movements to prevent stiffness of joints are necessary for the fingers when pedicle grafts are transferred from the abdomen or elsewhere by means of the arm; and for the toes when the legs are immobilized for cross leg grafts. Such movements must be commenced immediately after operation and be sufficiently frequent to prevent stiffness. The test of efficiency of the Physical Medicine Department is that stiffness is prevented rather than function restored.

Œdema of a limb due to trauma or hypostasis is troublesome to the plastic surgeon and leads to stiffness of joints. It should be controlled as soon as possible by elevation, frequent massage, static contractions of the large muscle groups of the limb and occupational therapy performed with the limb in the elevated position. As soon as the œdema is under control the dependent position is resumed by graduated stages.

The President expressed surprise at the scant use which was apparently made of physical methods in the preparation of the receptor areas in grafting. Much excellent work done by Nutini and his co-workers had proved beyond dispute that raw areas treated by ultraviolet light were not only sterilized superficially but that the cells damaged by this agent produced substances which provoked proliferation in other cells. It would seem that irradiation with ultraviolet light might be indicated before grafting to ensure taking.

[*June* 21, 1944]

The Electron Microscope: Its Application to Medicine

By G. E. Donovan, M.Sc., M.B., D.P.H.

Function depends on structure. It is also true that structure is altered or moulded by function. Any advance which makes the perception of the finer details of structure possible is of interest to the doctor.

Resolution and Visibility

The resolving power (as apart from magnifying power) of a microscope is its capacity to separate two adjacent points, and this property determines the amount of structural detail that can be observed. The maximum resolving power of the "naked" eye is 0·1 mm. (100 microns). The limit of resolution of the light microscope is attained, using visible light of the shortest wavelength, when the magnification reaches approximately 2,000 diameters. Theoretically, with axial illumination, two points closer together than half the wavelength of the light used cannot be resolved. It is not possible to attain this theoretical limit under normal visual working conditions and, in practice, the limit is reached at about 0·25μ (0·00025 mm.). It is to be remembered that an average human red blood corpuscle is about 7·5μ.

According to Abbe, the smallest distance d of two parts of an object which can be resolved with light of wavelength λ is given by

$$d = \lambda / (n \sin \alpha),$$

where (N sin α) is the numerical aperture of the objective, N being the refractive index of the object space and α the semi-vertical angle of the cone rays entering the objective. If the wavelength λ is decreased, this resolving distance d can be reduced.

Resolution, however, must not be confused with visibility, because it is possible to see "elementary bodies" (of virus diseases) as small as 0·074μ with ordinary white light, and even smaller, 0·0673μ with green light. The difference between visibility and resolution can be illustrated if a printed page be placed about a distance of 10 feet away. It is possible to see that the print consists of a number of letters, but it is not possible to distinguish the form and shape of the actual letters as such at this distance. The letters are visible but their details cannot be resolved.

The ultraviolet microscope.—If ultraviolet light is used instead of visible light, a 50% improvement in resolving power can be obtained, but special quartz lenses and photographic registration must be employed. By this means, J. E. Barnard has succeeded in photographing several of the filterable viruses.

Electron Rays

The limitations imposed when using light radiations have largely been removed as the result of recent progress in electron physics. It has been found that moving electrons behave as if they were associated with a wavelength; this wavelength being an inverse function of their velocity. Some photographs have been published which show diffraction rings produced by light passing through a minute hole in an opaque screen. These rings are due to the fact that light is propagated by wave motion. Other photographs show similar diffraction rings and patterns produced by electrons passing through a thin gold film, and by electrons reflected off a small face of gold. That this does not result from X-rays produced by the electrons striking the gold leaf is proved by the fact

that the whole system of light and dark rings is deflected when the beam of electrons emerging from the gold leaf on its way to the photographic plate is passed through a strong magnetic field. Such a magnetic field would have no effect on light waves or X-rays.

The fundamental theoretical investigations of L. de Broglie in 1925 and the experimental researches of G. P. Thomson in 1928 established the existence of a wavelength of the electron which was found to be extremely short in comparison with the wavelength of light. The electron wavelength measured in cm. is

$$\lambda = \frac{1{\cdot}22.10^{-7}}{\sqrt{V}} \times \frac{1}{\sqrt{(1+10^{-6}V)}}$$

λ depends only upon the electron energy V, which, in the equation is measured in ev.

Electron rays of 20 to 100 kv. energy can easily be produced by electrical discharges in gases or by an acceleration of electrons emitted from a hot cathode. A stream of electrons can easily be given velocities up to 100,000 miles a second by the influence of high voltages. With an accelerating voltage of about 60,000, which is commonly used in the high voltage cathode-ray oscillograph, the velocity attained is about 150,000 km. per second (about half that of light), and the associated electron wavelength is then about 100,000 times smaller than the wavelength of visible light. If such a beam of electrons could be used as light rays are in the microscope, one would expect a corresponding increase in magnifying and resolving power One red blood corpuscle would be enlarged to seven metres. This does not work out in practice, as there are physical limitations, which greatly reduce the useful magnification obtainable.

Electron Optics

A beam of electrons is a stream of negatively charged particles and can be bent by means of magnetic or electrostatic fields to bring them to a focus. A procedure of this kind is followed in the electron microscope. The optics of electron rays are in some ways comparable to those of light rays, but instead of using glass lenses, the focusing agents are electric or magnetic fields (*see* fig. 1). The bending does not take place suddenly as in glass lenses, but gradually.

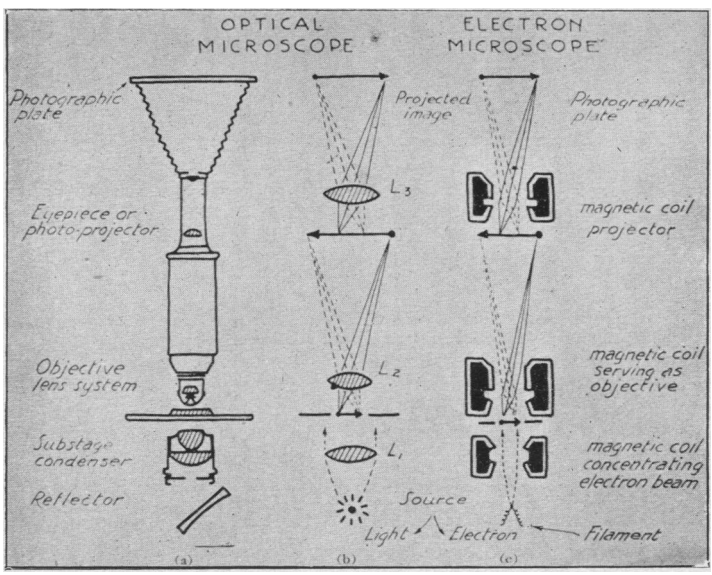

FIG. 1.—Comparison of light microscope and magnetic electron microscope. (Drawings supplied by the Radio Corporation of America.)

H. Busch showed in 1926 that the action of short, axially symmetrical, magnetic fields on electron rays was similar to the action of a glass lens on light rays. It was to be expected that electron optics soon would be used to overcome the limits to microscopy. M. Knoll and E. Ruska in 1932 published their first experimental results on the electron

microscope. They obtained poor pictures and relatively small magnification, but the development of the new technique by E. Ruska, H. O. Muller, H. Krause and others produced gradual improvement. By 1935, the resolving power of the best optical microscope was reached, and in 1937 this was surpassed. B. V. Borries and E. Ruska in 1938 described a technical electron microscope which they designed for the Siemens' Company in Berlin. Meanwhile, successful models were developed by L. Marton in Brussels in 1934, L. C. Martin and his associates at the Metropolitan Vickers Company in 1936, and by Prebus and Hillier at Toronto University in 1938. Hillier in 1941 co-operated with Zworykin and Vance of the Radio Corporation of America to produce a commercial and mass-produced electron microscope capable of magnification up to × 150,000. Work on the electron microscope of high magnification was begun in many other laboratories, and only some of the more outstanding contributions are mentioned here.

The Magnetic Electron Microscope

The electron microscope has individual parts serving the purpose of lenses, but these lenses have no material existence, as they are magnetic or electric fields (*see* fig. 2). A

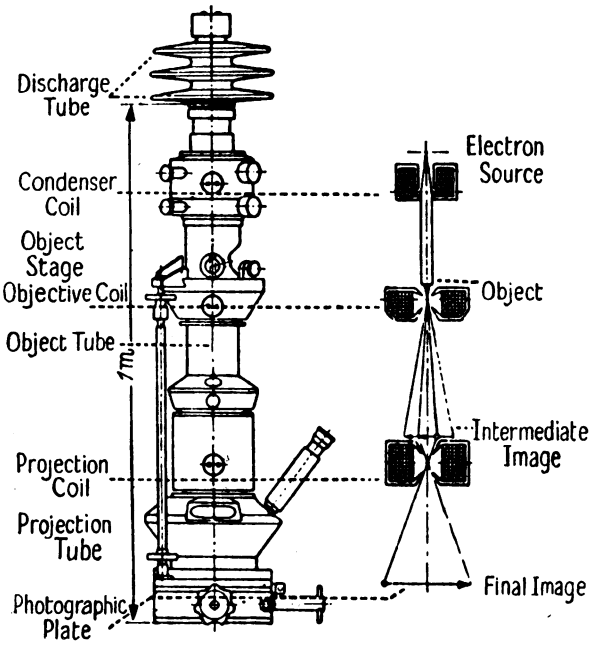

FIG. 2.—Scheme of Siemen's magnetic microscope.

heated filament emits electrons which are accelerated to about 60 kv. *in vacuo*. The actual voltage used depends on the electron wavelength required. The electron rays are concentrated on to the object by means of a focusing magnetic coil. The specimen to be examined is brought into proper position by means of a micrometer adjustment. The electron beam modified by its passage through the specimen is focused by the objective coil and forms an intermediate electron optical image, which is projected on to a fluorescent screen or to a photographic plate by means of a magnetic projection coil. A high speed diffusion pump which maintains high vacuum inside the microscope is incorporated in its stand. The specimen and photographic plates are introduced from outside by means of air-locks, without breaking the main vacuum, so that only a few minutes after their introduction the vacuum is complete enough to use the instrument again. The cathode-rays strike the relatively delicate specimen for the short time of exposure only. For the rest of the time, the beam is deflected by means of a magnetic field set up in the deflection chamber. The magnetic lenses used in the electron microscope have focal lengths of a few millimetres.

The R.C.A. high voltage electron microscope has an upper fluorescent screen upon which the first image is focused, and which can be viewed through one of the upper peep-holes. This enables the required part of the specimen to be located. The main screen can be examined with both eyes through the six ports at the base. This screen

can be replaced by a photographic plate when a permanent record is wanted. The magnification can be varied by manipulation of the electrical controls, and a further enlargement of up to six or seven times these values is obtained by photographic means. Zworykin (1941) and his associates of the R.C.A. have further developed a high voltage electron microscope which uses 300 kv.

The Electrostatic Electron Microscope

Since the beam of cathode-rays can be focused by electrostatic lenses, it is not surprising that models of electron microscopes have been introduced which incorporate this principle. Instead of the magnetic fields produced by coils, electrostatic fields produced by electrically charged diaphragms are employed as electron lenses. As focusing in the General Electric Company instrument is achieved by means of electrostatic instead of electromagnetic fields, the apparatus is smaller and simpler than the electromagnetic model—only a single unregulated voltage to earth is needed. The length of the main tube which is mounted horizontally is only 11 in. from the hairpin-shaped hot cathode to the fluorescent screen, which is viewed and photographed through a glass lens. External photography removes the need of the insertion chamber for the photographic plate. The whole of the energy contained in the electron image is concentrated into a smaller area on the screen, with corresponding greater brightness, while the amount of light gathered by the optical lens from the image on the screen increases with the magnification. A magnification of only × 500 is required from the electron lenses, which, however, can be increased to 7,000 or 8,000 by optical or photographic enlargement before blurring occurs. The instrument requires 35 kv.

Electrostatic and Electromagnetic Microscopes

The electrostatic lens used in electron microscopy to-day is of the unipotential type, the so-called *einzel-lens*. The focal length of such a lens is fixed. In order to bring the image into focus, the object distance is varied mechanically.

Electronic Aberrations

Chromatic aberration.—All lens systems, whether they be optical, electromagnetic or electrostatic, are liable to chromatic aberration, and this is due to the radiation, whether visible or not, consisting of mixed wavelengths, which normally come to a focus at different points. Visible light is a mixture of different colours, but the difficulty is compensated to a sufficient extent by employing two different kinds of glass, each having complementary effects on the most important wavelengths. For electron beams, the wave-length is a function of the anode voltage, and can be kept constant by generating the electron rays at exactly the predetermined voltage, and maintaining a high degree vacuum in the tube, to minimize collisions with molecules of residual air. Means are employed in practice for limiting fluctuations to within about $\pm 0{\cdot}002\%$ of the correct value for the electromagnetic instrument. Chromatic aberration is also due to dissipation of the electron energies in the specimen under examination. As the mass thickness of the usual electron microscope preparation is generally very small, the mean loss of electron energy is also very small.

Spherical aberration.—Spherical aberration sets an all-important limitation for existing electron microscopes. With optical lenses it is minimized, either by the use of a small stop (or aperture), or by an elaborate arrangement of elements in each lens, the former necessitating an exposure varying inversely with the square of the aperture. With electron lenses, there is also a choice between a small stop and a special design of the pole-pieces, or electrodes. The resolving power of an optical microscope depends on having a lens of large numerical aperture. In the electron microscope, however, physical factors compel the opposite course to be followed, or the definition suffers. A very fine cone of rays is all that can be tolerated. A stop, which can transmit less than 1% of the radiation falling on it, and 1/1,000 of an inch in diameter, is employed. This explains why the resolving power of the electron microscope, which, theoretically, should be 100,000 times, is restricted to 50 to 100 times, that of the ordinary microscope.

Unusual Electron Microscopes

Two interesting attempts have been made to obtain electron microscopes of high magnification on rather different and novel lines.

Scanning microscope.—M. v. Ardenne (1938*a* and 1938*b*), and Zworykin, Hillier and Snyder (1942) have developed scanning microscopes by applying methods used in television. A magnetic scanning field such as is generally used in television tubes is employed to move an exceedingly fine electron beam "probe" line after line over the surface of the object to be examined The electrons transmitted through the object (or in other

constructions, those reflected from the object) are collected by the plate which is connected with the grid of the input valve of an amplifier. The amplified currents are then applied to the modulator grid of a television tube, which is scanned in synchronism with the electron probe so that the magnified picture of the microscopical specimen can be viewed on the large fluorescent screen of this cathode-ray tube. From pictures obtained in this way it seems that the resolving power of the scanning electron microscope surpasses that of the optical instrument, but the scanning microscopes are still inferior to the highly developed projection electron instruments.

Shadow electron microscope.—Another type of electron microscope with high magnification is realized in the point-projector or shadow microscope. There the specimen to be examined is brought very close to a minute electron source, casting an electron shadow on to a relatively distant fluorescent screen. The main problem in the method is the production of the point electron source. G. A. Morton and E. C. Romberg (1939) used etched tungsten points of less than 5×10^{-5} cm. as cathodes in their point-projector microscope. H. Boersch (1939*a* and 1939*b*), in his shadow microscope, uses two stages of electrostatic lenses in order to reduce the electron optical image of a hairpin cathode. He thus obtained an electron source of minute dimensions. This type of shadow microscope is better than the scanning microscope of v. Ardenne, but still is inferior to the projection electron microscopes.

Characteristics of Electron Micrographs

The chief advantage of the electron microscope is its great resolving power, but sufficient has been said about this property.

Electron micrographs may be considered analogous to X-ray pictures, inasmuch as the darkness and brightness depend on the thickness and density of the specimen as distinct from micrographs obtained with the light microscope where an image is formed due to differences in the amount of absorption or refraction within the object. The presence of very small particles in specimens for examination under the electron microscope will cause perceptible scattering, and the image formed of an object thicker than about $0{\cdot}5\mu$ is merely an enlarged silhouette.

Another characteristic, which is usually an advantage, is the great depth of focus. This is useful for stereoscopic work.

Specimen Mounting

The vast majority of microscope specimens must be mounted upon a transparent support. Glass of a convenient thickness is the most suitable material when the illuminant is visible light, but it is opaque to an electron stream, and a new technique has therefore been elaborated whereby specimens may be adequately prepared for examination. A very thin, uniform film of collodion or nitrocellulose is used. It produces a uniform diminution of intensity, and if the film is thin enough, the amount of scattering and spread of velocity caused by it does not cause much interference with the picture. A very thin film is obtained by dropping a small quantity of a 1·5% solution of collodion in amyl acetate on amyl-acetate-saturated water. The film spreading over the surface is taken up and dried on a small circular disc of 200-mesh wire gauze, less than $\frac{1}{8}$ in. in diameter. Gentle pressure on the diaphragm causes it to adhere to the film. Films of this kind are thinner than the length of a collodion molecule. The coated discs are separated from the rest of the membrane by means of delicate handling tools, lifted from the water, inverted so as to bring the film side uppermost, and placed upon a miniature pedestal. There the water clinging to the surface is removed, and a drop of a fluid containing the specimen in suspension or solution is placed upon it, and the fluid allowed to evaporate. The whole is then placed in position on the cartridge, which in its turn is inserted through the air-lock into the microscope tube's interior, i.e. into the space about to be evacuated.

Casts of specimens.—The surfaces of certain materials, for instance, metals and alloys, can be studied by light reflected from them in the optical microscope, but this is generally impracticable with electron rays. A cast of the surface can be made by using some sort of plastic in solution and allowing the solvent to evaporate: a negative solid replica of the surface structure can be produced by peeling off the film from the original, and can be examined like an ordinary specimen in the electron microscope. An electron image of such a film will develop more strongly where the plastic material is thinnest. In some cases, where a replica cannot be stripped off, satisfactory results can be got by dissolving the original in some acid or other solution which the plastic film can withstand. The cast technique may be useful for examining the surface of such structures as metals, teeth, &c.

Practical Applications

Until very recently, the electron microscope remained an experimental instrument in the hands of the physicists, and it is only in the last few years that any serious attempt has been made to exploit its possibilities for research. Most of the examinations so far reported have been directed towards the discovery of possible fields of research, rather than towards the solution of particular problems. It holds great promise in almost every field of science, especially in chemistry, metallurgy, medicine and biology, as it reveals many important structural details and reactions, which have hitherto been inaccessible to direct observation and measurements.

Dusts and smokes are among the simplest kind of materials to view in the electron microscope, revealing groups of ultramicroscopic particles that float in the air. This type of research is of interest to the public health worker, and those interested in environmental diseases such as the industrial doctor, &c. A great number of the particles found in human lungs are smaller than 5μ in diameter, and an appreciable number less than 0·2μ. Electron micrographs have been published of smoke particles resulting from the combustion of zinc, magnesium ribbon, aluminium, &c. The physical structure of these differs, and the electron micrograph reveals how magnesium oxide consists of small cubic crystals, aluminium oxide smoke is made up of strings of spherical globules, &c.

Powders are required for many purposes, and a knowledge of their physical structure is of importance. A sample of lead arsenate insecticide which possessed unusual covering power and toxicity showed under the electron microscope—magnification × 56,500—that the particles consisted of extremely thin flakes, which naturally possess a large surface and clinging power. A popular face powder owed much of its popularity to the fact that it did not easily come off. The electron microscope showed that its particles were of a highly angular shape, capable of hooking themselves into the epidermis.

It has many uses in organic chemistry, for instance, an electron micrograph has been published (*Trans. A.I.E.E.*, April 1940), showing a specimen of polyvinylchloride. The magnification × 100,000 shows the specimen to be mottled with an evenly spaced succession of spots. The spots are considered small enough to be of molecular dimensions, and there is little doubt that visual confirmation is here obtained of the truth of the molecular theory. It has been used in the study of protein molecules (Stanley and Anderson, 1942).

It is now possible to obtain electron micrographs of the location of certain chemical reactions incident to the metabolism of the bacterial cell. The reduction of potassium tellurite by *C. diphtheriæ* has been studied (Morton and Anderson, 1941). It has been demonstrated that tellurium crystals form in all parts of the micro-organism, in some cases puncturing its walls. A method of selective microchemical analysis has been developed (Mudd and Anderson, 1942) by taking electron pictures of bacteria after exposure to salts of heavy metals. The electron microscope has demonstrated changes in the bacterial cell brought about by the action of germicides and antibacterial substances (Mudd, 1943). The recording of the action of germicide agents on individual bacterial cells is a promising field of application of microchemical analysis.

Electron micrographs of bacteria have been published (Mudd, Polevitzky and Anderson, 1942). The *Myobacterium tuberculosis hominis* shows that its cell wall appears to be very delicate. Many small dark granules appear throughout the field and, in particular, adhering to the cell wall. Large black granules are shown within the protoplasm. A strain of Fusobacterium shows dense areas, but in contrast to that of the tubercular bacilli the dense areas are not localized in definite circumscribed granules. Monotrichates, for instance, *Vibrio schuylkilliensis,* show a cell wall Definite circumscribed granules are again seen within the protoplasm. The flagella of monotrichates—for example, vibrios—are on the whole wider in diameter than those of peritrichate and lophotrichate species. Unstained diphtheria bacilli show definite polar bodies. *Treponema pallidum* appears to have flagellate processes at various points along its course. The morphology of *Leptospira ictero-hæmorrhagiæ* and *L. canicola* has been investigated (Morton and Anderson, 1943).

If suspensions of streptococci are subjected for a short period to sonic vibrations some of the cells are cytolysed (Sheffield, 1944). These bacteria retain their original outline, but become transparent to the electron beam, appearing as pale grey bodies and contrasting strongly with the opaque normal cell. *B. subtilis,* after subjection to sonic vibrations, shows the flagella to be continuous with the cell wall.

The combination of antibodies with flagellar and somatic antigens has been demonstrated by the electron microscope (Mudd and Anderson, 1941). It has long been known that the bacterial cell wall and flagella of organisms such as the bacilli of typhoid and paratyphoid are altered by the deposition of antibodies, and the combination of

antibodies and antigens at bacterial surfaces has also been shown by quantitative analytical methods. These sensitized surfaces have now been examined under the electron microscope, and, as a result of the deposition of homologous antibodies upon them, the walls are found to become opaque, and less clear-cut in outline. The flagella become thicker, but less sharp and less uniform in outline, and they tend to coalesce.

The various viruses differ greatly in size, although each kind of virus is itself very uniform in size. During the last decade, a few of the viruses which attack plants have been isolated. Although they differ from each other in stability and analytical composition, all those purified have been shown to consist solely of nucleoproteins of high molecular weight. These viruses seem to be a connecting link between living and non-living matter. They are actually protein molecules possessed of certain definite biological acitivity. On the other hand, there are viruses, that of vaccinia, for example, and all the Rickettsia disease agents, which are very much larger, and cannot be regarded as single molecules. The larger viruses appear to be true micro-organisms which can only live a parasitic existence. One of the first viruses to be photographed under the electron microscope was that of tobacco mosaic, and it at once confirmed the suggestions, based on other methods, about the size and shape of this virus. It was a long rod about 300 mμ. Particles of tobacco mosaic virus appear in purified form as discrete rod-like units with a tendency to side-to-side and end-to-end aggregation. The electron microscope has also been used in the study of the virus of tomato bushy stunt. The reaction between tobacco mosaic virus and its antiserum has been studied by means of the electron microscope (Anderson and Stanley, 1941). This instrument has been used in the investigation of the morphological structure of the virus of vaccinia (Green, Anderson and Smadel, 1942). The elementary bodies of vaccinia are rectangular shaped, resembling a brick, and contain five areas of condensation, and are somewhat like the five spots of a dice. Sharp (1942*b*) and his colleagues have employed the electron microscope in their investigations of western strain equine encephalomyelitis virus. Taylor (*see* Sharp *et al.*, 1942*c*) and his associates have used this instrument on the eastern strain equine encephalomyelitis virus. Studies have been published (Chambers and Henle, 1943) on the nature of the virus of influenza with particular reference to the dispersion of the virus of influenza A in tissue emulsions, and in extra-embryonic fluids of the chick. The size of the infectious unit in influenza A has been investigated (Chambers, Henle and their associates, 1943). This instrument has been employed on the morphological structure of Rickettsiæ (Plotz, Smadel and Anderson, 1943). It has also been used in studies on the papilloma virus protein (Sharp, Taylor *et al.*, 1942*a*).

Studies of bacteriophages (Luria and Anderson, 1942) disclose an extremely constant and characteristic sperm-like appearance with a round head, and a much thinner tail; in many micrographs the head is filled with a dense internal structure (fig. 3). These are adsorbed to their specific micro-organisms by head or tail, and after contact it is possible to observe extensive damage of the bacterial cell. These results are interesting, as some years ago the bacteriophage was looked upon by some workers as of macromolecular nature. The discovery of such constant and detailed information is of interest also to geneticists, for genes are thought to be macromolecular entities. The sperms of the ram and bull, being extremely flat, lend themselves to examination and have already come under observation.

The electron microscope is of value in histological research. It has revealed characteristic cross-striations in collagen fibres, and the effects of various physical and chemical conditions on the fibres have been investigated (Hall, Jakus, and Schmitt, 1942) in a search for further knowledge of the molecular structure of collagen. To entomologists, this instrument shows hitherto unseen structures, and it allows the accurate measurement of those already recognized. The tracheæ, trachioles, air sacs, wing scales, and cuticle have been examined, and experiments (Richards and Anderson, 1942) on the mode of penetration of the cuticle by non-volatile oils serve as an example of future useful applications.

The foregoing are only some of the many fields in which an electron microscope is useful.

Some Disadvantages

The electron microscope is not yet an instrument for every pathologist's bench, due to its cost, size and complexity. Its immediate future lies rather in the research laboratory. The bombardment of specimens with high speed electrons produces changes in protoplasm, and in molecules. Entomologists have remarked on shrinkage, evolution of gas, discoloration, and increased friability of their specimens. As the specimen for study must be placed in a high vacuum, it must, therefore, be dry. Great difficulty is experi-

enced in viewing anything but "dead" specimens, and in consequence, movement must inevitably be "frozen", and require a number of successive and similar operations to show progressive action. The objects to be examined must be extremely thin.

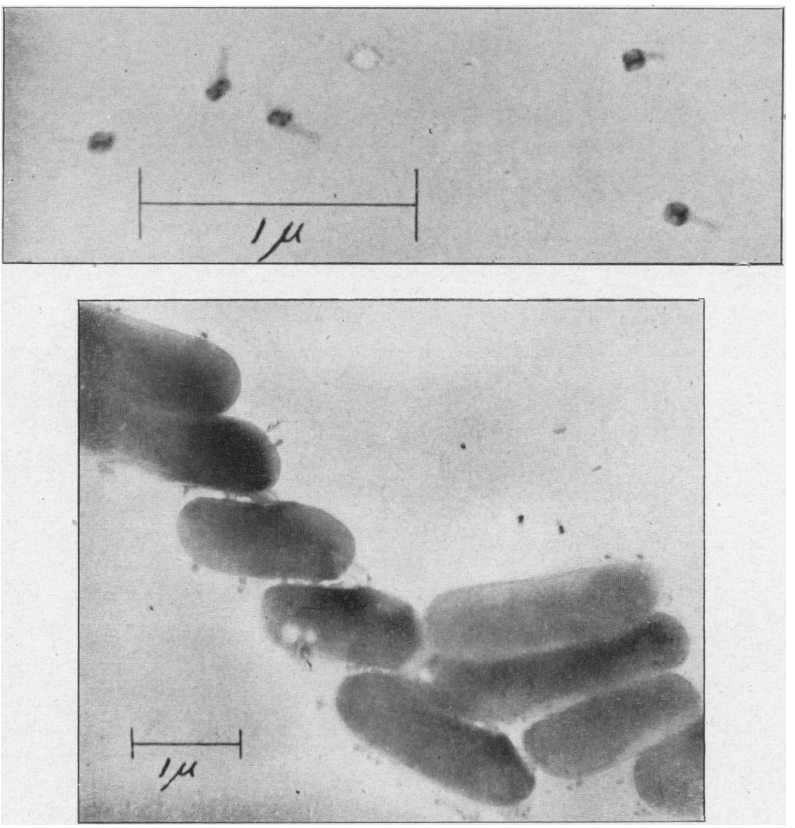

FIG. 3.—Bacteriophage. The lower picture shows bacteriophage attacking *B. coli*. (*From* " The Identification and Characterization of Bacteriophages with the Electron Microscope," by S. E. Luria and T. F. Anderson, *Proceedings of the National Academy of Sciences of the United States of America*, 1942, **28**, 127.)

Some Further Developments

Owing to the very small aperture of the electron rays, the electron microscope shows a surprisingly large depth of focus. Electron stereomicroscopy has been suggested by E. Ruska. M. v. Ardenne (1940) has further developed this idea, and introduces in his electron microscope a particular object carrier which can be tilted by a few degrees between two successive exposures. A vivid impression of solidity is produced if the two corresponding photographs are examined under a stereoscope.

M. v. Ardenne (1940) has successfully applied dark-ground illumination and obtained resolving powers down to 5×10^{-7} cm. M. v. Ardenne (1939) discusses in this connexion the possibility of viewing single atoms, and studying their distribution in the object plane. There are, however, great practical difficulties, for instance, the exposure time would have to be increased more than 1,000 times if ultramicroscopical methods were to be introduced.

O. Scherzer (1939) discusses the possibility of improving the resolving power of the ordinary electron microscope with direct illumination by an improvement of the electron lenses leading to larger numerical apertures. He mentions in this connexion the practicability of correcting spherical abberation by introducing space charges into the lens. F. H. Nicoll in his patent proposal of 1936 discusses the introduction of an electron mirror into the instrument. As it is feasible to construct mirrors with negative aberration, a useful opportunity of correcting the mirror-microscope is given.

The most direct method of improving the resolving power is to use appreciably greater electron energies, and thus shorter wavelengths. There is an upper limit to what we can hope for in this direction.

After this war is over, there should be great development in television, and some of this research work will be employed in improving the electron microscope.

My thanks are due to the Research Departments of the Radio Corporation of America; the General Electric Company of America; Metropolitan Vickers of England; Mr. G. Parr, Editor of *Electronic Engineering;* Dr. P. Bauwens, President of the Physical Medicine Section of the Royal Society of Medicine; Mr. T. J. Shields, Librarian of the British Medical Association; and Mr. G. F. Home, Librarian of the Royal Society of Medicine.

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