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DIAGNOSTIC ELECTRON MICROSCOPY

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Electron microscopy has become established as a useful diagnostic tool in pathology. Diagnostic electron microscopy refers to the utilization of electron microscopy and its associated methods in all of their ramifications for the study of human disease as well as animal disease. At the present time, electron microscopy provides crucial diagnostic information and also information of confirmatory nature of great educational value to pathologist and clinician. Pathologist relies increasingly on the electron microscope as an aid in the morphologic diagnosis of disease.

The field of diagnostic electron microscopy is closely associated with the field of cellular pathobiology. The power of concepts derived from cellular pathobiology and applied to human disease biology cannot be overestimated. Information derived on one especially suitable cell type can be rapidly applied, with a minimum of experimentation, to other cell types and other organisms leading to much more rapid progression of knowledge. An important concept in this renaissance of general pathology is the correlation between structure and function at the cellular level, which has been made observable through the integration of methods in the fields of microscopy, immunology, biochemistry and physiology. The electron microscope is, of course, a fundamental tool in those investigations because it is at the level of resolution provided by this instrument that most structural correlations with function and metabolism are visible.

Magnification has always fascinated the probing mind of man. Galileo Galilei was the first who developed the means of achieving it. Since then, improvements in the field of optics have brought us to the limits of resolution in light microscopy. Ruska conceived the first electron microscope in 1930. The evolution of his ideas has led to the development of the complex and sophisticated electron microscopes available today. These include scanning, high voltage, electron microprobe and X-ray analysis electron microscopes. It is now possible to identify individual molecules or individual constituents of tissue. This article attempts to briefly describe the variety of areas in which electron microscopy has a significant contribution to make in providing information that is reliable and of diagnostic value and that the electron microscopic examination of tissue can provide a greater understanding of well known disease processes.

Diagnostic electron microscopy in kidney is one of the longest and most well developed applications. Several forms of renal disease cannot be distinguished clinically. They differ in prognosis and response to therapy. By light microscopy, the lesions are very similar and almost identical in appearance. However, they are readily differentiated by electron microscopy.

Electron microscopy is found to be extremely useful in diagnosis of the etiology of infectious disease in surgical and autopsy pathology. This is of great importance since some causative organisms cannot be cultured or in others culture results are questionable or cannot be interpreted. For this aspect, in addition to the examination of standard stained ultrathin sections, negative staining of the specimens is also employed. The negative staining is useful for electron microscopic examination of small biological objects, such as viruses and bacteria, perticularly for material taken from cutaneous vesicular lesions, serum or stool filtrates.

Accurate diagnosis and classification of carcinomas and sarcomas are serious and critical problem. Classification and typing rely mainly on cytological and histological criteria. Application of histochemical methods and detailed ultrastructural examination of normal and premalignant cell of many neoplasms in both man and animals has added to the existing knowledge. The data obtained hopefully will provide a sounder basis for diagnosis than exists at the present time and should promise greater correlations between the etiology, prevention, treatment, antigenicity, clinical behavior and prognosis. Applications of electron microscopy coupled with cytochemistry give a new classification and histogenesis of lung carcinomas. This has previously been a difficult and controversial area. The diagnosis of soft tissue tumors which has for a long time been a very difficult area for surgical pathologist is considered and improved by electron microscopy. Combination of scanning and transmission electron microscopy greatly augments the knowledge of classification, typing and estimation of prognosis in prostatic carcinoma. The same is true in several other neoplasms.

The usefulness of electron microscopy, in particular X-ray microprobe analysis, in identifying with precision xenobiotics such as quartz, talc and asbestos fibers has been discussed in a number of papers. For most such substances, X-ray microprobe analysis is sufficient. In case of minerals such as asbestos, however, the simultaneous application of X-ray microanalysis and electron diffraction to the same particle is ideal and sometimes necessary to identify the exact mineral form. This new field of microanalysis is growing rapidly and has become so important that it is clear that every university pathology department should at least have access to this technology. It is true that whenever, possible foreign particulates should be identified with light microscopic techniques. Nevertheless, there was example, granulomas described by light microscopy as being caused by "particles of plastic" which were in fact caused by talc as proven by X-ray microanalysis.

There is a need for simplified methods of the tissue preparation that make possible the application of electron microscopy to diagnostic pathology. One strategy aimed toward this goal was to produce fixatives with which it is possible to fix tissues for both light microscopy and electron microscopy and, moreover to permit prolonged storage in the fixative, thereby permitting retrieval of specimens for electron microscopy when indicated by either diagnostic application or the interest and education of the pathologist. In this manner, all material fixed routinely would always be available for subsequent ultrastructural study if required.

Presently, attention is being focused on the improvement of techniques. Progress is being made in the consolidation of diagnostic criteria. In addition, both technical and medical personnels are being trained to achieve greater skills which are needed to continue the progress that has resulted in the establishment of electron microscopy firmly as an additional tool in the diagnostic armamentarium of the pathologist or biologist.