VIRUS DISEASES AND VIRUSES

The study of virus diseases and viruses is one of comparatively recent date, and yet in the course of the last few years it has become of outstanding interest to all biologists and many biochemists. Knowledge regarding this group of disease agents commenced in 1894, when Iwanowski showed that the disease of tobacco plants known as "mosaic disease" could be transmitted by an agent which would pass through the pores of filters which were sufficiently fine to hold back all ordinary bacteria. In 1898 Beijerinck, independently, discovered anew the filterability of the infecting principle of tobacco-mosaic disease and wrote of a *contagium vivum fluidum* as the cause of this disorder. This conception, which was contrary to accepted doctrine at that time, has not been destroyed with the growth of knowledge, but has, more recently, owing to Stanley's work with the same disease agent, gained in strength. In 1898, again, Loeffler and Frosch showed that the virus of foot-and-mouth disease of cattle would pass through filters which were impervious to

bacteria and that the disease could be transmitted in series from animal to animal by means of what appeared to be sterile filtrates. With these striking examples of disease, induced by agents which were apparently differentiated from bacteria by their minute size, it is not a little remarkable that recognition of the importance of viruses should have been delayed for so long, and it is perhaps the more remarkable since the early workers foresaw clearly the possible applications of their new knowledge to other diseases. However, if advance in the study of virus diseases was slow to commence with, it has proceeded with an ever-increasing acceleration, until to-day it has become exceedingly difficult to keep abreast with the advances which are made almost daily. There are still just a few workers who are sceptical regarding the existence of viruses and who endeavour to explain the essential experimental results in other ways, such as, for example, filterable forms of ordinary bacteria. But the number of the unbelievers is small and steadily diminishing. The great majority of competent observers recognise that a special group of agents called viruses can cause many diseases in man, animals, plants and even in bacteria themselves. These diseases are of great importance and the sum total of the dis-

harmony they produce rivals that caused by the visible bacteria.

In the case of man we now know that many of the acute infectious fevers are caused by these peculiar agents, as for example small-pox, measles and mumps, and probably chicken-pox. Each of these is responsible for much suffering, though the first-named is now, for us, of smaller importance owing to the introduction of Jennerian vaccination in 1796, long before the nature of the causative agent was appreciated. Warts, *Herpes febrilis*, epidemic influenza, yellow fever, infantile paralysis and some forms of encephalitis are all caused by viruses. Only those who have seen many cases of infantile paralysis can realise the damage it may cause to a population or the disability from partial paralysis which may be left behind on recovery from the acute stages of the disease. Yellow fever, once the most dreaded infectious disease of the tropics, is still a severe threat to the well-being of man in many parts of the world, but the pioneer work of Walter Reed and his co-workers, who proved that the infecting agent was filterable and transmitted by mosquitoes, did much to assist in combating the ravages of the disease. An intensive anti-mosquito campaign instituted by Surgeon-General Gorgas enabled him to rid Havana of

yellow fever for the first time for many years. Subsequently, by still more strenuous efforts on a wider front, he eliminated yellow fever completely from the Panama Canal zone and reduced the incidence of malaria to quite small figures. This allowed the completion of the great waterway between the Pacific and the Atlantic. Stokes, Bauer and Hudson showed that the virus could be transmitted to rhesus monkeys, and this led to an intensive study of the malady on an experimental basis. These studies cost the lives of some of the workers. Adrian Stokes did not live to see even the first-fruits of his discovery, and Noguchi and Young also died from the disease. Many who have worked with yellow fever have contracted the ailment, but now, thanks to much experimental work, we know of methods of immunisation which can be employed to protect laboratory workers and others exposed to infection. The methods are not easy to apply on a really large scale and yellow fever still remains to a large extent uncontrolled.

Typhus fever is included in the group of virus diseases by some authorities and excluded by others. Typhus is not now common in civilised communities, but it was once one of the greater epidemic scourges of mankind. It flourishes where

large numbers of people are herded together under insanitary conditions, such as have obtained during military campaigns. Zinnser, in his very interesting book, *Rats, Lice and History*, shows how important this disease has been in the past, how it has influenced crusades and interrupted wars. He states: "It is hardly debatable that the power of Napoleon in Europe was broken by disease more effectively than by military opposition or even by Trafalgar." And one of the more important diseases which ravaged Napoleon's armies was typhus fever. During the Great War typhus caused serious trouble in Russia and the eastern front, but very fortunately the western front escaped this deadly ailment, though that comparatively trivial kindred disorder known as "trench fever" was common enough.

To quote Zinnser once more: "The establishment of the Haitian Republic, though usually attributed to the genius of Toussaint l'Ouverture, was actually brought about by yellow fever. In 1801 Napoleon sent General Leclerc with 25,000 men to Haiti to put down the revolt of the Negroes. The French troops landed at Cap Français, defeated Toussaint, and drove him into the interior. The Negro army was rallied and reorganised by Dessalines, but could not have

successfully opposed the well-disciplined and well-equipped French troops had not an epidemic of yellow fever disorganized the invader. Of 25,000 Frenchmen, 22,000 died. There were only 3000 left to evacuate the Island in 1803."

Animals and birds suffer from virus diseases as commonly as man, and some of the disorders are of considerable economic importance. Swine fever and "hog-flu" have proved to be great sources of worry in pig ranches where large numbers of swine are herded together, and they are still sources of trouble, though not quite so serious, to those who keep pigs in small groups. Swine influenza is a particularly interesting example, because Shope proved that this disease was caused by the combined attack of a virus and a small haemophilic bacillus. Later Andrewes, Smith and myself, and Shope and Francis, showed that the virus element in this disease, though distinct, has close relationships with the virus of human epidemic influenza; moreover the human and porcine diseases show certain striking resemblances. Louping-ill of sheep, a tick-borne disease, causes much worry and loss to the sheep farmers in Scotland. It can infect other species, including man, but apart from its natural host, the sheep, it rarely causes serious

trouble. South African horse-sickness and equine encephalomyelitis, the latter another insect-borne disease, may be the cause of much anxiety and loss for the horse owner. Rabies is another example, but this is of little importance to Great Britain thanks to the rigid quarantine laws for imported dogs. Dog distemper, besides taking toll of many young dogs, is now recognised as a serious menace to the fur farmers, for silver-foxes, mink and fitches may suffer severely from the disease. The losses from virus diseases are greater when the affected animal population is crowded together, and this condition frequently obtains in fur farms when large numbers of susceptible young animals are coming to maturity. Three widespread outbreaks of dog distemper swept over Greenland in 1888, 1896 and 1904, with the result that sledge transport by dogs was seriously interfered with and this caused great hardship to the human inhabitants.

Foot-and-mouth disease, which is historically interesting, is also a disease of great economic importance, as is well illustrated by the experience on the continent during the latter half of last year. Foot-and-mouth disease is due to a very small virus (one of the smallest known), and this commonly infects cattle, sheep, pigs and goats, though

a number of other species are also susceptible. The disease is an acute infectious fever characterised by a vesicular eruption in the mouth and on the feet. The mortality from the virus disease alone in the adult animal is not high, though young animals suffer much more severely and serious losses may occur in young stock; but, as is often the case with virus infections, complications are common, and in this instance these may include the loss of a hoof, spreading septic infection up one or more limbs, local gangrene and occasionally pneumonia. From these complications losses are often very considerable. Even if no complications develop, the convalescent animal takes a long time to recover and regain a condition which will satisfy the farmer. Contact infection is easy to understand, but the precise mode of spread of this disease to remote places is not understood, and control has proved exceedingly difficult. In this country the disease is notifiable, and whenever an outbreak occurs which is confirmed by a Veterinary Inspector of the Ministry of Agriculture the whole of the affected herd is slaughtered and the carcasses burnt. Disinfection is undertaken and limitations regarding the movement of animals in the neighbourhood of an outbreak are imposed for a time, while a careful watch is kept for any

sign of further disease in the district. Put quite briefly, whenever this disease gains access to this country it is eliminated by a slaughter policy and compensation is paid to the farmer for the animals destroyed. In the greater part of the continent of Europe the slaughter policy is not in force, and attempts are made to control the disease in other ways. In 1936 there were a few sporadic outbreaks of foot-and-mouth disease on the continent and such as did occur did not spread to any significant extent. In May 1937 the disease broke out in the south of France, apparently introduced by sheep imported from Algeria, and gradually spread all over France, to Switzerland, Belgium, Holland and Germany. By the end of 1937 there had been at least 130,000 outbreaks in France, 63,000 in Belgium, 100,000 in Holland and 36,000 in Germany. Each of these outbreaks involved considerable numbers of animals, so that the total of cattle involved during the year must have been very large. With a disease of this type spreading so freely and widely on the continent it was impossible that Great Britain should escape, but thanks to the watchful eye of the Ministry of Agriculture and its officials, together with the loyal co-operation of the farming community, the total outbreaks in this country up to the end of the year

only reached 187. The epizootic was not over by the end of the year, but it is abundantly clear that it has cost the continent several million pounds and this sum is likely to increase, while Great Britain has suffered comparatively slightly.

Birds show many interesting examples of virus diseases, such as fowl plague, fowl-pox, pigeon-pox, canary-pox and infective laryngotracheitis, but there is one group of outstanding interest at the present time and that is the group of filterable viruses which were originally shown by Rous to be associated with the production of tumours indistinguishable from true sarcomata. In recent years there has been much work inspired by Rous's observations on fowl tumours, designed to explore the possibility that cancers in animals might be due to viruses. It cannot be said that any mammalian cancer has been shown to be associated constantly with, or caused by, a virus, but there is evidence from the work of Rous with the Shope papilloma virus and that of Andrewes, Ahlström, Gye and Foulds with the Shope fibroma virus that viruses may play some part in the production of malignant neoplasms. The work is in its infancy and what the ultimate outcome may be cannot be foretold, but the investigation is at a very interesting stage at the moment.