RENATO DULBECCO



A versatile virus man

R ENATO DULBECCO, Caltech Professor of Biology, is a man who apparently believes that there is no such thing as a thing that can't be done. In fact, he'll do it himself, if necessary. Which helps to account for the fact that, to date, he has become an accomplished plumber, mathematician, physician, carpenter, pianist, dentist and photographer—among other things.

These, of course, are merely sidelines. ("Hobbies" is too flabby a word to describe most of these activities—particularly as practiced by Dulbecco). His chief professional interest is in animal viruses—the viruses responsible for such diseases as influenza, polio, shingles and smallpox. He is in charge of animal virus research at Caltech, and his contributions to the field have not only speeded up this research enormously—they have even revolutionized it.

Renato Dulbecco was born on February 22, 1914, in Catanzaro, Italy, and grew up in Imperia, on the Mediterranean near the French border, where his father was a civil engineer.

At 16, he entered medical school at the University of Turin, and received his MD degree in 1936, at the age of 22. After graduation, he was obliged to serve a year and a half in the Army, and in 1938 he returned to the University as an assistant professor in the department of pathology. His work was going well, and his future seemed secure, so, in 1939, he was married to Giuseppina Salvo, a girl from his home town. Ten days later Italy declared war.

For four years Dulbecco served as a medical officer in the Italian Army. He spent eight months with the Italian troops in Russia, and there, fortunately, he suffered a broken shoulder and was sent home—fortunately, because his regiment was later wiped out at Stalingrad.

In 1943 Dulbecco packed up his family (there were two children now—Piero, 2, and Maria, just a few months old) and moved to Piemonte, an out-of-the-way village not far from Turin. The town had no doctor at the moment, so Dulbecco set up as a general practitioner, serving all the health needs of the grateful villagers—both medical and dental.

It was typical of the man that, though he knew nothing whatever about dentistry, when he found that the villagers needed a dentist, he studied and read and learned—and became an excellent one.

In 1945, when the war ended, Dulbecco was at last free to return to his scientific work. Professionally, he had lost six years, and he promptly began to make up for them. Even today he sometimes works at such a clip that he seems to be *still* making up for them. Uncertain, now, of what kind of scientific work he wanted to do, he returned to the University again and spent two years on the study of physics. During this time, because of his medical background, he became interested in the action of radiation on cells, and he began to study more about this, using some of the techniques he had learned in experimental embryology.

Bacterial viruses

S. E. Luria, at Indiana University, was making studies at this same time of the action of radiation on bacteriophage, the viruses found in the human body which attack bacteria. Hearing of Dulbecco's work, he offered the young man a job as research associate in Indiana's department of bacteriology. The salary was too small to support a family on, but Dulbecco was anxious to work with Luria, so he came to America alone, leaving his family in Turin. After a year, his wife and children joined him in this country.

At Indiana, while studying the action of radiation on biological material, Dulbecco made the accidental discovery that bacterial viruses which had been inactivated, or killed, by ultraviolet light could be reactivated by ordinary white light after 24 hours or more. Though he was interested in this merely as a piece of basic research, it did have possible practical applications, for anything that could be learned about how to correct radiation damage might reveal something about what causes it in the first place.

Animal viruses

In 1949 Dulbecco came to Caltech as a Senior Research Fellow in Biology. Shortly after his arrival, the James G. Boswell Foundation sponsored an international virus conference here, at which, for the first time, scientists working on the three different groups of viruses those which attack plants, those which attack man and animals, and those which attack bacteria—got together to discuss their research in progress.

The two most important facts that Dulbecco carried away from this conference were (1) that very little was known about some aspects of animal viruses, and (2)that Caltech had a fund for virus research.

Dulbecco knew no more about animal viruses than he had once known about dentistry, but he determined to work in this field. To familiarize himself with it, he had himself assigned a review of the field for the *Physiological Reviews*. He visited every animal virus lab he could get to, and read everything that had ever been written about animal viruses in the three languages he could understand. At the end of six months he not only wrote a respectable review, but he had compiled an index on animal viruses that would shame an IBM machine, and — not all incidentally — he had learned almost as much about animal viruses as a lot of the men who had been working in this field all their lives.

For many years viruses had been studied chemically and medically, but never very much biologically —until E. L. Ellis and Max Delbruck began working with bacterial viruses at Caltech 18 years ago. Dulbecco carried over this biological viewpoint to the study of animal viruses, and developed techniques which made it possible, for the first time, to make quantitative studies of them. Like Delbruck, who was trained as a physicist, and Ellis, a chemical engineer, Dulbecco was able to make an important contribution to virus research largely because he was trained in a different discipline, and so was unaware of the things that supposedly could not be done in this field.

Since viruses only grow in living cells, not much was known of the viruses that attack animals. Research was done primarily by infecting monkeys or chicken embryos with a virus, then observing the effect on the animal as a whole. The problem was to find an adequate way of studying the growth of a virus on animal tissue directly.

A practical technique

Despite steady skepticism from many of the pros in the field, Dulbecco quickly came up with a practical technique — adapted from methods used in studying bacterial viruses—for studying animal viruses. Working with the western equine encephalomyelitis virus (which causes horse sleeping sickness; though it is of no great medical significance, it is nevertheless a good research tool), he grew a single layer of animal tissue cells in a nutrient medium. A weak suspension of virus particles was then introduced into this, and, as the virus particles attacked the tissue cells, they multiplied and produced small visible areas of dead cells, known as plaques. In this way it became practicable to study the precise effects of a virus on a cell.

Research results

It was definitely established, for example, that infection in an animal, or human, can be produced by a *single* virus particle. Working with the polio virus (also an excellent research tool) Caltech researchers were able to isolate, for the first time, genetically pure strains of the three known types of polio virus, making it possible to start intensive studies of the development and hereditary properties of that virus.

Work is also now in progress at Caltech on a second group of animal viruses, which, instead of growing in a cell and eventually destroying it—as the polio virus does—induce it to grow tumors and stimulate it to multiply.

This research is supported by both the National Foundation for Infantile Paralysis and the American Cancer Society, not because any immediate, practical results are expected, but because it is work which may shed light on one of the most fundamental problems of biology. The more we can find out about how a virus grows in a cell, the closer we may come to understand how the cell works.