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SULFANILAMIDE, THE GERM FIGHTER

In December of 1936, when a son of the President of the United States lay in a Boston hospital dangerously ill of a streptococcal infection, and then suddenly recovered, newspapers reported that his cure had been wrought by a strange chemical just out of Germany, a reddish dye called "prontosil." The truth is that prontosil probably had nothing to do with the relief of young Roosevelt. Its administration was begun late one night, but hardly more than begun when the very limited supply of the chemical in the hospital ceased to be available, and it was only after a resort to surgery that the patient recovered. However, the wide publication of this "cure" spread the news of prontosil, and perhaps no pharmaceutical find of the 1930's has had so much favorable publicity.

Nor is the fame undeserved, despite the element of fiction in the reputed cure in Boston. For there are plenty of places in which the chemical was administered in doses sufficiently large to get results, and in scores of cases patients afflicted with blood poisoning and other germ diseases were restored to health.

Some months before the Boston episode, Dr. Leonard Colebrook and his associates at Queen Charlotte's Hospital, Hammersmith, London, tried the drug on women suffering from the streptococcal infection associated with puerperal or childbirth fever. By this treatment they reduced the death rate from such infections 25 per cent. The Foundation has a special interest in the results at Queen Charlotte's, for the study of puerperal fever there is supported by a grant of \$105,000 to the British Medical Research Council. The grant was made in 1931 for a seven-year period, payable at the rate of \$15,000 annually, and the 1936 experiments with the

chemical were conducted as part of this research. Today prontosil and its derivatives are coming into use in many maternity hospitals as a powerful ally against this highly dangerous disease.

But Colebrook and his associates were not the pioneers in the new chemo-therapy. For its beginnings we must go to Germany. In May of 1933, Dr. Foerster at Dusseldorf reported to a medical society that he had just cured a child of severe staphylococcal infection by using "streptozone." Streptozone was the trade name of a dye which the I. B. Farbenindustrie Werk had synthesized the year before. For some reason the company's chemists thought the preparation would have medical value; so they had sent samples to a number of physicians throughout Germany. Foerster was the first to report a favorable result, but he was followed by others, and the clinical records of these cures began to appear in medical journals.

Meanwhile, the I. B. F. changed the name of streptozone to "prontosil." Nobody knows why. Some wag suggested that it was coined from the Spanish "pronto," to suggest swift germicidal action, but Professor Horlein of the company's technical staff denies this. "It's just a convenient name - that's all."

Although there had appeared these reports of remarkable recoveries, there was no strictly scientific proof that the chemical was the curative factor. Other agencies might have been working for the patients, and it is never safe to generalize from a few scattered clinical results. But in February, 1935, a German scientist, G. Domagk, published the results of experiments with mice under carefully controlled laboratory conditions. He was able to show that of a group of mice of the same age infected with streptococci, those that were treated with prontosil

recovered, those that received no prontosil died. He was able to check further on the prontosil, and found that wherever it permeated, the activity of the white blood cells in attacking and destroying the streptococci was increased. Apparently the actual germ killers are the white blood cells, the function of the prontosil being either to stimulate them or to render the bacteria vulnerable.

Soon after Domagk's report, chemists at the Pasteur Institute in Paris subjected prontosil to organic analysis, and they made an interesting discovery. They found that its activity is localized in one distinctive part of its molecular structure. This active end, a grouping of one sulfur atom with atoms of nitrogen, hydrogen, carbon, and oxygen, is known as "sulfanilamide." Prontosil is red; sulfanilamide is colorless. Prontosil weighs 586 in the molecular scale; sulfanilamide weighs only 172 - but it is that 172 that is the potent factor in prontosil. Prontosil may be likened to a train of cars with its locomotive, and sulfanilamide to the engine alone. Ironically, we find, sulfanilamide is a well-known compound which has been used in the synthetic dye industry for a quarter of a century. So it turns out that the engine of our bactericidal attack has been with us all these years, its medicinal powers unsuspected, only to be discovered now hidden in the bulkier synthetic structure, prontosil! Today a doctor may give his patient prontosil or, if he prefers, he may administer only the active part, sulfanilamide. The I. B. F. is turning out sulfanilamide in the form of white tablets marked "prontylin," but that is only the trade name for a free compound which many pharmaceutical houses are now dispensing under its chemical name.

The first trials of the new drug in the United States were reported from the Johns Hopkins School of Medicine. Here in the fall of 1936 Drs. Perrin H. Long and Eleanor Bliss tested the chemical in mice infected with hemolytic streptococci, and confirmed the European findings of its effectiveness. In later experiments they tested it on pneumococcal bacteria, then on the gas gangrene effect known as Welch bacillus infection, using mice as experimental material, and obtained favorable results. At the Johns Hopkins Hospital Dr. Long was associated with Drs. F. F. Schwentker and F. F. Gelman in the first successful use of sulfanilamide in the treatment of meningococcus meningitis in human beings. Here, too, early in 1937, Drs. J. E. Dees and J. A. Colston, Jr., found the compound effective in treating gonorrhoea in men.

Many laboratories and hospitals, both European and American, have had part in the research with this sulfur compound. In addition to the diseases already mentioned, it has been found effective in the treatment of certain infections of the urinary tract, and meagre but favorable results are reported from its use with certain virus diseases.

Sulfur has long been recognized as a distinguishing element in many physiologically active substances. It is in insulin, as we have seen. It is the characteristic inorganic element of cystine. And now we find that in the form of sulfanilamide it helps the body to fight some of the more virulent bacteria.