings. We paint objects in brilliant hues, but nature tones them down. Corrosion, weathering, erosion, decay, and the creative forces of growth, synthesis, propagation, and rejuvenation are powerful agents of camouflage.

Some Camouflage Concepts

The bombardier is interested mainly in man-made objects, and since man-made objects are radically different in appearance from those found in nature, a naturalistic concept of camouflage is apropos. If installations are disguised so that they appear natural instead of man-made, camouflage has been achieved.

Man-made objects, in the main, are characterized by regularity, straight lines, and geometric patterns. They are recognizable because of symmetry, formal balance, repetition, sameness, orderliness, and concentration. At times, they are distinguishable because of smoothness and lavish use of colors seldom found in nature.

Nature's creations usually display opposite characteristics. Nature specializes in irregularity, unbalance, asymmetry, curvature, openness, dispersion, and randomization. Her color schemes are subdued and she avoids large untextured surfaces. Obviously, a naturalistic scheme of camouflage will emphasize these and avoid those that characterize man-made things.

It is not always possible or desirable, however, to achieve naturalistic camouflage. Man in his endeavors has often disrupted the natural scheme to such an extent that it is impossible to return to it. A large city, for example, cannot very well be disguised to appear as a forest or landscape scene, and vital installations within it may require an altogether different treatment. Hence, factories are made to appear as rows of dwelling houses or other harmless installations. Patterns are altered and dummies may be erected at new locations. Where the purpose is not so much to disguise as it is to hide or obscure, camouflage schemes involving toning down or the use of smoke, fog, or other means of obscuring, are used.

Long vs. Short Time Camouflage

Any well-conceived camouflage plan not only contemplates protection for the immediate emergency but takes cognizance of the future. At the close of the present conflict our country cannot, with safety, again retreat behind the ramparts of a once vaunted isolation. In spite of all that may be done to guarantee peace by covenants, we must recognize the fact that air power has annihilated distance and will remain a threat to all countries regardless of their geographic position.

For the present, however, the camouflage must direct his efforts to the immediate problem. Installations vital to the war effort must be protected at all costs. Needless to say this phase of the program involves many difficulties. The camouflage is handicapped by lack of time, and of needed materials, and he encounters a scheme of industrialization that does not generally lend itself to effective camouflage. Intense concentration of installations that were not planned with camouflage in mind is the rule. The camouflage must make the best of a bad situation.

The long-time program presents a more rosy picture. Vital industrial plants can be camouflaged effectively. The powerful tools of dispersion and randomization can be brought into play, and the camouflage can execute camouflage with permanent vegetation and durable materials as the basis.

Aside from the element of protection, the long-time program gives opportunity for an improved industrial system and a more desirable social order. Under it the dream of civic planners and prominent industrialists may come true. Decentralization gives promise of more desirable living conditions, more beauty of surroundings, and more opportunity for play and recreation.
I am going to take a considerable time to tell you something about the history and the people of Russia, then I will use the remainder to talk about science in Russia.

Looking at a map of European Russia, you observe that the rivers rise very far north. In the ninth century, the Norsemen, occupying and settling that part of Russia around Novgorod, began to establish trade routes along these rivers, to Constantinople and the East. The Russian people themselves had originated along with the other Slavs in the Carpathian Mountains, and a few thousand years ago there had been migrations north into Poland and Czechoslovakia, east into Russia and the Ukraine, and south into the Balkans, Croatia, Serbia, and Bulgaria. Then, as I mentioned, about the ninth century came the influx of Nordics establishing trade routes through Russia down to Constantinople. From Constantinople in 862 the Macedonian brothers, Cyril and Methodius, of the Eastern Orthodox Church, came up to Kiev on their mission to Christianize the Russians and the other Slavs.

The Slavonic Languages

And now a word about the Slavonic languages. They are divided into three groups: the western, the eastern, and the southern. The western Slavonic languages are the Polish and the Czechoslovakian, written with our Latin alphabet. The eastern Slavonic languages are: the White Russian, the Little Russian or Ukranian, and the Great Russian or Russian, which is spoken by 70 or 80 per cent of all the Russians. The Ukrainians or Little Russians number about 30 million. Then there are the White Russians of which there are six to seven million around Minsk. Their language, as you might suppose, would be somewhat of a mixture of the Russian and Ukranian. All three of the eastern Slavonic languages are written with the Cyrillic alphabet. The south Slavonic languages are written in the Old Slavonic, the Slovene, and the Serbo-Croatian. The Serbo-Croatian is really one language, the Serbs using the Cyrillic and the Croats the Latin alphabet. I have indicated the origin of the Russian alphabet, also of the Latin alphabet of western Europe. It all begins with the Egyptian, whence the Proto-Semitic, of which there were two branches: the South Semitic from which we derive the modern alphabets of India; the North Semitic producing the Aramaic (branching to the Arabic and the Hebrew alphabets), and the Phoenician, which gave rise to the alphabet of Greece.

The Greek alphabet was split into two divisions. We shall follow the Western Greek first. It is the alphabet of the Greeks who went over into Italy and from whom the Romans derived their alphabet from which we have the alphabet of modern western Europe.

When the Christian missionaries went into Russia in the ninth century, they found a people who had no written language. So Cyril, who was the student of two missionary brothers, went to work to devise an alphabet in order that he might translate the scriptures into the Slavic language. Starting with the twenty-four Greek letters, he added some from the Hebrew, invented still others, and finished with forty-eight letters constituting the original Cyrillic alphabet. Peter the Great dropped it down to thirty-six. The Soviet Government in a simplified spelling campaign threw out four more to reduce it to thirty-two letters. In Russian, each letter has only one sound, which arrangement is much preferable to our chaotic English spelling.

The English language is spoken all over the world by approximately 270 million people. Russian is spoken by approximately 170 million people. A recent edition of Life estimated the population of Russia as more than 193 million, of whom 170 million use Great Russian either as a native tongue or as a secondary tongue. Compare this with our American 130 million.

The United States has more than three million square miles. Russia contains somewhat more than eight million square miles, including Siberia. And the resources of Russia are enormous—just how great, no one knows.

Russian Scientists

My interest in Russia arose many years ago in connection with a research problem in synthetic organic chemistry, which had been begun by a Russian and discontinued. As I followed this work, I began to realize that there was in the Russian language considerably more in science, and particularly in chemistry, than I had suspected. Still I was surprised a few years ago on seeing a tabulation of the articles in the chemical abstracts for the year 1935. A midwestern professor had taken the trouble to go through the
abstracts and tabulate the language in which those articles had originally appeared. As might be anticipated, English led with 2,255, German was second with 1,200, French third with 660. Russian was represented with 535. In physical chemistry the number of articles in Russian exceeded those in French. That was in 1935, and it is obvious to anyone that the picture has largely changed now and will be greatly changed very shortly after the war.

Regarding Russian scientists, I should like to mention first a few early Russian scientific workers in various fields, the old timers. Lomonosov was born in 1711. He went to the University of Marburg, became interested in mines and mining and later in chemistry. He taught chemistry to Russian students in Latin because that was the language in which things were taught in those days. He checked Franklin's experiment with lightning and survived the experiment. His collaborator didn't. Lomonosov later became a writer and is regarded as the founder of modern Russian literature, because he first used the language of the people in literary composition.

Lobachevski, born in 1793, has been called one of the most outstanding mathematicians of all time. He created a new non-Euclidian geometry, won a master's degree at eighteen, and was a university professor at twenty-three. His work has been called "one of the great masterpieces of mathematics and a landmark in human thought."

Coming back to chemistry, Zinin first demonstrated that nitro-compounds could be reduced to amines for the production of aniline and all the derivatives which come from it.

Markovnikov was one of the early chemists to work on petroleum oils, in which field the Russians still excel, as they do in synthetic rubber.

A member of our own chemical engineering department, who was recently asked to prepare a bibliography on synthetic rubber, found that there were ten times as many references in the Russian language as in all other languages.

Chernov worked on the structure of steel and its thermal treatment. He illustrated how steel could be thermally treated to withstand high pressure and made it possible to build modern artillery out of steel instead of bronze.

Shukhov published a study and patented a process for cracking oil under pressure. At the Tentelev chemical plant was employed the first contact method for preparation of sulfuric acid.

Kucherov in 1880 discovered that under the influence of mercury salts you can produce an addition to the acetylene gas and water vapor, leading to acetic acid which is the starting point of many war materials.

Ladygin, while a student at St. Petersburg, in 1874, devised the Ladygin-Didrichson lamp which was demonstrated in Paris and Berlin. In 1876, during the construction of Alexandrovski Bridge, this lamp was used. Another Russian, Yablochkov, produced the carbon arc lamp commercially in 1876, and not until 1878 did Edison get the idea.

Aleksander Popov, professor of naval engineering, in 1895 demonstrated wireless telegraphy to his class, sending messages from the chemistry laboratory to the physics lecture room. By 1897 he had improved this machine to send messages five kilometers. Marconi published his first papers on wireless telegraphy in 1897, wherefore Russian scientists regard Popov as the inventor of the wireless.

Those of you who are working in physiology know of Ivan Pavlov's work on digestion and on nervous and mental phenomena related to sleep and to the conditioned reflex. You remember Pavlov's experiment with the dog, how he tied off a portion of the submaxillary gland of the dog and measured the flow of saliva while holding meat before the dog's nose and ringing a bell. Later, the ringing of the bell, alone, produced the reaction. Pavlov was the recipient of a Nobel prize in 1904.

Mechnikov, who was educated in Germany, did pioneer work on the intercellular digestion of lower animals. He later became a director of the Pasteur Institute. He investigated intestinal flora with particular reference to immunity and in 1908 shared the Nobel prize with Ehrlich.

**Modern Russia**

And now a word with reference to modern Russia. I was interested in a statement made in this week's issue of *Life* that the Soviets are responsible for teaching 100,000,000 people to read. In this connection, I remember an old professor of mine who many years ago said that in Russia only 2 per cent of the people were really educated but that these 2 per cent constituted the highest educated body of citizenry in the world. But this left in Czarist Russia an enormous number of illiterates.

*Life* indicates that the number of illiterates in Russia has dropped from 75 per cent to 20 per cent, and these are largely old people. It says that the Slavic languages are spoken by 170 million out of 193 million people. That includes
Ukrainians and White Russians. In Turkestan and some of the Asiatic countries, the policy of Russia has been to set up schools in the language of that particular country, but Russian has been put in as a secondary language.

We come now to the scientists of modern Russia. Kapitza, who was a student of Rutherford in England, devised a method of liquefying helium without using liquid hydrogen for cooling and thus eliminating the explosion hazard. He too, won a Nobel prize.

Of contemporary physicists, Savinov worked on the polarization of electrolytes, Plotnikov and Kistianovski on conductivity of solutions. They are now outstanding physicists in the Soviet Union.

Among chemists I have mentioned one or two, but I want to mention some others. Kalichevsky was one of the first to work out successfully a chemical process for the refining of petroleum; Mithov and Schimanski studied thermal cracking; Nemzov, Sokind, Lebedev, Orlov, Kozlov, Fedoseev, polymerization of olefines, thus making many new petroleum products now available for commercial use. That leads us to the production of synthetic rubber. Kolachov, who is now working in this country, has devised a continuous alcohol production program which is going to be pretty important.

In genetics, some of you are familiar with Oparin, who is attempting to trace back as far as possible the origin of life itself; Serbrovsky, who worked on hybridization; Karpechenko, plant cytogenetics; Ilyin, animal pigmentation; Dobzansky, Lysenko, Michurin, Kostov, Balinsky, all eminent biologists; Filatov, amphibians; Sevitski, who worked on plant growth, and many others.

In morphology there are many names known to every student of this science.

Russia boasts two outstanding men in agriculture, Lysenko and Michurin, who have been nicknamed "the Soviet Burbanks." In biochemistry, Engelhardt; in ecology Fenyuk, Kalabukov, Vinogradov, men who are becoming known the world over.

Research Institutes

I came across a recent article published by Ipatiev, who is now with a well-known oil company in Chicago. He came here from Russia, stopping in Germany long enough to pick up $40,000 on a patent. He has now become an American citizen. When he celebrated his seventy-fifth birthday last November he also celebrated his golden wedding anniversary and fifty years research in chemistry.

For 1935, which seems to be the latest you can find out anything about Russia, Ipatiev lists the research institutes that were under the control of the Commissariat for Heavy Industries.

Under physics are listed six main institutes with no branches; chemistry with twenty-seven main institutes and five branches; fuel, five main and two branches; energetics, seven main and one branch; electrotechniques, six main; ferrous metallurgy, six main; nonferrous metallurgy, five main; mining, four main and ten branches; geology and geodesy, three main and two branches; machine building, fourteen main and three branches; building construction, twelve main and three branches; and organization of labor, four main with one branch institute.

The research institutes in these fields total 126, with a staff of more than 33,000 of whom 11,000 are specialists, the others being part of the engineering staff and the laboratory assistants. They carry a budget of 269 million rubles.

I tried to find comparable information for the biological institutes in Russia, and again I could find no data later than 1935. I have a list here of thirty-one research institutes of medicine and allied sciences, such as the Institute of Research in Municipal Sanitation and Hygiene, the Regional Institute of Tuberculosis, the Regional Institute of Physio-therapy and Physio-prophylactics, the Institute of Infectious Diseases, the Regional Institute of Psychoneurology, the Central State Scientific Institute of Public Feeding, etc. Thirty-one research institutes are devoted to medicine and nineteen are devoted to biology.

That makes a grand total of 176 research institutes in Russia for scientific research in physical and biological sciences and the fields dependent upon them.

A Challenge

What does all this mean to us? It means two things: That we have to know what the Russians are doing in science. That is first. Second, it is up to us as scientists to bring this tremendous program to the attention of the proper authorities in this country so that following the war we ourselves may undertake a similar, and at least equal, program of research. If we don't do that, then it appears obvious that within twenty-five years following the end of the war Russia is going to occupy in science the position that Germany occupied between 1870 and 1914 and that we in this country are going to take second place.
BACTERIOLOGICAL AND SANITARY PROBLEMS OF WARTIME

J. E. Simmons

Today we are engaged in global war such as we have never before experienced. Wars, together with droughts, floods, earthquakes, frosts, blights, and plague of insects, have shown their devastating power from time to time to cause famine, and always the aftermath of famine is pestilence. No matter how famine is caused, pestilence always stands by to add to the misery and a wide assortment of infectious agents quickly devitalize multitudes. Unfortunately the poor suffer out of all proportion to others.

Famine is usually applied to the condition of a marked dearth of food. As food scarcity increases, poverty likewise increases and with it disease occurs with increasing incidence and a corresponding higher death rate. It is quite commonly accepted that the death rates of tuberculosis and pneumonia vary inversely with economic status. It has been shown that the mortality rates of pneumonia are about twice as high among people on relief as among those under more comfortable circumstances. We have nearly always observed that typhus fever increases in years of scarcity especially among those where privation is greater.

In former wars pestilence affected mainly the armies in the field. In the present conflict, conditions are somewhat different. The long barrier of distance has to a very marked extent been entirely wiped out. High speed aeroplanes span the distance from America to Europe or Africa in a few hours. With long range bombers, no area in the civilized world is beyond the reach of 2 and 4 ton block busters. This has brought poverty, poor living conditions, and infectious disease to civilian populations among the countries within striking distance. Starvation and malnutrition occur, the health of the entire populace is endangered, and general misery, famine, and destitution follow. Dissemination of disease follows with pollution of water supplies; rats and lice breed in the ruins of bombarded areas, shortage of fuel and food with the gnawing pangs of hunger become widespread, and people gradually lose the incentive to observe even the simplest rules of hygiene.

Constant vigilance of public health authorities is necessary to prevent the recurrence of the common scourges of the 19th Century, such as smallpox and diphtheria. Only a few days ago an announcement was made in Washington, D. C., by the U. S. Public Health Service that smallpox vaccination of the entire population of that city is urgent. Two reasons appear for this request. In the past few months there has been an alarming outbreak of smallpox of unexpected severity in Pennsylvania; there is fear that the area of this outbreak may become greatly increased. The other and more significant reason is that Washington, D. C., is the meeting point of tremendous numbers of visitors gathered there from all continents of the world, and it is not unreasonable to think that sometime an individual may bring the virus of smallpox from some distant land.

With the finding of the bacillus that is the causative agent of diphtheria by Klebs-Loeffler, it was only a few years later that an effective antitoxin was developed by Bering-Roux and others. Resistance to infectious agents depends upon defensive mechanisms either acquired or inherited, neither of which is absolute but always relative. Acquired resistance, or acquired immunity as we commonly speak of it, is quite well studied and understood. Inherited or natural immunity is still a complex quite far removed from understanding and solution. It is through our knowledge of acquired immunity that we have reduced the rate of incidence of some of our common infectious diseases among both civilians and our military forces.

For an infection to take place in an individual, several conditions are necessary. The mere presence of a bacterium or a virus in or on the body does not constitute infection. The bacterium must be able to produce a local process during its growth. It must reach the tissue for which it has great affinity. To do this it must overcome the defensive mechanism of the body. Time plays an important role in this procedure and if conditions are such that they can be controlled the course of the infection may be very effectively altered; such control occurs daily with the administration of antisera or with the aid of chemotherapy. In the use of both of these agents, much has been accomplished in the past few years. I need only mention the extensive use of the sulphamides in their present usefulness. In the case of antisera not so much has been accom-
plished in spite of the fact that we have known for a long time the close association of them with globulins. It is only recently that perhaps an antibody has been chemically produced mainly through the effort of Dr. Campbell and one of our own graduates, Dr. Linus Pauling, at California Institute of Technology. If, as is now definitely established, there is a close relationship between antibody and globulin, then we must believe that diet is an essential factor in resistance to disease. If there is an inadequate intake of protein, then the amino acids necessary in the synthesis of globulin will be sadly lacking and soon deterioration of the population continues until catastrophe overtakes them.

One of the problems that is ever present is that of educating the civilian population relative to the value of immunization. That there is need of a widespread public health educational program is illustrated by a survey concerning immunization procedure, in which a questionnaire was sent to groups of individuals in a nationwide poll. One of the purposes of this questionnaire was to obtain the opinion of these groups regarding the value of immunization in respect to some common infectious diseases. Let me briefly summarize the results of this poll. Only 65 per cent of those replying believed that typhoid immunization prevents the development of typhoid fever, only 72 per cent believed diphtheria could be prevented by immunization, while 77 per cent thought smallpox vaccination was effective. The replies appeared to indicate that most people were aware of the value of immunization and the seriousness of these diseases but "put off" being immunized. It appeared that the public was not well informed concerning how often or when they should be immunized.

In the past few years much has been accomplished in the discovery of the causative agents of well-known diseases, but much more information is urgently needed. I can illustrate the urgency by giving a few figures from a recent number of the Public Health Reports. In Algeria, Morocco, Tunisia, and Egypt last year, more than 110,000 cases of typhus fever alone were reported. There were probably many additional cases that were never diagnosed and reported. That is an area where our boys are now actively engaged in terrific battle. Incidentally I should be somewhat remiss if I did not mention that 37 cases of typhus were reported for the week ending February 20, 1943 within the confines of the United States. I could give some recent statistics regarding other diseases such as plague, yellow fever, and malaria, but since they are spread mainly by insects they will probably be discussed by following speakers.

I have made no particular effort to separate the problems of bacteriology and sanitation in our civilian and military groups. Perhaps the basic concepts are very similar or identical but they can be more drastically and effectively carried out under military regulations than among the civilian population.

Since most of us, for one reason or another, may very likely continue to be civilians for the duration of the war, it might be worth while to mention briefly some of our problems and how to cope with them. It is absolutely vital to our armed forces that the nonmilitary portion of our population be healthy so that we may be able to produce the maximum of the various commodities needed in warfare. I believe it is commonly accepted that about half of all illness may be attributed to infectious agents. It behooves us then to prevent illness from these agents as much as possible. It has been said that if anyone who is harboring an infectious agent would keep it to himself for a determined period of time, many diseases would disappear.

**Food Research for the Army**

**Dr. Pavcek**

Our committee is a part of the National Research Council, more closely related to the Food Nutrition Board, and was organized specifically by order of the Quartermaster General. It will probably function a little later on with Lend-Lease. It is a very interesting position that I find myself in and quite an honor to work with a man as brilliant as Professor Elvehjem. An Army general was faced with the problem of collecting data on food which was hard to evaluate because of variations in assay techniques. He thought if he could put it in the hands of a committee that was qualified to evaluate such data, a lot of his problems would be solved. We hope they will be.

We have been engaged in the past three months in collecting literature. We have furnished the Army with mimeographed lists of 204 food items. A recent request is concerned with dehydrated foods which the Army is buying a lot of, vegetables specifically.

As a part of this trip I have contacted various laboratories to arrange for assays on our various projects. Many dehydrated foods sold to the Army are being tested. The thing that strikes me is the willingness with which the people cooperate. Go to a university and ask them to make analyses; they will turn over their laboratories. Another study that seems to be developing is the study of the losses of cooking. There are various projects throughout the country that are studying cooking losses in foods. It does not mean anything to say that a certain vegetable contains certain units of vitamins or carotene because they might not be there after you cook it.

*Stenographic report of remarks at luncheon.*
Mr. Chairman, I have a very special interest in the subject of epidemic meningitis because upon entering the Army May 3, 1917, the first thing I did in military service was to catch meningitis myself. Later, at Fort Riley, Kansas, I was one of about eight physicians and an equal enlisted personnel who were engaged in running down meningococcus carriers in the two divisions at neighboring Camp Funston. Cases of meningitis were frequent, deaths were occurring at the rate of several daily, and a survey became correspondingly important. A colossal program of culturing was carried out, for which I disclaim any responsibility. Every soldier in each command was cultured at least once, usually several times. An estimated quarter million culturings of normal and abnormal nasopharynges were made, transferred and subjected to agglutination tests. As a result an average of about fifteen hundred soldiers were in isolation much of the time. Meanwhile the epidemic continued unabated, and the deaths went on.

Three renowned scientists of that time arrived on a tour of inspection—Gen. W. C. Gorgas, Dr. Victor C. Vaughan, and Dr. William Welch. They inspected our laboratory routine, failed to detect its flaws, and gave it carte blanche. They even made it the type for all similar surveys in the Army. But another eminent authority—the late Dr. Hans Zinsser, then of New York and later of Harvard—arrived at a different conclusion. Without seeing our set-up at all he wrote us expressing doubt as to the correctness of our findings, and asked certain poignant questions. For example, were we sure that the agglutinations we observed were really meningococci or were they ordinary sediment—in simple terms, dirt? There was no question in my mind that he had diagnosed the situation correctly.

The upshot of it all was that a new commanding officer came to Fort Riley, followed by a shift of personnel, and I suddenly found myself in charge of the laboratory division. The next day, at a meeting of the efficiency board, the new C. O. asked me for a report and recommendation. I told the plain truth: we had done a foolish and needless bulk of work, a quarter of a million cultures, including entire regiments and divisions, with the result that about fifteen hundred recruits had been kept in isolation at all times. I recommended that routine repeated culturing of entire commands be discontinued and that the search for carriers should be confined to the immediate contacts of the meningitis cases. The C. O. ordered that such a change be made at once. The outcome was most gratifying. Within a few weeks the number in isolation as meningococcus carriers was reduced from fifteen hundred to about fifty. Meanwhile the number of active cases decreased, and likewise the number of deaths.

Such is the lesson that can be learned from World War I, when we had to depend solely on epidemiological studies and a proper use of specific sera and ordinary care. Statistics show that we had relatively few cases of meningitis in France, in spite of the fact that we did comparatively little routine culturing for carriers. This satisfactory result was due largely to the fact that a thorough study was made of immediate contacts, without complicating the picture by wholesale culturing of commands.

CAPT. HERMAN BOLKER

I am very happy that Dr. Benson opened this subject which is very near to me now. I am at Camp Adair and have just gone ahead with some work on meningitis and profited considerably from many of the errors that were made in the last war. There are many things that I am not privileged to talk about. The important thing is that while we went ahead with culturing our suspected carriers, the contacts of a known case, the fact remained that every time we got a new case it never came from an outfit that had been cultured and the carriers removed. In about December of this year an article in the Military Surgeon reported definitely that carriers could be cured over a period of three months with sulfanilamide. The important thing now is that such a thing is done without interfering with the training period, and we have had what appears to be a very successful experiment with it which I am not as yet privileged to discuss except to say that Camp Adair has had no meningitis following this work. The carrier rate will drop with small doses of sulphadiazene to next to nothing in four to five days. Since the night we started this, on January 29, the only cases have come from outlying out-
fits. This matter is being reviewed by the Surgeon General at this moment, and maybe some day I will be able to say more.

You can get enlisted men to do the culturing. Meningococci can now be cultured with ease. I do not think the chapter on meningitis has been closed. (Note: Prophylaxis use of sulaphadiazene is now officially the subject of a letter from the Surgeon General’s office.)

DR. WEINZIRL

I am most interested in the discussion of meningococcus meningitis. Anyone who deals with that disease either in the laboratory or in connection with epidemics or in the sick room is apt to have many fascinating experiences, even including a personal attack of the disease. That happened to Dr. Benson and that happened to me. I should like to ask the medical officers of the Army what the present view of the effectiveness of this program is? That the camp type of outbreaks of meningococcus meningitis can be controlled simply by separating the heads of the beds in sleeping quarters and more or less ignoring cultures and carriers was clearly demonstrated during the last war.

Further, during the depression the outbreaks that occurred in the many transient bureau dormitories were controlled simply by separating the beds.

VENEREAL DISEASE CONTROL IN WARTIME

DR. ADOLPH WEINZIRL*

I was asked to discuss the relationship between biology of the war and the venereal diseases. The thing that happens as a result of war is an increase in delinquency, including sex delinquency. The advent of war aids delinquency, and the reason for it lies in the fact that those social pressures that operate not perfectly, but with remarkable effectiveness, on every individual living in his home community are lessened. The influence of the home and the church and the school and the opinions of one’s associates are strong. With the advent of war, young persons, at an age when the forces are so strong toward the exercise of the reproductive instinct, are removed from the influence of these social pressures and are sent to camps or industrial centers. The result throughout the past has been a rise in venereal disease in the armed population and among civilians during times of war.

But the problem is being met in this war with remarkable effectiveness by a four-point program. It consists of an expanding health service program, bringing about treatment for the infected and prophylaxis for the exposed. Secondly it consists of repression of organized prostitution. That in many minds is a very controversial subject, but among the informed there is no longer any question about its effectiveness. The repression of commercialized prostitution has been accepted not only in this state, not only in this nation, but in Canada. It is the quickest way in which a marked drop in the prevalence of venereal diseases can be made up to 50 or 60 per cent. The third part of the program consists of providing recreation. You can not walk through any town or city without seeing a USO or welcome group. The recreational facilities are to combat loneliness.

The fourth part of the program consists in providing public information. There are two phases of it. One undertaken by health agencies consists of providing adults with information concerning what the community should provide as a means of prevention, particularly with a view to securing community support in behalf of local authorities who have a responsibility for providing health services, recreational facilities, and repression of prostitution. The other phase is undertaken by the schools and has become a concurrent part of the Victory Corps program. The Victory Corps program consists of physical development on the one hand and health knowledge on the other.

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Introduction

Since the advent of man, insects and their kin have been man's chief competitor in peacetime and his greatest enemy during wartime. They destroy his dwellings, devour his crops, raise havoc with his domestic animals, and cause sickness and death by the transmission of disease. In wartime, the insect plays an important role, that of the vector of disease. Diseases have caused more deaths on the battlefield than bullets.

In the Old Testament we read: "And there came a grievous swarm of flies into the house of Pharaoh, and into his servants' houses, and into all the land of Egypt: the land was corrupted by reason of the swarm of flies." Elsewhere in the Bible, one finds mention of plague as occurring centuries before the Christian era in the land of the Philistines. Mention is also made of disease breaking out during military operations against the Israelites. It is reasonable to suppose, of course, that many of the pestilences of ancient times and the middle ages were typhus fever.

Typhus was prevalent during the Great Plague of London, spread throughout Europe, and persisted in epidemic form throughout the duration of the Napoleonic wars. Napoleon was a great general, nobody denies, but the louse, Pediculus humanus, was greater, for it was the louse that contributed most to the great retreat from Moscow. In the French Revolution and the Seven Years' War, typhus killed more men than bullets.

A number of these diseases are characterized by a high fever and a stuporous state. Delirious, the soldier loses his sense of caution, may expose himself, and become a target. When shot he is listed as "killed in action." Also, the soldier, because of his stuporous state, lacks alertness and allows the enemy to gain the advantage.

We know the part played by insects in the transmission of disease in past wars. The question arises, will history repeat itself in World War II? Also, we know that the incidence of disease rises during wartime. What will be the status of disease after this war? Also, how long will it be before man will be free from pestilence?

There are about 60 diseases of man that are transmitted by insects. Five of these, malaria, dengue, yellow fever, plague, and typhus fever, have been chosen for discussion to give some insight into the medical entomological problems of the war. Some of the other diseases, for example, are: tularemia, undulant fever, cholera, amoebic and bacillary dysentery, yaws, relapsing fever, sleeping sickness, spotted fever, tsutsugamushi, trench fever, and filariasis. Some of these undoubtedly are playing and probably will continue to play an important part in this war.

Malaria

Hippocrates wrote about malaria in 400 B.C. In his book on epidemics he noted the existence of periodic fevers, divided them into four types, and referred to the enlarged spleen. The term "malaria," however, was not introduced into English literature until about 1829. Malaria or "bad air" was considered to be due to poisonous emanations from the damp ground from marshes. It was not until 1880 that the parasites of malaria were recognized in the blood and in 1900 Manson proved the mosquito transmission theory. Malaria is transmitted by the bite of certain Anopheline mosquitoes. To date, 60 out of 180 potential vectors have been incriminated.

Malaria is widely distributed over all parts of the tropical and subtropical world and much of the temperate regions and exists on all of the active battle fronts. Already affecting millions of people, it is an ever present danger. The severity of malaria cannot be over-emphasized. In India, for example, out of a population of 353 million, about 100 million (or one-third of the population) are reported as having malaria. Figures indicate that the annual death rate from malaria in India alone exceeds the 3 million mark. Even in the Western Hemisphere, where it prevails so widely, it is a disease causing great mortality, though of course not with such magnitude as in India.

Malaria is a protozoan disease characterized by chills, fever, and a terminal sweating period. Headache, mental confusion, even a delirious stage and for short periods total blindness may occur. A soldier with malaria may become an easy target for the enemy.

Preventing the soldier from contracting the disease is of prime importance. This may be done in several ways: (1) by the destruction of the Anopheline mosquito and its breeding places;
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(2) by protecting the individual from the bites of the mosquito; and (3) by drug prophylaxis.

The destruction of the mosquito may be accomplished: (1) by the spray killing of the adult mosquito using an oil-pyrethrum extract; (2) by the destruction or removal of breeding areas using, actively, the pick and shovel; (3) by the spray killing of the immature forms using oil or Paris green; and (4) by the use of fish and other natural enemies.

To combat the Army's No. 1 disease, malaria, a section of the Preventive Medicine Service is devoted entirely to the control of malaria and is directed by an eminent malarialogist. Besides the anti-mosquito campaign in permanent camps and the Caribbean bases, the Army has established small and highly mobile "malaria survey and control units."

The soldier may be protected from the bite of the mosquito by the use of screens and netting, gloves, protective clothing, citronella; proper instruction in this use is imperative and essential.

Another method of prevention is the use of drugs, quinine and atabrine, as a prophylaxis. Should the soldier, however, get malaria, he can be treated. Quinine stands preeminent in the field. Because of the shortage of quinine, a number of synthetics, plasmochin and atabrine, and substitute drugs, certuna, totaquine, and sulfanilamide, have come into vogue.

It must be borne in mind that malaria is a disease for which there is only treatment, not a "cure." This is so, because after the treatment has been taken, some of the protozoa may hide out in tissues like the liver or the spleen and pop up to plague a "cured" man months or even years afterwards. Also, even a patient who has become completely free of the parasites has no true immunity and is liable to be reinfected if an infected mosquito should bite him.

Bearing these facts in mind, what do you suppose will be the status of malaria after the war? Also, how long after the war will it take man to reduce the incidence of malaria to a state of tolerance or to free the world of this pestilence?

Dengue

Dengue was not recognized until the end of the 19th Century. It is remarkable that it was not noted earlier. The explanation is that it was confused with other known diseases, malaria and yellow fever. From its wide distribution and numerous names, breakbone fever, blackwater fever, dandy fever, etc., it has probably existed for centuries.

Dengue is a widespread disease in tropical and subtropical regions, particularly in the Philippines. It is also found in temperate climates, e.g., Texas.

_Aedes aegypti_, commonly referred to as the yellow fever mosquito, is the vector of dengue. Other mosquitoes (_Aedes albopictus_ and _Culex fatigans_) have also been incriminated.

Dengue is a virus disease characterized by sudden attack of high fever, severe chill, nausea, and the passage of black urine, followed by rapidly developing anaemia. It is a disease in which fatalities have been as high as 50 per cent (Japan, India, and Rhodesia) although normally the death rate is low.

Little has been said about dengue in World War II. But from what I have been able to gather from purely hearsay evidence, it is my opinion that historians will record dengue as having played an important part in World War II.

The normal methods of control employed for the yellow fever mosquito, _Aedes aegypti_, also apply here.

As in malaria, quinine and atabrine are used as prophylaxis, but care must be exercised because of haemoglobinuria.

Yellow fever

Yellow fever is one of the more complicated and most dangerous of the infectious diseases of man. In recent years rapid strides have been made with this disease, because a number of efficient workers have devoted their energies to its study. A great deal has been learned about the pathology, the characteristics of the causative virus, its behavior in man, and the vector, _Aedes aegypti_. Nevertheless, there is no specific therapy once the infection becomes established. Immunity, however, is achieved through the use of a vaccine.

Africa is considered as the original home of yellow fever, with western Africa and South America as the endemic foci. The disease and the insect vector probably came into the New World during the days of the slave trade. Numerous severe epidemics followed in Philadelphia (1793), Memphis (1878), New Orleans (1905), and the Panama Canal. The Orient, however, despite its susceptible population and its abundance of suitable mosquitoes, has remained free yellow fever.

_Aedes aegypti_ remains as the vector responsible for the extensive urban outbreaks of yellow fever. It is a domestic mosquito, living in homes and feeding on man.
Yellow fever is a disease of populated centers. The disease is characterized by an abrupt rise of temperature of short duration, followed by a remission of longer duration, jaundice, prostration, and black vomit.

Considerable disagreement exists as to proper therapy. Rest is essential, even in mild cases. Individual prophylaxis consists of avoiding the mosquito, and the use of a vaccine. The efficacy of vaccination has been proved by its use in endemic zones of yellow fever.

Control *Aedes aegypti* and you control yellow fever. The method is simple, but requires strict and meticulous inspection with an iron-hand rule. The favorite breeding sites are in small jars and vessels, flower pots and discarded tin cans, wells, tanks, and other containers of drinking water. Frequently the ingenuity of the mosquito is greater than that of the inspector.

**Jungle yellow fever**

The Rockefeller Foundation in 1927 reported no cases of yellow fever. It was assumed that the battle that had cost the lives of research workers and millions of dollars had been won. Then, almost without warning, the South American jungle struck back and in a few years’ time the strategy of the battle had to be altered. Evidence pointed to infection occurring either in clearings next to uncleared jungles or in the jungle itself. The presence of the virus in mosquitoes caught in the jungle was demonstrated. Also, monkeys tested were found to have an immunity naturally acquired in the jungle. Therefore, the jungle must be considered as a possible permanent source of virus for the reinfection of cities and towns where *Aedes aegypti* is allowed to exist.

The question arises, with airplane travel as it is today, what will be the status of yellow fever after this war?

**Plague**

Plague is the most fatal of all epidemic diseases and its tragic history is full of interest. Plague is mentioned in the Bible as occurring centuries before the Christian era. It still exists in many parts of the world. Although not rampant, it remains as a potential threat and may at any moment lead to an explosive epidemic.

Hippocrates in 400 B.C. wrote about plague. The Great Plague of the 6th Century, starting in Egypt, spread to Syria and Europe, carried off about half of the population of the Roman Empire. During the 14th Century, the "Black Death" wiped out one fourth of the population of Europe. Successive epidemics occurred in Europe during the 15th, 16th, and 17th centuries and in 1665 the Great Plague of London killed 60,000 out of the population of 450,000. Plague continued throughout the 18th Century until 1841 when it seemed to have disappeared, only to return in the pandemic of 1894. Originating in China, it spread to India, Singapore, the Philippines, Arabia, Turkey, Egypt, Europe, North, Central and South America, to nearly every country in the world.

Bubonic Plague, the "Black Death" of the Old World, is commonly transmitted from rat to rat and from rat to man through the agency of the rat flea, but fleas from other infected rodents may give rise to the infection. Occasionally, the disease is transmitted from man to man by direct contact. The bacillus gains entrance through the broken skin or through the mouth, nose, and even the eye, if rubbed by a hand which has previously been contaminated.

Sylvatic plague, a plague of wild rodents, is transmitted to man through their fleas, and very commonly by handling or skinning the animals. Plague is an acute, infectious disease with a high mortality. It occurs in three forms, bubonic, septicemic, and pneumonic. The onset is abrupt with temperature rising to as high as 107°, rapid pulse, severe headache, backache, mental dullness, nausea, and vomiting. Death usually occurs in three days.

Rodent control is highly important. Once plague has broken out, prophylaxis consists of isolation and the extermination of rodents and fleas. For soldiers the best advice is to avoid plague-infected districts and when in such districts to leave wild rodents alone and stay out of buildings that might be infected with rats. Also, all wounds, no matter how small, should be treated instantly. Approved vaccines should be used. The treatment of plague is largely symptomatic, if one lives long enough.

**Typhus fever**

Europe has been the principal center of the Great Typhus epidemics of the world, Russia and Poland being the great endemic foci. It is a disease worthy of note and may be a deciding factor in the outcome of World War II. Typhus is an acute infectious disease, with a sudden onset, fever, and rash. The victim has a maddening headache and the fever may reach 109 degrees. Coma usually follows, men lie unconscious with their eyes open and staring, in a low
muttering delirium. Men with typhus make poor soldiers and good targets.

It is reasonable to suppose that many of the pestilences of ancient times and the middle ages were typhus fever. It was not until the 16th Century, when typhus was described (1554), that the disease was differentiated from plague.

During the Post War I period, a great effort was made to wipe out typhus from Europe, all of which has probably been in vain, because the eradication of typhus in Europe has again been set back by this war. Little has been said about typhus in World War II. Although the word "typhus" is "verboten" in Germany today, some information has leaked out. Poland is hard hit; in the spring of 1941, Warsaw had 26,000 cases. In 1942, deaths in Warsaw's Ghetto, where half a million Jews were huddled together, reached a daily rate of 400 deaths; bodies were left in the streets to be picked up by the police. Cases of typhus have been reported in Finland, Yugoslavia, Rumania, and parts of occupied Russia, Belgium, and the Netherlands.

This is undoubtedly the result of Hitler's strategy. Not that we suggest that he transplants the disease, but probably little is done to control the disease among the non-Aryan races. Of course, that frees Greater Germany from taking care of the "unwanted" and leaves more room for the expansion of the "purer races." It is said that a case broke out in Eastern Germany immediately, all traffic in the town was halted. A 20-mile quarantine belt was established and the town was "cleaned."

The Germans have said little about typhus and the Russians have said less, but it is a known fact that typhus is endemic in Eastern Europe, also that the laxity of personal hygiene and sanitation in such areas is conducive to rapid multiplication of the louse and typhus follows. Answer the question yourself. Look at the condition of the German prisoners in news reels recently released from Russia. Yes, the efficient Germans have freed Greater Germany from taking care of the "unwanted" and leaves more room for the expansion of the "purer races." It is said that a case broke out in Eastern Germany immediately, all traffic in the town was halted. A 20-mile quarantine belt was established and the town was "cleaned."

The United States is less than a day by plane from the jungle type of yellow fever of South America, less than two days from sleeping sickness of Africa, and less than three days from cholera and plague; hence the world has apparently become so small that our medical and sanitary responsibilities regarding tropical diseases have been greatly increased.

People talk today about peace after this war. They want freedom from fear, freedom from want, freedom of the press and freedom of speech, and freedom of worship. Let us add one more, namely, freedom from disease. Everyone in this room has a big job to do after this war and that is to help free the world from pestilence. Let us all hope that we shall live to see the day when the treatment of disease will be considered an admission of failure.
DISEASES CAUSED BY FLUKES AND OTHER WORMS
DR. MATTHEW C. RIDDLE*

Practically all of the parasitic diseases and the worm infestations are transmitted either by mosquitoes, insects of one sort or another, or lower animals that are referred to as vectors. As most of these parasites also infect animals other than man which act as a host or an alternate host, the subject is a very complicated one. Not being bound by military secrecy as Captain Ellsworth was, I want to make a few remarks. I promise you I'll reveal no military secrets because the silence of the armed forces has been so successful that I don't know any military secrets.

But I do know some of the background of these diseases. From what one obtains in the newspapers as to the nature of the warfare and what is happening to some of the enemies in this respect, it is easy to conclude what is happening to our soldiers over on the tropical battlefields. It has been stated that Japanese troops operating in Malaya and the Philippines were infected practically 100 per cent with malaria, and I think that that is probably correct. The mosquitoes that carry malaria are not particular about race or political opinions, so I think it is safe to say that practically every man that we have in the military services in heavily infected areas in the South Seas has either had malaria or the various kinds of dysentery either singly or in groups. It is a serious situation. The medical profession of this country has rather abruptly come to the realization that these various tropical diseases with which they have had very little experience, particularly in this part of the country, are going to become real problems. Not only are the physicians in uniform going to have to take care of soldiers with these parasitic diseases in the Army, but men will return to our country in tremendous numbers in the course of time infected with various parasitic diseases; and the civilian physicians will have to take care of them. This fact imposes many problems that we shall have to solve.

I propose not to discuss these various parasites in detail, but I want to give you a formal introduction if you are not familiar with them and give you their present address and let you meet them very much as you would meet a person on the street—enough of a background so that you will be familiar with them when you see them next. Many diseases are transmitted to the human being by the various human excreta. I am not including such filth-borne diseases where lack of hygienic habits or contamination of food is a factor because the military services are capable of handling those relatively well even under the difficult conditions under which our boys fight overseas. The parasites I am going to introduce you to are parasites that are hard to control by hygienic measures. They are carried by vectors—mosquitoes or snails, or by direct contact of the human being with infected soil or water without the intermediate transmission.

Hookworms are transmitted by way of the feces through contact with the infected soil. Their larvae develop in sandy, moist soil; and when the larvae are developed they can go through the unprotected skin of a person's bare foot within the matter of minutes. That is the way a man acquires hookworms. They offer a rather severe problem, not because it is difficult to get rid of the worms but because it is difficult to avoid getting them in heavily infested areas, particularly where you can not avoid contact with the soil.

Sleeping sickness is the disease caused by infection with either trypanosoma gambiense or trypanosoma rhodesiense. Sleeping sickness is a very difficult problem in the communities where it is present, including the neighborhood of Dakar, across which our transport planes fly. There has been the tendency to move out everything, people and cattle which act as a host, when a region becomes infected. The organism is a protozoan and is carried by the tsetse fly. Trypanosoma cruzii is another interesting organism but not of great military importance; it is transmitted by a group of vicious blood-sucking bugs. It usually affects children. The bites are on the face near the eye. It causes serious disease. African sleeping sickness can be treated, if not too far advanced, with some success. In the case of trypanosoma cruzii there is an infection in bugs in our southern states of South Carolina, New Mexico, and Texas, but no clinical cases.

The Leishmania is a relative of the trypanosomes. Leishmania donovani causes the Kala azar. Leishmania tropica is a species involving the skin and mucous membranes. These
diseases are all serious diseases. They are subject to treatment but are dangerous. They are not worked out completely as far as transmission is concerned but supposedly are carried by biting flies and intermediate hosts such as cats, dogs, sheep, etc.

The fluke, *Clonorchis sinensis* occurs particularly in China. We may not encounter this, particularly at this stage of the war. *Fasciolopsis buski* is an intestinal fluke. *Paragonimus westermani* is a lung fluke.

Some of the flukes show a very interesting life cycle. Near the head of the larvae are very prominent secretory glands that secrete a substance that is capable of digesting away human tissue. If the fluke egg is laid in the blood stream, it can travel to regions such as the bladder and be excreted that way, causing a good deal of trouble enroute. It hatches into a little larva, a miracidium. Flukes belong to the flatworm family. The life of a miracidium is very short, and it has to find a suitable host within a short time or it dies. It is very particular about the host which it enters. There is usually one particular species of snails which acts as a host for each particular species of fluke. The larvae are attracted to snails, going directly into the snail and within a matter of minutes setting up housekeeping there. The inner walls of the viscera become the home for the little larva. There is a later stage in which they become little tadpolelike larvae by budding from the inner cell wall of the larva. They become cercariae, which are the organisms infecting the next host or man. The cercariae are mobile organisms with a tail. They leave the snail and seek out various types of hosts. The *Clonorchis sinensis* seeks out the fish and is transmitted to man when he eats an infected fish. The lung fluke uses crabs and crayfish in a similar manner as an intermediate host. Others settle down on water plants; and man acquires them by eating the plants. Another alternative among these flukes is that the second snail may develop more of the cercarial larvae which are freed in pools of water. A moment's contact with water so infected will result in the penetration of this larva into the skin. All that is necessary is to get the skin wet, and by the time it has dried off the larvae are inside. This is the method by which the blood flukes are transmitted. Blood flukes are a serious problem because you can imagine that soldiers living in swamps and foxholes and ditches can scarcely avoid getting their skin wet.

The *Schistosoma haematobium* is the bladder fluke. Its habitat is in the veins supplying the pelvis and the bladder; it is not injurious to the human being except from the passage of its eggs or its larvae through the tissues in and about the bladder. But it is very injurious in that respect and can cause tremendous difficulty in the urinary organs and thereabouts. Many of our soldiers will undoubtedly pick up some of these Schistosoma. Other similar Schistosoma are blood flukes living in the veins supplying the colon and small intestine, and they create most of their damage by the penetration of their eggs into the blood vessels and all the tissues of the bowels and mesentery organs on their trip to the lumen of the bowel to be eliminated in feces and transmitted to others. These are also acquired by contact with water.

The adult worms live in the blood vessels. The female worm has a groove and fitted into that groove is the male worm, which is the smaller worm; and through their adult life they remain constantly in copulation. They live from the food derived from blood. The worms hang on to the vein walls by suckers, moving from vessel to vessel as the walls of the vessel become injured. The female lays tremendous numbers of eggs in the course of her life.

*Onchocerca volvulus*, a filarial worm, causes the development of lumps on the skin. The infection was originally found in Africa. The adult worm locates and curls up, forming quite an inflammatory nodule at the site of the location. It also attacks the eyes and may cause blindness. It is transmitted by a coffee fly. The scientific name of the fly is *Simulium damnosum*, which indicates its nature as a pestiferous, biting, annoying insect.

*Dracunculus medinensis* is a worm about three or four feet long. It travels underneath the skin around the body, causing considerable cutaneous inflammation. It is difficult to get rid of because of its dimensions and is hard to pull out because of the hooks on the tail. When it becomes sexually mature and ready to lay eggs, however, it travels down the leg so that the head causes a little blister on the lower part of the leg or foot; and when the infected individual steps in a pool of water, the blister breaks and immediately the worm discharges a group of eggs. These eggs develop and are taken up by crustacea commonly known as water fleas, which act as immediate host and vector. The infection is acquired in man by accidentally drinking water that contains some of these little crustacean organisms. The proper time to start treatment is when the worm sticks its head out of the blister. This treatment was devised thousands of years ago and it has not been
improved upon since. When the worm has its head in the blister, tie its head onto a twig or match stick and attach the twig to the side of the leg and leave it until the worm has come out an inch or two more. Then roll it out a little more, day by day, until ultimately the worm is extracted.

*Wuchereria bancrofti* is important from a military standpoint. It is reported that hundreds of our men have returned from the South Seas with this worm. It causes filariasis or elephantiasis and there is no very effective method of treating it. It causes sickness by mechanical obstruction of the lymph channels to the lower extremities. It is transmitted by mosquitoes and is very difficult to avoid in the type of general warfare that occurs in the South Seas.

### Meeting to Consider Proposals for Organization of an Oregon Academy of Science

The meeting was called to order by Mr. Gilfillan as temporary chairman at 5 p.m., Saturday, April 3, 1943, in the Memorial Union at Corvallis.

Mr. Gilfillan stated that in response to his enquiry, numerous letters had recently been received indicating a need for an Academy of Science, while a few other letters raised questions as to whether or not this was the proper time for such an organization, and also questioned the possible relationship of such an organization with the Northwest Scientific Association. Following a discussion of these questions by Messrs. W. M. Wood, W. D. Smith, S. N. Wycoff, H. B. Yocom, H. J. Andrews, E. C. Gilbert, C. Grobstein, J. E. Simmons, and others, the following action was taken:

The first motion, by Mr. Wood, was that the chairman appoint a committee whose work would be primarily to discuss with the Northwest Scientific Association, first, the establishment of the Oregon Academy of Science in affiliation with the Northwest Scientific Association, and second, some agreement to be made with the Northwest Scientific Association so that its meetings would be scheduled so as to be more convenient to people in Oregon.

Motion seconded by Mr. Smith, and after discussion, motion was called for and lost.

A second motion, by Mr. Grobstein, was that a committee be set up to investigate the needs of science in Oregon and that any organization formed be coordinated, if possible, with similar organizations in the Pacific Northwest. This committee was to report by June. Motion seconded and carried.

The third motion, by Mr. Wood, was that one member of this committee be also a member of the Northwest Scientific Association. Motion was seconded and carried.

The fourth motion, by Mr. Simmons, was that the present chairman of the meeting select a committee of five to "go ahead with this organization." This motion was amended so that the chairman of the meeting shall be chairman of this committee and that the membership of the committee be set at a minimum of seven. This amendment was accepted, the motion was seconded and carried.

The meeting was adjourned.
THE PHILOSOPHY OF A BIOLOGIST

A. L. STRAND

In their philosophies of life people fall generally into two classes: the hermit-crab type, and the Caddice-fly larva type. The hermit crabs are willing to confine themselves as well as they can within the philosophical shells of some by-gone gastropods. This is rather easy and the method affords some protection and from time to time it is possible to move into more commodious quarters. But by and large it's pretty much the same old house. It is safe, however; the tender parts are shielded, and little thought or preparation is required. It is just a matter of acceptance. Most of us belong in this category. A few there are like Caddice-fly larvae, who prefer to seek in the stream of life little bits of sand or particles of wood, fit them closely together, bind them with the silk of thought into the philosophical case about them. The partially completed structure, to the outsider, may look like the devil himself. However rough and irregular it may be on the outside, though, it is smooth in spots within and at least temporarily comforting. There usually won't be anything new about the particles of material used in building this abode, pretty much the same old material that has been washing down the stream for ages. The essential difference is that it allows for alterations and improvements; parts that are wont to crumble on account of faulty binder material can be rebuilt. Indeed the thing is never done up to the moment the builder is swept off to another world.

This is what Overstreet expressed in much better language than I have used when he wrote in the foreword to his Enduring Quest:

Very deeply and persistently we seek a philosophy of life. Our existence, for the most part, is a kind of puzzle picture which we feel we must in some way put together. We have, indeed, a fairly convinced notion that we shall never quite get it all together, but, as we fit piece to piece, there is a curious delight in each momentary triumph. And despite our notion to the contrary, there is always the hope that, by a stroke of good fortune, we shall come upon some master clue which will sweep the thing into an illuminating unity.

Now I should say somewhere here in the beginning that I do not pose as very much of a Caddice-fly larva and certainly not as an Overstreet picture puzzler who has found some key sections of the great design. But I am a biologist and it seems to me that it requires little perspicuity to see that some pieces do not fit, to see that some of the old shells in common use are very incommodious indeed. Philosophy, as Emerson said, is Man Thinking, past, present, and future; the present state of affairs must be considered in relation to how they got to be that way. Certainly that brings in the biologist. Furthermore, such reflection and observation is inescapable. Was there ever a more portentous period in man's existence when he needed more desperately an "illuminating unity" to give his life purpose and meaning? Of wars there have been plenty before. Man's inhumanity to man is one of the oldest of the "crooked knarls and knobs in a tough old world." Periods of depression, of deep mental and spiritual despair, have probably been the rule rather than the exception through countless generations. But when it comes to mass bloodshed, hunger, torture, mass murder, and misery, there could not have been before anything like we have seen since Hitler marched into Poland in 1939. There could not have been any time to compare with these present years in the magnitude of these things because never before were there so many souls to be so subjected.

Saying such as this has become trite, it is all so obvious. But two circumstances seem very pertinent to biologists and scientists generally. The first is that the breakdown has occurred in Western Europe which has been the seat of learning for over four centuries in continuous line of development. The second is that the struggle in which we are engaged is not confined to the things over which nations have commonly fought in the past. It digs deeper into ideas concerning the Nature of Man, his development, his morals, his "inalienable rights," his striving for "the good life." The ends to be achieved through victory, therefore, were never more divergent. The amplitudes of departure, from peace to war, from a scientific age of plenty to deepest misery, from democracy to nazism, from reason to unreason, from Jesus to Nietzsche, were never brought so in contrast.

There is a sentence of Sumner's that has intrigued me with its historical inclusiveness since the first time I read it. In one of his essays he says:

The great stream of time and earthly things sweeps . . . on. It bears with it now all the errors and follies of the past, the wreckage of all the philosophies, the fragments of all the civilizations, the wisdom of all the abandoned ethical systems, the debris of all the institutions, and the penalties of all the mistakes.

Certainly the banks of this stream of time and
earthly things are running full today, running full of humanity, full of blood, sweat, and tears, full of penalties. There are whirlpools of revolution, eddies and backwash of conservatism, but the crest is running high and fast. Where is it taking us; what sense is there in it?

In such a crisis it is not surprising that some of our beliefs that seem quite tenable in the complacency of peace are all but undone in a world of war. The old shells are cramping and uncomfortable even to those accustomed to see only what they want to see and who ordinarily get through life in a state of intellectual somnambulism. Certainly to a biologist, trying to put some pieces together and keep them in place, the workings of nature in the raw as we see it now furnish a fertile field for testing and observation. In my feeble attempt this evening to bring Homo sapiens into a more reasonable relationship to the world in which he lives, I wish to discuss two concepts that, at least to me, are very germane to the hour. They constitute, for me, some background on which to build any satisfactory philosophy that will fit our most conspicuous needs. These two things have to do with (1) misery — yes, I said just plain human misery — as part of God's universe, and (2) evolution as it relates to naziism and democracy. Evolutionary doctrine I might warn is concerned even more in number one than in number two.

All of us have heard the question raised as to why all this malefaction should come upon us. Why should such misery beset the world and fall so harshly upon God's fairest creation? We see what appears to be such unnecessary human suffering, such tremendous sacrifice of the innocent, the perversion of things fundamentally good and some of the noblest works of man to the forces of darkness and evil. Yet it is all part of the universe and we pray to the God who created it. Thus the subject of misery brings us at once to our conception of God. Recently I read the statement that "there is no scientific difficulty in the belief that God, if He exists, controls the universe completely." Perhaps no scientific difficulty but certainly there is a religious difficulty, a very old one, and the very difficulty to which my first subject, misery, is very definitely related. It has to do with the moral nature of God. Is God moral or amoral? No less a mind than that of H. G. Wells found it necessary in getting around this dilemma in his God the Invisible King to postulate two Gods. One was the God within humanity; the other the Veiled Being, the inscrutable power behind creation. Personally I don't believe that was up to Wells' usual standard for it is just the old dualism, which is unacceptable. We can't have one God to which we pray who admittedly has no control or responsibility over another part of His Being out of which come the "forces of evil." (At least in my universe God is responsible for the devil and there is no way out of it.)

I have gained a great deal of satisfaction in recent years from Bishop Ernest William Barnes' Gifford lectures at Aberdeen, published in book form under the title Scientific Theory and Religion. We all like safety in authority. If you examine his qualifications you will see what I mean. He is a scientist and theologian of distinction with a refreshing willingness to look facts biological squarely in the face. I intend to quote him freely in the next few paragraphs for he has furnished some of the material that has gone into my philosophical case, as it were. He says in relation to this general subject of the moral nature of God that "in the end all attempts to take from God responsibility for the nature of His creatures must fail." He points out that a Hebrew Psalmist in a flash of insight long ago recognized this truth when he wrote: "The lions roaring for their prey do seek their meat from God." There can be no reason to deny that the evolutionary process, for instance, "is as clear a revelation of God's creative activity as we can have. Its apparently non-moral character must be with His permission. For some unknown reason, He permitted death, disease, struggle, the instincts which have led to selfishness and lust in man, because He willed that higher, moral, intellectual and emotional development which in man is such an unexpected outcome of the process."

"Our present difficulty," Barnes says, "is not merely that in humanity sin [and misery] exist. There is a far more fundamental source of perplexity in the fact that the whole process of creation now appears to be non-moral. There is no evidence to lead us to infer that variations in the genes are directed towards ends which in our judgment are good. In such variations there seems, in fact, to be no ethical quality whatever." (Darwin, I might interpolate, said "there seems to be no more design in the variability of organic beings, and in the action of natural selection, than in the course which the wind blows.") Such variations "have led to odious parasitism, to the carnage of the jungle, to the microbic diseases that cause such suffering to humanity, to those animal appetites which are useful in the struggle
for survival and are the basis of sin in man. This, the immoral, brutal, lustful side of creation is as characteristic as the parental self-sacrifice, the adventurous curiosity, the instinct for truth, the enthusiasm for righteousness, the beauty of form, and the physical wellbeing which equally result from the evolutionary process. No revolt of angels, no theory of a fall, will account for such facts."

Barnes emphasizes that "we cannot postulate that God resembles his creative process in being Himself non-moral: to do so is to leave the moral nature of man unexplained and inexplicable." The highest consequence so far of the progressive development of terrestrial life is civilized man with his ethical sensitiveness and his regard, at least part of the time, for ideal goodness. So far he is God's finest achievement upon earth; and the best that is in man must reveal, as fully as we can know it, God's nature.

The Bishop of Birmingham admits frankly that in this situation we are confronted by a dilemma from which there is, at present, no escape. "Verbal dexterity," he says, "and the skillful use of those evasive phrases which are too common in modern theology might seem to offer escape to some; but to the man of science evasion is high treason against truth. We must apparently allow that genetic variation, the raw material of evolution, seems to be as often for worse as for better: if it is good, it is also evil: it leads alike to progress and to degeneration"; to the glory of man in his times of greatness, and to his misery.

It seems to me that possibly here is the particle of sand, or better yet, here is the unfinished location for that particle or several particles. If the structure could be finished, if we could make a tenable separation, we could achieve a unity of Goodness; our philosophy would be complete, and a priori too, the whole thing would have been different. We really wouldn't need a philosophy; all would be perfect. Man instead of being on his road somewhere, would have long since arrived. Here is where, though, I gain my greatest admiration for the Great Impersonal Designer, for He must have willed that, for man, life should not be a matter of just being, but of becoming. Take out the struggle, take out the misery, and you would also take out the achievement and greatness. A frightful price—but an invaluable gain.

I come now to the second phase of my discussion, that which relates nazism and democracy to organic evolution. It will be brief and I'm afraid rather sketchy for it is a large order. The possible connection between these things may seem odd to some but I am sure not to biologists or social scientists. The fact that one can interpret nazism and democracy, as the one is set off against the other in basic ideals, in terms of evolutionary doctrine is merely recognizing again the universality of this fundamental concept. The idea of evolution is integral to my philosophy. Even yet, I know, there is a type of religious thought that refuses to admit the truth of man's evolution from lower forms of life. It is repugnant to the extent of stopping all clear thinking on the subject, thus standing in the way of the possible perception of a grander unity in the universe. For me man's dignity needs no defense save that provided by his own conduct. Actually "he is what he is, and whether evolved long ago from some anthropoid ape or specially created in the image of God, his present faculties, aspirations, and achievements determine his worth." But to perceive the origin of his deficiencies, to account for the warts on his humanity, what does a man do without some idea of evolution? What hope unless there is built into the design of things some unfolding of man's higher nature together with the decline of his baser motives?

No one to the extent of my reading has covered so meticulously the underlying ideologies of World War II as W. T. Stace in his Destiny of Western Man. Never dogmatic, he has traced the opposing doctrines with a very discerning hand. I have found in his book much good material to replace some very weak spots in my own larval casement and I recommend it to you as an expert and inclusive treatise on only a small part of which I can give but an outline. I am indebted to Stace for much that is to follow.

I said a few moments ago that the ends to be achieved through victory for one side or the other were never so widely divergent as in the present conflict. Our common arguments and disagreements are seldom if ever over ends but concern only means. We agree on the ends, for unless there is agreement on ends an intelligent argument cannot be developed. But this is precisely what has happened in the modern world as between the two opposing forces. The totalitarian nations dispute our axioms and deny what we have taken to be the supreme values of political life. They do not admit that all men are created equal. They do not agree that the individual has any inalienable rights. They do not think that liberty—at least in our sense—is a
good thing. The happiness of individuals to them is a poor and contemptible end. Thus our controversy with them is not about means, but about ultimate ends and ideals. They have developed a different conception of the good life from ours. Our life with its emphasis on the individual, on human personality, is set off against the "new order" with its emphasis on the state and its concomitant Weltanschauung.

This basic conflict over ends arises in part out of divergent interpretations of organic evolution. One only has to glance at Stace’s book to realize that this is a small part of the initial differences between democratic and totalitarian political philosophies, but nevertheless a very important part. The virus that has been running through German politics for the last several generations stems from Schopenhauer and his student Nietzsche. Perhaps the necessary tendencies were already present in the German makeup. I suspect they were. But these men furnished the Anschauung out of which the virulence of the modern Nazis seems to come. Schopenhauer, of course, in a way anticipated Darwin but Nietzsche embraced the idea of the survival of the fittest as the ultimate basis for power and the ruling human motive.

Darwin furnished the biological basis for the eternal law of struggle. This has been used to justify the exploitation and oppression of the weak by the strong. Nietzsche’s ethics, and especially the version of it that has influenced Nazism, are full of it. Stace answers very well the question as to whether the theory of evolution justifies any such conclusion.

In the first place, no matter what the subject or theory may be, one is not warranted in lifting a particular point out of all the relationships that are associated with it and disregarding other points and facts that modify ultimate conclusions. The argument that the Nietzsche-Nazis have glorified is that competition has been the sole cause of evolution, granted the initial genetic variations necessary. But such a statement is untrue. Competition is not the only law of the animal world. There is decided cooperation in animal societies as well. The herd instinct among the higher mammals is a plain application of the cooperative principle. The best supported theory regarding the time of this development in mammals is that it came along with the evolution of the grasses, which makes it very old indeed. From that, one can argue very well that it has survival value and doubtless has been an instrument in the evolution of species.

Nietzsche professes a great contempt for the herd instinct among men. (I don’t imagine Hitler, if he thinks about the matter in terms of his own position right now, is very crazy about it either.) It is, he says, the main characteristic of the slave mentality as distinguished from the master mentality. But this attitude is entirely unjustified by the doctrine of evolution upon which it is supposed to be based. His fundamental principle is that whatever has helped forward the evolutionary process is good and should be encouraged. But the herd instinct is one of the things which has helped forward that process. To condemn it, therefore, is arbitrary and inconsistent with his own ideas.

If we turn from the pure animal to the human world we find that Nietzsche’s glorification of struggle and competition is even less justified. Human progress, as distinguished from the biological evolution of species, has resulted far more from cooperation than from competition. Doubtless in human life too, competition is necessary and makes for advance for it is commonplace that without it effort lags and men become slothful. Yet if we ask what has been the prime cause of the enormous advance which civilized man has made upon the condition of the cave-man—in the control over nature, in scientific discovery, in development of social and political institutions—the answer is organized cooperation. This has been rendered possible by man’s reason. But whatever has been the source of the principle, the fact seems indisputable that it has been a mighty force in human progress. The contention then that all progress has been everywhere the result of struggle and competition is false.

Stace goes on to show that all human progress, the whole of the advance which man has made beyond the animal, has consisted in some way in an advance on mere nature. Nature unassisted heals wounds and cures disease. But medical science, through antiseptics, drugs, surgery, etc., adds to nature’s means of restoring health. Countless other examples might be given.

What is more important, morality is an advance on nature for as we attempted to show before, nature is amoral. Hence morality, which definitely came into the world with the rise of man, had the function of supplying to human conduct that principle which nature failed to supply. Nature from the beginning has ensured struggle and competition. To do this is no part of the business of human morality. Therefore, human moralists are right to make cooperation
the sole principle of morality. Competition is not a part of morality but a part of nature.

When I was a graduate student at Minnesota there was a little old man with a pointed beard who could be seen any day putting quietly about the library or working in his office over some old, worn manuscripts which he had never been able to get published. He was unduly and unjustly discounted by some of us because he was an irreconcilable vitalist; we, of course, felt safe and aloof in the scientific security of our mechanism. However, I took a year's course of lectures from him and have never regretted it. Although a vitalist, he was an ardent evolutionist and I think I got from him a better understanding of evolution than from any other source. Evolution to him was not something that had stopped with man or with any other level in nature. He had a little diagram—he taught by means of simple little diagrams that he would draw on the blackboard—showing in successive steps the great major steps in evolution and would argue quietly and convincingly how they had to proceed in that order. It began, at the bottom, with the Protista, the old name for unicellular organisms used by Haeckel, if not coined by him. (Haeckel you know was the leading mechanist of Germany in the late 19th century and was truly hated by this old philosopher, but nothing Haeckel ever wrote I am sure ever escaped him.) Next, at a higher level, were the plants; then still higher, were animals. But the diagram didn't stop there as in ordinary biological descriptions of evolution, but went on to what he called the FOURTH EPOCH. This was the level of “mutuality” or “mutualism.” Fundamental to this man's theory of evolution was the striving of organisms to get into “a higher epoch.” Many lines on the diagram were used to show this. For billions of abortive efforts, there was one success. That was his law of nature; that was his key to evolution. He said also, and certainly with logic, that there was no reason to conclude that the process should stop with “the fourth epoch.” But we could never get him to elucidate any further.

Built into this simple diagram were all the mighty forces of nature; struggle and competition rampant at the lower levels, genetic variation, all the complicated mechanisms and associations of organisms, but the whole topped off by the slow evolution of cooperation and mutuality. Man, himself, gyrated between the third and fourth epochs and on brief occasions “as in a mirror darkly,” caught a fleeting glimpse of even a higher EPOCH.

I believe this. For me it unites the things which in my philosophy must be united. It brings in the “primacy of reason” of Plato, “the primacy of sympathy” of Jesus. It unites them to support the infinite value of the individual, out of which have grown the ideas of equality and liberty. It holds the possibility of man being on his road to some better place. It makes a place in my larval casement to fit liberalism and the backwashes of conservatism. It provides an explanation for forces such as naziism that reduce powerful minorities, with the great facilities of modern science as their sole weapons, to the level of the jungle.

Nature can be relied on to continue to supply the element of competition to human life, or any other life; and in doing so to provide automatically for the exercise and encouragement of those harder virtues that Nietzsche especially recommends. Morality growing out of mutualism is something that man has added to nature out of the stores of his own peculiar humanity. And what needed to be added, to be expanded beyond that found in nature, was the principle of cooperation. We need not worry that Christianity, or Socialism, or any other suggested system of living, will ever get rid of struggle and competition. You cannot get rid of it by any artificial means any more than you can separate man from the world in which he lives. Nature will eternally supply it.

Although death and destruction, disease, and starvation are rampant in this year of 1943, can we not have a sound faith that our ideas are rooted in reason and goodness, and that they are worth defending because they are right and true, because they are directed to a progressive evolution rather than a retrogression and a degradation of mankind? I close with one final quotation, this one taken from Emerson (it’s exactly 105 years old):

If there is any period one would desire to be born in, is it not the age of Revolution; when the old and the new stand side by side, and admit of being compared; when the energies of all men are searched by fear and by hope; when the historic glories of the old can be compensated by the rich possibilities of a new era?

And I might add to that, a higher epoch?
GEORGE WELLS BEADLE, Ph.D.
Leader of Sixth Annual Biology Colloquium
Sixth Annual Biology Colloquium

Theme: Genetics and the Integration of Biological Sciences
Leader: GEORGE WELLS BEADLE, Ph.D., Geneticist and Professor of Biology, Stanford University

Discussion Leaders:
Vernon H. Cheldelin, Ph.D.
Associate Professor of Chemistry, Oregon State College.
Robert E. Fore, Ph.D.
Professor of Farm Crops and Agronomist, Agricultural Experiment Station, Oregon State College.
Charles S. Holtom, Ph.D.
Plant Pathologist, Division of Cereal Crops and Diseases, Bureau of Plant Industry, United States Department of Agriculture, cooperating with and stationed at Department of Plant Pathology, State College of Washington.
Ralph R. Huestis, Ph.D.
Professor of Biology and Curator of Vertebrate Collections, University of Oregon.
Frank H. Smith, Ph.D.
Assistant Professor of Botany, Oregon State College.

Chairmen of Sessions:
Nathan Fasten, Ph.D.
Head of the Department of Zoology, Oregon State College (afternoon session).
Margaret L. Fincke, Ph.D.
Professor of Foods and Nutrition, Oregon State College (afternoon session).
Sanford Myron Zeller, Ph.D.
Professor of Plant Pathological Research and Plant Pathologist, Agricultural Experiment Station, Oregon State College (morning session, dinner session).

Address of Welcome by:
August Leroy Strand, Ph.D.
President, Oregon State College.

Introduction of Colloquium Leader by:
Francois Archibald Gilfillan, Ph.D.
Dean of the School of Science, Oregon State College; Dean and Director of Science, Oregon State System of Higher Education.

OPENING OF THE COLLOQUIUM

Dr. Zeller: The Sixth Biology Colloquium has convened. There was some doubt in the minds of individuals as to whether we should hold a colloquium this year because of the war conditions, but the committee decided that the continuity of this function should be maintained. It would look from the attendance this morning that the colloquium is filling a need and that the committee was justified in continuing.

At the opening of one of our colloquia the statement was made that “the colloquium is not for the scientist but for the intelligent man.” I am sure that you are both here and that it will make for a happy mixture.

I have asked Dr. A. L. Strand, President of Oregon State College, to give a word of welcome from Oregon State. Dr. Strand.

President A. L. Strand: Drs. Zeller, Beadle, ladies and gentlemen, biologists, and relatives of biologists, I am very pleased to welcome you to this Sixth Biology Colloquium. On a day like this you hardly need a welcome. Our distinguished guest from California claims the honor of having brought this weather to Corvallis this morning. I think perhaps we might dispute that a little bit, but certainly it is very easy to welcome strangers to Corvallis on a morning like this.

It seems to me that the subject or the main motif of this colloquium is rather appropriate because the biology colloquium, I think, emphasizes the integration of biology more than anything else—that is, it brings biologists together from all the various fields. I would say from my observation in the short time I have been here that they like it. They like to get together with others from other fields in biology, so integration is certainly a good theme.

I have experimented a little bit in years past with students, even some senior students, in regard to their ideas of the organization of biology. Too often and in too high a number of cases their first idea of the divisions of biology is botany and zoology because—that's the way we organize it on the campus. Why should they know that we are organized into rather illogical divisions?

Biology does need some integration. Certainly genetics is one field that can lead in that integration for the simple reason that to become a science a subject should have reached the stage of prediction. All sciences seem to go through the stages of description and observation and then some synthesis, then the development of the experimental method, and finally the stage of prediction. If it doesn't get to the stage of prediction, it isn't much of a science. Genetics cer-
Certainly has gone through those stages and has reached the stage of prediction more than any other phase of biological work.

Finally, and at the risk of being embarrassed later by what our guest speaker will say, I have a little diagram that was given to me long ago. It shed much light for me on the organization of biology and its possible integration. It might be helpful to some of those who haven't thought of it that way. It is easiest set up in the form of a star.

![Diagram of star with labels: Phylogeny, Morphology, Genetics, Embryology, Physiology, Ecology]

Morphology is related to physiology; physiology to ecology; morphology to embryology; and embryology and the rest of them to phylogeny. I was always bothered about genetics, and I decided we would have to write genetics in the middle; so I say it is quite an integrating theme for the whole subject of biology.

We are very pleased to have so many visitors today at this colloquium.

Dr. Zeller: Thank you, Dr. Strand.

If you look over the program, you will find that there are about forty-five minutes allotted to each speaker and the discussion of his paper. We hope that the discussion will be very free and informal and that everyone will feel at liberty to take part. If we have to ring the bell, we will do it; and we hope that no one will take offense if we cut him short.

If we have had any criticism of past colloquia, it has been that our discussions have been too much limited and that perhaps we have had too many papers. But it is better to have plenty of discussion than none. We are going on the assumption today that we will have plenty of discussion and that we will take the liberty to close the discussion if necessary.

I think it is very fitting for the dean of the School of Science to introduce our leader for the day. I am therefore calling on Dean Gilfillan of our School of Science to introduce Dr. Beadle, who will open the program this morning.

Dean F. A. Gilfillan: Dr. Zeller, President Strand, and members of the colloquium. For more than a thousand years now there has been current among the desert people in the East a proverb which I should like to call to your attention. Translated from the Arabic it runs something like this: "Consider well, my son, does wisdom issue from the mouth of a fool? Can a she-ass bring forth camels?"

Now, the old Arab is not asking you, he is telling you. He knows the answer, and he is assuming that you cannot do other than agree with him. And yet, I would venture to disagree. Many a time and oft have I seen a she-ass bring forth camels and considered it no miracle but only a sad reflection upon our national over-indulgence in the use of tobacco.

However, it is scarcely fair to meet the old Arab except on his own ground so let us go back. It is not to be expected that he could foresee the social habits of the people in a country which was not to be discovered until five hundred years after he had uttered this "eternal truth." Now I think we agree that it is not well that we let one of these "eternal truths" stand too long unchallenged. It is fitting that we re-examine it from time to time in the face of new evidence that may have arisen.

Can wisdom issue from the mouth of a fool? On that I would say with Einstein that "fool" and "wisdom" are relative terms. We know the reverse is often true, that from the mouths of wise men often issue words that are quite foolish, and I am sure that under certain circumstances we may hear words of wisdom from some who are not considered so wise.

Now, can a she-ass bring forth camels? Well, I wouldn't maintain that. Certainly if a she-ass continues to be associated only with other asses her progeny is likely to be just another ass. But we know that by cross-fertilization it is possible for her to bring forth progeny different from what she may have thought possible in her wildest dreams. Of course, this crossing is usually made the other way, but the result, as every old army officer and every citizen of the sovereign
state of Missouri well knows, is a creation absolutely essential to the U. S. Army and to agriculture in southern and central United States.

If we can anticipate these startling results in biological cross-fertilization, is it not well to assume that we may reach similar results in an intellectual cross-fertilization? That is what we have hoped to do at these biological colloquia. We know that all scientific experiments should be controlled, so this experiment also should be conducted under control. It is well that such experiments be carried on under the direction of someone who is well qualified to know and to judge the results. For the Sixth Biology Colloquium we have such a scientist, a man who is a specialist in genetics.

Dr. George Wells Beadle is a native of Nebraska. From the University of Nebraska he received his bachelor's and master's degrees and from Cornell his doctor's degree. For two years he was national research fellow at the California Institute of Technology and later assistant professor of genetics at Harvard. He also was a guest instructor at the Institute of Biology in France. In the field of genetics he first carried on extensive work on Zea mays and then upon Drosophila (which is the geneticists' first love, I believe), but more recently he has gone into a new field, investigating the genetics of some of the lower biological forms. He is now working on Neurospora, investigating the inheritance of biochemical activity as influenced by genetics.

So we proceed with our experiment today with all assurance that under Dr. Beadle's capable leadership and through this intellectual cross-fertilization, some of us mental she-asses may bring forth brain children that may startle the scientific world.

THE NEED FOR INTEGRATION IN THE BIOLOGICAL SCIENCES

G. W. Beadle

I should like to say first that I very much appreciate the honor of being asked to take part in this colloquium. One of the difficulties involved in this is that those of you who have taken part in the first five colloquia have set the standards so high that it is going to be difficult to maintain them.

I should like to add that I am particularly pleased to visit this institution. As I walked across the campus this morning and saw buildings marked "Agriculture," "Dairy," and "Agronomy," it made me feel very much at home. I did both my undergraduate and graduate work at agricultural colleges and it is a real pleasure to see these names again.

Our subject "Integration of the Biological Sciences" assumes, in the first place, that we have something to integrate. Fortunately, in the biological sciences we do have something both worth integrating and capable of being integrated. All of us can see various ways in which it can be done. What I should like to emphasize as my contribution is how this can be accomplished from the standpoint of genetics. Others of our speakers will contribute further to the general theme.

I am sure all of us would agree that one of the finest examples of integration in the biological sciences was given to us by Darwin in his theory of common descent with modification. This is certainly one of the greatest biological generalizations of all time. It shows us how organisms are interrelated, how one came from another—and presents the organic world as a unified whole. Darwin's generalization as we understand it today includes a concept that Darwin did not appreciate. This is the way in which heredity permits variation and at the same time preserves general themes in evolutionary lines. As we are all aware, this concept was first appreciated by Mendel.

Mendel had a remarkably clear conception of what was going on, but I suspect that he didn't really appreciate its importance. He saw the beautiful mechanism of heredity at work in the garden pea, but when he attempted to apply it to other organisms such as Hieraceum and the honey bee he did not find segregation of clear-cut alternative characters. We know now that this is because the hawkweed reproduces asexually and the male honey bee arises from an unfertilized egg. But Mendel did not know of these idiosyncrasies. This must have been a terrific blow and his consequent failure to confirm his theory generally must have been a major disappointment to him. Our textbooks say that Mendel's work was
not recognized because his paper lay buried in an obscure journal for 35 years. I am more inclined to believe that the reason that it was not generally appreciated is that he himself lost faith.

We know from work beginning in 1900 that the Mendelian Principles are as general as those of Darwin. In fact, "Mendelism" is basic to the theory of common descent. Accordingly, it is appropriate that we should examine exactly how the science of heredity has developed and exactly how it has related itself to other phases of biology.

It is unfortunate that in its early stages, at least, genetics developed more or less autonomously. Its methods are peculiar to itself and its terminology is a special one. For these and other reasons many "old-school" biologists remained for years antagonistic to this new upstart science. There still exist some who hold out, and I have no doubt there are others who do not clearly see the light as to what the gene theory has done and exactly what its implications are. If today we can indicate what some of these implications are, I am sure this colloquium will have served a useful purpose.

There are a number of fruitful unions that genetics has made with other branches of biology. I should like to enumerate and discuss briefly some of these. Several will be developed more fully by other speakers.

One of the first ties that genetics made with another branch of biology, as you know, is that with cytology. Very early after the rediscovery of the Mendelian Principles, cytologists saw that they had the physical basis for them in the chromosomes. All of you know the history of the development of the chromosome theory of heredity with its final irrefutable confirmation coming in 1916 in Bridges' classical paper on nondisjunction in the vinegar fly, *Drosophila melanogaster*. This field of cytogentic has been especially active in recent years under the able leadership of such people as Belling, McClintock, Darlington, and many others. Dr. Smith, who is to be the next speaker on this program, will have a good deal more to say about cytogentic.

A closely related aspect of this interrelation is what we sometimes call experimental taxonomy or cytotaxonomy. As all of us appreciate, genetics includes the mechanisms by which species have become differentiated. Cytotaxonomy together with genetics is devoted to telling us how species originate. Such men as Rosenberg, Winge, Karpechenko, and Dobzhansky have been active in this field. The mathematical approach has been effectively made by Wright, Fisher, Haldane, and others. Dr. Huestis will develop further the general topic of speciation including its bearing on geographical distribution of species and varieties.

Another field that is an active one at the present and, it seems to me, one that has more promise than almost any other in which different sciences are brought together is that of "immunogenetics"—the relation of immunology to genetics. I hope this evening to be able to develop a little more in detail some of the ideas that help us to understand this relation. Immunology is concerned to a large extent with protein specificities and many of us believe that the primary role of genes is in the determination of such specificities. Our blood groups, for example, are determined by our genetic constitutions through the control of specificities of antigens. In immunogenetics belongs the classical work of Landsteiner and his co-workers and more recently the work of Irwin and Cole and others.

One of the outstanding immunogenetic contributions that has been made recently and which is still being actively worked on is the transformation of one Pneumococcus type into another. Within the past few months Avery of the Rockefeller Institute has shown that by adding a very small amount of nucleic acid from one Pneumococcus type to another a permanent transformation of type can be brought about. Types result from specific polysaccharides in the capsule of the organism and this presumably is under genetic control. It is too early to generalize from these results, but their implications are almost certainly going to be of great significance to both genetics and immunology.

Immunogenetics is intimately related to the problem of disease resistance, a subject of particular importance to medical people and agriculturists. The disease resistance of cultivated plants is a subject in which agricultural people are forced to take an interest. Dr. Holton is going to summarize certain aspects of this field for us.

Plant breeding, about which Dr. Fore is going to talk, is a field in which genetic principles have been applied in solving practical problems. In this connection I should like to tell a story because it illustrates the unpredictable nature of science, and is an example in which we start with something that seems to be absolutely and completely useless and end up with a valuable application. Some thirty-five years ago a U. S. Department of Agriculture man, G. N. Collins,
found in upper Burma a peculiar variety of Indian corn. Its endosperm has a “waxy” appearance. He worked with it genetically and found that it differed from ordinary starchy corn by one gene. The waxy character soon became a standard genetic tool, but to the layman it remained just a curiosity. No one ever had any notion that it might have a use.

Four or five years ago Doctor Sprague and Professor Hixon of Iowa State College got together to see what Iowa could do with all its corn. With the geneticists increasing the yield some twenty per cent and the economists proving it under, this problem had become acute. One obvious thing to do was to find new uses for corn. An appreciable fraction of the corn crop is converted into corn starch. The ramifications of the starch industry are many and a whole segment of our economic system has been built around a type of starch imported from the Dutch East Indies known as tapioca starch. Imports of about 350 million pounds of this tapioca starch per year were interrupted when the Japanese took over the Dutch East Indies. Offhand this would not seem to be of great importance. Tapioca starch is used, it is true, for tapioca, but this is a very minor use. Much more significant are its other uses. For example, most of the “remoistening” mucilages such as are used on stamps and envelopes are made from tapioca starch. Tremendous quantities of it are used in this way. Cloth sizing consumes large quantities as well. Ordinary corn starch does not have the right physical properties for many of these purposes for which tapioca starch is usually used.

Hixon and Sprague decided in this search for new uses for corn that they would investigate the starch types of the various genetic kinds of corn. Much to their surprise they discovered that waxy corn starch has almost identical properties with tapioca starch. They then set out to introduce this gene into the best Iowa strains of corn. By a year ago this spring they had enough waxy seed to plant fifteen hundred acres of this new waxy corn. From this they harvested enough to plant fifty thousand acres this year. Their timing was perfect and waxy corn starch can now be used to replace tapioca starch. We need never again be dependent on an external source for this type of starch.

It is also true for medicine that advances are frequently made by biologists who investigate phenomena that appear to have no possibility of practical application. Penicillin was discovered as a result of a study of the ecology of micro-organisms—following a chance observation. It is unlikely that this most miraculous drug would ever have been discovered by a medical man deliberately looking for it.

Recently Lennox, Gibbs, and Gibbs, working at the Massachusetts General Hospital, have made an important discovery in neurology as related to epilepsy. This disease has been thought for some time to be a simple recessive mental trait in man, but it was never clear cut. If two electrodes are properly placed on the head of a normal person and the potential set up between them measured, a smooth rhythm with a frequency of about 10 per second is obtained. If such electrodes are put on a person who is subject to epileptic seizures, a very different wave with a lower frequency is found. All persons who have epilepsy have this type of pattern even when they are not having a seizure. Still more curious, many people who have never had epilepsy and who are perfectly normal have this type of brain wave. The irregular wave pattern is inherited as a simple dominant but the expression as epileptic seizure is dependent on other factors—perhaps how we live and probably what modifying genes we have. One person in ten has this irregular rhythm, but only one person in twenty with the irregular wave pattern ever shows epilepsy.

This is an indication of a field in which we are certainly going to see advances in the future. As to exactly how our brains work we know practically nothing either from a biochemical standpoint or from any other. Genetics will provide one of the ways by which we are going to make progress in the future. There is another example I should like to use which illustrates how genetics may be related to neurology, and which tells us something as to how the brain works. This involves a relation between what goes on biochemically in the body and genetic constitution. Phenylalanine, one of the amino acids, is one constituent of proteins. Some of the protein of the diet is burned as an energy source. The final product is often carbon dioxide and water. Exactly how proteins are burned no one knows. But in the case of phenylalanine one way involves a conversion to tyrosine, followed by oxidative deamination to form a substance called p-hydroxyphenylpyruvic acid. This in turn can be oxidized to give another compound, homogentisic acid.

A German worker, Fölling, discovered that there is a type of abnormality in which there accumulates in the urine phenylpyruvic acid. The
difficulty with individuals who show this trait is 
that they cannot carry out the oxidation of phenyl-
pyruvic acid. A significant fact is that such per-
sons are invariably feebleminded. Obviously this 
reaction has something to do with the normal 
functioning of the brain. Some day we shall 
know more about it. The interesting point from 
the present standpoint is that the normal form of 
a particular gene is necessary to make this re-
action go. Inability to oxidize phenylpyruvic 
acid further is inherited as a simple recessiv 
trait.

Still another field that is, I think, very closely 
related to genetics is that of viruses. Unfortu-
ately, about all we can do at present about this 
relationship is to say that viruses show similarities 
to genes. The virus does essentially everything 
that a gene does; it reproduces, it mutates, and if 
it doesn't mutate, it maintains itself in constant 
form from generation to generation. Virus spe-
cificity is certainly related to protein specificity. 
Some day we are certainly going to know more 
about viruses and what, if anything, they have 
to do with genes.

The last relation that I should like to mention 
is one which I have already mentioned in connec-
tion with phenylketonuria. This is a relation 
sometimes referred to by the term “biochemical 
genetics.” One of biochemical genetics’ most im-
portant questions is: How does a gene act in 
terms of what goes on chemically? Ultimately, 
of course, everything that happens in the organ-
ism must be resolvable into what goes on chemi-
cally. I like to believe that biochemical genetics 
provides one of the ways in which genetics can 
be put in its proper place in relation to biology in 
general.

At this point I should like to tell you some-
thing about the man whom I like to think of as 
the father of biochemical genetics. He carried 
on work of the kind that we are doing now and he 
did it forty years ago. He was an English 
physician, Sir Archibald Garrod. His father, 
Sir Alfred Garrod, also a physician, was an au-
thority of his time on gout. The Garrod family 
is itself a good example of heredity. Sir Archi-
bald had a brother who, like himself, was a mem-
ber of the Royal Society, and his daughter, Doro-
thy, is at present a professor of archaeology at 
Cambridge. In 1909 Sir Archibald wrote a book 
“Inborn Errors of Metabolism,” in which he 
summarized the status of several hereditary dis-
cases. A second edition of this classic was pub-
lished in 1923. Garrod was interested in pig-
m ents of the urine and through this he ran across 
several abnormalities of metabolism that are ex-
pressed through abnormal excretions in the urine. 
One of the most interesting of these is alcapto-
urnia, a simple recessive trait in which, instead of 
undergoing further oxidation to CO₂ and H₂O, 
homogentisic acid is excreted in the urine. On 
exposure to air this acid, known chemically as 
2-5 dihydroxyphenylactic acid, forms a black 
pigment. The characteristic blackening of the 
urine provides a ready means of diagnosis. From 
a genetic standpoint the significant point is that 
here we have a specific gene identified with a 
specific chemical reaction.

DR. ZELLER: Dr. Beadle’s talk is open for dis-
cussion. Are there any questions or comments?

DR. W. J. VAN WAGTENDONK: Are the sub-
stances formed by the gene or does it mean that 
the gene is absent?

DR. BEADLE: This does anticipate an idea that 
I hope to develop tonight. In its normal form, 
the gene provides something necessary for the 
reaction. If the gene isn’t in the right condition, 
the reaction is blocked. One might draw an 
alogy between the defective gene and a missing 
gear in a machine. An important question is how 
does the gene control the chemical reaction? I 
can say here that nobody knows positively the 
answer to this question. We can make several 
guesses. At least one guess is that genes work 
through the enzyme systems. I should be in-
clined to guess that the gene controls the protein 
specificity of the enzyme; if the gene is in the 
wrong condition, the enzyme is in the wrong 
condition, and the reaction can’t go.

DR. VAN WAGTENDONK: Is there a possibility 
of cancer being caused by irregularities of the 
amino acids? Is there a possibility that there is 
an absence of the amino acid oxidase in people 
having cancer?

DR. BEADLE: The d and the l forms of a mole-
cule are like right- and left-handed gloves. One 
rotates the plane of polarized light in one direc-
tion; the other rotates it in the opposite direction. 
A chemist, unlike an organism, can’t synthesize 
one of these without synthesizing the other. He 
always makes equal amounts of the two isomers. 
Nobody knows why or how the organism makes 
only one. The organism has an enzyme which is 
called d-amino oxidase; if you give the organism 
the d-form—the unnatural form—it will immedi-
ately take off amino group and replace it with 
the oxygen atom. The enzyme is specific for the 
unnatural form. One of the very important ques-
tions is why does an organism have a system for 
working on something it doesn’t make? Perhaps
it does make the unnatural form but destroys it as fast as it makes it. In the case of amino acids, the $d$-amino oxidase may immediately oxidize the $d$-form giving the keto acid which has no optical activity. The organism can then reaminate this. This may be the mechanism for asymmetric syntheses generally. If enzymes are controlled in their specificities by genes, then geneticists ought to be able to induce mutations so the organism would make both optical forms of a given compound. At present, so far as I know, no chemist or biologist knows for certain why $d$-amino oxidase is present. Obviously this is a basic question and until we can answer it there is not much point in discussing the relation of optical isomerism of the amino acids to cancer.

**CYTOGENETICS**

Frank H. Smith

Cytogenetics provides one of the best examples of the results that can be obtained by the integration of the different branches of science. Cytology and genetics are both comparatively new sciences. They have developed together and are, to a considerable extent, mutually dependent. The accusation has been made that too many cytologists do not know that there is anything in a cell except the nucleus or chromosomes. To a certain extent this criticism is justified. In the beginning, cytological research was very important in laying the foundations for the chromosome theory of inheritance.

One of the early cytogenetical problems to be solved was that of establishing the individuality of the chromosomes of a complement. The discovery of the sex chromosomes resulted in definite proof of a functional differentiation of chromosomes. Sex determination is, of course, not as simple at XX and XY, but the presence of definite, recognizable chromosomes associated with sex did establish the fact that a functional differentiation of the chromosomes of a complement does exist. Sex was thus the first character to be assigned to genes in a given chromosome.

Structural differentiations in the chromosomes of a complement were also established early. It was found that chromosomes in certain species could be identified by differences in size and by the presence of such morphological features as constrictions, satellites, and knobs that are relatively constant in size and position from one generation to the next.

With improved techniques an internal differentiation of chromosomes was also demonstrated. Without going into detail, it is probably safe to say that most cytologists now accept the idea that the chromosomes which usually appear as solid structures are actually composed of at least two spiral threads embedded in a lighter-staining matrix. Each spiral undoubtedly represents a main axis along which the genes are arranged in a linear order.

During the reduction divisions the exchange of threads between homologous chromosomes that must accompany genetic crossing over is evident. While this is fairly good cytological evidence that genetic recombination is due to an exchange of portions of homologous chromosomes, it is not conclusive. It was not until 1931 that definite cytological evidence on this point was obtained in corn by Creighton and McClintock and in *Drosophila* by Stern. Since the evidence is essentially the same in both forms, that obtained from corn will suffice here. Chromosome 9 of corn normally has a knob at one end that can easily be recognized during the early prophase of the first reduction division. A plant was obtained with a heteromorphic pair of chromosomes. One member of the pair had the knob at one end and a portion of a non-homologous chromosome attached to the other end. It carried the dominant gene $C$ for colored endosperm and the recessive gene $wx$ for waxy endosperm. The other member of the pair had no knob and no translocated piece and carried the recessive gene $c$ for colorless endosperm and the dominant gene $Wx$ for starchy endosperm. The plant was crossed with a strain having two knobless chromosomes carrying both genes in the recessive condition. In the offspring there appeared four types, two like the parents in their chromosome morphology and character combinations and two others which showed in their chromosome morphology that an exchange of portions had occurred, while the characters due to the genes involved had been recombined. Thus a recombination of characters was proved to be associated with an exchange of visible characteristics of the homologous chromosomes known to carry the genes responsible for these characters.

The behavior of the knobbed chromosomes in
corn has also provided direct proof that exchange may occur between only two of the four chromatids at a given level. The chromosomes considered by Creighton and McClintock were involved with another pair in a ring as the result of reciprocal translocation. The chromosome without a translocated piece had a small knob while the chromosome with a translocated piece had a large knob. When brought together the four chromosomes form the configuration characteristic of a reciprocal translocation. Some of the rings showed knobs of the same size on the two chromatids of each chromosome, while in other rings the knobs were of different sizes. That it was not whole chromosomes that had exchanged was shown by the presence of the translocated piece and the synoptic relations in the ring.

The geneticists have drawn up linkage maps of the chromosomes of some species, based on genetical crossing over. These maps show the relative but not the actual positions of the genes along the chromosomes. The greatest ambition of many cytologists at present is to see a gene and, of course, to recognize it as such. No one has as yet seen a gene, but several methods have been used to locate within narrow limits the actual positions of certain genes in the chromosome.

The key to the more exact localization of the genes was given by Muller when he found that if mature germ cells of Drosophila are exposed to X-rays, the chromosomes are often broken and the material rearranged in a new order. From genetic data Muller was able to determine which genes were separated by a given break. Muller and Painter were thus able to construct maps of the metaphase chromosomes that indicated with a fair degree of accuracy the actual position of the genes in the chromosome.

This method has limitations, however, because the chromosomes at the equatorial plate are shorter than any other stage of the entire chromosome cycle. Any foreshortening would introduce a considerable error in the calculations. The early prophases of the first reduction division provide a better stage at which to study the chromosomes; at this stage they are greatly extended and homologous chromosomes appear side by side so that more careful comparisons may be made. Chromosome 9 in corn is favorable for study because the presence of the knob makes it easily recognizable. Near the knob is the gene Yg which results in a normal green color in the plant in the dominant condition, while the homogogens recessive yg results in a yellow-green color.

Miss Creighton used a yellow-green plant, in which chromosome 9 had a small knob, as the female parent and treated this with irradiated pollen from a green plant in which chromosome 9 had a large knob. Most of the offspring were green in color as would be expected of the heterozygote. Cytological examination showed no change in the structure of the chromosomes. Some of the yellow-green plants showed chromosomes with large knobs but the chromosome was shortened. A second class of yellow-green plants showed the knob itself shortened, indicating a deletion including part of the knob. Of course, the smaller the deletion that can be recognized, the more accurately the gene may be located. A single plant was partly green and partly yellow-green. Cytological examination showed that in the yellow-green portion a truly terminal deletion had occurred in the embryo. A terminal deletion is a comparatively rare occurrence.

The giant chromosomes in the salivary glands of the fly larva provide an even more favorable situation for the determination of gene locations. The salivary gland chromosomes of Sciaria are about 125 times as large as the normal chromosomes that had formed the basis for previous study. The large size possibly is the result both of multiplication and of growth of the chromosomes. There is a definite pattern of banding across the chromosomes, a banding that is constant in its finest visible detail. A second very important feature of the salivary gland chromosomes is the close pairing of the homologous chromosomes in what has been termed somatic synopsis. During this process similar bands on the pairing chromosomes are so accurately matched as to become continuous. Thus it is possible to make very exact comparisons between homologous chromosomes. Deletions of only one or two bands from one of the chromosomes are recognizable and indicate with a high degree of accuracy the location of the gene or genes involved. We cannot as yet place the gene exactly because we do not know whether each band represents a gene locus or whether some of the colorless material between the bands is also involved.

The duplication of genes is also demonstrable in the salivary gland chromosomes. The dominant mutation in Drosophila known as bar-eye was shown by Painter to be the result of duplication.

When the chromosome map constructed on the basis of such data is compared with the linkage map for the same chromosome, it is found that the two agree with respect to the serial order of
the genes. This is excellent proof of the value of the cross-over method long used for the determination of gene arrangement. The spacing of the genes, however, differs in some regions, showing that the occurrence of crossing over is not uniform in frequency throughout the length of the chromosome. This was originally assumed but has been questioned for some time. The differences show up especially near the spindle-fiber attachment and near the ends of the chromosomes.

It would seem then that in at least two organisms, corn and Drosophila, the cytogeneticist is well along on the problem of determining the actual location of genes along the chromosomes, and thus is nearer to the gene itself.

Another favorable field of cytogenetics, on which we can touch only briefly, is the study of chromosome behavior in species hybrids. Such a study provides one of the best bases for determining evolution and relationships in a genus or family. Because plant hybrids are more easily obtained and propagated, most of our information has been obtained from plants. The amount of pairing or synopsis between chromosomes from different species is a more or less direct indication of the degree of similarity or relationship between the two species.

One of the most interesting as well as important phases of this study in recent years has been in connection with amphidiploidy. An amphidiploid is an organism that possesses in the somatic cells the diploid complement of both the parental species of an F1 hybrid. Amphidiploids may arise in various ways but the most frequent method of origin is probably by chromosome doubling in somatic tissues. This results in the formation of strictly homologous chromosome pairs and a plant that is probably fertile. In order for an amphidiploid to be perpetuated there must be enough harmony between the two sets of genes for them to function in the same soil, but they must be different enough so that only the homologous chromosomes will pair. If there is pairing between the chromosomes from different parents, the result is irregular chromosome distribution and sterility.

At present about as many or more amphidiploids have been produced experimentally as have been identified in the field. The evidence suggests, however, that many, if not most, of the natural polyploids are the result of amphidiploidy. Some of the amphidiploid species found in the field have been reproduced experimentally.

The Triticum-Aegilops-Secale complex indicates the possibilities of amphidiploidy in the evolution of species. From the primary species with a haploid number of 7, which has persisted in the Einkorn wheats, the 14 and 21 chromosome wheats have been built up as distinct species by amphidiploidy. The degree of pairing in species hybrids in this group supports this theory. As the amphidiploids Hynaldtricum, Aegilotricum, and Secalotricum were produced experimentally, their relationships with the other species are known.

The cytogeneticists have accomplished much with regard to the two problems considered here, the interpretation of gene and chromosome behavior with regard to the evolution of species and the localization of the genes on the chromosome. The former problem is being attacked more systematically at present than has been possible before. The experimental taxonomy of Clausen, Keck, and Hiesey at Stanford is an indication of the future possibilities in this field. It is possible that the localization of the gene has progressed as far as we can go with the present microscopic technique. There is always the hope that still more favorable material for study along this line will be discovered. We may have to wait until the chemist can see a molecule. Then perhaps he can show us a gene, which is probably on the order of a molecule.

DR. ZELLER: We have a little more time for questions if there are any.

MR. JOHN BURTNER: Has the use of the electron microscope had much effect on these studies?

DR. SMITH: My last impression was that they were still trying to interpret what they were seeing.

DR. BEADLE: I think Dr. Smith has indicated the correct answer to your question. Those who work with the electron microscope have so far had their hands full in dealing with techniques of getting the chromosomes mounted. So far as I know, no one has ever seen anything that couldn't be seen with an ordinary microscope.

DR. ERNST J. DORNFELD: In view of genetical advances, it is rather amazing that the biochemistry of the chromosomes has not received more attention. I think it was back about 1870 that Miescher and Kossel studied the chemistry of nucleoproteins extracted from various cell preparations, and for a long time no one paid any further attention to the matter.

About 1900 genetics began to flourish. It was fully realized that the chromosomes were concerned with genetics but still no great attention
was paid to the chemistry of the nuclei. Levene in 1921, however, finally gave us a long treatise on the nucleoproteins, and only in recent years have those things been studied with real care.

I think, Dr. Smith, you are familiar with the Feulgen reaction that was developed in the late twenties. That is about the first microchemical test applied to chromosomes based on the known composition of the nucleic acids. It was ten years later, 1936, that Caspersson, working in Sweden, applied the principle of ultraviolet absorption spectra to the analysis of chromosome chemistry. Using wave lengths of 2600 Å, which give characteristic maxima for molecules with pyrimidine groups, he was able to photograph the precise location of nucleic acid within individual chromosomes. He found that these nucleic acids are concentrated in the dark bands of the salivary chromosomes, but the question of whether the genetically active portion of the chromosomes lies in the nucleic acid or in the histone matrix is still unanswered.

Caspersson combined that work with enzyme digestion experiments. Combining trypsin with lanthanum he got these nucleic acids to precipitate exactly in the dark bands. Digestion with pepsin, however, clearly showed that the chromosome has a continuous protein structure. Experiments with polarized light and x-ray diffraction studies suggest that the nucleic acid units are oriented parallel to the lengthwise chains of the histones or polypeptides.

Dr. Smith: It has been suggested that the nucleic acid material is in the clear spots.
THE IMPORTANCE OF VITAMIN RESEARCH
TO THE BIOLOGICAL SCIENCES

Vernon H. Cheldelin

Dr. Margaret L. Fincke: In past colloquia we have had several reports on the relation of nutrition to the biological sciences. This time we will depart a little from that. We haven't had many reports on the relation of nutrition to microbiology and medicine, so Dr. Cheldelin, who is associate professor of chemistry at Oregon State College, will report on that side of the vitamin work. Judging from what I know of his work he will probably emphasize the microbiological side.

Dr. Cheldelin: Madam Chairman and members of the colloquium: At the outset of our discussion it seems advisable to define the term "vitamin" and to delimit somewhat the scope of our survey. Vitamins have been identified as organic chemicals which are necessary in the diet in small amounts and which do not themselves furnish energy to the organism. In this respect they differ from hormones which are necessary to the body processes just as the vitamins, but which are synthesized within the organism. This draws a sharp delineation, for purposes of definition at least, between vitamins and amino acids, since the latter are essential units in protein structure and are energy-yielding compounds.

Also, for the present we shall admit into the group of vitamins any member that has known vitamin properties and is essential to at least one animal. Ascorbic acid, though it is not needed in the diet of the rat, is necessary for guinea pigs and human beings; likewise nicotinic acid is not required for the rat although it is for several species.

If we consider a list of the known vitamins, we will realize that this list has grown considerably since 1918 when only vitamins A and B were known:

A Thiamin (B1) Biotin (H)
B Riboflavin (B2) Inositol
C Nicotinic acid Folic acid
D Pantothenic acid —aminobenzoic acid
E Pyridoxin (B6)

There are others which yet are rather poorly defined and about which little is known.

More than one thousand papers dealing with vitamins have been published during each of the last four years. This is eloquent testimony to the importance of vitamin research. This display of interest is easily understood, for all of us are anxious to know more about these substances which are so necessary for our well being. In addition, the prospect of rich financial gains may have had its part in the choice of research problems. This influence was emphasized in the decade 1930-40, when intensive research on the structure of several vitamins was under way in many laboratories. Work of this nature is still being done; the structure of biotin was elucidated in 1942, and progress is even now being made toward the proof of structure of folic acid—but the peak has probably passed. Much literature has appeared in the last three years. The great volume of research in recent times has been devoted to the study of the action of the B vitamins—on microorganisms, on laboratory animals, and on ourselves. It is this latter trend that I wish to discuss, especially as it is related to the biological fields, including physiology, microbiology, psychology, and genetics.

Considering first physiology, it would appear safe, I believe, to say that vitamin research is capable of making great changes in the science of physiology and of enriching it in every subdivision. Vitamins may be regarded from the physiological standpoint as a heterogeneous collection of indispensable tissue constituents that were discovered by nutritional investigation. Through nutritional studies on guinea pigs and dogs two highly important constituents of rat tissues were discovered—namely, ascorbic acid and nicotinic acid. Nutritional investigations on various microorganisms have brought to light several other such constituents of tissue—namely, biotin, inositol, p-aminobenzoic acid, and folic acid. Many of these function as vitamins, but from the physiological standpoint their internal physiology may be just as great whether they arise from outside or within the organism.

Several surveys have been made of the distribution of vitamins in tissues in an effort to obtain information on their broad physiological significance. It would appear that vitamin A is not essential to the colorless plants, fungi or yeasts, or even to so highly organized a member of the biological kingdom as the cockroach, which can complete its entire life cycle completely devoid of vitamin A either in its diet or tissues. Vertebrates, on the other hand, utilize it and store it in their livers, depot fats, and elsewhere. Thus the best sources of vitamin A may be more than
100,000 times as rich as the poorest sources. Vitamins E, K, and C are found rather widely throughout the biological kingdom, although not everywhere. The information concerning vitamin D is not sufficiently conclusive, but it appears that this vitamin's occurrence is not at all widespread.

The family of B vitamins is found in every portion of the organism. There are no very rich or very poor sources. Even throughout a wide range of organisms the best sources are seldom more than 15 times as rich as the poorest. Even among the tissues of the poorest organisms there is not a widespread difference in concentration. Furthermore, there appears to be a high degree of mathematical correlation among the B vitamins. Thus, when the concentrations of the several B vitamins in a wide variety of tissues are correlated with the concentration of nicotinic acid in the same tissues, the correlation value for thiamin is .52; for riboflavin, .67; and for pantethenic acid, .72. Correlation coefficients are also high between respiration rates and the concentrations of ascorbic acid, riboflavin, biotin, and inositol in tissues. This information would suggest then that these four compounds are involved in cellular oxidation systems. Unexplained, however, is the lack of correlation between respiration rates and the concentrations of thiamin or nicotinic acid, which are established members of the enzyme systems. Of special interest here is the high correlation value of ascorbic acid, which is believed to be involved in some way in oxidation-reduction reactions.

Although the literature dealing with the effect of individual vitamins on metabolism is almost legend, I think it would be well not to attempt to examine it here. There are, on the other hand, experiments dealing with metabolic effects of groups of vitamins—thiamin, riboflavin, pantethenic acid, and pyridoxin—which under certain experimental conditions appear to be intimately related in the function of glycogen formation and hydrolysis. Any of these four vitamins produces about the same effect under controlled experimental conditions, and all seem to be necessary for a balanced metabolism. It is possible that a synergy exists between pantethenic acid, pyridoxin, and vitamin E, perhaps in a manner similar to the synergy that is known to exist between vitamins A and E in tissues; that is, vitamin E will spare to a large extent the requirements of other vitamins.

B vitamins are known to be related in an important manner to embryonic development. These tissues are, in general, richer in the vitamins than are the tissues of adult animals. The injection of thiamin, riboflavin, nicotinic acid, or pantethenic acid into hatching eggs produces changes in hemoglobin concentration and in the size of feet and brains of the chicks. Feeding extra pantethenic acid to laying hens will produce defects similar to those produced by injecting pantethenic acid into the hatching egg. Better hatchability of eggs and increases in the litter size of rats are observed upon inclusion of mild excesses of pantethenic acid in the diet of the mothers.

The relationships that have been shown to exist between vitamins and hormones are very few. A study of twelve endocrine glands of cattle has revealed little relationship between hormone and vitamin distribution. The adrenal has been found unusually rich in vitamin C, but there has been no explanation for this observation. One of the best examples for this lack of relationship is that the anterior and posterior pituitary glands of cattle contain the same amounts of B vitamins in spite of the vast differences in physiological functioning of the two glands. It would seem that propinquity, rather than function, may determine the vitamin contents in this case. Vitamin E, on the other hand, seems to exert a synergy or sparing action on the corpus luteum hormone and on progesterone. It is thought that this and other cases of sparing action by vitamin E may be due to its function as an antioxidant—that is, protection of the other vitamin or hormone against oxidation, the vitamin itself being destroyed.

Various members of the B complex have been shown to be active protective agents against malignant growths. Riboflavin has been shown to be especially effective against certain types of artificially induced liver cancer. Under other conditions biotin seems to promote tumor growth. An extensive study of the distribution of B vitamins in cancer tissues has indicated that cancers of different types and from different animals are very similar in their vitamin contents. Cancer tissues seem to constitute a tissue type in the same sense that heart muscle or brain does. Folic acid is very high in cancer tissues, as it is in embryonic tissue. Additional information regarding the distribution and functions of the various vitamins should shed further light on the peculiar nature of cancer metabolism.

Turning our attention next to the portions of vitamin research which affect microbiology, we find that microorganisms are important for several reasons. First, there is a widespread use
of microorganisms as testing agents whose vitamin requirements can be observed with very great savings in time, cost, and labor. By fashioning a growth medium complete in all respects except the vitamin being tested, growth responses may be obtained by adding small known amounts of the vitamin to the growth medium. The growth can be measured and used as a standard against which other colonies, grown upon unknown quantities of the vitamin, can be compared.

Generally speaking, those vitamins that are needed by higher animals are also needed by microorganisms, especially by certain groups of bacteria and yeasts. The bacteria that have received particular attention are the genus Lactobacilli, and the yeasts are various strains of the species Saccharomyces cerevisiae. Undoubtedly these methods have a wide field of application, and they are becoming increasingly important in vitamin research.

Most of the foregoing experiments have involved assaying. A second, and possibly even greater application of vitamin research in this field, lies in the complete determination of the nutritional requirements of certain bacteria which are either (a) pathogenic or (b) important commercially. Relatively little is known concerning the nutritional requirements of many pathogenic organisms. Some, especially those indigent to tropical climates, are relatively strange to us, but we may become introduced to them by the returning servicemen after the war.

The potentialities for combating these microorganisms are as follows: Organisms which require p-aminobenzoic acid as a vitamin can for the most part be killed by sulfonamides or other sulfonamides.

The sulfonamide presumably competes with the vitamin at enzyme surfaces and since it is present in greater concentration it enters into combinations normally held by the vitamin. It fails, however, to carry on the normal metabolic activities which the vitamin ordinarily conducts. The organism thus dies. The infected host, being larger, is not affected to so great an extent. The mechanism of sulfonamide action is not always so simple as pictured here, but the explanation is a good approximation.

Sulfur analogues have been prepared which correspond to certain of the other B vitamins, and in the case of pantothenic acid, at least, the sulfur compound is completely effective against organisms that require the vitamin.

Commercial bacteria that are receiving study include those that produce alcohols, acids, and related compounds, as well as the high protein and high vitamin yeasts. Synthesis of vitamins by organisms is important because it proceeds continually in our own intestinal tract where at least a part of our necessary supply is made up by the intestinal bacteria. A deficiency of biotin would be very unusual for this reason.

In pointing out the ubiquitous nature of the B vitamins, it should be emphasized that any localized pain or lesion which may accompany a vitamin deficiency is probably incidental to the general impairment of cell functions. Among the effects that would be expected from such a condition would be a general lack of well being. This might in turn be reflected in the psychological state of the individual. With the development of a fuller understanding of vitamin deficiencies, it is not unreasonable to suppose that measurable "psychological lesions" may some day be demonstrated, which would be more subtle than the usually recognized types of vitamin deficiency and which could be correlated with improper nutrition.

Progress has been made in this direction in the borderline field between biochemistry and psychology. The brain potentials of thiamin-deficient pigeons have been found to increase greatly before any sign of deficiency is indicated. Convulsions in rats have been shown to be caused by vitamin deficiencies. Maze activities of human beings have been shown to be impaired by thiamin deficiency and improved by readministration.

It is doubtful whether it was ever thought that contributions to vitamin research would be made by genetics. The work of Dr. Beadle and his co-workers, however, using mutant strains of Neurospora, has been of great scientific interest and application. These organisms, which Dr. Beadle will undoubtedly describe tonight, have been treated with x-rays to render them in-
capable of synthesizing certain vitamins. They have thus provided extremely useful tools for further vitamin research; the mutant requiring choline is the only organism that has been used for assay of this substance.

In conclusion, the vitamins appear to occupy a unique position in the fields of science since they serve to bring together on common ground the physical and organic chemists, biochemists, physiologists, microbiologists, and nutritionists. It is thus often difficult to distinguish the principal application of a particular research project. As the biological sciences are integrated more completely, I believe we may hope to see vitamin research catalyzing further this important process.

Dr. Fincke: Any questions? There is one thing I should like to ask. Do any of these bacteria ever become resistant to the sulfa analogues?

Dr. Cheldelin: Yes, they do. Much research is being carried on to find new compounds that are sufficiently different from the previously administered drugs to provide new angles of attack in combating bacteria. The different drugs could presumably be alternated, providing a "cross-fire" effect on the organisms.

Dr. Fincke: That would tend to explain why human beings fail to react to some of the sulfa drugs after awhile? What protection is there against the advertising of the vitamins? Do Pure Food Laws hold?

Dr. Cheldelin: If you go into a drugstore and buy a packet of vitamins, you have little protection unless the content is labeled. If you wanted to get some pantothenic acid, for example, you would find that each pill contained several milligrams of it. The B vitamins, so far as I know, are not deleterious, but the fat soluble vitamins may be. In the enriching of cereals, on the other hand, we are pretty well protected. This is true whenever large groups of people are involved, but in the promiscuous eating of vitamin pills you have no protection except your own conscience.

Question: What about taking it the other way? What if it is advertised to have a plentiful supply? How is the public to judge whether it contains the advertised amount? If they state that the pill contains a certain amount, and nearly all of them do, does the Pure Food Act cover that?

Dr. Fincke: Yes, it does. If it is advertised as a source of those particular vitamins it must contain the minimum requirements of the National Council. There are beginning to be regulations; I don't think they are complete yet, but I think that they will be more carefully worked out in the future. The National Research Council has set up minimum requirements for those vitamins that are known to be required by man. For some of these others we have no standard as yet for man.

Dr. Beadle: I should like for you to summarize the evidence for believing that choline should not be considered a member of the B complex.

Dr. Cheldelin: I think the chief reason is that it is required in such large amounts that one begins to feel that the inclusion of choline might warrant the inclusion of other materials. Another is that it can furnish energy by itself. Its function as a methylating agent is not specific for it at all. Thus, you could use methionine as well. I think, however, that your question is a valid one. The present definition set up for B vitamins, namely, that they furnish no energy, will of course exclude it.

Dr. Beadle: We have a Neurospora mutant that uses choline in such small amounts that energy is out of the question. One gamma is sufficient to bring a culture up to full growth.

Dr. Cheldelin: The group of B vitamins is growing so fast that we may in the future find it necessary to consider vitamins largely on the classical basis.

Mr. Elmer Hansen: I don't think we should overlook our Victory Gardens as a source of vitamins. In the field of agriculture there are two problems with which we are concerned in relation to vitamins: One of these is how can we by practical means increase the vitamin contents of our plants during the growing season? Another problem is how can we retain the vitamins from the time of harvest until the plants are finally consumed?

In relation to the first problem there are practical means of increasing vitamin content: first, by alteration of the environment in which the plant is grown; second, by altering the genetic constitution of the plant. In regard to the first method, there has been, so far, little success. Fertilizers appear to have little effect on vitamin content. Certain environmental factors, such as light and temperature, have an effect on the synthesis of at least some of the vitamins. Tomatoes grown in the greenhouse under reduced light intensity contain only about half as much vitamin C as tomatoes grown outdoors. There has been some work to show that vegetables grown during cloudy weather contain less vitamins than those grown during clear weather.

Another approach to the problem of increasing the vitamin content is by breeding and selection.
At the present time this seems to hold most promise. There are several projects throughout the country along this line. In one of the southern states an endeavor is being made to increase the ascorbic acid content of cabbage by breeding and selection. Certain strains have been obtained that are nearly three times as potent in ascorbic acid content as other varieties. With sweet potatoes in one of the southern states, they have been able to increase the carotene content by breeding and selection. In Oregon we have been able to obtain, by breeding, varieties of small fruits that are higher in ascorbic acid content than the commercial varieties. Genetics has an important practical application in obtaining fruits and vegetables uniformly higher in vitamin content.

**GENETICS AND GEOGRAPHIC DISTRIBUTION**

**RALPH R. HUESTIS**

Dr. Fincke: The next speaker needs no introduction. He has appeared before and always with pleasure to his audience—Dr. Huestis of the University of Oregon.

Dr. Huestis: I might say one of the reasons I am very pleased to be here myself is because it removes a kind of mental impasse. We had a professor at the University, Dr. Clancy, who was a colleague of Dr. Beadle's, and he talked a good deal about him. I couldn't see how, with the name of Beadle, that he could know so much. We are influenced by early training, and I was thinking of the Beadle in Oliver Twist.

One of the greatest advances made in biology was made by Charles Darwin, who came to his conclusions as a result of studying geographical distribution. He began the study of geographical distribution by a matter of accident. He was a curious “duck.” He flunked out of a very good institution, the University of Edinburgh. I imagine if they put up a plaque, they would have to put up, “Charles Darwin slept here.” He never got his degree at Edinburgh, but managed it at Cambridge after which he took a job going around the world. At the Galapagos Islands he found a distribution that could be explained only by the theory of evolution which he presented to the world. The discovery of local island distribution was an accident, also. Darwin was dining with the governor. Governors know quite a bit. This fellow knew that the tortoises from some of the Galapagos Islands were better tasting than those from other islands in the same group. “I can tell just where the tortoises came from,” he remarked, “They look different.” Darwin was always inclined to be a disbeliever. But he found this to be true and that the birds from one island were different from those of a different island. He went on from there to elaborate the idea of evolution by natural selection acting locally.

Gregor Mendel, who flunked out of a more famous university, the University of Vienna, was a man who required explanations of things also because he followed them as they seemed to occur to him; and his performance was a matter of very careful planning and exceptional ability in understanding his results. To Mendel we owe our first idea of particulate inheritance, that behind characters are entities which can readily separate from one another.

That it wasn't discovered before Mendel's time was not because people weren't smart, but because people were studying characters whose particulate origin was not obvious. So they missed the point. Particulate inheritance is difficult for anyone to understand. In regard to people with good looks and various abilities and things of that sort, the character is dependent on a very large number of individual genes; as Dr. Beadle has said, the writers of textbooks sandwich in genetics someplace. It isn't related very much to the things that come before nor is it commented on in the material that comes after. It is just there, and the students are supposed to learn it. But they fail to apply it to anything else they know. If they look within the inheritance of their own families, there is little they recognize; and they think Mendelianism is just something to learn in school.

I might say with regard to an examination of the distribution of the differences between wild animals the same difficulty obtains. The characters by which organisms are arranged taxonomically are not characters which are readily reducible to particulate inheritance. So for a considerable period of time people interested in wild species and wild life didn't believe that Mendelianism had anything to do with it. That, of course, is due to the difficulty that I have outlined and also to another point. Most of our illustrations in genetics have to do with domestic creatures, and in domestic creatures variability is somewhat rampant. It comes up in all ways. There is no conservatism to it. You can have
anything appear. You look over any domestic animals. There are different spots and sizes, etc. Anyone familiar with animals picked up in the wild knows there is variability in quite a number of different things but it has a general and controlled appearance. I have here a few mice that undoubtedly had their origin among the wild creatures but have grown up in captivity. I thought I would show them to you. (Shows a mouse with gray and white coloring.) You wouldn't see a mouse like this in the wild state. It is a piebald, like the spotted or the white-faced cattle you see anywhere in Oregon.

Anyone knows that if you have domestic animals and breed together relatives quite a large number of new colors and sizes and other characteristics appear, and you can use those for genetic illustrations. Here is a mouse whose tail doesn't grow straight. These are a couple of characteristics which we wouldn't suppose would help the mouse get along in the wild state, and so would be restricted in nature. These exceptional things are the "stuff" that people associate with Mendelian characters. You can use these for illustrations, but it doesn't prepare you for the situation you see with regard to wild creatures.

I have some deceased mice, the skins of which will give you an indication of what the mouse looked like when it was running around. These were all wild mice. These in the upper row are deer mice; starting at the coast (very dark); Roseburg (lighter); top of Cascades (still lighter); between Silver Lake and Harney Lake (lighter). These mice all show a gradation of color. These (Cascades and Silver Lake) are much brighter yellow in color; the white parts are a paler white. These western coast mice tend to be dull. If you captured specimens along between the points indicated, you would have a large number of intergrading mice. You can see a gradation, also, in the length of the tails.

The mice in the bottom row represent other species of mice in the same group. This mouse is Peromyscus californicus. This is a mouse from the desert. Island types differ rather nicely from kindred types on the mainland. Along the mainland you often find such fine intergradations that you don't notice them. There are some species of animals that look pretty much the same no matter where you find them. The barn owl is the barn owl here or in Europe. Wherever you go it is the barn owl. It is a single type of owl. The individual variations among these owls don't fit into any particular racial or color scheme. There are other species that come in rather pronounced differences—polymorphic phases (two different colors) are not rare. The Olympic Black Bear is an example. We human beings come in brunets, blonds, and redheads. Even if we don't come in all these in this room, we would probably have all the blood groups.

I am going to tell you about the species which comes as a black or a brown bear. We supposed at first that there was some specific difference in these two bears, but now we know that the species can be either color. You might suppose that they just came blacks or browns according to chance and there was no organized arrangement about it, but we know that this is not so. Counts made of the number of blacks and browns show that they differ regularly in different parts of the country, and a very good test was made by investigating records of the Hudson's Bay Company, who kept track of all the skins and where they were collected. They made three copies of the reports and sent them by different routes to England. With those data we are able to tell what used to be the situation during the time the Hudson's Bay Company occupied the country.

In the North and West the black bears are more numerous. In the South and East the browns are more numerous. It is a very regular distribution. It seems obviously so to casual observation; and if you make counts enough today, it works out like that. We feel very confident that the difference in color is just a Mendelian difference, the brown being recessive to the black. You can also get light and dark browns and lighter and darker blacks. You can understand that Mendelianism is working, but you can't explain why the proportions are arranged geographically. Usually if an animal is being hunted and if it has dark hair, the country it is found in is dark, the vegetation heavy, and there are clouds in the sky. If the country is light, the animal is light. Also, if it is a predator, creeping up on its prey and it has a blending color, it can be concealed while creeping up. That is so with regard to foxes. But with regard to bears, there are no bears that creep up on their prey. They don't creep up on anything, and you lack that explanation in terms of concealment. The brown gene may have occurred in the southeast and gradually spread out. It is curious if this is so that it coincides in color arrangement with that of the other animals that are concerned with hunting and need to be concealed or those that are hunted and need to be concealed.

I am coming to that type of species difference in which I am particularly interested, differences
in geographical races or subspecies. This mouse we could be certain was \textit{rubidus}, this \textit{gambelli}, and this one is called an intergrade. Intergrades occur right along if you want to put them in. The taxonomist is rather stumped at times, and that is where genetics can sometimes help him out. We may find out just how some of these organisms are genetically separated. We have investigated characteristics such as coat color and tail length in mice but haven't got very far with a partuculate analysis. We know that if you take some of these mice that are greatly different and keep them in cages and apart they don't converge in appearance. At the end of a number of generations the races that were, in appearance, separate from one another when the experiment was started have descendants that are just as different.

If you select in any group parent mice with longer tails or the shorter tails, in not many generations you produce a considerable difference in the progeny of the two groups. If you mate together mice that are sufficiently different, the hybrids are rather typically intermediate not only in one but in all the characters in which the mice differ. It is very hard to make up your mind what the limits of any of these characters are so that they may be tested for Mendelism.

If you mate the first hybrid generation mice with one another, you tend to get those which are like the original parents and also those like the hybrids. The variability is typically greater in the second hybrid generation. The more genes involved the more hybrids you have to raise to get the old parental types again. I am supposing that we are talking about polymorphic species in all these characters. I think all of them are polymorphic. We have a greater concentration of genes that make these mice darker over here, and less concentration where mice are lighter over there. In a long stretch of country where the mice in each end are very different, you would have a regular gradation all along. You may find many genes involved in the tail length and many others involved in the color differences.

With regard to the color of mice, you have a pattern that can be modified readily in either geographic direction and that is the way the inheritance appears to be organized. I might make some comments on the way the mice work this out. They have lots of hairs in the coat, but the hairs come in different sizes. They have little hairs, heavy long hairs, and intermediate ones. The big ones that stick up are always black all the way through. In the other hairs there is a place, the agouti band, where hairs have yellow pigment showing. Yellow seems to be independent of the black but is always present in the little hairs which are the commonest ones in the coat. If you were investigating the hairs in a mouse of the darker kind, you would find that these yellow agouti bands were quite narrow and most of the large hairs lacked a band, and also that the amount of black in any place in the hair was considerably greater than in a paler mouse. The black is in little granules throughout the hair. The number of those granules is greater in the blacker hair. All through the hair the black pigment is concentrated in the medulla of the hair. At the hair tip there is some black pigment on the outside, also. I think the virtue of that is that it will fade during the season. Mice in the springtime are relatively dark. In the fall most of them have lightened up. The most superficial pigment at the hair tip fades along with the vegetation. This is a special seasonal arrangement. If you go into the desert, the yellow agouti bands are longer and there are fewer hairs that carry nothing but black pigment. But the colors appear to the eye in a very complex way. More of this and less of that. You have that play of very complex factors throughout which it is most difficult to investigate from the standpoint of particular inheritance.

I am busy trying to get some genetic tools to work with that will analyze some of the things that these mice exhibit but that are too complex for our present techniques.

With regard to the way these differences among wild organisms and among domestic organisms occur, the people who work with Drosophila flies have told us a good deal. There are many ways in which mice and plants and flies and people can get to look less like each other. That is to say, a gene can take on a new way of doing things and produce a different effect. If it produces a much different effect, it may not work into the general genetic system, and that new gene may be eliminated; but if it produces a little different effect, it may be useful to nature and be preserved and added in with the going organization of things. The chromosomes also get rearranged in many ways. We don't know that that sort of change works with these mice; but when we investigate species of Drosophila flies, we find that the chromosome picture is different as we get geographic differences among the flies. They have flies no one suspected would be possible. They are separated quite a bit genetically even if they haven't got something on the exterior that betrays the chromosomal difference. Among ani-
mals we discover cases where you get the poly-
ploid condition where the number of chromo-
somes is doubled. The abnormal arrangement of
the body cells which this may cause upsets the
nice adjustment of one cell with another, and in
the investigation of some animals—salamander
embryos—it was found that the ones who have
the extra number of chromosomes per cell don't
get along as well as those that have the normal
number of pairs of chromosomes typically found
in salamander cells. So there are many ways that
these entities, the animal groups, can come to be
separated from one another genetically.

There is another point. Just as Darwin found
out, separation aids in species forming because
groups of any kind isolated by space or lack of
association do not get their chromosomes together
in maintaining the standard type. This segregati-

donfronts us first of all as we go around
setting traps at random. We will find that the
mice are just in certain places. There are certain
kinds of country that they agree suits a mouse
and there are certain areas mice avoid. If you
go all through the fields without any brush cover,
you won't find any *Peromyscus*. Probably these
mice have certain ecoologic necessities which sep-

arate them into little groups here and there. That,
according to the evolutionary theorist and those
who check theories with mathematical formulae,
is the sort of thing you need to form new species.

Separation typically leads to differences even
if you don't get, in the case of the two groups,
real adaptation. If you need to find a difference
in mice, get one mouse from one place and one
from another. One becomes adapted to place A
and one to place B. The organism also tends to
become different in a new place even without
adaptation just as words differ in England and
the United States. Recently reporters investi-
gated a young woman who was working for the
British Government in Washington. She said
she liked it here "where you get lots to eat and
have a good time; but I have to wash my own
'smalls'." The Americans didn't recognize
"smalls" as underwear. These are not necessarily
adapted words. Such word differences are due to
the fact that when you get creatures apart you
get divergence due to different developments.

There is just one final point I want to leave
with you in our discussions of genetic differences.
In thinking of a brown and a black bear you
think of them as being quite different bears. But
in regard to all of their other characters, they are
quite similar. This modification of the pattern is
usually the difference you find in organisms.
Actually all vertebrates have the same body pat-
tern which is modified as development takes place.
I have as my hardest job the teaching of pre-
medical students embryology. I give them pro-
jected slides on the screen, and they identify the
different characters of the organisms. I give
them stages from a 24- to a 96-hour chick. They
have had successively 24, 33, 48, 72 and 96 hour
chick slides but never the whole chick. Instead
of giving them any chick slides for the final I
give them a 5 mm pig, and they do just as well
identifying the parts of the pig as of the chicken.
The best students do the best identifications of
characters in either type.

In the earlier stages these different organisms
are so much alike that students trained on one
will know the other. When I am talking about
the early stages, I am talking about such funda-
mental things as the relative size of the parts,
the position and parts of the heart, the main blood
vessels, the brain and ganglia and the location of
the gut. I am talking about the important things
that make up the body. These animals are about
the same to start with and gradually move apart
so that you finally get the adult chicken and the
adult pig. We think this has been due to a long
period of separation and different adaptations.

In Oregon we have a nice little ecologic group
of the chicken, the cow, the pig, and the Oregon-
ian; if the adults of those groups now look differ-
ent, it is due to long wandering in foreign parts.

Dr. Fincke: Thank you, Dr. Huestis. Are
there any questions?

Mr. Lawrence: With reference to the differ-
ences in the densities of populations you have
shown a series of local races which present quite
a uniform increase or decrease in racial charac-
teristics. Do you find that the density of popula-
ton is equally distributed?

Dr. Huestis: I don't find any differences in
density of population correlated with characters.
The groups each have an area and they keep
other mice out. No trespassing. They will be
spread out. There is a mouse here and another
there, etc. Investigators have worked on spe-
cific areas, tracked mice and marked them. If
the home is an extra good one, other mice will
take it when the owner dies. Where you get
brush on uniform territory like our sagebrush
plateau you get considerable densities of popula-
tion. Along the coast you might have to travel a
long way to get enough mice to make a showing.
Sometimes you get a surprising number in one
place. It depends on the presence of predators
and the amount of food, but I don't know of any
way in which these numbers can be correlated with these characters. There doesn't seem to be any difference in population density due to appearance.

Dr. Zeller: Do not some of these same relationships hold for salmon and trout in various streams?

Dr. Huestis: That has been discovered in all the streams that salmon go up. Investigators follow the little fish from where they start out and find different races in different streams. With regard to fish culture, you can do much better by selection than if you just feed them optimum food. If you experiment with food, you can get some size results, but selection of the faster growing fish is more effective.

Mr. Lawrence: Dr. Huestis, you have indicated that it is difficult to explain the correlation between racial characteristics and surroundings. Do you think you would get the same range of character difference along the environmental gradient if there were no Cascade Mountains?

Dr. Huestis: I am sure if there were no Cascades you would have some gradation but not the same amount. Close to the coast you would presumably have more rain and it would become less as you got farther inland, with consequent vegetation and genetic racial character differences in the mice.

GENETIC RELATIONSHIPS IN PARASITIC FUNGI AS A FACTOR IN THE PERPETUATION OF PLANT DISEASE PROBLEMS

Charles S. Holton

Dr. Nathan Fasten: We have had Dr. Beadle from California. We have had Dr. Chekdelin, Dr. Smith, and Dr. Huestis from Oregon. The next speaker comes to us from our northern state, the state of Washington. Dr. Holton.

Dr. Holton: Plant disease problems have confronted mankind for hundreds of years and, quite naturally, efforts to combat these diseases have extended over a similar period. Much success has attended these efforts and it seems more than probable that the development of certain flourishing crop industries of today would have been impossible without successful disease control. Nevertheless, paradoxical though it may seem, there is at present a greater multiplicity of plant diseases than ever before. Furthermore, some of the plant diseases that plagued the ancients still constitute major hazards to crop production throughout the world. Notable among these are the rust and smut diseases of cereal crops. The organisms that cause these diseases have demonstrated remarkable capacity for survival against natural hazards as well as those created by the plant scientist. At least one explanation for this appears to be found in their genetic attributes.

The use of disease resistant varieties is one of the generally recommended methods of plant disease control. Difference in varietal susceptibility of crop plants to disease was observed more than a hundred years ago, but the application of Mendelian principles to the development of disease resistant varieties did not begin until about forty years ago. Since that time much has been learned about disease resistance in plants, including its nature and its mode of inheritance. During the same period knowledge of genetic relationships in the fungi has likewise been greatly expanded.

The importance of the genetic relations in certain phytopathogenic fungi as a factor in plant disease control is now generally recognized.

In its original concept, the theoretical possibilities offered for plant disease control by breeding resistant varieties were so promising that some of the pioneers in this field felt justified in hoping for the total elimination of certain diseases through this method. They reckoned, however, without sufficient knowledge of the genetic constitution of the fungi that cause these diseases. In other words, it was assumed that the pathogenic properties of the causal organisms would remain fixed while the host reaction was being altered. Thus, plant breeders and plant pathologists alike were more or less unprepared for the rude awakening that came when varieties that once had been resistant to disease suddenly exhibited susceptibility. For example, certain varieties of hard red spring wheats became susceptible
to stem rust after having exhibited more or less resistance for a number of years. Other varieties that were resistant in one locality proved to be susceptible in another. Similar experiences were had in connection with the bunt disease of wheat, both in the hard red spring wheat region of the Midwest and in the winter wheat region of the Pacific Northwest. Various explanations were offered for this failure of resistant varieties to remain resistant but it is now common knowledge that the "apparent loss of resistance" in these varieties was due to pathogenic specialization in the rust and smut fungi. (Pathogenic specialization is simply the occurrence in a morphologic species of entities that differ from each other in pathogenic properties.)

Although pathogenic specialization in the rust fungi was known as early as 1894, the real implications of this phenomenon were not fully appreciated until the discovery of the sexual stage of the rust in 1927. This discovery, one of the really epoch-making contributions to the science of phytopathology, opened up a new field of research that has led to a better understanding of the origin and nature of pathogenic races in the rust fungi. Prior to this there was much speculation as to the possible origin of races of stem rust, but since that time it has been amply demonstrated that new races may readily be produced by artificially hybridizing already existing races and varieties. Furthermore, there is convincing circumstantial evidence that hybridization occurs frequently under natural conditions on the aecial host, resulting in the production of new races, which in some instances are capable of attacking new resistant varieties. Indications of this are found in the results of studies on stem rust epidemiology. Over a long period of years a different race of stem rust was identified out of every five aecial collections studied, in contrast to one race identified out of every 75 uredial collections studied. In addition, several races have never been isolated except from aecial collections and there are several instances in which new races were identified first from aeciospores. Therefore, through the operation of genetic factors the stem rust fungi have been able to keep pace with the development of new host varieties and thus to perpetuate the stem rust problem.

As already mentioned, the persistence of the cereal smut problem has been no less troublesome than that of the stem rust problem. The first systematic attempt to breed wheats resistant to bunt began in 1901, and much work has been done along this line. But the development of smut resistant varieties failed to eliminate the smut menace, primarily because of the frequent occurrence of new pathogenic races of the smuts. The durum wheats of the hard red spring wheat area were highly resistant to bunt for many years until about 1928 when smut became an acute problem in these wheats. A similar situation developed in the case of the common spring wheat variety Marquis, in the same region. In the Pacific Northwest the bunt-resistant varieties Ridit, Albit, and Turkey exhibited high susceptibility after one to several years of commercial production. In every case the susceptibility of these varieties was attributable to previously unrecognized races, each capable of parasitizing its own particular variety.

The oat smut disease presents a comparable problem. For a long time the variety Victoria exhibited a high degree of resistance to all known races of the oat smuts. Consequently, much of the breeding program for the development of smut-resistant varieties of oats has been based on the Victoria type of resistance. Within recent years several new varieties possessing this type of smut resistance have been developed and released for commercial production. Recently, however, a new race of loose smut was discovered that is pathogenically specialized to Victoria, and, therefore, to these new varieties also. To be sure, they are still resistant to all other races, but actually the appearance of this new race definitely limits their possibilities in solving the oat smut problem, especially since the new race was found on a commonly grown variety and may already enjoy wide distribution. We have, therefore, definite indications that the inherent nature of the oat smut fungi is sufficiently adaptive under natural conditions to enable them to withstand adverse circumstances and thus to contribute materially to a continuation of the oat smut problem.

Inevitably, the demonstration of physiologic specialization in the cereal smuts and the rather frequent occurrence of previously unidentified races, especially when these occurred on new varieties that were developed for smut resistance, stimulated interest in the investigation of the importance of this factor in the control of these diseases. The possible role of hybridization and mutation in this respect has been intensively studied within the past twenty years. In that period it has been demonstrated that genera, species, and races of several smut fungi hybridize more or less readily. This discussion will deal primarily with studies on hybridization in the smuts of oats and the stinking smut or bunt of wheat.
Characteristically the oat smuts are good material for studies on genetic relationships in the smut fungi. The two types of oat smut, loose and covered, are caused by two species of the same genus, one of which has rough spores and the other smooth spores. The life cycles of these species are essentially identical and they cross readily. Thus, there is opportunity for studying the heritability of their various characters, such as gross morphology of the diseased oat panicles, morphology of the spores, and pathogenicity. Some studies of this nature have been made and the results show rather clearly the genetic nature of these characters and, to some extent, their mode of inheritance. For example, in interspecies hybrids the loose and covered characters of diseased panicles were clearly controlled by genetic factors, although in an irregular pattern. On the other hand in a hybrid between two races of the loose smut species, one of which had the typical loose smut panicle and the other an indurate type of panicle, the loose type was dominant over the indurate type, both types segregating in a 3:1 ratio. Similarly, the rough spore character of the loose smut species was dominant over the smooth spore character of the covered smut species and these characters segregated in a 3:1 ratio.

During the course of these hybridization studies with the oat smuts an albino type of oat smut appeared in the experimental material, having resulted from mutation in the covered smut parent. It is similar to the covered smut in all respects except that the spores are hyaline instead of olive brown. Since in gross morphology the diseased panicles are buff in color this smut has been designated as the buff smut of oats. It crosses readily with the loose and covered smut species and the brown color of their spores is dominant over the hyaline character of the buff smut spores. In the segregating generation brown and hyaline spores occurred in a simple 3:1 ratio.

That pathogenicity is likewise genetically controlled in the oat smut fungi is clearly shown by studies with races having distinct pathogenic properties. From a cross between a Gothland race of loose smut (infects Gothland but not Monarch) and a Monarch race of covered smut (infects Monarch but not Gothland) it was possible to select a race of covered smut that is capable of infecting both of these varieties. In another cross, this time between the Gothland loose smut race and a Monarch buff smut race (infects Monarch but not Gothland) a buff smut race was selected that was capable of infecting both varieties. Further studies along this line proved that it was possible to produce a buff smut race equal in pathogenicity to, or more pathogenic than, any known race of the loose and covered smuts, simply by making the cross and selecting a buff segregate from the appropriate variety. In addition to proving the heritability of pathogenicity these studies also showed that its inheritance is independent of the inheritance of other characters, such as spore markings and color. Ratio determinations on the mode of inheritance of pathogenicity could not be made, however, owing to the high degree of lethality in the F1 gametes. And there is some evidence that the degree of lethality is associated with pathogenicity.

Results similar to those obtained with the oat smuts have also been obtained in studies with the fungi that cause bunt, or smitting smut, of wheat. There are two species that cause this disease and they, like the oat smuts, are distinguishable on the basis of rough and smooth spores. But taxonomically and biologically they are distinctly different from the oat smut fungi, and incidentally, more difficult to handle in experiments than oat smuts. Nevertheless, their principal characters are genetically controlled. In the case of spore morphology, however, the operation of genetic factors appears to be less regular and precise than in the oat smuts. For example, in most of the species hybrids roughness of the spores was dominant over smoothness while in some of them the reverse was true. Furthermore, when roughness was dominant the degree of roughness was less pronounced than in the rough-spore parent. In subsequent generations segregation and recombination of factors occurred in such a way as to produce not only spores representing both parent types but also spores with different degrees of roughness. In degree of roughness, therefore, these spores stood intermediate between the rough parent type and the smooth parent type. Intergrading types of this nature frequently are observed in material collected from commercial wheat fields, which suggests that hybridization between these species occurs under natural conditions. Obviously this creates problems for the mycologist since the intermediate types frequently are sufficiently atypical to be regarded by some as different species.

From the standpoint of control, pathogenicity is the most important single character of physiologic races of bunt. It seems especially significant, therefore, that variability in this character may be determined by different combinations of genetic factors. That is to say, when two patho-
genic races cross, new factor combinations may result in the production of one or more races with pathogenic properties distinctly different from the parent races, either by being more virulent or by being less virulent. This, then, is a basic fact which, if properly applied, could be of practical value in the development of bunt resistant wheat varieties. More specifically it makes possible the production of pathogenic types which are not known to occur in nature but which might reasonably be expected to appear in the future, if proper conditions should prevail.

The possibilities in this respect are further emphasized by the behavior of several artificially produced hybrids, of which the following are representative: A cross between Hohenheimer race T-9 (which infects Hohenheimer but not Oro) and Oro race L-8 (which infects Oro but not Hohenheimer) produced a segregate capable of infecting both of these varieties. Another cross between these two races produced a segregate to which both Oro and Hohenheimer are resistant. From a cross between Hussar race T-8 (which infects Hussar but not Hohenheimer) and Hohenheimer race T-9 (which infects Hohenheimer but not Hussar) a segregate was obtained which is pathogenic, not only on both Hussar and Hohenheimer, but also on a variety that is highly resistant to all known naturally occurring races.

Thus, if it is possible to produce a variety of wheat that is resistant to all known races of bunt, it also is possible to produce a race of bunt capable of infecting that variety. And if one pursued the theoretical possibilities further, perhaps to an impractical extreme, it should be possible to produce a race that would be pathogenic on all wheat varieties. As yet this has not been attempted. But fundamentally, if the most bunt-resistant variety of wheat is one that is resistant to the greatest number of races, then the use of artificially produced races in a breeding program should enhance the possibilities for the development of such a variety. In any case, the genetic nature of these fungi would seem to guarantee that this disease will continue to be a threat, at least potentially, for a long time to come.

By way of summary, therefore, it may be said that, in general the morphologic and physiologic characters of the rust and smut fungi are determined by genetic factors and that the occurrence of new types frequently may be due to new combinations of these factors resulting from hybridization between species and races. The mode of inheritance of these characters apparently is simple in some cases and complex in others, but more important is the evidence that genetic relationships in these fungi probably are the primary contributing factor to the perpetuation of these plant disease problems.

Dr. Fasten: I am sure there must be some questions on this very interesting paper.

Dr. C. E. Owens: Just a few years ago we heard a lot about the great advances in science and technology and how this increases unemployment and social unrest. Are these discoveries going to put the plant breeders out of business, or, conversely, perpetuate their jobs?

Dr. Holton: I don't believe any plant pathologist is going to put any plant breeder out of a job. I think the most that can be said for this kind of work is that it explains a lot of things that have been hard to explain before, things that have been theorized and speculated on for a good many years. I believe if you want to get the most disease resistant variety of any plant, the thing to do is to subject all the available breeding material to a test against as many of the races of the disease as you possibly can and then go on from there. I might say, in this connection, in the work that we are doing we have accumulated quite a quantity of material for the plant breeders to use, and they are using it every time they have an opportunity.

Comment: I marvel at the wheat farmers letting you stay in the Palouse Country.

Dr. Holton: That question naturally has come up. My answer to anyone who would seriously want to criticize the possibility that we might release some super de luxe race of smut is that we have these races developing in natural conditions anyway, and we allow farmers to ship their wheat back and forth, thereby spreading new races, and no one says anything about it. But some farmers might be the first to criticize this kind of work. I maintain, however, if the farmers ship their wheat back and forth, they are going to spread smut races around. Furthermore, if a man is working on something like this and doesn't have an appreciation of the consequences if he allows artificially produced races to escape, it would be better for him not to be working at all. In other words, our practice is to keep this material pretty well corralled. Significantly, the areas where we find the largest number of resistant wheat varieties are also the areas where we find the most virulent races of smut. It would appear, therefore, that natural processes of production and distribution of races of bunt probably are more efficient than artificial ones.
There is a close interrelationship and interdependence between practical plant breeding and the science of genetics. Practical breeders who were good biological artists were able to produce improved varieties of plants before the laws of genetics were known. The knowledge of how inheritance works has, however, enabled breeders to go farther and faster with fewer mistakes. Plant breeding in one form or another has been practiced from the time plants were first cultivated for human food but greater advances have been made since the rediscovery of Mendel's laws in 1900 than occurred during the thousands of years preceding that time. Genetic discoveries have made it possible to avoid many mistakes and have pointed out a great many shortcuts that can be taken in breeding for certain specific purposes. Scientific discoveries have made possible rapid advancement in breeding techniques and methods. Improved techniques and methods have in turn made possible the discovery of new facts and laws. Some of the new scientific discoveries have come from research undertaken because of problems encountered in practical breeding. Much of the foundation work and many ideas for fundamental research programs have come from plant breeding experience. Thus the science and the art complement each other and are mutually beneficial.

The interrelationship of the science of genetics and practical plant breeding is well illustrated in the breeding of the crop that occupies a greater acreage in the United States than any other—namely, corn. I should like to cite briefly the history of corn breeding and a few examples from our own experiences in the breeding of this crop.

Corn is a distinctly American crop, being unknown until America was discovered. The origin of the crop is lost in antiquity as no wild forms have been found. The nearest wild relative of corn, teosinte, resembles corn in some respects and can be crossed with it, but is not thought to be a direct ancestor of corn. I should like to cite briefly the history of corn breeding and a few examples from our own experiences in the breeding of this crop.

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Early corn breeders, including the Indians, who developed the different types of corn were artists at selection. Corn being a naturally cross-pollinated crop is particularly susceptible to change by selection. Numerous variations are produced by the natural recombinations of hereditary characters occurring under conditions of open pollination. The success of the breeder up to the time of the discovery of the laws of genetics depended largely on his artistic ability at selecting rather than on following any scientific facts or laws. The breeder would select what appeared to be a desirable type and would perpetuate it. If he had the ability to select properly, improved varieties were developed.

In 1897 B. G. Hopkins of the University of Illinois started a new method of corn breeding that he hoped would result in more rapid improvement and would place corn breeding on a more scientific basis. This method was known as ear-to-row selection. The method consisted essentially of selecting a large number of good ears from an open-pollinated variety of corn. A portion of the seed from each ear was planted in an individual ear row and only a few of the higher yielding ears were saved for seed. The seed from these few high-yielding ears was bulked and planted in a seed plot from which a new variety was selected. It was hoped by this method to eliminate the types that were inherently low yielding and hence bring about more rapid improvement. Numerous variations of this method were tried by Hopkins and others but all proved to be failures. The method violated what we now know to be a scientific fact. Inbreeding of an open-pollinated crop such as corn will reduce general vigor and yield. The ear-to-row method of breeding caused inbreeding as the ears selected in following this method were closely related. Hence the method was discarded.

During the period from 1870 to 1900 a number of workers tried making crosses between various open-pollinated varieties but this method did not prove popular. It was necessary to make the crosses each year and the advantages proved
The rediscovery of Mendel's laws by de Vries, Correns, and Tschermak in 1900 gave immediate stimulus to research on heredity among scientists in both the theoretical and applied fields. Corn was used by two of the rediscoverers of Mendelism, de Vries and Correns, in their research and has played an important part in many of the genetic discoveries made since that time. A major portion of the research on the inheritance of quantitative characters has been with corn. The first known case of linkage of genes was reported in corn. Theories to explain hybrid vigor have resulted from research with this crop. The method of inheritance of approximately 400 genes has been worked out. The 10 linkage groups have each been associated with their particular chromosome and the linkage relations of a large number of genes studied. Corn is also being used in much present-day cytogenetic research.

Several workers began inbreeding corn shortly after 1900 to produce pure lines for use in making hereditary studies. These workers found that inbreeding reduced vigor and yield for several generations but that eventually the inbred lines became pure for the inherited characteristics and constant for vigor. Upon crossing these inbred lines they found that the vigor was regained in the F1 hybrid and that in many cases the hybrid was much more vigorous than the original variety from which the inbreds came. A great many of the hybrids were found to yield 25 to 30 per cent more than the original varieties. Many of the corn breeders at this time considered that these interesting scientific facts adding to our knowledge of heredity but thought that no practical applications could be made because of the difficulty of producing large quantities of seed. A few breeders were quick to grasp the practical possibilities of these new discoveries, however, and began working out methods and techniques for putting them into practical use. As early as 1909, Shull suggested a corn breeding program based on (1) the isolation of true-breeding inbreds, (2) the determination of which inbred lines produced the best crosses, and (3) the utilization of superior crosses in the commercial production of hybrid corn. A number of other workers also continued research along somewhat similar lines, although breeders in general did not take up the new program for several years. The original suggestion was to use single crosses or crosses between two inbred lines for commercial production. This necessitated the production of seed on inbred lines that were lacking in vigor and low in yield. Single crosses were also found to be rather limited in their adaptation. To avoid these difficulties, D. F. Jones of Connecticut suggested the use of double crosses or crosses between four inbred lines. It was found that double crosses could be used without reducing the expected yield and that they were more widely adapted as they were somewhat diverse in genetic characters. It was also feasible to produce large quantities of commercial seed since the seed was produced on vigorous single cross plants. This method with certain modifications and improvements is the one being used at present to produce the seed for planting 90 to 95 per cent of the corn acreage in the midwestern corn belt and more than 50 per cent of the corn acreage of the United States as a whole. Approximately 70 per cent of the corn acreage in Oregon is being planted to hybrid seed at present.

To illustrate more specifically the interrelationship of genetics and plant breeding, I shall outline the breeding methods we are using here at the Oregon Experiment Station. We are carrying on a breeding program for the development of improved corn hybrids for the various corn-growing areas of the state. The first step is to produce good inbred lines. This is accomplished by self-pollinating the existing open-pollinated varieties or hybrids. The shoots or young ears are bagged with a special waterproofed parchment bag before the silks appear to avoid possible contamination from wind-blown pollen. When the silks are about two inches long under these bags and when the tassels are shedding pollen, a bag is placed over the tassel to catch the pollen. The pollen is then placed on the silk of the same plant by hand. Each self-pollinated ear is tagged, harvested, and shelled separately and the following year the seed is planted in an individual ear row. If 1,000 ears are self-pollinated in one season, the following year 1,000 rows of corn will be planted. The best plants in each row are again self-pollinated. This process is continued for five or six years until the inbreds become pure for their inherited characteristics. Large numbers of the poor inbreds are discarded each year. After the inbred lines become practically pure or homozygous for their inherited characteristics they can be carried on either by inbreeding or by growing in isolated plots. The inbreds will remain unchanged and can be used year after year as parental stock. The
crossing of two inbreds will always give the same results. The method used in developing inbred lines is based upon the scientific fact that in-breeding will purify strains genetically.

The testing of inbred lines for yield and various other characteristics is started in the second or third year of self-pollination. It has been found that the yielding ability of an inbred line is established early in the inbreeding process. The first test used for inbreds, other than general observation, is to cross all inbred lines with an open-pollinated variety. The resulting seed is grown in a yield trial and inbreds producing poor crosses are discarded. This type of cross is known as a top-cross. The open-pollinated variety is diverse in its genetic makeup and hence any inbreds carrying factors for high yield will produce a combination with the open-pollinated variety resulting in a high-yielding hybrid. Large numbers of the poor inbreds can be discarded on the basis of the top-cross test.

The next test used for inbred lines is to cross the inbreds themselves in all possible ways to determine which produce the best combinations. A certain inbred may produce a high-yielding hybrid when combined with certain inbred lines that may produce low-yielding hybrids with others. It is necessary to select inbreds that carry genetic factors for high yield and that can be combined to produce a good hybrid. Inbred A may produce an excellent hybrid when combined with inbred B but may give very poor results when combined with inbred C. Yet it may be possible to use a cross of A x C in combination with two other inbreds and thus secure a high-yielding double cross.

The majority of commercial field corn hybrids now being grown are double crosses, or in other words are made up from four different inbred lines. It is possible to combine four inbreds into six different single crosses and three double crosses. Each single cross and each double cross may give different yields. To produce all possible double crosses and grow them in yield trials would require a great deal of land, labor, and time. It has been found possible to predict accurately double cross yields from the yield of the single crosses, thereby saving considerable time in a breeding program. To illustrate the method used we will designate the four inbreds to be combined in a double cross hybrid as A, B, C, and D. The six single crosses that can be produced from these inbreds are: A x B, A x C, A x D, B x C, B x D, and C x D. The three possible double crosses are: (A x C) (B x D), and (A x D) (B x C). The expected yields of each double cross can be predicted by averaging the yields of the single crosses not appearing in the double cross. The following example giving yields of the six single crosses and expected yields of each double cross will clarify this method:

<table>
<thead>
<tr>
<th>Cross</th>
<th>Yields</th>
<th>Expected Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>A x B</td>
<td>57 bu.</td>
<td></td>
</tr>
<tr>
<td>A x C</td>
<td>89 bu.</td>
<td></td>
</tr>
<tr>
<td>A x D</td>
<td>88 bu.</td>
<td></td>
</tr>
<tr>
<td>B x C</td>
<td>85 bu.</td>
<td></td>
</tr>
<tr>
<td>B x D</td>
<td>79 bu.</td>
<td></td>
</tr>
<tr>
<td>C x D</td>
<td>52 bu.</td>
<td></td>
</tr>
</tbody>
</table>

1. \((A \times B) (C \times D) = (89+88+85+79) ÷ 4 = 85.3\) bu.
2. \((A \times C) (B \times D) = (57+88+85+52) ÷ 4 = 70.5\) bu.
3. \((A \times D) (B \times C) = (57+89+79+52) ÷ 4 = 69.3\) bu.

These data indicate that the highest yields can be expected from double cross No. 1. By using this method the breeder is able to determine the best possible combination of inbred lines without having actually to produce and test the double crosses.

Inbred lines used in the production of improved hybrids must transmit many other factors as well as high yield. Inbreds differ markedly in resistance to diseases, insects, cold, drought, and lodging, and in composition of grain. Numerous special tests have been devised for determining the value of inbreds with respect to these characters. We shall mention just a few. The seed and plants can be inoculated artificially with disease spores. Cold chambers in which temperature and humidity can be accurately controlled have been devised. These machines are portable and can be taken to the field for trials under natural field conditions. Machines for determining accurately the strength of roots and stalks are available. Considerable research is being conducted in an attempt to find visible plant characters that are correlated with high yield and other desirable traits. Some correlation has been found between the amount of chlorophyll in the leaves and yield.

The fact that the success of hybrid corn depends on hybrid vigor or heterosis has given considerable emphasis to research on the fundamental genetic and physiological phases of heterosis. Hybrid corn maintains its high yield and other good qualities for only one generation, hence necessitating the production of new freshly crossed seed each season. Numerous genetists and plant breeders have worked on heterosis and many theories have been advanced to explain the phenomena. It appears likely, however, that no one has as yet discovered the complete explanation. Discoveries to date along this line have
been helpful to plant breeders but a complete explanation of all of the phenomena involved in heterosis would be very helpful. Further fundamental research along this line is needed.

It is now possible to breed crops to specifications with almost the precision used in building a machine. Inbred lines of corn can be made to order by the back cross method. As an illustration, assume that inbred A carries many desirable hereditary characters but is weak-stalked and hence lodges badly. Inbred A is crossed to inbred B carrying resistance to lodging. By back crossing the offspring to inbred A for several generations and selecting among the offspring it is possible to develop an inbred having all of the characteristics of the original A inbred plus lodging resistance. A number of wheat varieties resistant to bunt and stem rust have been developed by Briggs and coworkers in California by the back cross method. Rex wheat, which is now the most widely grown variety in the Northwest, was produced by hybridization at the Sherman Branch Experiment Station at Moro. This variety was obtained from a cross between White Odessa and Hard Federation. The winter habit and smut resistance of White Odessa were transferred to the Federation type wheat. Multiple crosses or crosses involving a large number of varieties are being used, particularly with barley. Santiam, a new barley variety recently released by the Oregon Agricultural Experiment Station, came from a multiple cross.

The only hop breeding project in the United States was started at the Oregon Agricultural Experiment Station in 1931. Progress in hop breeding has been slow as it was necessary to work out many problems in breeding technique before rapid progress toward the production of new varieties could be made. The value of accumulated knowledge gained through the many years of research in genetics and breeding of crops such as corn, wheat, and barley has been fully demonstrated during the course of these hop breeding experiments. It was necessary to determine the proper techniques to use in all of the various procedures necessary to breeding hops as scientific literature contained few references to hop breeding. The proper techniques for crossing, germination of seed, and testing hybrids had to be determined. After approximately twelve years' research, sufficient knowledge of hop breeding methods has been obtained to allow the breeding program to proceed on a basis somewhat comparable to that being followed with the more common crop plants.

Rapid progress is now being made in the breeding of small fruits and other horticultural crops at a number of experiment stations throughout the United States. Several new varieties produced by hybridization have been released by the Oregon station. The Corvallis and Brightmore strawberries were bred for canning and preserving qualities. The Cascade and Pacific varieties of blackberries came from crosses between Zielinski, a selection of the native wild trailing blackberry, and the Loganberry. This cross was made to obtain the flavor of the wild berry in combination with the size and other good characters of the Logan. The Willamette variety of red raspberries was developed from a cross of Newburg by Lloyd George.

The newer developments in practically all fields of biological sciences are proving of value to the plant breeder. We are probably now on the threshold of discoveries that will revolutionize plant breeding methods. Practical applications of some of the newer discoveries are becoming apparent at present. A great deal of the newer work in cytogenetics appears to have great practical possibilities. We are learning to manipulate and control chromosomes and genes almost at will. Haploids and polyploids are being produced. Plant chromosomes, genes, and characteristics are being changed by means of translocations, inversions, deficiencies, trisomes, and other types of mutations. These new discoveries are being made by workers in the fields of both pure and applied sciences and are of value in advancing both scientific knowledge and practical agriculture.

In closing I should like to state again that the discovery of scientific facts and laws and practical applications go hand in hand and are mutually helpful to each other. There are many practical breeding problems whose solutions definitely wait on the results of further genetic research. These problems act as a stimulus to research workers in fundamental sciences.

Dr. Huestis: I have found the hybrid corn is not as good tasting as the original bantam corn. Is anything being done to improve this?

Dr. Fors: There is a good deal of work on hybrid sweet corn. There is no question as to whether the hybrids are better than the open-pollinated group. Golden Cross Bantam hybrid corn is grown throughout a wider area than any other kind in the United States. It is used for canny purposes more than any other hybrid due largely to the high quality and uniformity in maturity.
THE INTEGRATION OF GENETICS WITH THE OTHER BIOLOGICAL SCIENCES

GEORGE WELLS BEADLE

DR. ZELLER: Ladies and gentlemen, we are very sorry that conditions are such that it was impossible to reserve places at the tables for everyone who wished to come, but I guess we shall have to live with such circumstances for the duration. You can readily see that many more would have attended the dinner tonight if we had had all the facilities necessary at our disposal.

I am not going to take long for a preliminary meeting tonight. We had several introductions at the luncheon this noon, and we shall pass those up for the evening, but there are some guests here who were not at the luncheon whom we should like to recognize at this time: Dr. Larrsell, dean of the graduate school of the State System of Higher Education; Dr. Riddle of the Medical School, who has always cooperated with our colloquia; Mr. Rex Putnam, superintendent of public instruction; Mr. Frank McKennon, of the state department of agriculture, and Mrs. McKennon.

In order to organize the colloquium it is always necessary to have a number of good workers. I should like to read to you the names of the colloquium committee who are responsible for the program and who have worked laboriously to organize the colloquium: G. V. Copson, E. M. Dickinson, R. E. Dimick, Ernst J. Dornfeld, Nathan Fasten, Margaret Fincke, F. A. Gilfillan, D. D. Hill, D. C. Mote, C. E. Owens, J. E. Simmons, F. H. Smith, Frederick Meyer, and Virginia Weimar. I think they need a hand.

The punch served this afternoon instead of tea was under the auspices of Phi Sigma and Omicron Nu. We thank these young people for this fine service. The luncheon was under the auspices of Sigma Xi, and in the absence of Dr. Britt, Dr. Fincke, acting president, made arrangements for the luncheon.

The colloquium has, from the start, been under the sponsorship of the Oregon State chapter of Phi Kappa Phi. It was organized during the year when Mr. D. M. Goode was president of the Oregon chapter. The idea of the colloquium was entirely his, and I think we have had six examples of his good judgment. I should like to present Mr. and Mrs. Goode at this time.

Dr. Peterson of the department of English is the present president of the chapter, and I have asked him to say a few words for Phi Kappa Phi.

DR. SIGURD H. PETERSON: Mr. Chairman, ladies and gentlemen, now that we are nearing the end of our colloquium I think we will all agree that it has been very pleasant and very successful, and it becomes my happy duty to say just a few words on behalf of the organization that sponsors this program with Sigma Xi.

It is going to be a very few words, because it is not the main purpose of the evening to listen to the representative of Phi Kappa Phi. I think that the occasion certainly calls for thanks to the person who has done more than any one individual, aside from Dr. Beadle whose contribution we all recognize, to make these meetings a success, and that is Dr. Zeller.

I think not many know, probably not many stop to think, how much actual work, how much time, it takes to organize a thing of this sort, to make it go smoothly and effectively as this series of meetings has gone. Most of the credit belongs to Dr. Zeller. He started early and has worked diligently.

Then, of course, I wish to thank Dr. Beadle for his coming up here. We certainly appreciate it. We will long remember the excellent talks. As a non-scientist I can say that even I enjoyed the meetings, and I think I understood them pretty well in spite of all the big words. I know I am going to enjoy tonight.

I want to thank all of you, especially the members of the committee, in making the occasion a success.

We are very glad to have such a fine attendance because we feel, as has been expressed several times today, that continuity in the colloquium is a very desirable thing. We thank you on behalf of Phi Kappa Phi for being with us and hope that in another year you will be back again to enjoy another series of successful meetings.

DR. ZELLER: Thank you, Dr. Peterson.

I know now I was right in calling on him.

I should like to thank Dr. Gilkey and Miss Hughes for the beautiful decorations on the tables. I think they did a marvelous job. I hope I haven't forgotten anyone. You know, we are absent-minded professors around here the
same as at other similar institutions. That reminds me of a professor on the Oregon State campus who I think gives a good illustration of the absent-minded professor. He met a student one day on the campus. She inquired about some class work and when they were through, he said, "By the way, which way was I going when I met you?"

"You were going that way."

"Oh, all right. Then I've had my luncheon."

It is with some reluctance that I present to you the speaker of the evening because I know that when he is finished, the colloquium is over.

I hope, Dr. Beadle, that you will come back and visit us many times and that when you come again you will have been acclimated to Oregon weather. I am not so sure that you will like it. Perhaps you have heard the story of the fellow who went up to the Pearly Gates, and St. Peter said, "Well, where are you from?" He said, "I'm from Los Angeles."

"Oh. Well, you can go in, but you won't like it."

We have had a marvelous day together, and we thank Dr. Beadle tremendously for his contribution to the colloquium. With these few words I present him to you for the talk of the evening, Dr. Beadle.

Dr. Beadle: The title of the talk I shall give tonight is somewhat of a misnomer. I do not presume to be able to do what the title implies and integrate genetics with all the other biological sciences. Rather what I should like to do is give you an example of one way in which some of genetics can be integrated with some of the rest of the biological sciences. This attempt will be built around work that we have been doing at Stanford in the past two or three years, and represents what, in my opinion, is one way in which problems of this sort can be tackled.

With the increasing amount of information that we have about the various fields of science it becomes almost impossible for any one human being to know enough about enough branches to put our knowledge together in the best possible way. Accordingly, it is becoming more and more essential that many of these problems be attacked by groups of investigators working as teams. On the Oregon State campus you have seen a number of examples of this. One is the vitamin investigations started at Oregon State College by Dr. Roger J. Williams. Another is the work now under way on the campus under the direction of Dr. Wulzen and Dr. van Wagendonk. In both of these examples investiga-
not reverse the procedure? Instead of selecting a character and then trying to work out its chemical basis, why not first decide what chemical reactions we could best study and then find genes influencing them? This sounds simple and actually it is. But at first, as is so often the case, knowing what we wanted to do was very much easier than knowing how to do it.

It finally occurred to us that what we ought to do is select reactions, the products of which are essential for the life of the organism and can be supplied from the outside, and then look for gene mutations affecting these reactions. Thus if we obtained a mutant individual unable to carry out a vital reaction we could prevent the death of the organism by supplying the product of the reaction from an external source. These considerations suggested the use of the reactions concerned with vitamin and amino acid synthesis.

We know in the case of ourselves that we get our vitamins from an outside source. We know further that lower plants and lower organisms make their own. The same is true of amino acids. We get our vitamins and amino acids in our diets. The organisms that make these in the first place are, in general, plants. If these essential substances are made under the influence of genes, it should be possible to take an organism that makes a specific one of them and induce a mutation that will modify the organism in such a way that it can no longer make the substance in question. For example, we know a corn plant makes vitamin B₁ because it can be grown in the complete absence of this vitamin and after it is grown we can extract B₁ from the tissues. The organism obviously must make that vitamin from inorganic substances taken up through the roots and leaves.

It should be possible to make a corn plant unable to make B₁ by causing the right genes to become inactive or to mutate in some other way so that it would be dependent on an external source of B₁, if B₁ is necessary. We are reasonably sure this vitamin plays such a fundamental part in cellular metabolism that no organism can live without it.

The corn plant, however, is not a favorable organism with which to carry out this experiment. For one thing it requires too much space. More important, an adequate control of its nutrition, although possible, is out of the question from a practical standpoint. Protozoa are possible but are unfavorable organisms from the standpoint of nutrition. Bacteria do not have sexual cycles and hence are not favorable organisms for genetic studies. The algae offer possibilities. They have the advantage of being completely autotrophic, and some are favorable in other respects. Unfortunately, they are not ideal from a genetic standpoint. The fungi seemed to us to offer a better bet. In considering members of this group it occurred to us that Neurospora, which has been worked on since 1928 by B. O. Doge, Lindegren, and others, was practically ideal from both genetic and biochemical standpoints. Its one serious drawback is that it is difficult to observe its chromosomes in any detail. At the outset of our work with Neurospora we knew very little about its nutrition. On investigation it became evident that it could make everything it needed in the way of vitamins and amino acids except the one vitamin biotin. It will not grow unless supplied with this substance, but fortunately this recent member of the B-Complex had just become available in pure form. More recently it has become available in synthetic form. With this exception Neurospora must make everything it needs from a carbon source and from inorganic salts, that is, sugar, nitrate, phosphate, and other inorganic salts.

On the assumption that this organism requires vitamin B₁, it must make it. We ought to be able to produce a series of mutant strains by treating with X-rays or ultraviolet rays, and if we look long enough, we should find a strain that can no longer make this substance. The simplest way to do this experiment is to treat the organism and establish homogeneous strains of it in the presence of B₁. Loss of ability to make B₁ can be tested for by transferring asexual spores to a medium containing no B₁. Failure to grow on such a medium is indicative of loss of ability to make B₁. The inheritance of this character can be easily tested by crossing the strain that cannot grow in the absence of B₁ with the original and observing the descendants. What this procedure amounts to is growing the organism in the presence of what you want it to lose the ability to make, inducing mutations, and then testing by taking the substance away—in this case B₁. Since we could be unlucky and not find a strain unable to make B₁ in a reasonable number of tests it would be wise to increase our chance by looking for more than one kind of a mutant. This can be done by adding B₂ to the original medium. The test for loss of synthetic ability can then be made by transferring to a medium deficient in both B₁ and B₂. If the strain tested does not grow, it lacks the ability to make one or the other of these substances. We
can determine which it is by supplying each alone. Actually, as you can see immediately, one might as well keep on adding to the original medium. For example, B₆, nicotinic acid, pantothenic acid, choline, folic acid, p-aminobenzoic acid, and other vitamins could be added. We might also just as well add the known amino acids, the building blocks of proteins. All organisms have to have a certain group of these amino acids and the same reasoning can be applied to their synthesis as that outlined for vitamin synthesis.

After we have added all the known vitamins, we might just as well include some that are unknown if there are such. The organism cannot know whether we know the chemical nature of a certain vitamin or not. It is just as likely to lose the ability to make one we do not know about as it is one we do. Theoretically, these substances can be added by grinding up the organism being worked with and adding this to the medium. In this way all the unknown vitamins that it needs can be added unless some are destroyed in the grinding. Known and unknown amino acids are also added. Actually what is used is a commercial preparation known as yeast extract. This is the water soluble portion of a yeast antolyzate. Since yeast is a fungus belonging to the same group as Neurospora, it presumably contains the growth factors necessary for almost any mutant that might arise.

In terms of the procedure actually used, we x-ray the fungus at some convenient stage in the life cycle, pass it through meiosis and isolate single ascospores to insure genetic homogeneity. These are cultured on a medium to which all available growth factors have been added—the so-called “complete” medium. Tests for loss of synthetic ability are made by transferring asexual spores to a medium containing only the minimal requirements of the original wild-type strain—a “minimal” medium. Strains that do not grow on minimal are further investigated to determine what it is they have lost the ability to make. These tests are made in a systematic manner by adding to minimal medium one vitamin, amino acid, or other growth factor at a time. If the ability to make one specific substance is lost through mutation, this particular substance and no other will produce a growth response when added to minimal.

As an example, strain 5531 grows on complete but not on minimal. Minimal supplemented with known vitamins supports growth but a supplement of the amino acids found in casein is without effect. When added individually, pantothenic acid promotes growth. No one of the other vitamins gives this response. We conclude from this that strain 5531 has lost the ability to synthesize pantothenic acid.

Several methods of studying growth are used. In one, horizontal tubes half filled with an agar medium are used. If these tubes are inoculated at one end, the normal wild type will grow down the tube at a steady rate which is about 4 mm. per hour under standard conditions at a temperature of 25°C. On unsupplemented medium the wild type will grow perfectly well. A mutant strain such as 5531 which cannot make pantothenic acid will not grow.

If a small amount of pantothenic acid is added, slow growth results. With increasing amounts of pantothenic acid, increasing growth takes place. If the right amount of pantothenic acid is supplied, growth takes place at a normal rate. This behavior shows that the only thing wrong with strain 5531 is that it cannot make pantothenic acid.

To make the story brief, by making this type of test on something like 90,000 different strains we have found about 250 that cannot make various specific compounds.

If the one strain that cannot make pantothenic acid is crossed with wild type and the resulting ascospores removed from the asci in order and planted in tubes containing media containing pantothenic acid, all the spores will germinate and all resulting mycelia will grow normally. If conidia are taken from each of these tubes and transferred to a set of tubes without pantothenic acid, four of them will grow and four will not. This result indicates that the difference between the wild type strain and strain 5531 that cannot make pantothenic acid lies in a single gene. Actually, this result has been obtained repeatedly with mutant 5531. Incidentally, in Neurospora, because of the manner in which the meiotic products are recovered, ratios are mechanical, not statistical. There can be no deviation from the 4:4 ratio in a single set of eight ascospores.

Other similar examples [illustrated by slides in the oral presentation] include strains unable to synthesize vitamin B₆, vitamin B₃, nicotinic acid, and choline. In all cases these "errors in synthesis" are inherited as single gene characters. By crossing two different mutants, double mutants that must be supplied with two growth factors can be built up.

It is clear that genes are vitally concerned in the biosynthesis of vitamins in Neurospora. This
is just as true of other substances. For example, we know that Neurospora can build up its nitrogenous compounds from nitrates supplied in the medium. Among such compounds are the amino acids. In such a plant as Neurospora it is supposed that the first step in the utilization of nitrate involves a reduction of nitrate to nitrite, a reaction catalyzed by the enzyme nitratase. Further reduction converts nitrite nitrogen to ammonium nitrogen, which is then built up into various kinds of organic molecules including amino acids. We know that the first step in nitrate utilization is genetically controlled because we have found in Neurospora a mutant strain unable to grow on nitrate nitrogen, but able to utilize nitrate or ammonium nitrogen quite satisfactorily. This strain differs from wild type in a single gene.

We have obtained a series of mutants in which individual amino acids such as lysine, leucine, methionine, arginine, tryptophane, proline, and others cannot be made. Again, these mutants differ from wild type in single genes only.

Aside from telling us something about what genes are and what they do, there are at least three ways in which induced mutations concerned with specific reactions are of use to the biologist, viz.: (1) in providing material for biological assays for known compounds of biological significance; (2) in providing means of detecting and measuring substances of unknown chemical nature that are of concern to the organism, e.g., new vitamins, amino acids, and other substances; and (3) by making it possible to identify precursors of biologically important compounds that are accumulated by mutant strains as a result of genetic blocks.

As an example of the first use, mutant strain 4545 cannot make the essential amino acid lysine. It responds quantitatively in growth to lysine in the medium, and accordingly it can be used in measuring the amount of lysine in a protein, crude food material, or other mixture of substances containing lysine.

If a mutant strain requires a growth factor not identical with any known vitamin, amino acid or other known growth-promoting substance, it is useful as a specific qualitative and quantitative test for the new growth factor. As we are all aware, the known vitamins were first identified as such in essentially this way. It is a trivial difference that the organisms used for this purpose in the past have been naturally occurring ones rather than ones modified deliberately by man.

The third suggested use of mutant strains is not essentially different from the one just discussed but, being more general in its application, it is perhaps more important to biology in general. The identification of precursors of biologically important substances is synonymous with increasing our understanding of biosynthetic processes. This is important because biosynthesis is a field about which relatively little is known at present. Until recently I have had little appreciation of the extent of our ignorance in this field. I had naively imagined, as I suppose other biologists do, that if one wanted to know about the biosynthesis of the amino acid lysine, all one needed to do is to look in a treatise on biochemistry and find out. After all, are not questions concerning how organisms make their constituent chemical compounds ones which biochemistry might properly be expected to answer? As a matter of fact, very little is known about how any organism makes any compound of biological significance. How man does it in a test tube often tells us very little as to how the organism does it in vivo, for the methods of in vitro synthesis are usually much more violent than those available to the living cell.

Homogentisic acid in man is an example of the accumulation of an intermediate in metabolism by a mutant form. The study of alcaptonurics has shown the relation of this substance, not found in normal persons because it is immediately transformed, to phenylalanine and tyrosine. Were it not for the existence of alcaptonurics with their genetically defective metabolic machinery, the role of this substance, or even its existence, might never have been discovered.

Examples similar in principle can be cited in Neurospora. One of these involves the so-called ornithine cycle. It is known that in the mammalian liver the amino acid arginine is enzymatically hydrolyzed to give rise to ornithine and urea. Ornithine is converted to arginine through the intermediate citrulline. Ornithine combines with CO₂ and NH₃, to give citrulline. Citrulline plus another molecule of ammonia goes to arginine. The process is repeated in a cyclic manner. With each turn of the cycle one molecule of urea is formed. Srb and Horowitz working at Stanford with various mutant strains of Neurospora have shown that the ornithine cycle is present in Neurospora. Some mutant forms are unable to make ornithine. They are enabled to grow normally if supplied with ornithine, citrulline, or arginine. Others are unable to convert ornithine to citrulline and require for growth either citrulline or arginine—ornithine will not do. A third genet-
succeeded in making this reaction take place in a test tube.

All this is very fine, but how are indole and serine made in the organism? Unfortunately, we cannot answer this for serine, but an extra step can be taken in the case of indole. Tatum and Bonner have shown that there are two types of Neurospora mutants that cannot make tryptophane. Both types are able to convert indole to tryptophane according to the reaction described. But one accumulates a precursor of the indole nucleus which has been isolated from the culture medium and shown to be anthranilic acid. The second type of mutant is able to use this anthranilic acid to replace indole in tryptophane synthesis. Anthranilic acid is a precursor of indole. Tryptophane synthesis therefore takes place as shown at the bottom of the page.

In mutant type b anthranilic acid cannot be further converted and therefore accumulates. This cannot be synthesized from anthranilic acid but can convert it to indole and tryptophane if it is supplied from an external source. Theoretically, it should be possible by studying additional mutant types to determine how anthranilic acid and how serine are made.

The method of using genetics to help work out sequences of synthesis in the organism can be applied to many systems of reactions, although one might expect to run into complicating factors such as toxicity of accumulated precursor, irreversible transformation of precursors, etc. The implications of the type of work described with regard to nutrition are clear. All organisms require certain basic organic compounds for use as building blocks, as parts of enzymes, or for other reasons. Some organisms such as photosynthetic plants make all of these substances from inorganic materials. Parasitic and saprophytic organisms in general differ from their autotrophic ancestors in being less complete synthetic machines. We, for example, have lost the ability to make carbohydrates, the ability to make amino acids from inorganic nitrogen, and the ability to make vitamins and other growth factors. We
must therefore have in our diets a carbon source, proteins or other sources of amino acids, plus an array of vitamins. These losses in synthetic ability presumably represent genetic changes. By combining the right genes, we could make an artificial form of *Neurospora* very much like man from a nutritional standpoint.

I now return to the basic questions of biochemical genetics. What is a gene? What does it do? And how does it do it?

Various lines of evidence converge in indicating that a gene is an entity like a virus molecule, made of nucleoprotein, capable of reproducing, and in some way determining how the organism of which it is a part will develop and function. This summarizes in a very brief way the best answer I can give to the first question.

We have already seen numerous examples of what genes do. We believe that these various activities can be reduced to the control of specific chemical reactions—one gene, one chemical reaction. This is at least a tentative answer to the second question.

The answer to the third question involves even more speculation and accordingly should be regarded as correspondingly less satisfactory. Most biochemical reactions are enzymatically catalyzed. The enzymatic catalysts, unlike inorganic catalysts, are remarkably specific. These specificities are based on protein configurations and these in turn are presumably under direct genetic control. How this genetic control of protein specificity is brought about is not understood but it is possible that genes control the configurations of cellular proteins generally in essentially the same way in which they control their own specificities during reproduction. This may involve the gene acting as a model or template. This amounts to saying that daughter genes that remain in chromosomes are genes while those that do not remain in the chromosomes become nuclear or cytoplasmic proteins—antigens, antibodies, enzymes, structural proteins, etc. Summarizing this view of gene action, we can say that reactions are controlled by enzymes, that each enzyme is characterized by a specific protein, and that each specific protein has its specificity set by a particular gene. This is not to say that one gene has control of the entire synthesis of a particular protein but rather that it oversees the final putting together of the constituents to give a particular pattern. The synthesis of the constituent parts such as the individual amino acids requires the intervention of many other genes and, as one goes from primary to secondary to tertiary genetic control, the interrelations become more and more difficult to comprehend. This is why the problem of how genetic control is brought about appears in so many instances to defy solution. We can at least hope that when we have put our fingers on the primary control, the manner of action of the gene will prove to be simple.

**DR. ZELLER:** Dr. Beadle has opened up some problems here in pathology, physiology, biochemistry, mycology, and the whole category of biological sciences. I think that if he is not too tired we could spend a few moments asking him questions, if you so desire.

**QUESTION:** Are there any group reactions that are common to two different substances?

**DR. BEADLE:** We have one mutant, studied by Bonner and Tatum, that is concerned with the synthesis of two amino acids. One of these is isoleucine and the other is valine. These are closely related, differing by one methylene group. It is probable that the gene concerned in this mutation controls a reaction which both substances have in their synthesis.

**DR. SMITH:** Have you found any need for two genes to control a single reaction?

**DR. BEADLE:** Every time we find an instance in which two genes are concerned, the mutant strain requires two substances. We have not found a case in which two genes control a single reaction.

**DR. ZELLER:** That was an inspiring talk on your inspiring work, Dr. Beadle, and you have let us in with you on some very basic facts and knowledge.

**DR. BEADLE:** Thank you very much. I have thoroughly enjoyed my visit to Corvallis and want to thank all of you for your hospitality and kindness.
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