obituary

Jacques Trefouel

PROFESSOR Jacques Trefouel, Director-General of the Pasteur Institute in Paris from 1940–1965 and a figure of great influence on the French scientific scene during this period and for many years after his retirement, died on 11 July 1977 at the age of 80.

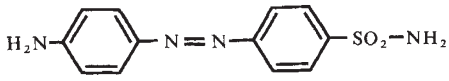
He was an outstandingly capable and skilful organic-synthetic chemist who dedicated his whole active scientific life to the field of chemotherapy. He entered the Pasteur Institute at the age of 23 when he became a student of the great master of French chemotherapy, Ernest Fourneau, head of the Department of Chemotherapy created by the then Director-General of the Pasteur Institute, Emile Roux. A year later he married a colleague of his, Thérèse Boyer, who was not only an equally brilliant synthetic organic chemist, but also an exceptionally attractive lady of great charm and elegance. Nearly all his original papers were published jointly with his wife, and Jacques and Therese Trefouel became one of the most productive and best known scientific couples. They stayed at the Pasteur Institute until their statutory retirement.

Their first papers, most of them published jointly with E. Fourneau, followed Paul Ehrlich's lines and led to a series of substances active against trypanosomes, spirochetes and plasmodia.

The most important contribution of the Trefouels made in collaboration with their brilliant colleagues the pharmacologist Daniel Bovet and the microbiologist Frederico Nitti, which earned them a position of immortality in the biomedical sciences, was the discovery in 1939 of the chemotherapeutic properties of sulphanilamide against bacterial infections.

During his extended histological studies, at the end of the last and the beginning of this century, Paul Ehrlich had become aware of the strong antibacterial properties of some of the synthetic aniline dyes, but unfortunately all of these were far too toxic for systemic chemotherapeutic use. However, Paul Ehrlich hoped, in view of the fact that dyes were capable of specifically staining some part of cells while leaving others unstained, and in view of his firm belief that the possibilities of synthetic organic chemistry were practically unlimited, that one day a synthetic dye would be discovered which would specifically kill bacteria without affecting the host organism they had infected. He was encouraged in these thoughts by his finding that the dyes trypan blue and trypan red, were moderately effective in the chemotherapy of trypanosomal infections.

Stimulated by Paul Ehrlich's ideas the pharmaceutical divisions of the German dyestuff industries, then leading the world, made a tremendous effort to test thousands of dyes for chemotherapeutic efficiency in bacterial infection, but without success. In 1935 G. Domagk, of Bayer's, reported the sensational news that finally he had found an azodye, prontosil



which was capable of protecting mice against streptococcal infections and was also effective in man. This dye had been tested for over two years before its chemotherapeutic properties were released for publication. It thus seemed that Paul Ehrlich's ideas, after a period of over 30 years, were finally vindicated. However, the Trefouels, Bovet and Nitti proved conclusively a few months later in the same year that the chemotherapeutic properties in bacterial infections of prontosil had nothing to do with its dye nature, but resided totally in the non-coloured moiety sulphanilamide of the prontosil molecule. They postulated that prontosil was reduced to sulphanilamide in the animal body, an hypothesis which was later proved correct experimentally and explained why prontosil was inactive *in vitro*, but active *in vivo*.

There can be no doubt that the discovery of the chemotherapeutic properties of sulphanilamide marked a major revolution in therapeutic medicine, both with regard to its practical use and theoretically. Sulphanilamide, synthesised as early as 1908, is a very simple molecule and can be readily modified. The Trefouels synthesised over a hundred derivatives, among them the sulphones which later were recognised to be valuable chemotherapeutic agents in the treatment of leprosy. Since then many thousands of sulphonamides have been synthesised in the laboratories of numerous pharmaceutical firms, and the advent of the antibiotics has not eclipsed them. They are still widely used in the clinic, particularly for the treatment of urinary infections caused by *E.coli* in combination with folic acid antagonists of 2,4-diamino pyrimidine structure (sulphanilamide itself was shown in 1940 by D. D. Woods in this country to antagonise the structurally similar para-amino benzoic acid, a part of the folic acid molecule, a discovery which, on its own, signified a major advance in the science of biochemistry).

Professor Trefouels scientific achievements were rapidly recognised and rewarded inside and outside the Pasteur Institute. He was promoted to Head of the Laboratory and, a few years later, to be Head of the Division of Chemotherapy. In 1940 he reached the administrative pinnacle of the Pasteur Institute when he was nominated Director-General. He was put into this prominent position while France was passing through some of the most difficult years of its history.

In 1939 World War II broke out and a year later France was conquered and humiliated by Germany. Jacques Trefouel, thanks to his inexhaustible spirit of enterprise, his great diplomatic talent and flexibility, his courage and his firm, deeply felt and uncompromising patriotism, managed to steer the Pasteur Institute successfully through very stormy waters with dignity and determination, and to preserve the essence of its unique historic scientific traditions and patrimony. He conceded nothing of importance of the possessions of the Pasteur Institute to the enemy, and his authority inside the Institue remained untarnished and undisputed.

He was a very courteous and polished personality, unruffled in situations of difficulty, and his radiant smile was irresistible. He was very erudite and wise, and was always very

kind and friendly, though he could be quite firm in relation to the people with whom he had to deal. He was gifted with a quick intelligence which enabled him to understand complex situations in a few moments, and he was endowed with a very refined, inimitable and typically French sense of humour.

His exceptional human qualities enabled him to keep on good terms with the majority of his senior colleagues and they made him popular among the staff of the Pasteur Institute. He appointed judiciously and, on the whole, successfully, new members of the staff and succeeded in maintaining the very high scientific standards of the Institute. He also created and maintained close contacts with the French pharmaceutical industry, to both its own benefit and that of the Pasteur Institute.

In my view, the Pasteur Institute never had a more dedicated and successful director than Jacques Tréfouël.

Throughout his onerous social duties as Director-General of the Pasteur Institute, Jacques Tréfouël received extensive, continuous and competent support from his wife who combined the properties of an excellent scientist with those of a perfect hostess. Time passed quickly during the animated and witty conversations covering a wide range of subjects at their elegant parties, which remained an unforgettable experience in the memory of those privileged to participate in them.

Jacques Tréfouël received numerous high honours from the French and other Governments and scientific societies. Among these were his nomination to the grade of a Grand Officer of the Legion d'Honneur, to the Membership and later Presidency of the French Academy of Sciences and the National Academy of Medical Sciences, many honorary degrees in the Universities of Europe, including Oxford and Cambridge in this country, and the Americas, and membership of many foreign academies and learned societies.

The passing of Jacques Tréfouël marks the end of an era in European science.

Ernst Chain

G. K. Green

GEORGE KENNETH GREEN, or Ken Green as he was known in the world of particle accelerators, died on 15 August 1977 of a heart attack while visiting his son at Brownsville, Texas. He was 66 years of age and had lived through, and taken a leading part in, one of the most extraordinary technological developments of our time.

Ken Green was born in St David, Illinois, and retained all his life the looks and the dry humour of a Mid-Westerner. He went to Illinois University, obtained a Ph.D. degree in physics there in 1937, and stayed on a year afterwards as an Associate in Physics. His first experience with what became his life's work was at the Radiation Laboratory of the University of California where he did design work on cyclotrons and nuclear physics research. It was there, at what was then the fountainhead of accelerator developments, under the inspiration and leadership of Ernest Lawrence, that Ken Green must have fallen in love with accelerators. He also spent a short time at the Department of Terrestrial Magnetism of the Carnegie Institution of Washington D.C.

He spent the war years with the Army Signal Corps, joining in 1942 as a second lieutenant, and in 1946 he was Army Electronic Representative and Technical Head of the Signal Corps Group at Operation Crossroads at Bikini. Later, he became principal physicist at the Evans Signal Laboratory of the Signal Corps at Belmar, New Jersey. During this period he worked on sonar and was one of the inventors of the proximity fuse, an important advance in firing rockets and artillery. At the Bikini test of atomic bombs he was involved in the development of instrumentation to study nuclear explosions. For his services during the war he received both the Civilian Distinguished Service Award and the US Army Legion of Merit.

Ken Green joined the Brookhaven National Laboratory in 1947 to work on the 'Cosmotron' and he never left that laboratory nor accelerator building for the rest of his life. The Cosmotron, in its time, was the largest accelerator in the world, and with a top energy of 3 GeV it was the first accelerator to exceed one thousand million electron volt particle energy. Ken Green was involved in the design and construction of every part of this machine. Formally, he was a senior scientist; in practice he combined a considerable design ability across the whole field of accelerator technology with a remarkable talent for supervising the construction of this giant machine—a talent rather rare in those days. The result was that Ken Green knew every detail of the Cosmotron, the reasoning behind its design, how it was constructed, and how well or badly it operated. No wonder that he earned the name of 'Mr. Cosmotron.'

The construction of the Cosmotron was finished in 1952, and many improvements were made to it subsequently, in all of which Ken Green was intimately involved. Meanwhile, another, even bigger accelerator project was being quietly conceived at Brookhaven, and in Europe a new international laboratory was being set up, called CERN, which aimed at building a similar machine. Then followed one of those unofficial and extremely effective collaborations between two laboratories which prove so beneficial to the course of scientific research, and Ken Green entered whole-heartedly into this collaboration.

The two machines, the 30 GeV AGS at Brookhaven and the 25 GeV CPS at CERN were essentially designed together. The principle of alternating gradient focusing was discovered at Brookhaven at this time, and the two teams worked out the consequences of this important idea together, and based the design of their machines on this new principle. Brookhaven staff came to Europe, CERN staff went to Brookhaven, and the success of these two machines owed much to the close collaboration between Ken Green's team at Brookhaven and the CERN team at Geneva.

The two machines came into operation at about the same time in 1960, and the two teams celebrated each other's success. The AGS and CPS were for many years the highest energy accelerators in the world. Ken Green became the Chairman of the Accelerator Department of the Brookhaven National Laboratory in 1960, having first served for a while as deputy-chairman under Leyland Haworth, and he held that post until 1970.

His last most notable contribution to accelerator design was the electron machine for the National Synchrotron Light Source which he started before his official retirement from Brookhaven Laboratory and continued for the short while afterwards until his death. Construction of this machine is due to start at Brookhaven towards the end of 1977. His last appearance in Europe was in the spring of this year when he came over to CERN to participate in the inauguration of the European 400 GeV SPS machine.

Ken Green has earned an immortal place in the ranks of the great accelerator builders with the Cosmotron and the AGS which were not only the highest energy machines of their time but also very challenging projects, involving many technological advances. All his many friends and colleagues throughout the world, in all the laboratories where these giant machines exist, will mourn his death, and remember with gratitude the help and encouragement he has given them.

J. B. Adams