New Strategy in the T. B. Campaign

Therapeutics

By Edwin E. Slosson

The turning point in the Great War was 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 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 large 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 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.

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 for the disease. 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 have got to 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 undertook to cultivate the creatures 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.

Although the chemical work may be said barely to have begun, yet it has already resulted in startling discoveries. Two, especially, 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 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 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.

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 others, 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 (*Turn to next page*)

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Toxic Sugar is Tuberculosis Poison

Pathology

The world's first poisonous sugar has been discovered lurking within the tuberculosis germ. Although it is harmless to uninfected animals it is death to those suffering from tuberculosis. Produced by the tubercle bacillus itself it is probably the stuff that slowly poisons the victim of the white plague.

Such is the latest news from a great cooperative research effort directed at a greater knowledge of the disease and an eventual use of this knowledge in saving human lives. To the National Tuberculosis Association meeting at Atlantic City last Tuesday, Dr. William C. White, of the Hygienic Laboratory of the U. S. Public Health Service at Washington, brought his test results that showed the deadliness of the new polysaccharide isolated from tuberculosis germs by Dr. R. J. Anderson, Yale chemist.

Never before in medical or chemical history has a sugar been shown to be poisonous. But a small amount of this white, innocent looking sweetish substance injected into a tuberculous animal causes its death in four to five hours. A well animal similarly treated shivers, then runs a temperature, its white blood cells decrease, showing that the sugar has some effect on the healthy body even if the consequences are not tragic.

This is the second startling discovery in the course of cooperative research by twenty-one organizations and dozens of scientists under the general directions of the National Tuberculosis Association. Last month Dr. Florence R. Sabin of the Rockefeller Institute for Medical Research, New York City, revealed that a germ-free fat, obtained from chemical analysis of the tuberculosis germ and similar in composition to food fats, will cause the characteristic tubercles of the disease. This inaugurated a new technique in disease study.

As a necessary preliminary to these discoveries of new roles for sugar and fat, Profs. Treat B. Johnson and R. J. Anderson at Yale undertook large scale chemical separations of bacteria into their component compounds. H. K. Mulford Company and Parke, Davis and Company grew many pounds of various sorts of tubercle bacilli under rigorous conditions to supply the raw materials for the separations.

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.

Other phases of the National Tuberculosis Association's cooperative attack on the fundamentals of the disease were discussed at the meeting during the past week. Among the organizations joining with the association in its attack are: U. S. Public Health Service; U. S. Bureau of Animal Industry; National Research Council; American Sanatorium Association; Henry Phipps Institute, Philadelphia; Edward L. Trudeau Foundation, Saranac Lake; Rockefeller Institute for Medical Research; University of California; University of Cincinnati; University of Chicago; Cornell University Medical School; 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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New Strategy in the T. B. Campaign—*Continued*

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 fatal 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.

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 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 tubercle bacilli into glucose or other harmless substances.

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 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 until they get to the muscle where they are needed. But there he loses track of them. 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 get hitched up wrongly in disease and finally how to correct the blunder.

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