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Nobel Prize in Medicines 1948

Paul Hermann Müller

The Nobel Prize in Physiology or Medicine 1948 was awarded to Paul Müller "for his discovery of the high efficiency of DDT as a contact poison against several arthropods".

The discovery of the insecticidal properties of dichloro-diphenyl-trichloromethylmethane, abbreviated as DDT, has a short and crowded history which, from the medical point of view, is closely connected with the fight against typhus during the last World War. In order to give my presentation the correct medical background, I will first mention one or two points concerning this disease.

Typhus has always occurred as a result of war or disaster and hence has been named«Typhus bellicus», «War- » or «Hunger-Typhus». During the Thirty Years' War this disease was rampant, and it destroyed the remains of Napoleon's Grand Army on its retreat from Russia. During the First World War, it again claimed numerous victims. At that period more than ten million cases were known in Russia alone, and the death rate was great. Admittedly, the famous Frenchman Nicolle had already, in 1909, shown that the disease was practically solely transmitted by lice - for which discovery he received the Nobel

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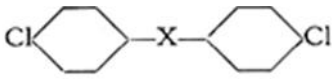
Prize - and thus paved the way for effective control; but really successful methods for destroying lice in large quantities, thus removing them as carriers, were not yet at hand.

Towards the end of the Second World War, typhus suddenly appeared anew. All over the world research workers applied their energies to trying to discover an effective delousing method. Results, however, were not very encouraging. In this situation, so critical for all of us, deliverance came. Unexpectedly, dramatically practically out of the blue, DDT appeared as adeus ex machina.

A research group in Switzerland, under the leadership of Paul Läuger and H. Martin and other collaborators had been engaged since 1933 upon the preparation of oral toxins against textile parasites. This work led to the discovery of a moth-control agent «Mitin» which, on the wool-fibre, looked like a colourless dyestuff. It was discovered at the same time that chemical combinations of the general formula:



X=S, SO, SO_2, O, etc.

often showed good oral toxicity to moths.

Paul Müller went his own way and tried to find insecticides for plant protection. In so doing he arrived at the conclusion that for this purpose a contact insecticide was best suited.

Systematically he tried hundreds of synthesized organic substances on flies in a type of Peet-Grady chamber. An article by the Englishmen Chattaway and Muir, gave him the idea of testing combinations with the CCl_3 groups, and this then finally led to the realization that dichloro-diphenyl-trichloro-methylmethane acted as a contact insecticide on Colorado beetles, flies and many other insect species under test. He determined its extraordinary persistence, and simultaneously developed the various methods of application such as solutions, emulsions and dusts.

In trials under natural conditions Müller was able to confirm the long persistent contact action on flies, Colorado beetles and gnats (Culex).

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Recognition of the intense contact activity of dichloro-diphenyl-trichloromethylmethane opened further prospects: indeed, the preparation might be successfully used in the fight against i.e. bloodsucking and disease-carrying insects such as lice, gnats and fleas - carriers incapable of being reached by oral poisons. In the further trials now conducted, DDT showed a very large number of good properties. At requisite insecticidal dosages it is practically non-toxic to humans, and acts in very small dosages on a large number of various species of insect. Furthermore, it is cheap, easily manufactured and exceedingly stable. A surface treated with DDT maintains its insecticidal properties for a long time, up to several months.

A short story perhaps illustrates better than many words how the substance acts. In 1945, when DDT was still relatively untried, I met an English Major in Germany who told me he had treated the window pane of his room with DDT since he was plagued by masses of flies. After the DDT solution had been sprayed on, the flies died and lay in heaps on the window ledge. The following morning a German soldier entered and thoroughly cleaned the window. When the Major noticed this he couldn't help crying «Goodbye my DDT!». But this farewell was uncalled for. In spite of the thorough cleaning, the window pane retained its deadly action on the flies. This little story amply illustrates how persistent DDT is and how small the dosage required.

A number of Swiss research workers such as Domenjoz and Wiesmann now concerned themselves with further trials of the substance. Mooser's researches aimed directly at a prophylaxis of typhus. On the 18th of September 1942, he gave a significant lecture to the physicians of the Swiss First Army Corps, on the possibilities of protection against typhus by means of DDT.

At that time, the Allied Armies of the West were struggling with severe medical problems. A series of diseases transmittable by insects, diseases such as typhus, malaria and sandfly fever claimed a large number of victims and interfered with the conduct of the War. The Swiss, who had recognized the great importance of DDT, secretly shipped a small quantity of the material to the United States; in December of 1942 the American Research

Council for Insectology in Orlando (Florida) undertook a large series of trials which fully confirmed the Swiss findings. The war situation demanded speedy action. DDT was manufactured on a vast scale whilst a series of experiments determined methods of application. Particularly energetic was General Fox, Physician-in-Chief to the American forces.

In October of 1943 a heavy outbreak of typhus occurred in Naples and the customary relief measures proved totally inadequate. General Fox thereupon introduced DDT treatment with total exclusion of the old, slow methods of treatment. As a result, 1,300,000 people were treated in January 1944 and in a period of three weeks the typhus epidemic was completely mastered. Thus, for the first time in history a typhus outbreak was brought under control in winter. DDT had passed its ordeal by fire with flying colours.

Since those days DDT has been used in large quantities in the evacuation of concentration camps, of prisoners and deportees. Without any doubt, the material has already preserved the life and health of hundreds of thousands. Currently DDT treatment is the sovereign remedy the world over for the prophylaxis of typhus.

The application of DDT has also proved effective in the fight against several other diseases transmitted by insects. Thus malaria is spread by several mosquito species. In the fight against malaria, the control of the adult mosquito as well as the larval state form essential part treatments. Under the leadership of Missiroli and the Rockefeller Foundation, large-scale field trials have been held in the old Pontine marshes and in Sardinia as well as in Greece. By simple means excellent results have been obtained there. In consequence the incidence of malaria in these areas has been greatly reduced. In Greece, where before in certain districts 80-85% of the population suffered from malaria, the frequency has been reduced to 5% and the ancient Pontine marshes are now as good as free of malaria.

In DDT therefore, we also possess an extremely valuable remedy in the fight against malaria, this the most widespread of all contagious diseases which yearly affects about 300,000,000 people and causes a yearly death rate of at least 3,000,000. In the cases of

many other diseases spread by insects, diseases such as plague, murine typhus and yellow fever, significant results have been obtained.

In our temperate climates these extensive contagious diseases spread by insects have, under normal circumstances, little actuality. In this respect the normal house fly must, however, be regarded as a dangerous intermediate carrier. Several intestinal diseases such as paratyphoid and paradysentery are transmitted by flies whilst a series of facts also point to the possibility that infantile paralysis is thus transmitted.

Generally speaking the housefly is very susceptible to DDT; unfortunately some fairly resistant species of fly have lately been observed. Early observations of such a resistant species were made in Arnäs in Sweden, and this species has consequently come to be referred to as the Arnäs fly. Research on this aspect continues; the discovery of DDT has stimulated further research and there are signs of substances to which even the Arnäs fly is susceptible.

The story of DDT illustrates the often wondrous ways of science when a major discovery has been made. A scientist, working with flies and colorado beetles discovers a substance that proves itself effective in the battle against the most serious diseases in the world. Many there are who will say he was lucky, and so he was. Without a reasonable slice of luck hardly any discoveries whatever would be made. But the results are not simply based on luck. The discovery of DDT was made in the course of industrious and certainly sometimes monotonous labour; the real scientist is he who possesses the capacity to understand, interpret and evaluate the meaning of what at first sight may seem to be an unimportant discovery.

Dr. Paul Müller. I have tried to give a brief survey of the historical development of DDT. Your discovery of the strong contact insecticidal action of dichloro-diphenyl-trichloromethylmethane is of the greatest importance in the field of medicine. Thanks to you, preventive medicine is now able to fight many diseases carried by insects on a way totally different from that employed heretofore. Your discovery furthermore has, throughout the world, stimulated successful research into newer insecticides.

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