Science's Mass Attack on Tuberculosis

Physiology

By Watson Davis

Hundreds of pounds of deadly microbes, carefully tended and amply fed, are now being turned over to the chemists to be torn into their constituent chemicals. The most intimate, deadly secrets of the germs are at last being revealed by orderly chemical analysis and biological experiments.

When the secret of the pestilential activity of these parasites of the cell is found out, the doctors will be in a position to devise methods of counteracting it, for they will no longer have to work in the dark as they do today. And the results so far of science's mass attack on tuberculosis, the first disease thus attacked, foretell the revolutionizing of present methods of treating and controlling disease.

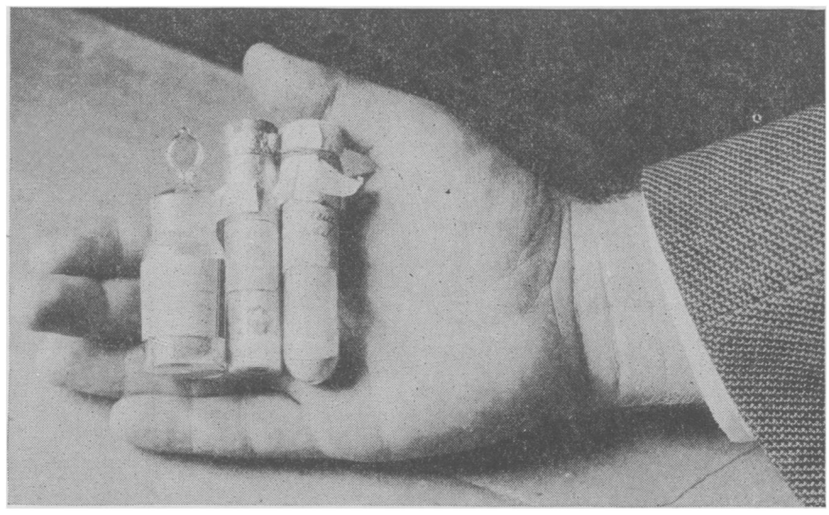
Out of the chemists' test tubes into which great masses of tuberculosis bacilli had been fed there came the world's first poisonous sugar, worth hundreds of dollars an ounce, armed with the ability to cause the death of a sufferer from tuberculosis if only a small amount got into his blood.

Out of this large scale analysis of germs there also came a fatty substance which, though containing no living germs whatever, could produce the characteristic tubercles or clumps of changed cells caused by the germ of tuberculosis.

Because of these novel methods of attack upon the great white plague, there is hope that the tuberculosis bacillus may be checked in its invasion of the human race.

Dozens of chemists and medical research scientists are now engaged in medicine's greatest offensive drive against tuberculosis. Marshalled under the auspices of the National Tuberculosis Association and financed in part by the pennies that little children provide through the purchases of Christmas seals, these medical warriors are using a new method of medical warfare. They capture the germ itself and split it up into its parts and then determine which of the chemicals within the germ are guilty of producing the harmful effects.

The turning point in the Great War came when the Allied forces fighting the Germans joined in a single coordinated plan of campaign under unified control by the appointment of General Foch as commander-in-chief of all the armies. The turning point in a greater war may likewise date from the day when the allied forces fighting the germ of tuberculosis thus joined in a single coordinated plan of campaign under unified control in charge of the Research Committee of the National Tuberculosis Association. This means a revolution of the major strategy in the conquest of disease, the adoption of the policy of siege tactics and trench warfare on a larger scale instead of relying upon accidental advances and the casual attacks of individual investigators as in former times. Progress under the new plan may be slow, but it is sure, for each foot of ground gained in advances into unknown territory is securely held. A small army of experts has volunteered service in this field—chemists, bacteriologists, druggists, physiologists and physicians, more than a hundred of them, working in various parts of the country on the common problem.



EACH KIND OF BACILLUS has its own kind of sugar. In these small bottles are, from left to right, sugar from the timothy grass bacillus, from avian tuberculosis bacillus and from human tuberculosis bacillus

The first objective of the new campaign is the discovery of the cause of the disease. After that is attained the way will be opened for the discovery of a cure.

It has long been known that tuberculosis is due to certain plant-like parasites, bacilli, or in plain English, "little rods", which find a lodgment in the cells in the lungs or other parts of the body and there form nests or colonies, in the shape of little nodules, the characteristic "tubercles". But we must know more about these bacilli before we can fight them effectively. How does it happen that these little creatures have the power to pull down a strong young man? Why is it that a little local colony of these microscopic invaders can set up fevers and sweats in the entire frame and cause him to weaken and waste away? Do they poison him or what? Do the dead germs or the live ones do the damage? What are they made of? What do they give off while living? What do they leave when dead?

Obviously, the first step in the investigation was to set the chemists to analyzing the T. B. bugs. But the chemists demanded that they be supplied with the material to be analyzed by the pound, even by the hundred pounds in the long run. So two of the leading manufacturers of medicines, H. K. Mulford Company and Parke, Davis and Company, undertook to cultivate the creatures that they proposed to destroy. Fortunately, it was found that the tuberculosis bacillus, unlike many microbes, could be made to grow outside of animals and without any animal matter. They would thrive in glass flasks filled with nutrients of known composition, made up of pure chemicals. Consequently, any new substances discovered in the dead and dried germs, or in the solutions where they had lived, must be such as have been formed by the creatures themselves and such as they release inside the body. In this mass of crude material, then, we may expect to find the products that exert the deleterious effect upon the human system. (*Turn to next page*)

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SOME OF THE SCIENTISTS who engaged in the great drive against tuberculosis. From left to right: Dr. Esmond R. Long, University of Chicago; Dr. William Charles White, Washington, D. C.; Dr. Rudolph J. Anderson, Yale University; Dr. Florence R. Sabin, Rockefeller Institute for Medical Research, New York City; Prof. Treat B. Johnson, Yale University; and Dr. C. A. Doan, Rockefeller Institute for Medical Research, New York City

Although the chemical work may be said barely to have begun, yet it has already resulted in startling discoveries. Two, in especial, are altogether unexpected and without precedent. There has been found, among the toxic constituents of the T. B. germs, two that belong to two of our most familiar food families: an unknown fat that may form tubercles and an unknown sugar that may be fatal under certain circumstances. All the fats and sugars known hitherto are nutritious and innocuous. Not a disreputable member among the scores of fats and sugars found in nature or the hundreds that can be formed by the chemist.

But the newly found fat when injected into an animal will form the same sort of tubercles as are produced by the living germs. This fat is, of course, devoid of life; in fact, has been freed from all other substances in the complicated chemical process of purification. Probably when its structure has been worked out it will be found possible to make it artificially from mineral matter in the laboratory. It consists of an oil containing phosphorous and is a compound hitherto unknown to chemistry, although it contains the same elements as the common fats and it seems similar in constitution to the ordinary fatty acids of foods, such, for instance, as stearic acid. Yet it is capable of producing all by itself the same little nodules that are characteristic of the disease and have hitherto been found only in the colonies of the living bacilli. The first effect of the injection of this fatty fraction is to stimulate the growth of the particular kind of blood cells that the T. B. bug lives in, and the abnormal multiplication of these cells upsets the balance of the body cells. After twelve doses of this compound, each dose containing as much of the substance as is contained in a gram of the dried "bugs", the tissue shows lesions closely resembling those of the disease. If the injections are not continued the lesions become gradually absorbed and almost disappear in a few months.

Other fractions from the chemical analysis of the cultivated bacilli consist of fats and waxes that have a similar effect in stimulating and disintegrating the cells of living tissues. This action of this substance is similar to that of the unknown cause of cancer, since this likewise excites the cells to abnormal multiplication and later results in their destruction. The tuberculosis bacillus invades the living cells and there lives and multiplies. This causes the cells to enlarge to an abnormal size and shape and these clumping together form the nodules known as "tubercles". This disastrous effect is perhaps due to some substance such as these that are now being isolated, excreted by the living microbes or coming from the decomposition of their dead bodies.

The experiments showing that the characteristic tubercles could be produced by this new, germless chemical compound were performed by Dr. Florence R. Sabin and her associates, Drs. Charles A. Doan and C. E. Forkner, of the Rockefeller Institute for Medical Research in New York City. They worked with one of the fractions extracted from the tuberculosis bacilli by Prof. Treat B. Johnson and Dr. R. J. Anderson of Yale University.

The achievement of Dr. Sabin and her co-workers is revolutionary. By it the most characteristic change produced in the body by a germ-borne disease has been obtained without the germ entering the body. This is the first time this has been done for any disease and introduces a new technique into the study of disease.

The other discovery is still more unexpected. This is a strange sugar which, when injected into the blood of a tuberculous animal, will kill it quickly. Yet it is harmless to an uninfected animal. Somehow the sugar knows. It can make a diagnosis like a doctor—or better than some. Yet the sugar is a white, harmless looking powder, sort of sweetish like the other sugars, made of the same elements, so it is peculiar that it should prove to have poisonous properties. It seems to act directly on the adrenal glands, causing sweats and fevers, for the secretion of the adrenals controls the temperature reactions of the body. We may surmise in advance of evidence that the familiar symptoms of the disease and its final effects may be due, in part at least, to the constant leaking into the blood of this pernicious product from the T. B. germs as they die and decompose inside the cells of the afflicted individual and so slowly poison him.

These strange effects of this deadly sugar were discovered in tests made by Dr. William Charles White of the U. S. Hygienic Laboratory, who is also the chairman of the research committee of the National Tuberculosis Association. The sugar itself is another fraction split from the tuberculosis bacilli by Prof. Johnson and Dr. Anderson.

This is not the only case of sugar found in disease germs, for recently some unknown sugars have been extracted from pneumonia material.

The healthy person can for a time withstand the (*Turn to next page*)

Pavlov Reports New Theories on Brain

Psychology

The part of the brain lying immediately below the two cerebral hemispheres is the most important part of the nervous system in maintaining the relation of the individual to the outer world, Prof. I. P. Pavlov, famous Russian physiologist, told the International Congress of Psychology which has just closed its sessions at New Haven.

Prof. Pavlov, who is now 80 years old, is still eagerly carrying forward his quest for knowledge as to how the brain works. Describing the latest discoveries from his Leningrad laboratory, he stressed the close and strategic connection between the hemispheres of the brain which form the switchboard for the most complex conditioned, or learned, reflexes, and the sub-cortical part of the brain lying immediately beneath the hemispheres, which is the center for the most complex unlearned reflexes such as those dealing with food, sex, and self-defense.

"On the basis of the most recent experiments, I find it justifiable to separate the reflexes of these two centers from the rest of the nervous activity under the special name of the highest nervous activity," the physiologist stated.

The study of the mutual relation of these two highest parts of the brain must become one of the most important problems of the highest nervous activity, he declared.

"First of all," he explained, "the cortical conditioned reflexes are formed by means of the sub-cortical centers. A certain degree of excitability of these centers is the essential condition for the formation of the connection between cortical cells and sub-cortical centers. For instance, if an animal is already fed before an experiment, it is difficult or even impossible to form the conditioned reflexes on food."

Prof. Pavlov's experiments lead him to the conclusion that the strength and real significance of the activity of the brain hemispheres rests upon the activity of the centers just below the hemispheres. And, on the other hand, the hemispheres serve as regulators of the centers below.

The cells of the brain hemispheres are continually protected against over-stimulation, he pointed out. If a stimulus from without exceeds the maximum limit, inhibition sets in to prevent the brain cells from so intense a stimulation. The same sort of inhibition acts as a guard if the sub-cortical centers become over-excited and attempt to send in too intense messages of hunger, for instance, to the highest brain centers.

Referring to the inhibition resulting from too intense excitation in the sub-cortical center, Prof. Pavlov explained that "this fact is obviously a vital one, as it distorts the actual normal relations and furthermore gives a satisfactory explanation of hysteria."

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pernicious influences emanating from the infected area, but as these increase and his resistance weakens, he fails to react as at first and the rising and falling of his temperature becomes more extreme. We may hope that eventually the chemists will find something that will break down the waste poison of the tuberculosis bacilli into glucose or other harmless substances.

Out of these researches there may arise a new conception of life itself. It may prove that sugar is the basic life material. Heretofore fats and proteins have been considered the most characteristic substances that enter into living matter. Sugar seemed to enter into the composition of living things somewhat incidentally.

But these researches upon tuberculosis show that even the various strains of tuberculosis germs have their own, radically different sugars. The avian bacillus yields a sugar chemically and physiologically unlike that in the human or bovine sort. Recent research upon the sugars contained in the germs causing pneumonia, the pneumococci, shows that each germ of this group has its own sort of sweet.

So there is beginning to be built a new theory of the chemical nature of life, founded on sugar specificity. Even the green leaf of the growing plant in which the sunlight builds carbohydrates may have its secrets unlocked by a continuation of the investigations that the tuberculosis work has pioneered.

It is already obvious that the new tactics for the investigation of disease, while at first focussed upon the tuberculosis problem, will throw light upon other diseases and, in fact, upon the fundamental processes of human physiology. For the three grand classes of components found in these laboratory-raised bacteria, that is, fats, sugars and proteins, are the same as constitute our bodies and our food. But how these three kinds of compounds combine in the body is still a mystery. The chemist has isolated and determined the composition and construction of all the common fats, sugars and proteins. Some of them he even can make synthetically in his laboratory. He can figure out closely just how much of these various ingredients of the food are needed for a particular day's work. He can tell, for instance, just how many more foot-pounds a man can lift by adding an ounce of glucose to his ration. The chemist can trace the molecules of glucose through the blood stream till it gets to the muscle where it is needed. But there he loses track of it. He is still much in the dark as to how the protein in the muscle fiber seizes on to the sugar and gets energy out of it and what part is played by the phosphorized fatty acids present. If he can find out how these three substances are hitched up in normal life, he would most likely be able to find out how they hitched up wrongly in disease and finally how to correct the blunder.

Two major outposts have been taken, but the battle has not yet been won. Among the scientific organizations joining with the National Tuberculosis Association in the attack are: U. S. Public Health Service; U. S. Bureau of Animal Industry; National Research Council; American Sanitorium Association; Henry Phipps Institute, Philadelphia; Edward L. Trudeau Foundation, Saranac Lake; Rockefeller Institute for Medical Research, New York; University of California; University of Cincinnati; University of Chicago; Cornell University Medical School; the Johns Hopkins University; University of Nebraska; University of Pennsylvania; Vanderbilt University; University of Wisconsin; Yale University; H. K. Mulford Company; Parke, Davis and Company.

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