times with different catalyst preparations so as to make sure of the facts.

An alternative method is to study the poisoning effect under more severe conditions of time, temperature and pressure, choosing such conditions that pure copper may show sufficient activity to allow evaluation of the poisoning effect. The results are shown in Table 2.

TABLE 2

CATALYST COPPER POISONING BY BISMUTH, CADMIUM AND LEAD

Poison wt. per cent.	Hydrogenation of benzene		
	Bismuth	Cadmium	Lead
0.000	33	33	33
0.005	21	6	5
0.05	6	1	1
0.5	2	0	0
1.0	0	0	0

Conditions: T. 350°; reaction time: 12 hours; charge 50 cc of benzene, 5 gr catalyst, 100 atms of hydrogen; Apparatus: 850 cc Ipatieff rotating bomb with glass liner.

As may be observed, we obtained the same picture with poisoned copper at superatmospheric pressure as at ordinary pressure with poisoned 99.8 per cent. copper and 0.2 per cent. nickel.

We previously reported that nickel is more effective in the activation of 95 per cent. copper, 5 per cent. chromium oxide, than of pure copper. Table 3 shows the effect of lead on the activity of this catalyst.

A comparison of the data of Tables 1 and 3 shows us that 0.1 per cent. of lead lowers the activity of the nickel-promoted 95 per cent. copper, 5 per cent. chromium oxide, from sixty-two to twenty-three (63 per cent. drop) and that of nickel-promoted copper from 19 per cent. to 2 per cent. (90 per cent. drop).

TABLE 3

POISONING OF COPPER CHROMIUM OXIDE NICKEL BY LEAD

	Hydrogenation of benzene wt. per cent.
Copper	0
" – 5 per cent. Cr_2O_3	2
" – 5 " " Cr_2O_3 – 0.2 per cent. Ni	62
" – 5 " " Cr_2O_3 – 0.2% Ni	62
" – 5 " " Cr_2O_3 – 0.2% Ni – 0.1% Pb	23

Conditions: T. 225°; C.T. 12 sec. H_2/C_6H_6 7 Pressure: Atms.

As a result of these investigations with mixed catalysts containing activating and poisoning substances, we can make the following remarks. Our preliminary survey emphasizes the extreme delicacy of catalytic processes and the necessity of careful definition of purity before drawing conclusions as to the catalytic properties of any particular element of a catalyst. The sensitivity of the system benzene-hydrogen-copper competes with the spectroscope in the detection of traces of nickel, bismuth and cadmium, and it goes beyond the range of the spectroscope in its sensitivity to traces of lead. Therefore in the case of lead, at least, spectroscopic purity is no guarantee of catalytic purity, which means that in order to introduce into the catalyst traces of different promoters or poisons, it is necessary to prepare the catalyst by a special method to be sure of its composition.

In conclusion, I wish to state that for a thorough investigation of the mechanism of catalytic reaction it will be necessary to apply all the chemical and physical tools at our disposal.

VIRUSES AND THEIR PART IN DISEASE

By Professor W. G. MACCALLUM

THE JOHNS HOPKINS UNIVERSITY

WHILE we are very familiar with the details of the lives of animal parasites, fungi and bacteria which invade and live and develop in the tissues of other animals and plants, producing diseases and stirring defensive reactions, all consistent with their living activities and with those of the invaded hosts, there are many other diseases, both of animals and plants, in which the invading agencies have only recently been recognized. This is because they are so minute as to escape all our ordinary means of making such things visible or evident through most of our usual methods of study, but recently new methods have been devised which afford enough information to reveal a whole world of extraordinary active contenders for propagation at the expense of the living creatures with which we have been familiar. These are the viruses, so-called because of their harmful effects, but not yet sharply classified into groups since they vary so much in character, such as size and life history, that these subdivisions have not been completed. Some, such as those which cause typhus fever and related Rickettsia infections or those found in smallpox and vaccinia, are distinctly visible as very minute granules and can be traced in their relationship with the cells of the infected tissues, so that there is some question as to whether their nature may not be closer to that of the bacteria than is the case with other viruses which are so minute that they can never be seen.

But the matter of size, which in most cases is such as to allow the viruses to pass through a filter which has pores so small that no bacteria can pass and which has given rise to the name filterable viruses, is obviously not a fundamental distinction from larger incitants of disease. Other methods, such as differential centrifugation and ultra centrifugation, have been successful in separating these invisible germs from all bacteria and cells so that they can be obtained in pure concentration.

The further study has depended upon the demonstration of the relation of such purified viruses to susceptible animals, or to culture media, especially as to their power of multiplying themselves, their effect on tissues and the defensive response on the part of the invaded host. In general, it may be said that the virus purified by filtration or centrifugation so as to be concentrated quite apart from living bacteria, can be grown only on cultures of living tissue from a susceptible animal or on such embryonic tissue as the allantoic membrane of a chick's egg, and on no medium composed of non-living material such as is used for bacteria. Further the invasion and spread in the tissues of a susceptible animal allows of a very great increase in the virus. This results, as with the long-recognized bacterial infections, in the development in the animal body of antibodies, agglutinins, precipitins, etc. The preliminary injection of such immune serum from an animal which has recovered from a virus infection will prevent the invasion of the virus in a non-immune, inoculated animal but will not neutralize a virus already injected, because, as it is thought, the virus takes an intracellular position and is no longer exposed to the action of the immune bodies.

So far, then, the viruses in producing disease resemble pathogenic bacteria in their invasion of the body and in their production, in addition to the injuries which they cause, of a response on the part of the body in the formation of antibodies. They differ from bacteria in being dependent for their own reproduction on living cells in which they assume an intracellular protected position, and this suggests that they are dependent upon the cell for the production of something, probably of a protein nature, which they require for their nutrition and multiplication.

The diseases produced by viruses are very numerous and there can be mentioned here only types such as the tobacco mosaic in plants, psittacosis in parrots, encephalomyelitis in horses and encephalitis, poliomyelitis, influenza, measles, herpes and others in human beings.

Emphasis should be laid especially on one point which is commonly set aside, namely, the extraordinary predisposition to bacterial infection which results from the virus infection. Thus in an epidemic of measles in 1918, the deaths which occurred in great numbers were not due to the measles but to a secondary bacterial infection with a streptococcus. So, too, in the succeeding epidemic of influenza, the deaths were not due to the virus but to the following induced bacterial infection which varied in different parts of the country, sometimes streptococcus or pneumococcus or even staphylococcus, while in some places it was the haemophilus or Pfeiffer's influenza bacillus which had been erroneously believed to be the cause of influenza.

This relation has been particularly clearly studied by Shope in the case of influenza in swine, where the secondary invasion is what gives rise to the serious pathological changes.

In spite of the general understanding that scarlet fever is caused by a streptococcus, it is my belief that in this we have a typical virus infection with the characteristic secondary invasion of these bacteria. Of course, the immunological reactions which are regarded as distinctive of scarlet fever are readily explained as the effect of the secondary infection.

In many forms of virus disease the transmission from one person to another is by recognizable paths, such as the inhalation of infected spray from the breath of the diseased person, or by even more direct methods as by the bite of a dog with hydrophobia. But in many others, such as yellow fever and equine encephalomyelitis, there are intermediate hosts such as biting insects in which the virus is harbored for a long time and introduced with their bite. The control of such agencies of transmission and spread of the disease is of course of enormous importance as in the case of yellow fever.

Very important, too, is some comprehension of the conditions underlying the immunization of persons affected with such diseases. It is well known that the protection following vaccination against smallpox is of long duration and it is familiar that upon survival such childhood diseases as measles, scarlet fever, poliomyelitis and many others confer a lifelong immunity. Efforts toward artificial production of immunizing substances may depend upon various changes which can be brought about in the virus by inoculating it into less susceptible animals; thus the transfer of the yellow fever virus to mice results in the production of a type which invades the central nervous system. Most successful production of an immunizing substance has been produced by long-repeated culture of a virus in mouse embryo—Tyrode medium—and then in chick embryo. Such vaccination with a weakened virus seems to produce an effective immunization without any serious symptoms.

The principles of immunization are therefore similar to those applied in other infections, but the permanence of such immunity after recovery from the virus diseases is especially impressive. Andrewes emphasizes the persistence of viruses in the body with the antibodies which they have stirred into existence, and this may explain the prolonged immunity with apparent complete health, while disturbances of normal body conditions may temporarily diminish the immunity so that, as in herpes and some other diseases, the lesions produced by the virus may reappear.

The relation of viruses to the development of some tumors in animals has roused especial interest in recent years, and various papillomatous and other growths in rabbits have been described as well as extremely virulent and rapidly growing tumors in fowls, all of which can be transmitted to others by inoculation of filtered or otherwise isolated material from such growths. Rous and his associates have also found that the influence of tar rubbed on the skin is very effective in stirring the growth of a more malignant form of epithelial tumor growth after inoculation with the papilloma virus. Further studies of the part played by viruses in the production of tumors will be looked for in the future.

It is the extremely small size of the viruses which seems to offer the greatest difficulty in conceiving of their peculiar and specific activities such as might be more readily accepted in larger organisms. Thus in the case of the bacteriophages which are actually parasites, especially related to certain bacteria as hosts and invading their tiny bodies produce a ferment which causes the liquefaction or lysis of their bodies, setting free the bacteriophage to invade others. The story is a familiar one except that it is all on such a small scale, but the epidemic spread of this disease of the bacteria is like that of the diseases of large animals and seems to support surely the living character of these infinitesimal bacteriophages and their introduction from some source to the liquid medium in which the bacteria were alive, causing their death and destruction.

The intracellular growth of the viruses which makes them insensitive to immunizing antibodies injected later is of great interest. The nature of the inclusion bodies found within the cells in some such diseases has never been thoroughly cleared, but the general idea is that they represent accumulations of the virus. The dependence of viruses upon living cells for their multiplication and growth has led to the idea that they must find or produce within these cells some nutritive substance required by them for their maintenance. Thus in the case of tobacco mosaic there is produced by the infection a quantity of a very heavy molecular protein which is the virus. Stanley has isolated this protein and has even crystallized it, proving by all the methods at his command that these crystals of the heavy protein molecule are not merely contaminated with the virus but that they are in themselves the virulent agent.

The question then arises as to the chemical character of other viruses and as to the nature of the factors required in a protein to give it the power of causing a destructive disease, stirring immunological reactions and perhaps especially its power of reproducing itself and multiplying to such extremes at the expense of its host. We have tacitly assumed all this to be the generally accepted character of a living being, and the problem left is perhaps only as to the chemical limitations of living as contrasted with non-living proteins. If only the chemical structure of proteins were not so infinitely complex it would be interesting to reconstruct this heavy protein synthetically and having reached its precise constitution to see whether it had any virus character although synthesized from pure materials which had never had any contact with tobacco plants. As Stanley says, certain compounds act as hormones, others as enzymes, others on injection stir up an anaphylactic reaction—the transitions to those activities which we regard as characteristic of life are not insuperable.

OBITUARY

ADRIAN JOHN PIETERS

Dr. Adrian John Pieters, botanist, agronomist and administrator in the Department of Agriculture for nearly half a century, and world authority on forage and soil-conserving crops, died in Washington April 25 in his seventy-fourth year. Known, in recent years, as the Father of Lespedeza because of his apostolic leadership in making that soil-building legume a major crop in the South, Dr. Pieters had a part in a large number of the more significant contributions of plant science to agriculture during the past forty years. In his position as chief of the Office of Seed and Plant Introduction and Distribution he was one of the small group of able men who, in 1901, founded the Bureau of Plant Industry. Subsequently, as head of the section of Clover Investigations and of the Division of Forage Crops and Diseases, and as member of innumerable committees handling matters of Bureau policy, he had a large share in shaping the destinies of that Bureau and, correlatively, of applied plant science throughout the nation. The personalities, the ideas and the ideals of those who thus "set other minds in straight channels" are worth a moment's thought.

Dr. Pieters came to the science of agronomy when that earthy infant was in swaddling clothes. Its garments were sometimes of poor quality and often did not fit. Following horticulture, it was in the process of developing from an art to something approaching a science. Its devotees, of necessity, were mostly men of the soil who, on a foundation of hard realism, had to build a structure that would command the respect of eruditionists. There were not lacking those who scoffed.

Into this situation, in 1895, came a young graduate of