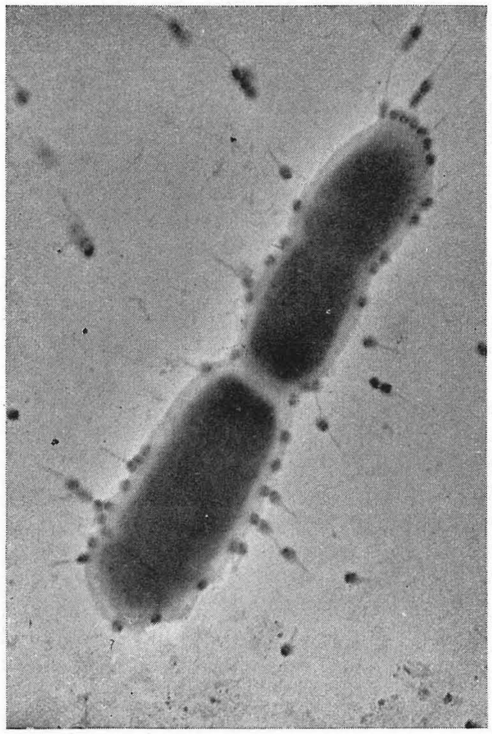
Research in progress

Magnified 25,000 times, this dividing bacterium coli is being attacked on all sides by bacterial viruses.



Caltech researchers are making spectacular strides in their war on the

VIRUS

CONTROL OF MANY serious virus diseases may come as a result of researches now under way in Caltech's Biology Division.

The same researches may also bring important knowledge of how certain kinds of protein—the stuff from which all living things grow—are created. The explanation of why these things are tied up together lies in the special nature of the virus itself.

Viruses stand at the borderline of life. Unbelievably small, they can be seen only with the newest kinds of electron microscopes. They can be crystallized, like salt or sugar—and after becoming crystals, and then being "decrystallized," they can actually "come to life" again and reproduce themselves. They can continue to live and reproduce themselves as long as they have some other living thing to grow on.

Viruses live and grow inside living cells. Some kinds of viruses live inside the cells of plants, and some inside the cells of animals and people. Still other viruses live inside bacteria, which are also cells—ones that live independently.

Viruses, however, are much harder to get at than bacteria. Many of the techniques for trapping bacteria—such as the use of fine filters—fail when tried on the virus. In many cases we can attack bacteria with drugs and kill them. But when we try to kill a virus, we are very likely to kill the cell in which it lives, too. Unlike bacteria, viruses resist many things such as penicillin and sulfa drugs. Like bacteria, to make matters worse, viruses can change—so that once a way to attack them

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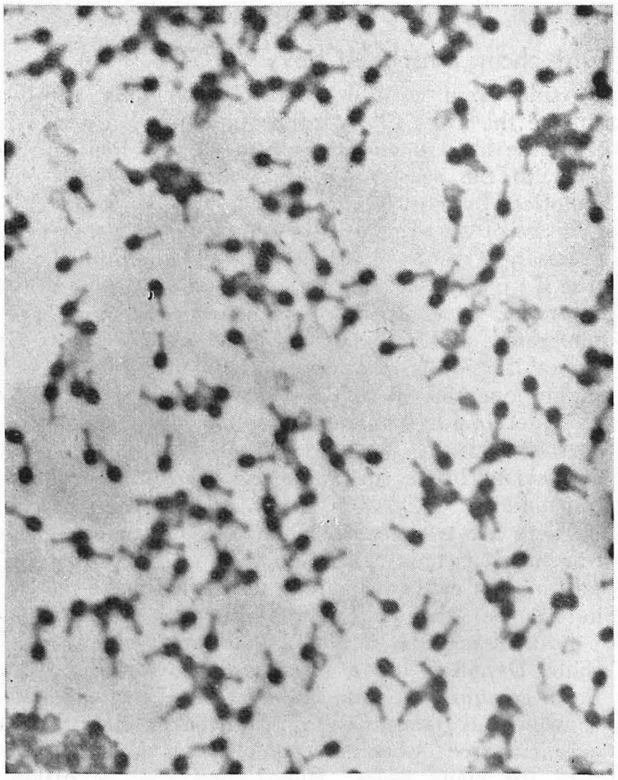

A concentrated culture of bacterial viruses is magnified 40,000 times by the electron microscope.

Researchers in bacterial virology meet at daily luncheon seminars in Dr. Delbruck's laboratory. From left to right group includes: J. Weigle, Geneva; O. Maaloe, Copenhagen; E. Wollman, Pasteur Institute in Paris; Merck Fellow G. S. Stent; Dr. Delbruck and G. Soli, graduate student from Italy.

At right, researcher in plant virology inspects mosaic-infected tobacco. Picture was taken through special plastic screen that protects plants from virus-carrying insects.

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is discovered, they can change themselves to a form which is immune to that attack.

For these reasons, viruses of all kinds are a major threat to plant and animal life. A virus is responsible for poliomyelitis, for example, and for such diseases as rabies, influenza, mumps and yellow fever. Plant viruses cause the sugar beet curly top, tomato spot and tobacco mosaic that are such serious crop destroyers. A plant virus got a foothold in a California orange grove some years ago and by last year this disease, known as the "quick decline," had killed whole large areas of orange trees. These are just a few of the diseases caused by viruses; there are hundreds of others.

Second front

For years, people have been trying to fight plant and animal viruses with such expedients as inoculation, immunization, spray, fumigation, isolation and the breeding of resistant strains. Valuable research on these lines is being followed at many centers today. Working along more fundamental lines, other researchers have accumulated a lot of sound knowledge about the nature of the abnormal, virus-infected cell—including the remarkable isolation of the virus itself. But research at Caltech is along radically different lines.

The Institute staff believes that the route to a truly complete understanding of the abnormal cell lies in an understanding of the normal cell. While this may sound like obviously simple reasoning, it is a fact that amid all this knowledge of virus-infected plants and animals there has been practically no knowledge of what a normal, healthy plant cell is really like.

Now, however, as a result of recent advances at the Institute, researchers feel that they know enough about the composition and inner workings of the normal cell to ask themselves how the virus fits into this machinery.

An answer to the question of what a virus makes itself out of is already foreshadowed in one line of research at the Institute. And if the answer is found, it may help to explain how all living matter gets made.

To see why this is so, it is necessary to remember that all living bodies are composed of cells. These cells in turn are made up chiefly of the fundamental life-stuff called protein. Viruses too are made up of protein, but it is different from healthy cell-protein.

Virus precursor?

Recently Institute researchers have discovered a normal plant-cell protein that is similar in its chemical makeup to virus protein. This recently-discovered protein lives in healthy cells, and acts like a healthy, harmless protein. Institute researchers, under the direction of Drs. S. G. Wildman and James Bonner, have set out to find the relationship between normal protein and virus protein.

Could it be that some slight disorder in the cell, they wonder, suddenly changes the normal protein into the virus protein? Is that the stuff from which the virus gets made?

Perhaps there is the possibility that this new protein is actually a precursor of a virus. It is an axiom in biology that "nothing grows out of nothing"; that everything must have something to grow on. And perhaps here in this virus-like protein the biologists have found the thing that virus grows on. In the case of the virus that causes the tobacco mosaic disease, a very large proportion of protein in the normal leaf cell is somehow converted into this foreign protein. Is it possible that the tobacco mosaic protein, then, gets made at the expense of normal tobacco leaf protein?

Whatever the answer, the Caltech virus researchers are probing extremely close to the question of how any virus—plant or animal—gets made.

As to the problem of how a virus reproduces itself, this question is being attacked not only through work on plant viruses, but through some unique work on bacterial viruses as well. These tiny particles that live inside the microscopic bodies of germs are just as deadly to their host, the bacterium, as the plant virus is to its host, the plant—thus proving the lines,

Big bugs have little bugs
  Upon their backs to bite 'em
And little bugs have littler bugs
  And so *ad infinitum.*

Caltech researchers, under the direction of Dr. Max Delbrück, have recently discovered that this "bug within a bug," the germ-inhabiting virus, has a sexual mode of reproduction. For these bacterial viruses have been found to be made up of sub-units, each of which is very like that ultimate particle of life, the gene. Furthermore, these same researchers have discovered they can breed special strains of bacterial virus.

In an ordinary living cell there are many thousands of genes, while in a virus there are but a few gene-like sub-units. Thus, in being able to breed strains of these viruses under carefully controlled laboratory conditions, and then to study their composition, these researchers have an unusually straightforward approach to the lowest known level of life.

Guinea pigs

So, while plant virus researchers breed special strains of virus-infected plants in their laboratory, the greenhouse, bacterial virus researchers breed special strains of germ-inhabiting viruses in test tubes. Thus, for both groups, the virus may become a kind of guinea pig that can tell us about the origin of new virus diseases, and about their epidemiology.

At Caltech, therefore—thanks to a unique staff and a unique approach to these problems—virus research has been established on a small but hopeful base. From this, research can go steadily ahead until, linking with researches in other lines at the Institute, it begins to piece together the total picture of virus life, of the abnormal or cancerous cell, and beyond that, of the ultimate nature of the living cell.

This account of the virus research program in Caltech's Biology Division is the second in a series of reports on research in progress at the Institute. Next month: the analysis laboratory and the electric analog computer.