

are almost always women, particularly dangerous when they live on a farm, or are cooks or other persons handling food. Centres of typhoid infection discovered in milk establishments, boarding houses and convents, are generally due to germ-carriers. Such persons must be forbidden all activities which might bring them in contact with food, and they should be obliged to observe the strictest personal cleanliness. Finally, people in their vicinity should be vaccinated.

Some countries are relatively well armed against typhoid fever. As soon as a focus of infection is reported, the patients are isolated, the threatened population vaccinated, and the above mentioned sanitary precautions taken. Then, going to the source of the evil, they protect wells, water-mains, water used in the manufacture of ice, and oyster-beds, and germ carriers are sought out. The best guarantee against typhoid fever is the extension of the water-main system. This, when inspected and chlorinated, gives complete security. In regions where water is so distributed, the only cases to be found are "imported" ones, that is, those due to milk, vegetables or oysters. The location of the infected persons enables us to discover the source of contamination and to remedy this immediately. In regions where the population is too scattered to permit the installation of a main-water system, the sick persons may be isolated, wells and cesspools improved, the necessary precautions taught, and eventually vaccination practised. Efficient sanitary services and education of the public will enable us to so reduce the incidence of typhoid fever as to make it exceptional.—*By courtesy of the League of Red Cross Societies.*

N.B.—The above account of the precautions taken in other countries make us realize how very far behind we are in India. It is hardly surprising that with us typhoid is endemic, and to find whole wards full of these patients. We not only need to educate the public but the municipal authorities; better water and conservancy systems are an urgent need. In the towns the latrines are totally inadequate and the country people have not been given sufficient help in making bore-holes etc. Public Health Acts, such as that passed by the Madras Government, should not only be passed but put into force, and this is not possible until public conveniences are adequate, and proper sewage systems are installed. These measures alone are insufficient. The public must be educated; for this hundreds, if not thousands of Public Health Nurses, Health Visitors and high grade Sanitary Inspectors are needed, under keen medical Officers of Health, who are not encumbered with other work.

In the meantime every health visitor and every nurse should do her best to teach and to help. We feel there should be a great opening for male nurses in this sphere of work.—*EDITOR.*

Blitzkrieg versus Conventional Warfare on Syphilis

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Recent developments in the treatment of syphilis have had many reverberations in the popular press. Rapid methods of treatment have captured the imagination of journalists. It was to be expected that the public would have a keen interest in newer methods of combating a scourge which has bedevilled the human race for centuries, and which has at least three million victims in the United States. For this reason a review of modern methods of the treatment of syphilis may be of interest.

It will be helpful in discussing the newer so-called "five day" and "one day" treatments, to consider the standard or conventional methods of treatment, together with a glance at the historical background of the development of modern specific chemotherapy of syphilis. In reality the entire romance of modern medicine is revealed in the unfolding of our knowledge of the treatment of syphilis.

The first phase begins with the appearance of the disease in Europe in 1493. The true origin of syphilis is still shrouded in mystery, and it is not the purpose of this brief paper to take sides in an old controversy—European versus the American origin of syphilis. Suffice it to say that in the four centuries which followed, consid-

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erable empiric knowledge of the disease was accumulated; that is, information derived through trial and error. It was soon learned that the disease was contagious, and indeed, records of the 16th and 17th centuries contain numerous references to epidemics of syphilis which caused great havoc in a number of communities. The fact that the disease was a constitutional infection, and not a local phenomenon, was noted, together with observations that it lasted for many years. Very early in this empirical era (Paracelsus—1534) the transmission of the disease from mother to unborn babe was suggested.

Early Treatment—Progress in the medical treatment of the disease was slow. Drugs, such as sassafras, gualiaum, china root, and other preparations were used with small success. Mercury was introduced in the treatment of syphilis late in the 15th or early in the 16th century. It was first used in ointment form and applied by vigorous rubbings, to be absorbed through the skin. The only criteria of its effectiveness were the reactions produced, among which were such conditions as severe inflammation of the gums and mouth with loss of teeth, severe gastro-enteritis with bloody diarrhoea, and even acute nephritis which often terminated fatally. It was not until 1750 that Van Swieten introduced a mercurial compound which could be administered by mouth, and which enabled the use of smaller doses with less toxic reactions.

Another great advance in the treatment of syphilis during this period was the introduction of potassium iodide by Wallace in 1835.

Modern Chemotherapy—The dawn of the 20th century, marking the end of the empiric era in the treatment of syphilis, saw a tremendous accumulation of detailed clinical experiences and observations, but no more. Moore has said, "In the first decade of the present century, the most expert physician was in little better position to deal with syphilis, either from the individual or public health standpoints, than his predecessor of 400 years before."

The early years of the 20th century, marking the beginning of the second phase in our knowledge of syphilo-therapy, witnessed a series of epoch-making discoveries which completely revolutionized pre-existing concepts and ideas. The discovery of the causative organism of syphilis, the pale spirochete, by Schaudinn in 1905, and the elaboration of the blood test for syphilis (Complement Fixation Reaction) by Bordet and Wassermann in 1906, set the stage for the discovery of arsphenamine by Ehrlich in 1907. This arsenical compound the 606th substance in the series studied for its lethal effect on the spirochete, was originally called salvarsan. The new drug was released two years later for general use in the treatment of syphilis. The chemotherapeutic problem involved is one of great delicacy: that is, to introduce a powerful germicidal drug in a concentration sufficient to kill the parasite without injury to the tissues of the patient. Ehrlich's ideal was a "therapia sterilisans magna" or rapid sterilization of the body by massive arsenotherapy.

The Arsenical Drugs—Arsphenamine or salvarsan was the first of a series of arsenobenzol compounds found to be of value in the treatment of syphilis. The drug contains about 31 per cent of arsenic and must be alkalinized before use.

Neocarsphenamine was the first of the derivatives of arsphenamine to be used clinically. It contains about 19 per cent of arsenic and may be administered immediately after dissolving it in sterile distilled water, requiring no alkalinization. Silver arsphenamine contains approximately 19 per cent of arsenic and 12.6 per cent silver, dissolves readily in water to form a black solution and requires no alkalinization. Sulphursphenamine is a derivative of neocarsphenamine, contains about 19 per cent of arsenic, and is very soluble in water. It is less irritating to tissues than other drugs of this group, and may be given intramuscularly, while all of the other arsphenamines must be given intravenously.

Mapharsen is an arsenoxide of arphenamine and was known to Ehrlich who, however, rejected it because of its supposed toxicity. It contains 29 per cent arsenic and is readily soluble in water.

Standard or Routine Treatment—Arsphenamine and its derivatives have been used with considerable success in the treatment of syphilis. In the United States

the most comprehensive study of the therapy of syphilis with the arsenical compounds, with and without the heavy metals, bismuth and mercury, was made by the Co-operative Clinical Group, composed of the chiefs of five leading syphilis clinics with the co-operation of the United States Public Health Service. In a series of brilliant studies published at intervals since 1932, many important contributions to American syphilology have been made.

The stage of syphilis which is of greatest importance both to the individual (because of the splendid opportunity for complete cure), and to the community (because of the existence of the communicable or potentially communicable stage of the disease), is early syphilis. The optimum treatment for early syphilis as determined by the studies of the Co-operative Clinical Group is a minimum of 30 arsenical and 40 heavy metal injections given continuously in alternating courses, without rest periods. The average duration of this treatment is about 18 months. Therapeutic results with this method of treatment are excellent; the one drawback is the length of time required. Because of the time element it is common knowledge that only a small proportion of patients persevere until discharged from treatment. The lapse rate, or the number of patients who fail to continue under treatment until cured, is distressingly large. Even in well organized and administered clinics, this loss of patients while still in the communicable or potentially communicable stage of the disease is as high as 80 per cent.

It was logical, therefore, for investigators aware of this unsatisfactory situation to seek "cures" for syphilis which could be achieved in a shorter time. The pioneer work of the investigators in this new method of using existing drugs marks the beginning of the third phase of our knowledge of syphilotherapy.

"Five Day" Treatment.—In 1932 Chargin, for many years chief of the Division of Venereal Disease of the New York City Health Department, proposed that the intravenous drip method, described by Hyman and co-workers in 1931, be used for the treatment of syphilis. Accordingly, Chargin, Hyman and Leifer treated 25 patients with early syphilis using large doses of neoarsphenamine administered by the intravenous drip method for five days. These results were published in 1935. Five years after treatment, 15 of the original group of 25 patients were still under observation. Thirteen of this group were completely cured clinically and serologically.

In 1938 this study was resumed on a larger scale with the active co-operation of the New York City Department of Health and the financial support of several philanthropic foundations.

The conclusion of the active phase of this study in 1940, saw almost 400 patients with early syphilis treated, the first series of 111 patients having received neoarsphenamine, and the remainder having been treated with Mapharsen. The latter drug was found superior to the neoarsphenamine originally used. Approximately 88 per cent of satisfactory results were obtained by the use of Mapharsen, given by the intravenous drip method for five days with an optimum total dosage of 1200 milligrams.

This study proved the stimulus to many variations of the general principle of massive dose arsenotherapy in early syphilis. Moore stated of this work that "This investigation may represent the most important advance in the treatment of syphilis since the original discovery of arsphenamine by Ehrlich in 1909.

Multiple Syringe Method—Seven Days—After observing the use of Mapharsen by the intravenous drip method of the Mt. Sinai Hospital, Thomas commenced rapid massive dose treatment by means of multiple injection at Bellevue hospital in December, 1939. (No facilities for the intravenous drip existed at the hospital.)

A series of 275 patients were treated with Mapharsen alone, 2 injections per day being given for 6 days. Subsequently, the treatment plan was modified to take advantage of artificial fever and the consequent use of less arsenic in the following manner:

2 injections of Mapharsen were given the 1st day;

1 injection of Mapharsen every day for 7 days;

On the 2nd, 4th and 8th days fever was induced by the intravenous injection of typhoid vaccine.