ground of the gas industry. It also gives a new perspective to the growth of experimental chemistry during the latter half of the eighteenth century; and it is worth bearing in mind that when Joseph Priestley discovered ammonia, he was exploring the properties of a substance of established utility as a saleable by-product of coal.

REFERENCES

S.L. = Library of the Writers to H.M. Signet, Edinburgh.
N.L.S. = National Library of Scotland, Edinburgh.

[1] Beckmann, J., "History of Inventions and Discoveries", **4**, 383 (London, 1817).
[2] Kay, John, "Original Portraits", etc., **1**, 55 (Edinburgh, 1842).
[3] Session Papers, 282, 14 (S.L.).
[4] Macintosh, G., "Memoir of Charles Macintosh, F.R.S." (privately printed, Glasgow, 1847).
[5] Dr. Joseph Black to Andrew Stuart, Edinburgh, January 25, 1783 (N.L.S.).
[6] Lord Dundonald to Andrew Stuart, Edinburgh, December 11, 1782 (N.L.S.).
[7] Session Papers, 380, 37 (S.L.).
[8] Ure, Andrew, "A Dictionary of Chemistry", Art. Ammonia, *Ann. de Chimie*, **19**, 61 (1797). Parkes, S., "Chemical Essays", **4**, 339–395 (London, 1815).
[9] Macintosh, G., *op. cit.*
[10] Sinclair, Sir J., General Report, App. Vol. 2, 310.
[11] Session Papers, 282, 14 (S.L.).

NATURE OF VIRULENCE

THE term 'virulence' has sometimes in the past been regarded as an intrinsic property of an infecting agent; that such a view is not entirely in accord with our knowledge of natural and experimental infections was apparent from the discussion on the nature of virulence at the meeting of the Society for Microbiology held in London on December 20. As virulence can only be measured in terms of the effect on the host by a micro-organism, using that term in its widest sense, it is obvious that the interaction between the micro-organism and host by which we estimate virulence will depend on many variables affecting both participants. Much of the discussion related to these variables and their effect on virulence. A very wide field was covered, contributions on the virulence of bacteria, of fungi and of viruses for both plant and animal hosts and of the parasitic protozoa being made by various speakers. It was generally accepted that multiplication of an infecting agent in the body of the host does not alone determine virulence, and that the term 'virulence' necessarily implies structural or functional damage to the tissues of the host.

It is clear that the morphology and physiology of plants are so different from those of animals that virulence of phytopathogens involves mechanisms different from those concerned in virulence of micro-organisms for animals. This point was clearly illustrated by Mrs. Dagny Oxford in her discussion of bacterial virulence in plants; the bacteria virulent for plants, unlike most of the animal pathogens, are free-living, relatively resistant and simple in their nutritive requirements. As most of these species do not split cellulose, they depend for their entry into plant tissues on abrasions or wounds. There may be some correlation of virulence of phytopathogenic bacteria with the power to produce pectolytic enzymes, and in some instances cell-free filtrates of bacterial cultures produce reactions in the plant tissues similar to those caused by the living bacteria. Mrs. Oxford pointed out that the resistance of plants to bacterial infection is a function of the local tissue cells and does not depend on any humoral mechanism such as operates in the resistance of animals to invading bacteria.

Fungi are, however, more important disease-producing agents in plants than are bacteria, and Prof. E. Gäumann of Zurich made a most interesting contribution in this field to the symposium. The necessary attributes for virulence were discussed in relation to different types of pathogenic fungi, the part played by the host tissues being emphasized. The damage to plant tissue appears in the case of one fungus to be due to a polypeptide which destroys the semipermeability of the plasma boundary layer; but the power to produce this substance *in vitro* is not of itself sufficient to determine virulence. The power to penetrate the plant tissues by the production of certain enzymes and to withstand the reactions of the host tissues are also necessary. In plant infections due to more than one fungus (mixed infections), the resulting disease may be dependent on the interaction of the infecting fungi and may not be controlled by the most virulent strain.

In his discussion on the virulence of bacteria in animals, Dr. D. W. Henderson pointed out that it is difficult to induce parasitism in normally saprophytic bacteria, and that this lack of virulence is due in some instances, although perhaps not in all, to their lack of power to multiply in the living body. In general, toxicity is inversely proportional to the degree of tissue invasion by a pathogenic bacterium. The species of the animal host, its physiological state, and its genetic constitution may all influence the virulence of a bacterial infection. Other points mentioned by Dr. Henderson as bearing on virulence concerned aggressins, route of entry of a bacterium into the body, and the synergistic action of other bacteria. The importance of the last two factors was later referred to by Dr. C. H. Andrewes in relation to the virulence of viruses for animals.

That apparent increase of virulence in a parasitic micro-organism may in fact be due to lessened resistance of the host was exemplified by Dr. J. T. Duncan in his contribution on virulence of ringworm fungi in animals. These fungi are frequently highly parasitic and highly infectious but of low pathogenicity, and the host parasite equilibrium may remain undisturbed for years. On the other hand, some of the normally saprophytic fungi may become highly pathogenic, producing severe systemic disease; and in some of these fungi pathogenicity is associated with the property of dimorphism, the organism being capable of developing, in place of the complex mycelial saprophytic form, a simple form adapted for rapid reproduction and invasion in animal tissues. In the case of such fungi, as with some of the ringworm fungi when implanted on an unusual animal host, high pathogenicity may be associated with low infectivity.

The parasitic protozoa afford instructive examples of variations in the host parasite relationship in relation to virulence. Prof. H. E. Shortt illustrated the state of true symbiosis between certain protozoa and their vertebrate or invertebrate hosts, and from the symbionts and commensals went on to consider the parasitic protozoa. Some of these may multiply without producing disease, but this balanced parasitism might be readily upset. The mechanism by which disease is produced by pathogenic protozoa is not clearly understood; no true toxins are demonstrable, and in some cases disease is due to mechanical

effects resulting from extreme proliferation of the parasites in particular cells or tissues; for example, certain trypanosomes in the reticulo-endothelial cells or muscle, and the malaria parasite in blood cells. Death of such highly parasitized hosts is frequently due to super-added infection with bacteria or other infecting agents. In the state of latent or chronic protozoal infection, it can be shown by transfer to fresh hosts, or by measures which lower the resistance of the chronically infected animal, that the protozoan has not lost its virulence. On the whole, it seems that for this class of micro-organism (as for the viruses and certain of the more parasitic bacteria) excessive virulence is a disadvantage to the parasite from the point of view of survival of the species, and virulence may represent the initial stages of association between the parasite and host, to be succeeded by commensalism or symbiosis.

The virulence of viruses for plants or animals must be considered only as a virus-host relationship, as the known viruses are essentially parasitic. Both Dr. Kenneth Smith and Dr. C. H. Andrewes stressed the variations in virulence manifested in virus-host associations according to variations artificially induced or arising naturally in the infecting virus, or depending on host factors and particularly on host species. The highly virulent virus which always produced death of the tissues or whole plant would, as Dr. Smith pointed out, have difficulty in transmission to fresh hosts and thereby in ensuring survival. Such plant viruses, however, while apparently possessing intrinsic virulence for one plant, usually infect other plant hosts without producing symptoms. Variations in virulence can be produced by various procedures which probably favour selectively the multiplication of a virulent variant already present in the virus strain. The emergence of virus mutants under laboratory conditions was also mentioned by Dr. Andrewes, who suggested that the selective survival of mutants showing antigenic variations from the original virus may explain the course of certain human epidemic diseases. From several viruses stable variants can be produced by adaptation to a new host species. The highly virulent virus is able to multiply extensively in invaded host cells, and to destroy these cells with liberation of virus for the attack on further cells. Although the mechanism responsible for cell destruction is not known, recent work with rickettsiæ and influenza virus suggests that these agents in the living state, if present in sufficient concentration, can exert a toxin-like action. Virulence of the animal viruses may also depend upon special tissue affinities, as in the neurotropic viruses. The adaptation of virus to host which results in latent infection may, as in other host-parasite associations, be readily upset.

Prof. A. W. Downie, in summing up the discussion, referred to various points made by previous speakers and suggested that the host-parasite relationship studied under experimental conditions might not show the manifestations of virulence which are evident under field conditions as shown by the behaviour of epidemic disease. We are ignorant of the mechanism by which damage to the tissues of the infected host is produced, and in this field there seems much to be done in the study of the biochemical interactions of parasitic micro-organisms or their enzymes and toxins with the metabolic processes of the host cells.

OBITUARIES

Prof. Robert Newstead, F.R.S.

ROBERT NEWSTEAD was justly proud of the fact that the high place which he achieved for himself in the scientific world, and the distinction which he brought to the Liverpool School of Tropical Medicine and to his adopted city of Chester, were won by him in face of almost insuperable obstacles, associated with an interrupted schooling and an absence of university training or contacts, until he was more than forty years of age.

Newstead, whose death occurred on February 16, was born on September 11, 1859, at Swanton Abbott, Norfolk, and received his early education at a village elementary school, from which he not infrequently played truant in order to be out in the fields and the woods, watching bird- and animal-life. At the age of ten he left school and was apprenticed to the village post and telegraph office, which included also a printer's and stationer's works. There, during the period of the Franco-Prussian War, Newstead became familiar with the processes of printing and studied telegraphy, in which he passed one examination. From telegraphy he passed to gardening and a little farming, devoting his spare time to the study of a small text-book of zoology, from which he taught himself the elements of systematic study, and to the collection of specimens of plant-, animal- and bird-life. One such collection, made primarily for his own pleasure, led to the beginning of his long connexion with Chester. In 1883, at the age of twenty-four, he was invited to exhibit a collection of Norfolk insects, birds and fungi at the Town Hall, Chester. His specimens attracted the attention of the late Mr. Alfred Walker, a disciple of Charles Kingsley and an ardent naturalist, who straightway offered him an appointment in his gardens, partly as gardener, partly as naturalist.

While holding this appointment, Newstead was present at the laying of the foundation stone of the Grosvenor Museum, Chester, and in 1886, when the Museum was opened, he realized one of his early ambitions by being appointed its first curator. The curatorship of the Museum was held for nineteen years, during which time Newstead was responsible for arranging and describing the exhibits in the natural history and archæological sections, both of which were enriched by many specimens which he personally prepared and mounted, not only during his tenure of office, but also long after his retirement; and I have seen him busy with this work after he had passed the age of eighty-five.

In 1906 Newstead was appointed lecturer in economic entomology and parasitology at the Liverpool School of Tropical Medicine, six years after its foundation as the first school of tropical medicine in the world, and at a time when it numbered on its staff such eminent men as Sir Ronald Ross and Sir Rubert Boyce. The importance of Newstead's work now began to receive wider recognition; in 1908 he received the degree of master of science *ex officio* in recognition of his scientific achievements, and in 1911 he was elected first holder of the Dutton Memorial chair of entomology in the University of Liverpool. From that time until his retirement from the chair in 1924, Newstead held a leading place in the world of entomological research. He was dispatched on two scientific expeditions organised by the Liverpool School of Tropical Medicine: first, to