Application of the Electron Microscope to Biological Research

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Research workers dealing with extremely minute particles now have the invaluable assistance of the electron microscope, enabling them to see objects or details not within the resolving power under previous microscopic conditions. In the field of biological research, the possible uses of the electron microscope are almost unlimited. Its application to laboratory problems may be divided into several types, such as routine study of vaccines, or of organisms grown under varying conditions or medicated with different solutions, or research into the realm of smaller bacteria or viruses never clearly observed or seen at all with the light microscope.

In the study of vaccines, the microscope has been used in these laboratories in connection with alum precipitated antigens. It is known that addition of more finely divided particles of alum gives better immunizing results and less reaction. Since this is not too well observed under the light microscope, the electron microscope has been of value in determining relative particle sizes found in various alum precipitated vaccines and in proving the consistency of the particle size in some of the vaccines.

There have been some interesting results of observing more closely the effect of different conditions imposed on the same organism. This has been noted particularly with *Hemophilus pertussis* and *Clostridium tetani*. *H. pertussis* was grown under conditions similar except for the varying use of human plasma and horse plasma in the media. Although there was no difference in the antigenicity of the two groups, there was a significant change in the appearance of the bacteria under the electron microscope. *Cl. tetani* was also grown under similar conditions with only a variation in the type of peptone used in the broth. Here a noticeable change occurred in the antigenicity as well as in the appearance of the organism.

A striking example of the change in medicated bacteria was found in a study of Staphylococcus and Streptococcus grown in inhibiting dilutions of penicillin. Pictures taken by the electron microscope when compared to normal controls showed considerable variation. Staphylococci were greatly enlarged and swelled to the bursting point, while Streptococci also enlarged and showed a tendency to have division inhibited although growth continued. *Cl. welchii* was found to be affected in the same manner.

A very apt subject for study with the electron microscope, and one of interest during the present war in connection with tropical diseases, has proved to be the Rickettsiae of typhus fever. A great deal of variation has been found within the rickettsial cells, which have always been too small to study well with the available resolution of the light microscope. From the small granular type to the larger bacillary form there are many

intermediary forms which might eventually be found to correspond to phases of a supposed cycle. It is hoped that further study might lead to information which will produce a better vaccine.

The only organism studied so far in these laboratories in or allied to the virus group has been that of a pleuropneumonia-like organism taken from the arthritic joints of the rat. Cultures usually appear as gram negative bacilli, but in some instances nothing at all can be seen under the regular light microscope. These latter cultures when observed under the electron microscope revealed very ghost-like forms which have been attributed to the virus form of pleuropneumonia. Some exceedingly bizarre but consistent forms were seen.

The advantages of the electron microscope are rather obvious, and it is easily seen that only a beginning has been made in the vast study of hitherto unknown organisms. It is hoped that some contribution to the fund of knowledge and some betterment to the field of therapy will arise from studies made with this microscope in the future.