1954

THE NATURAL HISTORY OF VIRUS ENCEPHALITIS

by Thomas A. Cockburn

On Cheviot, a few hundred yards from the Scottish border, the shepherd from Dunsdale pointed out to me a solitary weak-looking sheep with a peculiar gait, and informed me that it was "sick o' the loup". After five minutes meditation he added that some doctors from the South, beyond Newcastle, had been collecting ticks the year before and had said that the sheep should be well "dipped" next time, or many would die.

That was nearly twenty years ago, and although I did not realize it at the time it marked my introduction to the group of diseases known as the virus encephalitides.

"Louping ill" has been known on the borders for more than a century, but so far in nature the disease, which is caused by a virus and transmitted by ticks, has been confined to sheep. The virus is one of a wide group found in all parts of the world, but its nearest relation is a Russian form called Far Eastern virus. The Russian virus is also transmitted by ticks, and an ominous feature of it is that human cases of infection have been reported.

People often ask: "What is a virus?", and a really honest biologist will reply that he doesn't know, for he cannot even be really certain if it is a living creature or some inanimate molecule. The present most fashionable theory is that it is a bacterium that has learned how to live inside the cells of some organism, and become a kind

of parasite. Finding plenty of predigested food inside the cell, it has discarded as unnecessary much of its own metabolic system in true parasitic fashion, and in doing so has shrunk in size and complexity. Viruses have never yet been grown in the absence of living cells.

The cells that form a body like ours are specialised to form different organs such as the liver, skin, brain, spleen, and so on, and it would seem that certain viruses have adapted themselves to life in only one kind of cell. For example, smallpox has adapted itself to the cells of the skin, influenza to those that line the respiratory tract, yellow fever concentrates on the liver, while another group attacks the cells of the nervous system.

Those of the nervous system are quite numerous, and form one of the major problems facing the medical profession of this time. In many instances, the virus is unknown, or its method of spreading obscure, while the treatment or prevention is largely futile. Such a virus was that which caused Von Economo's encephalitis, called after the Viennese physician who first described it, which appeared in 1915, and swept the world to cause untold suffering. A peculiar feature of this illness was that the initial attack might in some cases be no more severe than an attack of influenza, but sometimes even years later, signs of damage to the brain would appear, to be called post-encephalitis paralysis agitans. In one's student days the chronic wards of most hospitals had many people suffering from this, with a slow-

ing

ing of the mental processes, muscular rigidity, and a constant shaking of the body, and an inability to look after themselves.

The organism was presumed to be a virus but was never isolated. No one knows how it was spread, and the acute disease disappeared in 1926.

Infantile paralysis (anterior poliomyelitis) is due to a virus that attacks certain cells on the spinal cord, and sometimes others in the brain, and as these are key cells in the spread of signals from the brain to the muscles, interference with them causes paralysis. The disease can be reproduced in monkeys, and using these as test animals it has been shown that the virus is excreted in the faeces of patients and sometimes of apparently healthy people. Yet the methods of sanitation that have wiped out diseases spread by sewage, like cholera and typhoid, have not prevented poliomyelitis epidemics, so other angles are being explored. The possibility that flies pick up the virus from faeces and so spread it is being considered, and large scale experiments are on the way to try out this possibility, but no one knows how to prevent or stop an epidemic, or cure a person with the disease.

Rabies is another virus disease of the nervous system and is spread by the saliva of infected animals. It is not confined to dogs and wolves for almost every animal is susceptible and the disease is found in almost all parts of the world. In England, rigid quarantine

reduces the problem to very rare cases in imported animals, but in America, Asia and Africa, the wild animals like foxes and skunks are infected and these sometimes bite cattle, goats or humans, and can set off an epidemic among the domestic dogs. In Trinidad, a fatal disease among the cattle was traced to vampire bats that were infected with rabies. These bats are so particularly quiet and gentle in their operations that they manage to knick open the skin of an animal or sleeping human and lap up the blood that wells out, but in doing so they may pass on the virus to the new host.

The ability to find new hosts is one of the most significant points of a successful virus, for if it is unable to do so it shares the fate of its host and dies when that does. The great majority of human viruses almost certainly evolved in the first instance in various groups of animals, until certain individuals of them managed to invade the human population and multiply there with success. In many, many of these viruses find themselves in a kind of blind alley, for they cannot escape from the body into which they have made their way, and so these particular ones are doomed. They are not successful until they learn how to travel from one human to another.

In louping ill the virus is still confined to the sheep and tick cycle; the Russian Far Eastern virus has made occasional invasions of human tissue; Von Economo's mastered some technique of transmission, but was too succ-

essful in spreading, for it burned itself out in a few years; polio might be classified as the almost perfect virus parasite, for it exists from year to year, seems to have little difficulty in passing from human to human, and only occasionally kills its host. But the ideal state, from the virus point of view, is attained by the Herpes virus, which is present in almost everyone but seldom gives any trouble. The Herpes organism must have been living with man for a very long time to have evolved so close a relationship, for its presence would be almost unknown did it not sometimes give rise to a few blisters around the mouth when the body temperature rose above a certain level, as happens during an attack of influenza or pneumonia.

In U.S.A. widespread disease has been known for many years in horses under the names of forage poisoning, botulism, sleeping sickness, but in 1930 a virus was recovered from the brain of a sick horse and the disease was called Equine Encephalomyelitis. A few years later, the first human case was confirmed as being caused by the virus. In 1933 a new disease due to a similar virus swept the area round the city of St, Louis on the Mississippi, with tens of thousands of people suffering from headache, coma and various forms of paralysis, while many died. Since then, Eastern, Western, Venezuelan and St. Louis strains of encephalomyelitis have been identified from numerous epidemics in various parts of the continent, involving both horses and humans, while in the Pacific, another type known as

Japanese B has caused considerable mortality.

It was not long before mosquitoes were regarded as being the means by which the virus spread to humans, and by now all types of encephalomyelitis virus have been recovered from the bodies of these insects on many occasions. To demonstrate this, large numbers of mosquitoes are caught and ground up, and the emulsion injected into the brains of mice. If infection is present, the mice suffer from a paralysis and die a few days later.

Once a mosquito is infected it stays that way apparently as long as it lives, and when it feeds on some mammal the virus is injected at the same time into the blood of the mammal. However, the virus does not stay long in the circulation, passing quickly to the nervous tissue of the brain and spinal cord, so that mosquitoes feeding later on the same mammal are unlikely to pick up a quantity large enough to infect them. The vast majority of mosquitoes die when the winter comes, although a small number manage to hibernate in sheltered places; the virus has never been shown to be passed from the female to its offspring through the eggs, nor found in hibernating mosquitoes. Since the mammals and humans seem to be dead ends as far as transmission is concerned, the important question remains to be answered ----- Where do the mosquitoes get the virus and where does the virus spend the winter? Until these questions are answered there can be little hope of controlling the disease over wide areas like the U.S.A. If it were possible

to kill all the mosquitoes then probably a few cases only would occur, but even with the assistance of chemicals like DDT the task would be an enormous one, and have to be repeated regularly. The only solution appears to be to find the reservoir that holds the virus all year round and then wipe it out.

A good deal of work has been done on those lines in the past decade. The first clue came when two separate occasions birds were seen to be sick, and on examination the virus of the Eastern kind was recovered from them. Then in 1941 in the big epidemic in North Dakota, a pheasant shot in a district that was severely affected was shown to have the Western virus. Experiments quickly showed that birds may hold the virus in their blood for many days, usually without having symptoms of illness, and that mosquitoes biting the birds could pick up the virus. Tests of bird sera for signs of past infection revealed that many had in fact had the virus in their bodies at various times, but this discovery only led to the question as to whether the mosquito was infected by the bird, or the bird by the mosquito.

To confuse the issue, an insect called a Triatoma sanguineus or kissing bug, one of the Reduviidae, that feeds on blood, was found to be infected in a field in Kansas in which horses had been ill with encephalomyelitis. It seems unlikely that these insects could cause an epidemic stretching over several states, but they could cause a small local outbreak.

The next step came when the St. Louis virus was found in Missouri in chicken mites, and this gave a hope that the reservoirs had at last been discovered. It would be an easy matter to spray all chicken houses with some chemical and kill all the mites, but a snag is that epidemics occur in parts of the country including certain valleys of California where there are no chicken mites. A search of wild bird nests for mites was begun, and in in California Western virus was found in mites called Liponyssus sylviarum, in the nest of a yellow-headed blackbird.

Experimental work on chicken mites indicates that the female mite can transmit the St. Louis strain to its offspring via its egg (trans-ovarian passage), but this work has not yet been confirmed. It is not unlikely that this should be so, for ticks and mites have been shown to do this with other infections, and if it is correct a plausible theory could be erected in which the mites are the permanent reservoir of the virus, infecting the birds in the spring and summer. The mosquitoes could feed on birds and then on horses and men, while various biting insects like Triatoma sanguineus could be infected occasionally.

But a lot of things remain to be proved. Do mites like Liponyssus really pass virus to their eggs? What happens to the mites in the winter time, and can virus be found in themmat that period of the year. Also Mallophaga, or bird lice, have been found infected, and where do they fit into the picture? It was long thought that these lice

fed only on feather and skin debris, but now it appears that some of them suck and digest blood.

Another angle not tackled yet is that of internal parasites. In Swine influenza the 'flu virus is picked up by the lungworm parasite in the pig; worm eggs are passed out in the sputum on to the ground; the eggs are eaten by earthworms in which they develop into larvae; and these finally grow into adult lungworms when the earthworms are eaten by other pigs. In this way the 'flu virus is passed from pig to pig.

Is it possible that encephalomyelitis virus is passed from bird to bird by some similar cycle? No one knows.

Then some workers are inclined to the belief that there are not a whole lot of differing viruses, but rather only one that manifests itself in various forms. ~~Confusion is added by the recent report of the Eastern strain in a sick monkey in the Philippines, where only Japanese B had previously been known.~~ Again, workers in Africa examining mosquitoes turn out quite a long list of new viruses, and it is difficult to fit them into the picture. Incidentally, this is the reverse of the past history of medicine, when a cause for a known disease was sought, for in Africa they find the virus first, and then look for the disease!

Some things about these encephalitis viruses are are clear; their distribution is world-wide; they are capable of causing much serious illness in man and beast; with speedier planes accidentally transporting insects to

all quarters of the globe the chances of spread of the viruses to new areas are very great; and control will mean application of knowledge and research in almost all brandes of biology.

Truly a problem of no little magnitude.