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Nobel Prize in Medicines 1939

Gerhard Domagk

The Nobel Prize in Physiology or Medicine 1939 was awarded to Gerhard Domagk"for the discovery of the antibacterial effects of prontosil".

The following account of Domagk's work is by Professor N. Svartz, member of the Staff of Professors of the Royal Caroline Institute.

Experiments in the treatment of inflammatory conditions by means of drugs and chemicals are known from earliest times, but for the most part the effects were nil or at best insignificant. With certain of these conditions, however, chemotherapy scored some first-class successes at an early date. Mercury is a very ancient, active chemotherapeutic agent, although it has now given place to more effective preparations. Another therapeutic agent which has been in use for a very long time is cinchona bark, the efficacy of which against malaria became generally known in Europe during the 17th century. Other experiments in anti-inflammatory treatment by chemical methods for the most part yielded but meagre results.

It is only during the past few decades that further advances of any great significance have been made in chemotherapy. In particular, experimental investigations with arsenical

preparations and the successes achieved with these preparations in cases of spirochaetic and trypanosome infections (relapsing fever, syphilis, African sleeping-sickness) provided a powerful stimulus to further experiments in the field of chemotherapy. Salts of other metals have also proved valuable in the treatment of specific types of inflammations - for instance, antimony salts have been used very successfully with certain tropical diseases. Particular mention must be made of the Bayer preparations «Plasmochin» and «Atebrin» for malaria and the preparation «Germanin» (Bayer 205) which has been successfully used in cases of tropical sleeping-sickness. In addition, bismuth salts have been found a very effective, though by no means infallible, remedy against syphilis, and have largely superseded mercury.

Thus, whereas it proved possible to attack certain diseases due to protozoa and spirochaetes by means of chemical substances, little success had been achieved with chemical preparations against infections due to true bacteria, namely cocci and bacilli. The theory that bacteria of the last-mentioned categories could not be combated by chemical means therefore continued to gain ground, and it was consequently assumed that serotherapy was the most practicable method of treating infections of this type.

Experiments with gold salts constituted an important phase in the more recent development of chemotherapy. A number of bacterial infections, e.g. septic conditions due to streptococci, rheumatic infections, etc., were found to respond in some degree to these salts, but it soon became clear that the effects varied very widely, and when the doses were increased in an attempt to produce a more vigorous effect serious symptoms of poisoning frequently appeared.

During the past 15-20 years a great deal of work has been carried out by various drug manufacturers with a view to producing less toxic but at the same time therapeutically effective gold preparations. The question of gold preparations and their applicability was also investigated at the great research laboratories of I.G. Farbenindustrie Aktiengesellschaft (Igefa) at Elberfeld. The investigations here were part of a series of experiments conducted with a view to discovering an agent effective against streptococcal

infections. The Igefa laboratory department in which this research was carried out is under Professor Gerhard Domagk, who planned and directed the investigations involving experiments on animals. The chemists Dr. Mietzsch and Dr. Klarer, working in close collaboration with Domagk, provided various chemical preparations for these investigations. It was decided to include sulphonamide compounds among the preparations to be tested. These compounds had previously been synthesized and had also been introduced into the dyestuffs industry by Hörlein and his co-workers. However, none of these compounds had been tested for their therapeutic action.

During the investigations conducted by Domagk and his co-workers 4-sulphonamide-2', 4'-diaminoazobenzene hydrochloride, among other substances, was tested. This preparation was subsequently named Prontosil. The earliest published experiments with Prontosil were begun in December 1932. The lethal dose, for mice, of a certain strain of haemolytic streptococci, which had been isolated from a patient suffering from blood poisoning, had previously been determined. A number of mice were injected with 10 times the lethal dose of this bacterial strain, and approximately half of them were given a specific quantity of Prontosil 1 1/2 hours after being infected.

On 24th December, 1932, it was found that in an experiment begun on 20th December, 1932, all the controls had died, whereas all the mice which had been given Prontosil were alive and well. This was the basis of the discovery which was destined to bring undreamed-of advances in chemotherapy.

The results of these and subsequent experiments, which aroused extra-ordinary interest, were not published until February 1935, whereupon Prontosil and its effects rapidly became known throughout the world. France was the first country apart from Germany where Prontosil was subjected to practical tests (Levaditi). Extensive experiments on, among other things, the mode of action of Prontosil were then conducted in France (Tréfouël, Nitti), America (Long, Marshall, and others) and Britain (Colebrook, Kenny, and others). One result of these investigations was the discovery that the favourable action of Prontosil was mainly due to the sulphonamide component of the preparation.

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From the outset Prontosil was described as being effective principally against streptococcal infections. Even in his first publication, however, Domagk had reported that the preparation had been found to have a therapeutic effect, although to a lesser extent, in staphylococcal infections, and that certain types of pneumonia had also responded to it.

At an early date sulphonamide preparations had proved extremely effective against erysipelas, and subsequent investigations completely confirmed this observation. Now, thanks to these preparations, erysipelas can normally be treated without difficulty.

It was also found that other streptococcal infections could be dealt with by means of sulphonamide preparations, although for the most part not so swiftly or surely as erysipelas. Although suppuration in the pleural cavity and meningitis due to streptococci are still serious diseases, they are much less so than they used to be. The same applies to puerperal fever and several other streptococcal infections. Even chronic general septicaemia with endocarditis, a condition hitherto regarded as incurable, has in isolated cases responded to sulphonamide preparations.

In addition, brilliant results have been obtained with certain infections not due to streptococci, namely gonorrhoea and epidemic meningitis, and, as already mentioned, an effect has also been shown with staphylococcal infections.

This preparation, which is so effective against various coccal infections, has also been used with success in the case of certain infections due to bacilli, e.g. cold infections. Sulphonamide is therefore now the best known remedy against infections of the urinary passages due to colon bacilli. Preparations of this group are also effective against undulant fever as well as, to a lesser extent, other bacillary infections which will not be enumerated here.

The discovery of Prontosil opened up undreamed-of prospects for the treatment of infectious diseases. Experiments with new combinations of sulphonamide preparations were everywhere conducted in the hope that new methods effective against other diseases might be discovered. Contrary to expectation these efforts were very quickly crowned with success.

Igefa reported that a new active sulphonamide preparation, Uliron, had been produced. In addition, the report, published in 1938 by the chemical firm of May & Baker of Dagenham, England, that a compound of pyridine and sulphonamide had been synthesized and had proved effective against pneumonia, was of major importance. This highly significant claim also proved correct. The preparation in question was put on to the market as M. & B. 693. It is now usually known as Sulphapyridine. Sulphapyridine is so far the most noteworthy derivative of Prontosil.

Simultaneously with the efforts to produce new sulphonamide preparations research workers in various countries are busy carrying out theoretical investigations into the mode of action of these preparations and their side-effects. Domagk himself has carried out some extremely fine investigations on these questions. Research in this field has also been conducted in France, Britain, America, Sweden, and other countries.

The foundations for this unprecedented expansion which chemotherapy has undergone in the brief span of less than five years were laid by Domagk and his co-workers. A new road leading to effective treatment of diseases which in the past were often fatal has been opened up. Reports on the most brilliant therapeutic results with sulphonamide preparations are streaming in from all parts of the world. Thousands upon thousands of human lives are being saved each year by Prontosil and its derivatives. Earlier, fruitless chemotherapeutic experiments often resulted in despondency, but now even the most pessimistic have gradually come to see the value of the results achieved. The imagination reels before the prospects of new chemotherapeutic victories which the sulphonamide preparations have unfolded before us.

The award of the Nobel Prize for Physiology or Medicine for 1939 to Gerhard Domagk has honoured a discovery which means nothing less than a revolution in medicine.

Professor Gerhard Domagk was awarded the 1939 Nobel Prize for Physiology or Medicine for the discovery of the antibacterial effects of Protonsil. Protonsil was the first of the so-called sulpha preparations, which have proved to represent one of the greatest therapeutic advances in the history of medicine. Professor Domagk was prevented from

accepting the prize at the time by political conditions. In 1947 he received the gold medal and the diploma.

Professor Domagk. It has become clear during the eight years that have passed since it was decided to award you the Nobel Prize that the sulphonamides have introduced a new era in the treatment of infectious diseases. What Paul Ehrlich dreamed of, and also made reality by using Salvarsan in an exceptional case, has now, through your work become a widely recognized fact. We can now justifiably believe that in the future infectious diseases will be eradicated by means of chemical compounds.

On behalf of the Caroline Institute I congratulate you most warmly, and ask you to accept from His Majesty the King the medal and the diploma.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1939/press.html