# DERMATOLOGIC ASPECTS OF ELECTRON MICROSCOPY*

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The usefulness of the electron microscope has increased rapidly since its introduction by Knoll and Ruska (1) some 20 years ago. Recent technical advances have converted this device from a laboratory curiosity to a practical and efficient instrument for the exploration of the sub-microscopic world. The potentialities of the electron microscope as a research and diagnostic instrument in medicine are great. This paper is a review of available information about the electron microscope which pertains to the skin and some of its diseases.

## *Description of the Instrument*

A microscope can only form a correct image of an object larger than one-half the wave length of the light passing through the optical system (2, 3). As the light microscope utilizes a wave length of about 5,000 Angstrom units, the shortest distance that can be resolved is about 200 millimicrons (2,000 Angstrom units). The only means of visualizing smaller objects is to use a beam of shorter wave length. Ultraviolet light can extend this limit somewhat further, but by using a beam of electrons vibrating at an extremely short wave length, particles as small as 10 millimicrons in diameter may be satisfactorily studied.

The principles of construction of the electron microscope combine the already familiar features of both the x-ray apparatus and the light microscope. The source of the beam is an electron gun operating at a potential of about 50,000 volts. The anode is made in such a way as to allow the passage of the electron stream through itself into a system of "lenses." These "lenses" instead of being constructed of glass as in the light microscope are electro or permanent magnets which are capable of focusing the beam on a fluorescent screen or photographic plate. This system of "lenses" takes advantage of the fact that electrons will deviate towards the axis when passing through a magnetic field.

The specimens to be viewed are placed in a chamber between the condenser and the objective "lenses." The object, depending upon its degree of density, appears as a more or less dark area on the viewing screen. The denser areas of the specimen deflect more of the electrons which strike them and prevent their impact on the corresponding portion of the screen, which will remain dark in contrast to the other areas of the screen which are subject to an uninterrupted flow of these particles. Thus the darkness of the image is proportional to the density of the material being studied, provided the thickness is kept constant.

As a specimen support, analagous to the glass slide of the optical microscope, a wire screen is used which has been overlayed with a monomolecular film of collodion or Formvar (4). Those portions of the preparation lying between the meshes of the screen are thus subjected to the beam and may be studied with the electron microscope. The correct preparation of the material to be studied is a major problem. The prime requisite is that the subject material be extremely thin. This is easily obtained in the case of biologic particles such

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as viruses and small bacteria because of their size. The visualization of thicker material such as tissue sections, thick fibers, etc., was impractical until the recent work of Pease and Baker, and others (5–8). These workers have developed microtomes which when used with special methods of tissue fixation and embedding will cut extremely thin sections of the size of $\frac{1}{10}$ to $\frac{1}{20}$ micron (5). Another important technical advance was the introduction of the shadow casting technic by Williams and Wyckoff in 1945 (9). This method takes advantage of the electron opacity of very thin films of certain heavy metals, which when coated onto particles gives them a three dimensional appearance which reveals otherwise hidden details of structure. Chromium, gold, palladium and uranium are the most satisfactory materials now in use (10–12).

### *The Skin Viruses*

The elementary bodies of all but the largest viruses are of insufficient diameter to be seen with the light microscope (13, 14). They were among the earliest objects of study by electron microscopists. Previous investigations of the appearance of these bodies using the darkfield technic have been recorded by Robinow and Bland (15), Eisenberg-Merling (16), Ebert and Otsuka (17), and others. However, the physical limitations of their equipment prevented a detailed description of these agents and their studies had to be confined to the larger viruses. Because of the ease of obtaining material from virus diseases of the skin, and the distinctive shapes of some of these agents they were among the first viruses characterized with the electron microscope.

Many diseased tissues have been used as a source of material for the extraction of the virus in question. Obviously, the more homogeneous this material and the more dissimilar it is in nature from that of the virus the less confusing will be the picture obtained after purification procedures. The most commonly used source is vesicle fluid and in general this material has given the most satisfactory micrographs. Successful examinations have been undertaken, however, with both skin scrapings and crusts of older lesions. The introduction of the thin sectioning technic may yield much useful information from biopsy material.

To study vesicle fluid after withdrawing it from the lesion it is placed on the collodion membrane of the objective screen and washed and dried. It is then examined directly or after "shadow casting" in the electron microscope. It must be emphasized that the washing-drying procedure is a necessary evil and may be responsible for some artifacts in the resulting photographs. Experience and a study of uninfected control tissue and vesicle contents, is of the utmost importance in the proper evaluation of the image on the viewing screen. When one considers the many normal tissue components which can mimic the appearance of the virus particle the care which must be taken in interpretation will be recognized (18). The possibility of viewing the virus in its intra-cellular position in tissue culture cells is promising (19). In this technic the infected tissue culture is allowed to grow out from the explant onto an electron microscope screen which is then removed and examined. The most recent advance is the technic of Green who advocates placing the electron microscope screen into the chorioallantoic cavity of the developing chick embryo (20). The cells surround and grow onto this foreign body and when the grid is removed the cells are in place and ready

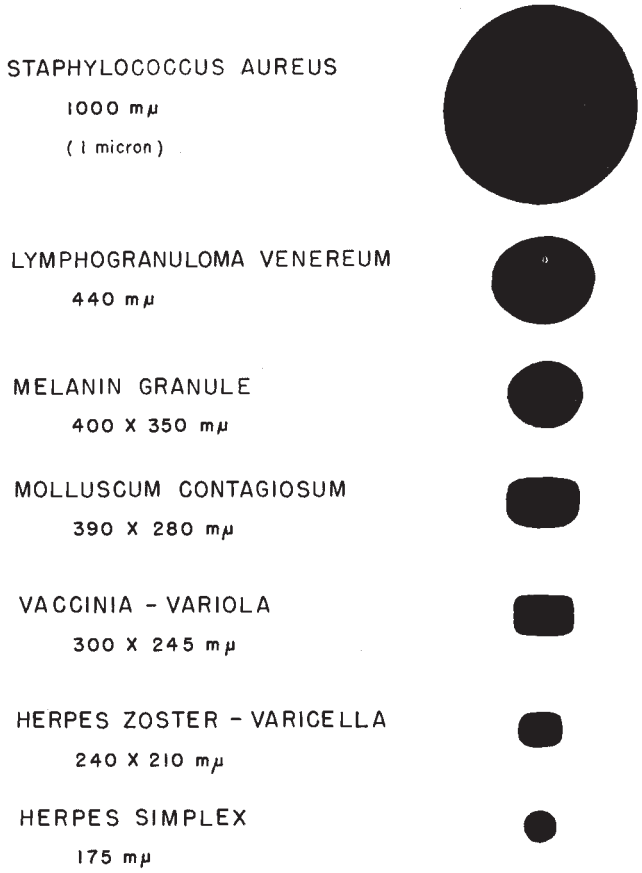



PLATE I

A diagrammatic representation to show the size and shape relationships of the skin viruses

for viewing. The advantage claimed for this latter method is the lack of any necessity for a supporting collodion membrane. Hence more contrast in the micrograph is obtainable.

### *Morphology of Skin Viruses*

Molluscum contagiosum is the largest of the skin viruses (21). The elementary bodies are rectangular in shape, measuring about 390 x 280 millimicrons. Small irregularities are to be seen on the surface but in general they are quite uniform in size and shape. There is some tendency toward chain formation and clumping as best demonstrated in the unshadowed preparation. Rake and Blank (22) have recently observed minute "sub-virus" particles of about 100 x 83 m$\mu$., which when aggregated occupy much of the substance of the large elementary body where they appear to be embedded in a homogeneous matrix.

The elementary bodies of vaccinia and variola are indistinguishable under the electron microscope, as would be expected from the close antigenic relationship between the two viruses (23–25). The rectangular individual particles have dimensions in the range of 300 x 245 m$\mu$. Favorable preparations will sometimes show dense areas in the substance of the body, which has been interpreted by some as evidence for a complex internal structure.

As shown in the accompanying photographs, the elementary bodies of herpes zoster and varicella are identical. These units are occasionally rectangular in shape, more often sperical and of an average size of approximately 240 x 210 m$\mu$. Electron micrographs have lent support to the argument that the viruses causing chickenpox and herpes zoster are closely related, if not identical (26, 27).

The virus of herpes simplex is the smallest of this group, measuring about 175 m$\mu$. in diameter. The extreme fragility of the virus increases the possibility of artifacts in preparation but the consistently spherical shape of these elements is demonstrated in the accompanying illustrations.

### *Clinical Uses in Virus Diseases of Skin*

As Van Rooyen and Scott have pointed out, the electron microscope is a "practical instrument for the diagnosis of smallpox" (28). They suggest that during the macular, vesicular or pustular stages of the disease when a rapid diagnostic method would be most valuable the electron microscope has a distinct advantage over rabbit cornea (Paul test) or chick embryo inoculation, which require several days to perform. Nagler and Rake (29) also demonstrated the value of the electron microscope as a diagnostic instrument to separate chickenpox and smallpox.

The confirmation of the view that a single virus is responsible for herpes zoster and chickenpox was effected primarily through the use of the electron microscope by Rake, et al. (30), who convincingly demonstrated the similarity of the elementary bodies obtained from each of these clinical conditions. The nature of the reaction between viruses and their corresponding antibodies has been well studied by Anderson, Wyckoff and others (31–33). These workers have found

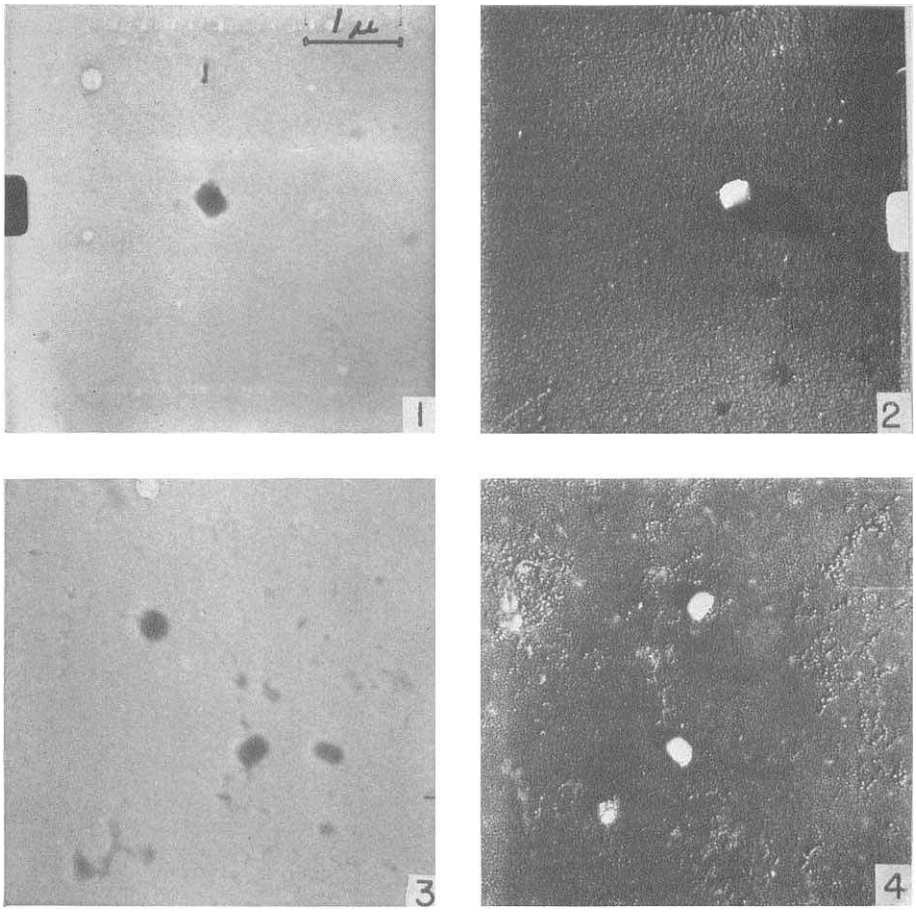



PLATE II

Fig. 1. Variola, unshadowed, ×15,000
Fig. 2. Variola, gold shadowed, ×15,000
Fig. 3. Vaccinia, unshadowed, ×15,000
Fig. 4. Vaccinia, gold shadowed, ×15,000

that there is first an absorption of the specific antibodies onto the individual virus particles which is followed in time by agglutination in the framework of the "microfloc." Wyckoff believes that this method of observation may be the basis for the development of "super sensitive diagnostic methods" in virology (34).

The method of multiplication of the viruses is under intense study, for until such information becomes known, effective therapeutic agents probably will not be available. The most direct means of observing the life cycle of the virus would be the actual observation of these processes in situ in the intracellular position. The thin sectioning, tissue culture, and implantation technics described have opened the door to this very promising aspect of study.

A number of interesting studies on malignant tissue have indicated the presence of spherical bodies of size such as to put them in the approximate virus range (35, 36). Hellwig and Alexander found bodies of this type in 23 malignant and 7 benign tumors. However, they did not believe them to be viral in nature, but rather aggregates of globular protein produced by alterations in the colloid state of the cancer cell (37). In two recent publications (38, 39) Passey and coworkers have presented electron microscope photographs of apparent viral bodies in extracts of breast tissue and milk from high breast cancer strains of mice. Control preparations of low breast cancer strains showed consistent absence of these particles.

### *Electron Microscopy of Spirochetes*

Mudd, et al. were among the early workers on the morphology of the treponemes. (40) In their studies on *T. pallidum*, *T. macrodentium*, and *T. microdentium* they visualized the presence of a definite cell wall which extended beyond the protoplasm at either end of the cell and was also visible between incompletely separate daughter cells. In all organisms studied, except *T. microdentium*, flagellae were distinctly seen along the sides of the organism but not terminally. Occasionally, they were grouped in tuft-like structures. Herxheimer's previous description of protoplasmic, granular structures was confirmed, and these dense spherical objects were found to be from 40 to 90 millimicrons in diameter. The so-called "granules spirochetogenes" which are irregular spherical bodies about 150 to 500 millimicrons in diameter were observed near the end of the organism and were thought to be "asexual, reproductive bodies." On the basis of their electron micrographs, these authors concluded that the treponeme probably divided transversely.

Wile, Picard, and Kearney in a later paper confirmed the existence of such flagellae (41, 42). The possibility of the introduction of artifacts by centrifugation, washing, and drying, necessary before examination, is admittedly very great and any interpretations made, must therefore be tentative. Wyckoff has also worked on this problem and his shadow cast photographs show the presence of terminal flagella. He demonstrated that side to side approximation of two spirochetes probably accounts for the old theory of longitudinal division.

In 1946 Tung and Frazier noted a loss of flagella and lengthening of the Reiter spirochete on contact with penicillin (43). More recently Morton and Oskay (44)

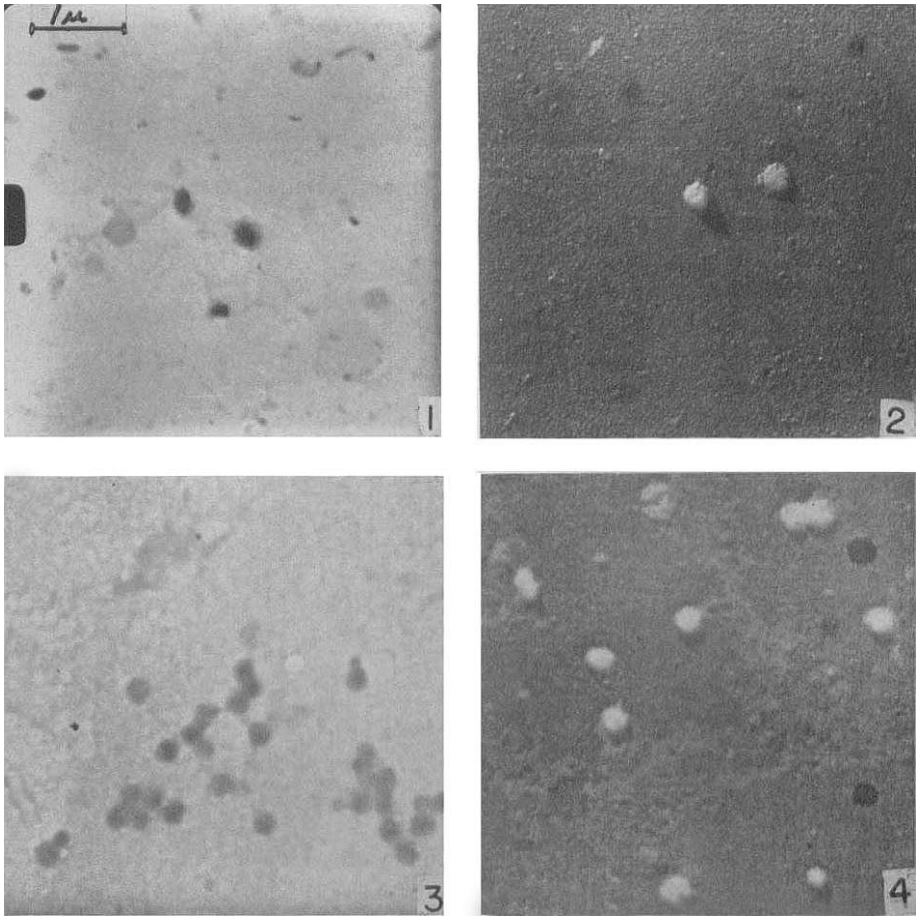



PLATE III

Fig. 1. Varicella, unshadowed, ×15,000
Fig. 2. Varicella, gold shadowed, ×15,000
Fig. 3. Herpes zoster, unshadowed, ×15,000
Fig. 4. Herpes zoster, gold shadowed, ×15,000

using the Nichols cultured strain have confirmed the increase in length but have also shown that there is a tendency for incomplete fission. They found organisms as long as 24 microns in the penicillin containing culture which was twice the length of the longest organism seen in the control media. Incomplete fission of the spirochetes resulted in chains measuring up to 51 microns. These latter workers did not observe the flagellar suppression described by Tung and Frazier but did note in some treponemes the development of fusiform swellings after contact with penicillin.

It would be of interest to examine with the electron microscope the effects of other agents upon the treponemes, such as Nelson's immobolizing antibody (45), and to study in finer detail the recently described stages in the life cycle of the spirochete (46).

### *Melanin Structure*

The fine structure of melanin from several different tissues has been described by Mason and coworkers (47). They ground the parent tissue and extracted the melanin by differential centrifugation. The melanin from mouse melanomas was found to be elliptical in shape and about 350 to 400 millimicrons in diameter, whereas control tissue consisting of amelanotic melanomas did not contain particles of this size. That obtained from beef eye structures was similar in appearance, but the particles were larger. The melanin from human skin, however, was quite different, being composed of both globular and rod shaped elements of from 100 x 400 to 180 x 600 millimicrons in size. They concluded that melanin is made up of specific "formed elements."

### *Protein Structure*

The electron microscope has made it possible to visualize individual protein molecules (48). As a result, the structure of a number of proteins such as myosin, thrombin and fibrinogen has been described (49–51). The important role of collagen in the several collagen diseases make this tissue element of primary interest to the dermatologist. Schmitt and his co-workers have demonstrated fibrils in collagen which have distinctive cross-striations (52–54). Their studies also indicate that contrary to the accepted theory, collagen is probably composed of protein molecules of the alpha or folded type and not the extended beta type structure. Human skin collagen fibrils are very similar to that of the other animals, although those in man seem to be buried in a non-fibrous matrix which was not seen in the other specimens. The extreme elasticity of the individual fibrils was demonstrated when it was discovered that they could be stretched up to 10 times their original size without fracturing. Astbury, however, in a recent paper retained the older concept and viewed the collagen fiber as being composed of long thread-like molecules which are twisted into "molecular yarn" (55). The nature of the molecular changes in degenerated collagen has not been investigated fully as yet. In a previously quoted paper (22) Rake and Blank noted the presence of what appeared to be collagen fibrils in a preparation from the inclusion body of molluscum contagiosum. It was thought possible, however, that

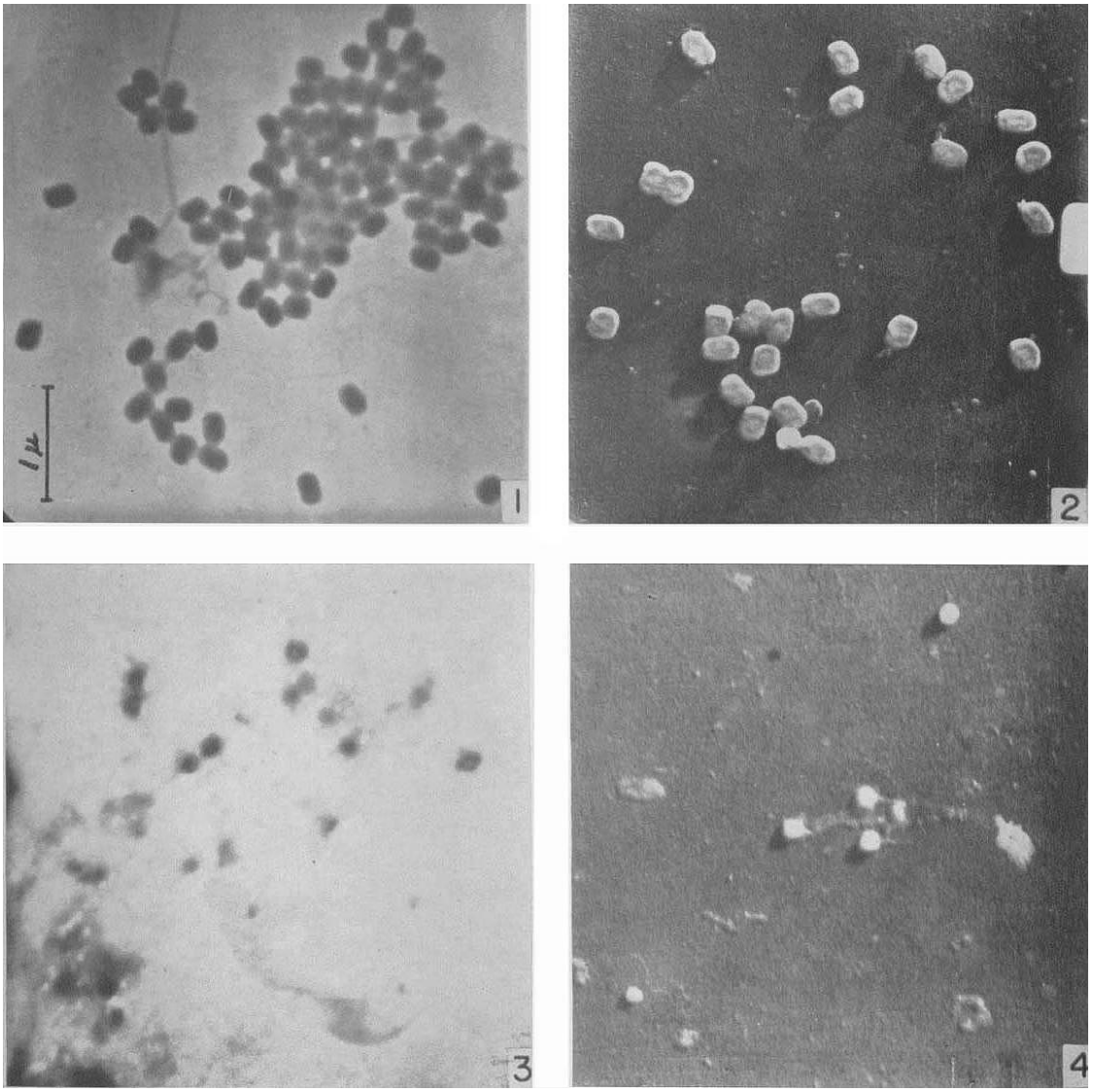
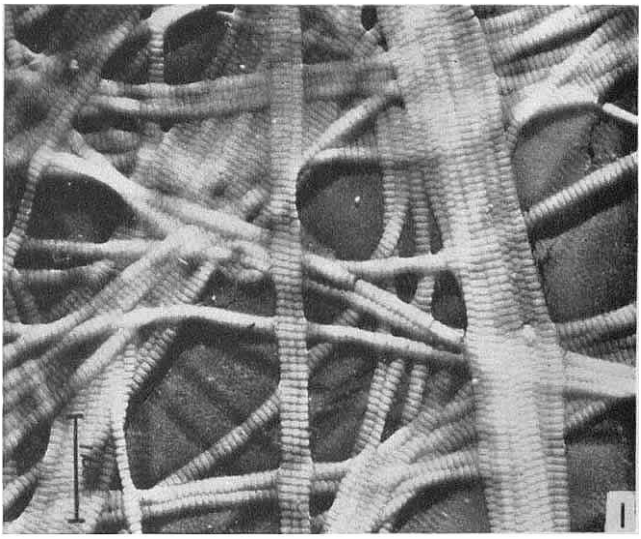



PLATE IV

Fig. 1. Molluscum contagiosum, unshadowed, ×15,000
Fig. 2. Molluscum contagiosum, gold shadowed, ×15,000
Fig. 3. Herpes simplex, unshadowed, ×15,000
Fig. 4. Herpes simplex, gold shadowed, ×15,000



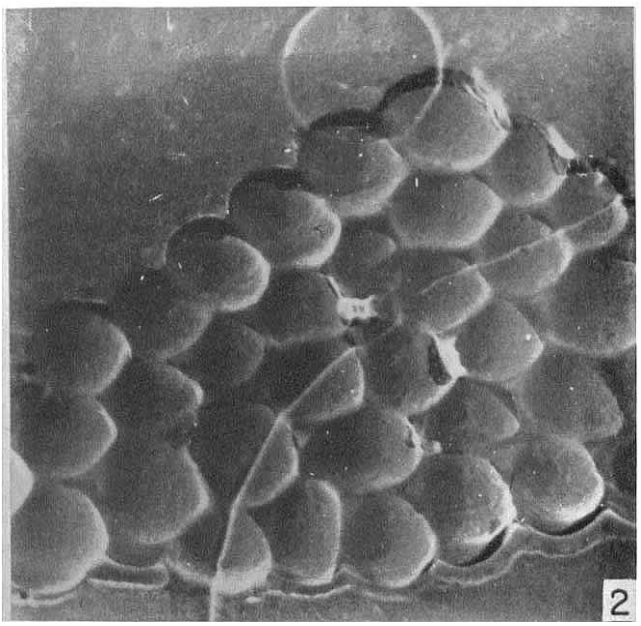


PLATE V

Fig. 1. Collagen fibrils from human corium, chromium shadowed, ×19,300. (Gross and Schmitt. J. Exp. Med. **88:** 555, 1949.)

Fig. 2. Staphylococcus aureus, positive replica, chromium shadowed, ×15,000.

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PLATE VI

Treponema pallidum from a lesion of secondary syphilis, chromium shadowed. (Courtesy Dr. Harry Morton and Dr. William Ford.)

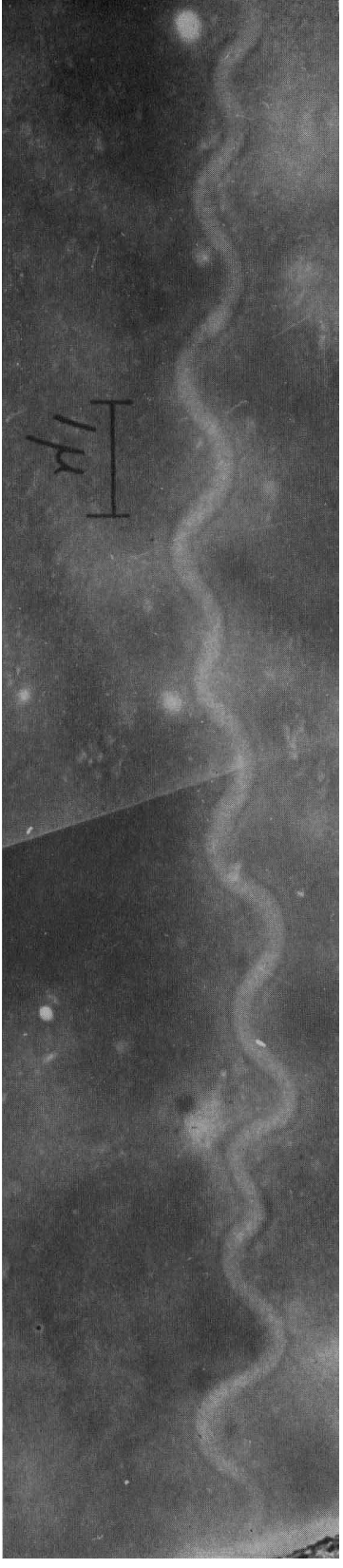


PLATE VI

these fibrils could represent fragments of the ribonucleoprotein matrix of these inclusions. Very little work with the electron microscope has as yet been undertaken as to the basic structure of keratin. Farrant, however, in a brief recent report indicated that fibrous keratin does not consist of long chains of folded or extended molecules, but rather is composed of strings of globular protein molecules (56). He also proposed the somewhat aberrant view that the beta keratin form arises not from the unfolding of the polypeptide change, but is more probably due to the addition of interfold water.

## CONCLUSION

A review of the various phases of electron microscopy of interest in dermatology has been presented. We have indicated those areas in which conclusive evidence is lacking and tried to point out some of the avenues by which they may be approached. The electron microscope will undoubtedly become increasingly valuable and practical as new technics and applications are developed. In the words of Wyckoff, "a new kind of embryology will rise which deals with units on the molecular instead of the cellular scale of organization."

## REFERENCES

1. Knoll, M. and Ruska, E.: Contribution to geometrical electron optics, I and II. Ann. Physik. **12:** 607, 1932.
2. Wyckoff, R. W. G.: Electron Microscopy. New York, Interscience Publishing Co., 1948.
3. Gabor, D.: The Electron Microscope. New York. Chemical Publishing Co., 1948.
4. Hass, G. and Kehler, H.: Temperature resistant and durable carrier for electron interference and electron microscope investigations. Kolloid Z. **95:** 26, 1941.
5. Pease, D. C. and Baker, R. F.: Sectioning techniques for electron microscopy using a conventional microtome. Proc. Soc. Exper. Biol. & Med. **67:** 470, 1948.
6. Fullam, E. F. and Gessler, A. E.: A high speed microtome for the electron microscope. Rev. Sci. Instr., **17:** 23, 1946.
7. Newman, S. B., Borysko, E. and Swerdlow, M.: New sectioning techniques for light and electron microscopes. Science **110:** 66, 1949.
8. O'Brien, H. C. and McKinley, G. M.: New microtome and sectioning method for electron microscopy. Science **98:** 455, 1943.
9. Williams, R. C. and Wyckoff, R. W. G.: Electron shadow micrography of virus particles. Proc. Soc. Exp. Biol. & Med. **58:** 265, 1945.
10. Williams, R. C. and Wyckoff, R. W. G.: Applications of metallic shadow-casting to microscopy. J. Applied Physics. **17:** 23, 1946.
11. Williams, R. C. and Wyckoff, R. W. G.: Electron shadow micrography of the tobacco mosaic virus protein. Science **101:** 594, 1945.
12. Williams, R. C. and Backus, R. C.: The electron-micrographic structure of shadow cast films and surfaces. J. Applied Phys. **20:** 98, 1940.
13. Krause, F.: Examination of viruses by the electron microscope. Naturwissenschaften, **26:** 122, 1938.
14. Stanley, W. M. and Anderson, T. F.: A study of purified viruses with the electron microscope. J. Biol. Chem. **139:** 325, 1941.
15. Bland, J. O. W. and Robinow, C. F.: The morphology of vaccinia. J. Path. & Bact., **48:** 381, 1939.
16. Eisenberg-Merling, K. B.: Observations on the living vaccinia virus in the corneal cells of the rabbit. J. Path. & Bact. **50:** 279, 1940.

17. EBERT, M. H. AND OTSUKA, M.: Virus diseases of the skin with special reference to elementary and inclusion bodies: variola-vaccinia and molluscum contagiosum: Arch. Dermat. & Syph., **48:** 635, 1944.
18. SCHWARTZMANN, G.: Some recent advances in bacteriology and virus research with special reference to electron microscopy. J. Mt. Sinai Hosp. **11:** 137, 1944.
19. PORTER, K. R., CLAUDE, A. AND FULLAM, E. F.: A study of tissue culture cells by electron microscopy. J. Exper. Med., **81:** 233, 1945.
20. GREEN, R. H.: Electron microscopy of embryonic avian tissues. Proc. Soc. Exper. Biol, & Med. **73:** 191, 1950.
21. BOSWELL, F. W.: Electron microscope studies of virus elementary bodies. Brit. J. Exper. Path. **28:** 253, 1947.
22. RAKE, G. AND BLANK, H.: The relationship of host and virus in molluscum contagiosum. J. Invest. Dermat. (In press).
23. GREEN, R. H., ANDERSON, T. F. AND SMADEL, J. E.: Morphological structure of the virus of vaccinia. J. Exper. Med., **75:** 651, 1942.
24. DAWSON, I. M. AND MCFARLANE, A. S.: Structure of an animal virus (vaccinia). Nature, **161:** 464, 1948.
25. SHARP, D. G., TAYLOR, A. R., HOOK, A. E. AND BEARD, J. W.: Rabbit papilloma and vaccinia viruses and $T_2$ bacteriophage of E. coli in shadow electron micrographs. Proc. Soc. Exper. Biol. & Med. **61:** 259, 1946.
26. AMIES, C. R.: Elementary bodies of zoster and their serological relationship to those of varicella. Brit. J. Exper. Path., **15:** 314, 1934.
27. KUNDRATITZ, K.: Experimentelle über tragungen von Herpes Zoster auf Menschen und die Beziehungen von Herpes Zoster zu Varicellen. Zeitschr. f. Kinderh., **39:** 379, 1925.
28. VAN ROOYEN, C. E. AND SCOTT, G. D.: Smallpox diagnosis with special reference to electron microscopy. Canad. J. Pub. Health, **39:** 467, 1948.
29. NAGLER, F. P. O. AND RAKE, G.: The use of the electron microscope in the diagnosis of variola, vaccinia, and varicella. J. Bact. **55:** 45, 1948.
30. RAKE, G., BLANK, H., CORIELL, L. L., NAGLER, F. P. O., AND MCNAIR SCOTT, T. F.: The Relationship of Varicella and Herpes Zoster. J. Bact. **56:** 293, 1949.
31. ANDERSON, R. F. AND STANLEY, W. M.: A study by means of the electron microscope of the reaction between tobacco mosaic virus and its antiserum. J. Biol. Chem. **139:** 339, 1941.
32. MUDD, S. AND ANDERSON, T. F.: Demonstration by the electron microscope of the combination of antibodies with flagellar and somatic antigens J. Immunol. **42:** 251, 1941.
33. WYCKOFF, R. W. A.: Electron microscopic study of viruses. J. A. M. A. **136:** 1081, 1948.
34. BLACK, L. M., PRICE, W. C. AND WYCKOFF, R. W. G.: The electron micrography of plant-virus antibody mixtures. Proc. Soc. Exper. Biol. & Med. **61:** 9, 1946.
35. GESSLER, A. E. AND GUY, C. E.: Notes on the electron microscopy of tissue sections—submicroscopic spherical bodies in carcinoma. Exper. Med. & Surg. **5:** 307, 1947.
36. GREGORY, J.: Electron microscopic findings in malignant tissue. Exper. Med. & Surg. **6:** 390, 1948.
37. HELLWIG, C., AND ALEXANDER, A.: Virus like globules in cancer extracts. Arch. Path. **48:** 436, 1949.
38. PASSEY, R. D., DMOCHOWSKI, L., ASTBURY, W. T., AND REED, R.: Electron Microsope Studies of Normal and Malignant Tissues of High- and Low-Breast Cancer Strains of Mice. Nature **160:** 565, 1947.
39. PASSEY, R. D., DMOCHOWSKI, L., ASTBURY, W. T., REED, R., AND JOHNSON, P.: Ultracentrifugation and Electron Microscope Studies of Tissues of Inbred Strains of Mice. Nature **161:** 759, 1949.
40. MUDD, S., POLEVITSKY, K., AND ANDERSON, T. F.: Bacterial morphology as shown by

the electron microscope. V. T. pallidum, T. macrodentium, T. microdentium. J. Bact. **46:** 15, 1943.
41. WILE, U. J., PICARD, R. G., AND KEARNEY, E. B.: The morphology of spirochaeta pallida in the electron microscope. J. A. M. A. **119:** 880, 1942.
42. WILE, U. J., AND KEARNEY, E. B.: The morphology of T. pallidum in the electron microscope. J. A. M. A. **122:** 167, 1943.
43. TUNG, T. AND FRAZIER, C. N.: Penicillin sensitivity and morphology of the Reiter strain of Treponema pallidum after cultivation in media containing penicillin. Am. J. Syph. Gonor. & Ven. Dis. **30:** 205, 1946.
44. MORTON, H. E. AND OSKAY, J.: The effect of penicillin on the Nichols strain of Treponema pallidum. Am. J. Syph. Gonor. & Ven. Dis. 34, Pg. 139, 1950.
45. NELSON, R. A. AND MAYER, M. M.: Immobilization of Treponema pallidum in vitro by antibody produced in syphilitic infection. J. Exper. Med. **89:** 369, 1949.
46. DELAMATER, E. D., HAANES, M., AND WIGGALL, R.: Studies on the life cycle of spirochetes VIII. Summary and comparison of the experimental results from various organisms. J. Invest. Dermat. (In press).
47. MASON, H. S., KEHLER, H., MACCARDLE, R. C. AND DALTON, A. J.: Chemistry of melanin IV. Electron micrography of natural melanins. Proc. Soc. Exper. Biol. & Med. **66:** 421, 1947.
48. PRICE, W. C., WILLIAMS, R. C. AND WYCKOFF, R. W. G.: Electron micrography of crystalline plant viruses. Science **102:** 207, 1945.
49. STANLEY, W. M. AND ANDERSON, T. F.: Electron micrographs of protein molecules. J. Biol. Chem. **146:** 25, 1942.
50. VAN ZANDT, H. C. AND PORTER, K. R.: The fine structure of clots formed from purified bovine fibrinogen and thrombin: A study with the electron microscope. J. Exper. Med. **86:** 285, 1947.
51. RANZI: Electron microscope investigation of the action of salt solutions on myosin. Nature **160:** 712, 1947.
52. SCHMITT, F. O., HALL, C. E. AND JAKUS, M. A.: Electron microscope investigations of the structure of collagen. J. Cell. & Comp. Physiol. **20:** 11, 1942.
53. GROSS, J. AND SCHMITT, F. O.: The structure of human skin collagen. J. Exper. Med. **88:** 555, 1948.
54. GROSS, J.: The structure of elastic tissue as studied with the electron microscope. J. Exper. Med. **89:** 699, 1949.
55. ASTBURY, W. T.: The molecular structure of skin, hair and related tissue. Brit. J. Dermat. & Syph. **62:** 1, 1950.
56. FARRANT, J. L. AND REES, A. L. G.: Structure of fibrous keratin. Nature **159:** 535, 1947.

## DISCUSSION

DR. MAURICE J. STRAUSS: I have had no great experience in identifying elementary bodies in tissue by this technic. I would be interested to hear whether the presenters have used it in verrucae, because we have tried it but with no success.

DR. G. DOUGLAS BALDRIDGE (Closing Discussion): We have used this technic chiefly in the common virus diseases—herpes simplex, etc., but have had no experience in the electron microscopy of the virus cited Dr. by Strauss.