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Problems of Immunity and Infection: the Filter-passing Viruses.

IN investigations on the effects produced in the body by invading micro-organisms, much attention has been directed towards an analysis of the defensive reactions of the former, but fewer observations have been made with regard to the offensive powers of the latter. Thus it is well known that the leucocytes or white cells of the blood, the wandering cells of the tissues, and certain of the endothelial cells lining the blood capillaries, are a part of the defensive mechanism of the body against bacteria or other particulate matter, which they ingest, and, if possible, destroy, whilst a further line of defence is represented by the different types of immune bodies which are present in the cells and tissue fluids or are developed therein in response to the invasion. The factors on which the infectivity, or virulence, of an organism depends are, however, less certainly understood, although variations in virulence quite apart from variations in the defensive powers of the host have been frequently observed. The "Report of the Medical Research Council for 1924–1925" lays stress on this aspect of the question, which has assumed considerable importance from the recent work of Gye and Barnard on cancer.

It has been known for some time that certain organisms are, by themselves, non-virulent: thus, the bacilli or spores of tetanus, or lockjaw, and those of gas gangrene, if thoroughly washed, produce no ill-effects on injection into the animal body. Gye and Cramer found that a minute quantity of a calcium salt, or of silica, both common constituents of the soil in which the organisms occur, injected along with them enabled them to act with their full virulence. A somewhat similar relationship was observed by Gye and Kettle with regard to the growth of the tubercle bacillus in the presence of silica, a relationship which is seen clinically in the association of pulmonary tuberculosis with silicosis in 'miners' phthisis.' It is of interest that some protozoa also seem to require the presence of some associated factor before they become virulent: thus, Dobell has found the *Entamœba histolytica*, the amœba responsible for one type of human dysentery, in the intestine of many people in Great Britain, yet the disease itself is very rare.

It will be recalled that the work of Gye and Barnard on cancer offers a very close analogy to the above-mentioned examples of the association of an organism with some 'specific' factor necessary for the development of the power of infectivity. The difficulty facing the hypothesis of the infective nature of cancer has always been the impossibility of transferring the tumour from one animal to another of a different species, and even in the case of animals of the same species,

transference is only possible with the living tumour cells. On the other hand, the microscopical appearances of a single variety of cancer in different species are the same, suggesting definitely a similarity of origin. The investigations of Gye and Barnard reconcile these two points of view by showing that the disease depends on the presence of a micro-organism acting in association with a 'specific' chemical factor.

Although usually the inoculation of an animal with a tumour only produces a growth when the living tumour cells are implanted, a few exceptions to this statement are known; thus, the Rous fowl sarcoma is caused by an agent which passes through the finest filters and has for long been believed to be a filter-passing micro-organism. Gye proved that this virus is actually corpuscular, since it can be shifted in fluids by the application of a centrifugal force and in pure culture, in the technique of which he was also successful, can be photographed by means of ultra-violet light by the method devised by Barnard. The presence or absence of the organism, determined experimentally by Gye, was confirmed microscopically by Barnard, thus increasing confidence in the results obtained by each author. But the greatest interest, perhaps, lies in the demonstration that the organism itself failed to produce any tumour when inoculated into fowls: it was only when an extract of tumour tissue in which there were no living organisms was inoculated together with the virus that a growth appeared. It was found on further work that the microbe could be obtained from other animals or tumours, but that the second non-living factor was 'specific,' in the sense that the type of tumour and its actual occurrence in an inoculated fowl depended upon the former's presence. The work suggests that the organism can only produce a tumour when the 'soil' is suitable for its growth: the many agents to which the origin of different cancers is ascribed, such as various irritants, may perhaps act by production of a favourable 'soil,' in other words, by causing the cells of the tissues to form, in the course of their, probably abnormal, metabolism, a chemical substance, which, in the present state of our knowledge, can only be described as the 'specific factor.'

The work of Gye and Barnard lends additional importance to investigations of the other filter-passing viruses and the diseases caused by them, among which may be mentioned canine distemper, 'sleepy sickness' (*Encephalitis lethargica*), herpes, vaccinia (cowpox) and variola (smallpox). That methods which are used for the investigation of the properties and effects of ordinary bacteria are applicable to the study of these viruses has been shown in the case of vaccinia and variola by Gordon. He has found that different samples of vaccine lymph obtained from calves and used in the vaccination of human beings against smallpox contain the same virus, and that the viruses from different smallpox epidemics tested against anti-vaccinia serum, all gave positive results. The fact that the immunity reactions given by this group of 'ultra-microscopic' organisms are similar to those given by the more common bacteria suggests that investigations on the other filter-passers, such as the viruses of cancer and canine distemper, can be undertaken with the hope of adding greatly to our knowledge concerning them. Work in connexion with the latter disease is being carried on in association with the *Field* Distemper Fund. It has been found that the disease can be transmitted to ferrets, which may thus be used for much of the experimental work; the virus is undoubtedly a filter-passer, although it has not yet been isolated or cultivated *in vitro*; the disease is extremely infectious, and it appears possible that the virus is air-borne, at any rate over short distances, necessitating adherence to a scrupulous technique on the part of all those concerned in the investigation.

Two further points may be very briefly considered. Although the chemical nature of Gye's 'specific factor' is quite unknown, there is no reason why further research should not throw light upon its general chemical properties, in the same way that recent work has brought an increased knowledge of the chemistry of the compounds involved in the immunity reactions of the body. Dudley and Laidlaw have obtained from tubercle bacilli a substance which forms precipitates in high dilutions with the serum of animals immunised against the whole protein constituents of the bacilli, although it will not itself evoke the production of such a serum. On analysis, the substance was found to be a complex carbohydrate of the nature of a gum, yielding pentoses and a more resistant nucleus on hydrolysis. Again, Hartley has shown that certain of the reactions between diphtheria toxin and antitoxin are caused by the ether-soluble constituents of the serum, whereas others occur independently of this fraction.

Finally, mention should be made of the question of treatment: the work on the filter-passing viruses having shown their close relationship with the microscopic bacteria, so far as the responses of the body are concerned, the outlook for a specific therapy is brighter than might otherwise have been the case. Meanwhile, the investigation of chemical compounds with a bactericidal action is being continued, especially in connexion with tuberculosis: both sanocrysin and certain oils have claimed the particular attention of numerous workers. An interesting point in connexion with the latter is the discovery by Griffith that the germicidal power of the oils is increased by exposure to the sun's rays, owing to chemical changes which they undergo in the light. One may recall the formation of the anti-rachitic vitamin

in similar circumstances, and the beneficial effects of sources of the fat-soluble vitamins in this disease.

The many points on which our knowledge of micro-organisms is advancing suggest a hopeful outlook with regard to the treatment of cancer and tuberculosis, two of the great scourges of mankind. Although a certain cure is not yet obtained, and may be still far distant, a cautious optimism with regard to the position appears to be justified.

Spitsbergen Papers.

Spitsbergen Papers. Vol. 1. Scientific Results of the First Oxford University Expedition to Spitsbergen (1921). Pp. xi+454+17 plates. (London: Oxford University Press, 1925.) 30*s.* net.

BRITISH tradition in Spitsbergen dates from Stuart times, when English sailors explored the coasts and fiords of that northern land. Later, Phipps, with whom was the midshipman destined to be Lord Nelson, and Lord Dufferin, added to our associations. Scientifically, however, the tradition is barely half a century old, Sir Martin Conway's expedition being virtually the first serious attempt of British men of science to grapple with the problems—geographical and geological—of Spitsbergen. Within the last few years, the exploration work of the late Dr. W. S. Bruce, the detailed geological investigations of the Scottish Spitsbergen Syndicate, and the results of the several Oxford University expeditions, have put the seal upon our interest and research.

The present work, which is the first volume of the results of the four Oxford expeditions and is devoted to the researches of the first (1921) party, consists of thirty-two reprints of papers, retaining the format and pagination of the scientific journals in which they originally appeared, with an appendix on Polyzoa and Tunicata which has not previously been published.

In the preface to the volume, the writer states that the original idea was that the expedition should be purely ornithological. Later, however, the personnel was increased to include representatives of the other natural sciences, with the result that the book contains articles on subjects ranging from rotifiers and lichens to topography, glaciology, and the courtship of birds. The party finally consisted of eighteen men under the leadership of the Rev. F. C. R. Jourdain, and with the title of the Oxford University Expedition to Spitsbergen.

The expedition consisted of two parties which spent almost three months in the archipelago, visiting Bear Island, Prince Charles Foreland, and the west coast of Spitsbergen generally, and Ice Fiord in particular. The scientific results obtained were published as soon as possible in the appropriate journals, so that specialists have already seen the results that most concern them.

The results may be divided into two groups: those which deal with topographical and geological work, and those concerned with the zoological and botanical observations made by the expedition. The former is represented by three papers of great interest. Mr. R. A. Frazer gives an account of the topographical work of the expedition, which was mainly in the nature of a reconnaissance and consisted principally of a sledge journey into the area north-east of Ice Fiord known as Garwoodland and New Friesland. In another paper Messrs. Huxley and Odell describe in detail the nature, and their theories of the formation, of the peculiar stone and fissure polygons and other surface markings seen so well in Spitsbergen. This paper is of special importance in view of the fact that it was only so recently as 1914 that Högbom, for the first time, put forward a feasible explanation of the phenomena. Mr. Slater's observations on the Nordenskiöld and neighbouring glaciers are also worthy of close study in view of the analogies (already noted by Garwood and Gregory) to be drawn between certain glacial phenomena in Spitsbergen and British drift deposits.

The biological papers are of exceptional interest from an ecological point of view. Spitsbergen occupies a peculiarly favoured position for such study, being a fairly accessible region for the explorer, yet sufficiently isolated to maintain a relatively simple fauna and flora. In addition, a great number of observations had already been recorded by other workers. Full advantage was taken by the Oxford Expedition of the opportunities thus afforded, as is evidenced by the published results. In a work of this kind, it is an invidious task to select papers of outstanding merit, but the "Contributions to the Ecology of Spitsbergen and Bear Island" by Messrs. Summerhayes and Elton is one of the most striking contributions yet made to Arctic biology. In this paper the authors describe the plant and animal communities of part of Bear Island and Spitsbergen (Prince Charles Foreland, Cape Boheman, and various parts of Ice Fiord). The succession of plant communities is traced, a noteworthy feature being the relative abundance of cryptogams, especially Bryophyta. The proportion of this group is particularly high upon the maritime coasts, which is no doubt due to the increase in humidity. The number of species, both plant and animal, is small, the severity of climatic conditions, geographical isolation, and the absence of distinct night and day being the chief factors held responsible. In addition, the authors give a sketch of the food cycle in Bear Island.

The remainder of the papers, apart from a few on ecological problems, are devoted to additions to systematic zoology and botany.

The volume, since it unites a somewhat scattered