There is evidence that one of the chief reasons why a balance is ultimately established in nature is that resistant plants survive, while the less resistant ones succumb. Therefore, in time, a certain amount of resistance to the attacks of parasite and animal enemies characterizes the native vegetation. Cultivated crops do not show this resistance unless resistant strains are selected by man to propagate the species or unless the crop has been grown in a fairly stable environment for a long time. There is further evidence that wild plants which exhibit certain degrees of resistance to enemy attacks in nature have this resistance factor weakened by a changed environment.[14] Native prairie vegetation may be losing some of its vigor, hardiness and resistance to its enemies by the changed environment brought about by present-day conditions.

The principle of biological control is to increase the natural enemies or checks of a species by additional species of parasites, predators, or diseases, or by releasing, after artificial propagation, a large number of individuals of a common species. Some outstanding examples of biological control of noxious weeds and insects have occurred. The control of the cottony cushion scale by the Australian ladybird beetle is a well-known example among insect pests. The present-day control of prickly pear in Australia, with the cochineal scale insect and the control of the sugar cane moth borer in Hawaii, are well-known outstanding example. In these and similar instances, man has aided nature in supplying the checks to certain forms which hold them to small numbers. Eradication has never yet been attained in biological control and probably will not be accomplished. It is a graphic example, enacted dramatically in a brief space of time of a restored balance.

Man with his agriculture has upset the age-long balance of nature in the great plains region, and a new balance has not been reached. It probably is a long way off, in fact, since man is constantly changing his agriculture. Nature works slowly and not necessarily for the benefit of man. New factors under modern civilization are always being introduced which tend to postpone attainment of the new balance. Most natural checks, such as parasites, spread slowly. Man is aiding them somewhat. The native wild insectivorous birds are becoming more scarce. Their place is being taken by such forms as the English sparrow, mourning dove, grackles, crows, pigeons, robins and domestic fowls. These birds are primarily seed and fruit eaters, being only in part insectivorous, or insectivorous for part of the year. What is lost for man's welfare in one sector must be made up elsewhere by some other advances.

Insect and plant disease problems are actually increasing, both in number and severity in the great plains region. Man, the disturber, will have to employ artificial control efforts for a long time, or be seriously handicapped in his labors. This biological complex reminds us of a complicated and delicate machine in which a slight misadjustment of a part affects all the others. It is as a stone dropped into a quiet pool. The ripples travel outward on all sides and upset the grains of sand all along the shore.

VIRUSES[1]

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THIS is an age of extremes. Very tall buildings, exceedingly large ships and unusually fast automobiles are indicative of modern trends. Moderation no longer satisfies. This desire for the superlative has taken possession of workers interested in infectious maladies, and now it is a common occurrence to hear talk about the minutest incitants of disease, namely, those that penetrate the "very finest" and "most impervious" filters. Extremely high buildings are not necessarily beautiful and profitable. Nor is the fastest mode of travel always the safest and most enjoyable. Large incitants of disease may be just as injurious to their hosts as are extremely minute ones. Yet the fact that a building is higher than all others and that certain etiological agents of disease are too small for resolution by means of a microscope lends an air of importance or mystery to the objects possessed of such unusual characteristics.

The sudden realization on the part of many workers that certain incitants of infectious disease may be very small and that types of infectious agents different from those already known may exist undoubtedly accounts for some of the present interest exhibited in viruses. These agents and the diseases caused by them are no more important now than they were formerly. Nevertheless, a concerted curiosity has served to focus attention upon them at this time. With this increased interest there have appeared in the literature many fantastic statements and unwarranted conclusions regarding the viruses. It is concerning some of these that I wish to make a few comments.

State College Jour. of Sci., 4: 49–179, 1930; J. E. Weaver, "The Environment of the Prairie," Bull. No. 5, Bot. Survey of Nebr., 50 pp., 1931.

[14] J. W. McColloch, "The Resistance of Plants to Insect injury," Bien. Rept. Kans. State Hort. Soc., 37: 196–208, 1924.

[1] Presidential address, the American Society for Clinical Investigation, Atlantic City, May 2, 1932.

Before protozoa and bacteria were known to exist, infectious diseases were thought to be caused by the wrath of the gods, miasmas, dirt and configurations of the stars. The idea that maladies might be induced by minute plants and animals seemed absurd. After much work and strife, however, it was clearly demonstrated that bacteria and protozoa do incite disease. Indeed, the fact was so firmly established that most, if not all workers, reasoning by analogy, came to believe that all infectious maladies are caused by fungi, bacteria, spirochetes, protozoa, or some form of these agents. The notion now held by some workers that primitive forms of life different from those mentioned may exist or that inanimate agents, reproducible in series, may cause infectious diseases has seemed ridiculous to many investigators. Although such ideas appear strange at first, there is no obvious reason, except analogy, to suppose that infectious diseases can be caused only by fungi, bacteria, spirochetes and protozoa, or that all infectious agents must be animate. One should not be dismayed by new ideas lest in future years one be listed with the skeptics who continued to believe the world flat in spite of proof to the contrary. On the other hand, one should not be too eager to embrace every new doctrine lest the mental tranquillity secured by the acceptance of a logical explanation—not necessarily the true one—blunt intellectual acuity.

Frequently one encounters statements that the virus diseases represent a group of infectious maladies of unknown etiology or that the virus group serves as a "catch-all" for infectious processes whose inciting agents are unknown. Such statements indicate that the etiological agents of smallpox, vaccinia, yellow fever, rabies and poliomyelitis are unknown. It is true that the exact nature of these agents is unknown, but to say that the agents themselves are unknown is somewhat of an exaggeration. Individuals who believe them to be unknown tacitly admit that they are incapable of knowing infectious agents that are invisible or unable to grow on lifeless media. Without going into a detailed philosophical discussion of what can and can not be known, one is justified in saying that the viruses of smallpox, vaccinia, yellow fever, rabies, poliomyelitis, herpes simplex, foot-and-mouth disease, fowl-pox, fowl plague, canine distemper and psittacosis are not entirely unfamiliar to the initiate. They can be separated one from another and from ordinary bacteria. Furthermore, in many instances their presence in a variety of materials can be ascertained with much more ease and assurance than is the case with certain bacteria. The old admonition regarding human beings, "Ye shall know them by their fruits," is quite applicable to the viruses, because they are known by their activities, that is, by the type of host or hosts attacked, by the clinical and pathological pictures induced, and by the immunological responses excited. In order to know an infectious agent it is not essential to see it or to grow it on laboratory media any more than it is imperative to see electricity in order to recognize it and to control it for our daily needs.

In 1873, Bollinger described in cells infected with the virus of fowl-pox large bodies that he considered the protozoan incitants of the disease. When it was demonstrated that the virus of fowl-pox is capable of passing through bacteria-tight filters, the Bollinger bodies, 7 to 25 μ in diameter, became discredited as the causal agent until Borrel and others showed that these structures consist of lipoidal capsules within which numerous minute coccoid bodies of uniform size are embedded in a protein matrix. At present certain investigators contend that the Borrel bodies are minute living organisms and represent the virus of fowl-pox. These contentions are based on the facts that the bodies are always present in infectious material, that they are uniform in size, that they have the appearance of minute organisms, and, finally, that they agglutinate in the presence of specific antisera. Such facts may be considered presumptive evidence that the Borrel bodies are minute organisms, but they are not conclusive, because as yet one can not by morphological and tinctorial data alone determine whether autonomous life exists in them. Furthermore, one dare not state that agglutination of particulate matter by a specific serum is proof of autonomous existence in such agglutinable particles, because it has been demonstrated that collodion particles treated with a variety of proteins and then thoroughly washed are specifically agglutinated by the proper antisera.

For a long time a few investigators have held that certain virus diseases are induced by ordinary bacteria. Now that attention is being focused on filterable forms of bacteria, workers in increasing number are adopting the belief that viruses are merely filterable, invisible and noncultivable elements of ordinary bacteria. Without going into details of the available knowledge of bacterial life cycles and their invisible and noncultivable forms, one can say that proof of many of the claims regarding them is lacking. Since even the existence of bacterial life cycles is doubtful, it seems unwarrantable to offer presumptive filterable forms of them as the explanation of another unsolved problem, the nature of the viruses.

Numerous workers seem to be convinced that the viruses are animate organisms, probably extremely minute bacteria. Yet they do not hesitate to state that the diameter of the etiological agent of foot-and-mouth disease is 8 to 12 $\mu\mu$. If such figures are accurate, then this virus is indeed very small, not much larger than a molecule of hemoglobin which is now believed to be approximately 5.5 $\mu\mu$ in diameter. Is it possible for an aggregate of so few protein molecules to be an organized living creature possessed of metabolic and reproductive powers comparable with those of minute bacteria? I am glad that I am not constrained to answer this question. Nevertheless, those who insist, without more evidence than is now at hand, upon the living nature or at all events upon the bacterial nature of the virus of foot-and-mouth disease, should at least manifest some appreciation of the difficulties of believing this.

As a rule viruses are smaller than ordinary bacteria. There is no reason to suppose, however, that all of them are of an identical order of magnitude any more than it is necessary to assume that all bacteria or all animals are of one size. Nor is there sufficient evidence to justify the belief that all viruses are of the same nature. Some may be inanimate transmissible incitants of disease, others may be primitive forms of life unfamiliar to us, still others may be minute living organisms. If it be assumed that the viruses differ in natures, one comes up against the question of why the diseases caused by them manifest many striking features in common. To find the answer to such a question may not be exceedingly difficult. At least a partial solution might well lie in the phenomenon of the intimate association of the viruses, animate or inanimate, with the susceptible host cells. Furthermore, the viruses may be situated near the line that separates inanimate transmissible incitants from minute living organisms. The transition from one side of the line to the other may be so gradual that no great difference in the types of disease caused by agents near the line is perceptible. Such a statement is strongly reminiscent of a remark by Aristotle that "nature makes so gradual a transition from the inanimate to the animate kingdom that the boundary lines which separate them are indistinct and doubtful."

To the naturalist it is undoubtedly of importance to know whether the viruses are living autonomous agents or products of cellular perversion capable of inciting similar perversions in other cells. Would a definite solution of this problem lead forthwith to great advances in the handling of virus diseases? At the moment I see no reason to suppose that it would. What, indeed, would be gained in this direction, were it possible to see, to define the nature of and to cultivate in abundance on ordinary media the etiological agents of poliomyelitis, smallpox, yellow fever, measles and varicella? Certainly nothing of a startling nature. Practical problems would for a while at least remain much as they are now, because already the viruses of smallpox, vaccinia, poliomyelitis, yellow fever and many other diseases can be handled, identified and kept free from bacteria. Moreover, many of these maladies can be experimentally induced in animals and highly protective and neutralizing sera can be obtained. Furthermore, there are successful methods of vaccination against many virus infections, notably smallpox, rabies, yellow fever, fowl-pox, canine distemper and cattle plague. I have little patience with those who state that just as soon as the viruses are cultivated on lifeless media, it will be possible to make vaccines to prevent and sera to cure the diseases caused by them. Had we waited for the cultivation of the viruses, we would still be without Jennerian prophylaxis and antirabic vaccination. Indeed, Jennerian prophylaxis was firmly established before it was known that bacteria cause disease. Furthermore, it is exceedingly doubtful whether viruses cultivated on ordinary media would lead to the production of antiviral sera superior to the ones already obtainable, for example, those against smallpox, measles, yellow fever, foot-and-mouth disease and poliomyelitis, the value of which as curative measures is questioned by many investigators.

Numerous diseases spread by means of water, milk, food, filth and insect vectors have been controlled not by preventive vaccines and curative sera, but largely through the improvement of sanitary conditions. Many viruses obtain entrance into their hosts by way of the upper respiratory tract. Our inability to control disorders arising in this manner is not due to the fact that we have not used some special kind of medium for the cultivation of the viruses, but because it is essential that we breathe, and as yet no one has suggested a practical method of obtaining uninfected air for human beings living amongst their fellows.

For more than thirty years investigators in considerable number have waited for the veil of mystery that surrounds the viruses to be lifted by deft hands capable of cultivating these agents on lifeless media. If the viruses are minute obligate parasites incapable of multiplication in the absence of living susceptible host cells, or if they are products of cellular perversion reproducible in series, then to wait for this to eventuate is a waste of time. Fortunately a number of workers are already attempting by other means the study of the virus diseases and their etiological agents. That a certain amount of success may attend these methods is proven by the results of recent work on vaccinia, psittacosis, canine distemper, poliomyelitis and yellow fever.