

have been confined to the possibilities of securing tremendously high magnification. In these studies the absorption of parts of an electron beam by the substance traversed gave rise to profile pictures, as it were, of bacteria, colloidal suspensions and in several instances epidermal cells. Another use of this new tool was in the examination of surfaces, particularly of metals, by means of the pictures resulting from thermionic excitation of electrons at the metallic surface. It occurred to us, about four years ago, that this latter adaptation of the electron microscope would be particularly useful in localizing minerals in sections of animal tissues.

It has been appreciated for some time that gentle and careful ashing of sections of biological tissues gives a remarkably faithful picture of the topographic distribution of minerals in such materials. Cells and their parts can be recognized with little difficulty. If material is prepared by a modification of the Altmann-Gersh<sup>2</sup> frozen dehydration method there is little chance that there is any perceptible shift in the cellular location of the inorganic constituents. Since most of the inorganic elements in tissues, particularly Na, K, Ca and Mg, are excited to thermionic emission of electrons at more or less specific temperatures, we expected to be able to differentiate between these various elements and localize them in cells. With this information at hand it seemed advisable to ash sections *in vacuo* on the surface of a barium and strontium coated cathode in the electron microscope.

After many experiments, both with apparatus and method, we have been able to secure pictures in which cellular structure in striated muscle, gastric mucous membrane, nerve and in other tissues can be clearly made out. So far the emission pictures which have been obtained have been due to magnesium and calcium only. It has been possible to localize these elements definitely in the contraction bands of frozen and dehydrated muscle. Epithelial cells of the mucous membrane of the stomach and intestinal tract show extensive concentration of magnesium and calcium in the free borders of the cells.

These results are being published in detail elsewhere, and the experiments are being continued.

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#### EXPERIMENTAL PROLIFERATIVE ARTHRITIS IN MICE PRODUCED BY FILTRABLE, PLEUROPNEUMONIA-LIKE MICROORGANISMS

A PROGRESSIVE, proliferative polyarthritis bearing a clinical and pathological resemblance to human

rheumatoid arthritis was produced experimentally in mice with a filtrable, pleuropneumonia-like microorganism which was recently isolated from the brain of a normal mouse.<sup>1</sup> Arthritis can be produced in practically 100 per cent. of mice when 0.5 cc of a 24-hour culture is injected intravenously or 1 cc intraperitoneally. Swelling of the joints may appear as early as 4 to 5 days. The arthritis is migratory, new joints becoming involved while others recede. Fusiform swellings of isolated digits, seen so often in human rheumatoid arthritis, occur frequently in these mice. The process is progressive and chronic in one or more joints, leading often to ankylosis, especially in the knees. By the method of "blind passage"<sup>1</sup> the microorganism has been cultivated from chronically affected joints as late as 70 days after intravenous inoculation. Tests revealed that the microorganism does not multiply in the brain, viscera, pleura or peritoneum. Excepting the arthritis, the mice appear in good health and not one of 150 with joint involvement has as yet died of the infection. Pathological changes are limited to the joints, and, as in the human disease, consist chiefly of proliferation in the synovial membrane, the capsule, the perichondrium of the articular cartilage, combined with a synchronous proliferation of the connective tissue and probably endosteum of the epiphyseal marrow directly below the joint cartilage. Intracutaneous, subcutaneous, intramuscular or intrathoracic injection or nasal instillation with or without ether anesthesia induced neither arthritis nor any local or systemic disease. Rabbits and guinea-pigs developed neither arthritis, fever or other signs of disease after inoculation with large amounts of culture.

A pleuropneumonia-like microorganism recently isolated from toxoplasma-infected mouse tissues<sup>1</sup> differs from the strain just described, in that it can also multiply in the brain as well as in the serous surfaces of the peritoneum, pleura and pericardium with the production of a characteristic exotoxin which has a special affinity for the cerebellum and can give rise to chronic choreiform signs when it does not prove fatal. When the rapid toxic death which follows intravenous injection of the culture was prevented either by the use of older mice (at least 2 months of age) or by injection of the centrifuged microorganisms, about 30 per cent. developed an arthritis similar to that produced by the other strain. The two strains are not serologically identical but possess a common antigen. Both strains have been found to pass through 500 m $\mu$  but not 396 m $\mu$  gradocol membranes (kindly supplied by Dr. J. H. Bauer), while on one occasion it was possible, by preliminary filtration through a 584 m $\mu$  membrane, to obtain a positive filtrate through a 322 m $\mu$  membrane; this suggests that the size of the smallest

<sup>2</sup> I. Gersh, *Anat. Rec.*, 53: 309, 1932.

<sup>1</sup> A. B. Sabin, *Science*, 88: 575, 1938.

unit capable of multiplication is in the same range of magnitude as that of vaccine virus.

The necessity of applying similar methods of cultivation and study to human arthritis of unknown etiology is obvious. Whether or not a similar microorganism shall be found to play a part in related human

affections, the experimental disease provides a useful tool in the investigation of many pertinent questions.

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## SCIENTIFIC APPARATUS AND LABORATORY METHODS

### DEVICES FOR VISUAL COMPARISON OF SPECTROGRAMS

IN the commonly used method of photographic spectrophotometry due to Howe, the absorption spectra of equal thicknesses of two substances which are to be compared, usually a solution and a sample of the solvent, are photographed side by side in as nearly perfect contact as possible. An essential part of the method is to determine the point or points at which the spectrograms are equally dark. The points usually are determined by visual inspection. They may be located by means of a microdensitometer, with a worthwhile increase in accuracy under certain conditions; but visual determinations are much more rapid and usually are sufficiently accurate.

It is well known that if the two spectrograms are not in perfect or nearly perfect contact, without visible gap or overlap, the accuracy attainable in visually determining the match points is greatly reduced. For this reason, great care is taken to obtain the best possible contact. This necessitates very careful and accurate adjustment of the relative positions of the light source and other parts of the apparatus. Indeed, while satisfactory contacts are usually attainable, perfect contact throughout the entire length of the spectrograms is impossible in practice, since the image spreads on the photographic plate to an extent which varies with the density.

Obviously the time and effort involved in obtaining accurate absorption data could be reduced greatly by eliminating the necessity for excellent contact of the spectrograms. A simple device has been found to do this very satisfactorily, making it possible to view the spectrograms in apparently perfect contact, even when there is a wide gap or overlap between them.

The device consists essentially of a biprism (Fig. 1-A) which is thinnest along the center line *e*. It is made preferably of a single piece of glass, but may be made of two prisms carefully ground and joined at the thin edges. It is held with its center line parallel to the lengths of the spectrograms and directly over the gap or overlap. Areas *ab*, *cd*, extending perpendicular to the plane of the paper, then appear at *a'b'*, *c'd'* in the visual field, with *b'* and *c'* apparently in coincidence. Thus the edges of the areas, at *b* and *c*, appear in perfect contact, with no visible dividing line. The area between *b* and *c* is invisible. The distance from *b* to *c* varies with the refracting angle and with the distance from biprism to spectrograms. By varying this distance, comparisons of the two spectrograms can be made at various distances from the edges.

The division between the visual areas remains sharp, while the distance between biprism and spectrograms is varied from zero to at least several millimeters. This range can be increased greatly by viewing the spectrograms through a small circular aperture (one eye) or (using both eyes) a narrow slit extending parallel to the center line of the biprism.

For convenience and accuracy in use, the biprism should be mounted in an apparatus in which it can be adjusted to any desired position above the photographic plate, with its center line parallel to the edges of the spectrograms. A low-power lens and a viewing aperture may be mounted above the biprism. Illumination of the plate should be uniform and by transmitted light.

The device can be used also for comparing the intensities, positions, widths or line shapes of the lines in two spectra; in comparing two parts of the same spectral line, as a check on uniformity of width and of illumination of the slit; in comparing the darkening at two different wave-lengths in the same spectrum; etc.

Instead of the biprism, the refracting unit shown in Fig. 1-B may be used. This may be made of two plane-parallel plates of glass cemented together at an angle, or, preferably, of a single piece of glass. Areas *ab*, *cd* of the spectrograms appear at *a'b'*, *c'd'*, in perfect contact, as when using the biprism. This unit is less useful than the biprism, however, as the distance between *b* and *c* can not be varied by varying the distance between the device and the spectrograms.

A biprism which is thickest along the center line

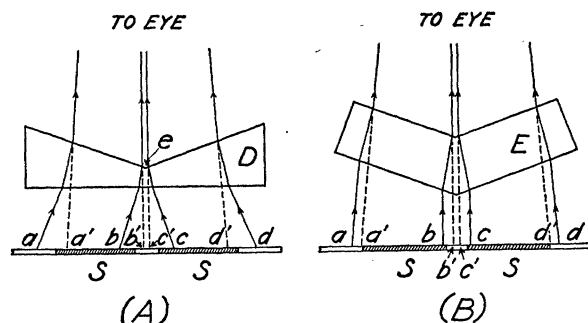


FIG. 1.