Meetings

Extracellular Matrices

Extracellular matrices are present throughout living multicellular structures and play a universal role in the organization, differentiation, function, aging, and degeneration of tissues. In order that biologists and chemists might learn from each other what is known and what needs to be known for an understanding of the structure and function of these matrices, the department of medicine of Columbia University invited 60 biologists and chemists to participate in a conference 1–4 November 1964 at Arden House in the Ramapo Hills. The chemical orientation of the biological specialties dealing with structure, formation, and differentiation and the biological orientation of biochemistry make the need for such a dialogue between the two groups obvious.

In the first session Keith Porter and Elizabeth Hay, on the basis of technically superb electron-microscope pictures, discussed the intracellular formation, the formation of the basement membrane, and the mode of transport of collagen into the basement membrane and of the protein complexes of the anionic mucopolysaccharides into the extracellular matrices. Production of collagen fibers was demonstrated in part with tritiated proline with and without collagenase, and mucopolysaccharides were made visible by means of colloidal iron and thorium. Porter and Hay agreed that collagen is formed by cells other than mesodermal cells and, especially, that epithelial cells contribute to the formation of basement membranes. The fibrous protein is assumed to be synthesized by polysomes of the endoplasmic reticulum and to migrate in small vacuoles to the Golgi apparatus. According to Porter, the microfibrils then become part of the cell membrane, whereas Hay believes that the collagen monomers are transported out of the cell directly into the matrices. The mucopolysaccharides also accumulate in the Golgi apparatus, where the sulfation presumably occurs. After the presentation of these reports, possible mechanisms were discussed for the beautifully regular plywood-like structure of the cornea and of the basement membranes of the skin of frog larvae and other aquatic chordates, in which the fibers of each layer run perpendicular to those in the adjoining layers.

Biological organization of a higher order was discussed in the next session. Clifford Grobstein, in a paper on morphogenesis and differentiation, analyzed what the chairman of the session, H. Holtzer, called the "cross-talk" between differentiating kidney, salivary gland epithelium, and chicken skin and their respective mesenchymal partners. The members of each pair were separated from each other by a porous membrane and grown in tissue culture. Tritiated proline and glucosamine were used to measure the contribution of each tissue to the synthesis of collagen, as tested by susceptibility to collagenase, and to the synthesis of mucopolysaccharide, as tested by hyaluronidase. Grobstein suggested that the collaboration of the two tissues resulted in the combined formation of an "intermediate relay" step which indirectly affects the synthetic activity within the cells.

One of the high points of the conference was the paper presented by A. Frey-Wyssling on the ultrastructure of the growing plant cell. In a discourse documented with beautiful histological and electron-microscopic pictures, Frey-Wyssling compared the matrices and fibrous elements of plants with those of animals. He demonstrated the striking similarities of the Golgi apparatus and synthesis of the "ground substances" (pectins and hemicelluloses) of the plant cells to the corresponding structures and processes of animal cells. The plant analogue of the collagen fibers, the cellulose, even shows laminated structures, as discussed by Grobstein. The mechanism of the formation of these structures in plants remains as unexplained as it is in the vertebrates. It appears almost certain that an understanding of the underlying mechanisms in the organization of multicellular organisms will come from botanical studies which deal with simpler components.

The discussion was opened by A. Moscona with a report on his latest studies of the secreted cell surface material and the species-specific cell aggregation of marine sponges. The secreted cellular surface substances appear to be particulate protein-carbohydrate complexes, similar but not identical in the specific aggregation reaction of two species of spongal cells.

The section on chemistry opened with a discussion by Philip Hoffman of the structure of the protein moieties and linkages to the carbohydrate chains of the protein-mucopolysaccharides of cartilage and other connective tissues. Paul Gallop reviewed the molecular structure of collagen and the evidence for the ester bonds between aspartic acid and a labile and as yet uncharacterized hydroxyaldehyde. S. M. Partridge reported on the isolation and characterization of desmosine and isodesmosine, the cross-linking branched amino acids of elastin, and their biosynthesis from lysine. T. Weis-Fogh gave a short report on resilin, the cross-linking amino acid of the insect cuticle, and its biophysical properties and biosynthesis.

The section on physiology consisted of four papers. Torvard Laurent of Uppsala discussed the physicochemical behavior of the various proteins and other solutes in solutions and suspensions of hyaluronate, of dextrans, of Sephadex, and of hyaluronate cross-linked with diepoxybutane. The sieve effects and exclusion of these macromolecules, first demonstrated by Ogston, were quantitatively described in various experimental procedures.

Chemical and physical differences between hyaluronate of synovial fluid and of mesothelioma were discussed by A. G. Ogston (Canberra). On the basis of measurements of viscosity and light scattering, he concluded that hyaluronate could not be considered as a straight-chain coil but as a cross-linked polymer.

Henry Wheeler discussed problems more immediately linked to physiology, namely, the transport of electrolytes and water through the gall bladder wall of the rabbit in vivo and in vitro. For the experiments in vitro, models were presented, based on calculations of Curran, which quantitatively accounted

for the movement of water and solutes and for the observed electrical potentials. The movement of water and of large and small molecular solutes of the corneal stroma was discussed by David Maurice of London, England. The high degree of reversible swelling of the cornea was shown by birefringence studies to be mainly confined to the ground substance. The ensuing discussion tangibly demonstrated the interest and the challenge presented by these reports.

In the last session, on pathology and aging, Leon Sokoloff presented an erudite analysis of aging of cartilage in osteoarthritis of various joints, illustrated by ingenious experimentation on the mechanics of compression of cartilage. This was followed by a presentation on the chemical changes in the mucopolysaccharides of cartilage and other tissues by Karl Meyer. The discussion of these papers brought forward many valuable suggestions and critiques.

It may be said in summary that the conference was successful. It neither exhausted the problems nor proposed final solutions of the many perplexing phenomena discussed, but the exchange of ideas which took place was an important accomplishment.

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Nuclear Medicine

Rapid growth and change in the use of radiopharmaceuticals have taken place over the last 5 years. In his opening lecture at the symposium on clinical applications of nuclear medicine (Shaker Heights, Ohio, 30–31 October 1964), Paul Numerof, of Squibb Institute, attributed this growth to the search for isotopes which will give maximum information to the physician and reduce radiation to the patient.

Short-lived isotopes were discussed at the symposium by William Myers (Ohio State University). Emphasis was placed on these isotopes primarily because with their use patients will receive less radiation. Secondly, scanning can be done in a shorter length of time and can be repeated at frequent intervals to study rapidly changing physiological functions. Also, because greater quantities of a short-lived isotope can be safely administered, counting accuracy will be improved.

George Taplin (University of California, Los Angeles) presented work done with macroaggregates of labeled albumin for lung scanning. The radioactive particles are temporarily retained in the lung capillaries. The scan image of the lung represents the pattern of the arterial blood flow. Tumor, embolus, pneumonia, emphysema, and infarct have been successfully diagnosed by scanning. Chest x-rays are essential in order to interpret correctly the lung scan.

N. David Charkes (Albert Einstein Medical Center) pointed out that scanning offers certain advantages in diagnosing renal disease. It is especially essential in patients suspected of having a renal disease who are allergic to iodides. This procedure was first demonstrated in 1960 with chlormerodrin-Hg^{203}. The iodinated agents which had been used prior to this were not retained long enough to give good results. The renal scan can confirm the presence of some common renal anomalies, such as space-occupying lesions, cysts, and tumors. Cysts and tumors, generally, are difficult to differentiate. Slight irregularity in outline and lower isotopic concentration indicate tumor.

Brain scanning has been studied for 17 years. Recent applications of this procedure were presented by Bertram Selverstone (New England Center Hospital). A frequent problem in brain scanning is that of locating tumors below the surface. An accuracy of 100 percent has been established in the diagnosis of meningiomas, as well as of astrocytomas, by the use of radioisotopes. When there is question of infarct, scanning should be repeated for confirmation.

D. Bruce Sodee (Doctors Hospital) discussed pancreatic scanning in which the Se^{75}-labeled selenium analog of methionine was used. With this agent and proper technique, excellent information on the pancreas has been obtained. The pancreas was visible in 90 percent of the patients scanned. Uptake of Se^{75}-labeled SeMe in damaged tissue is decreased much in the same way as that of I^{131} in cases of thyroiditis. In tumors this compound is not concentrated as it is in normal tissue. Therefore the tumor appears as an irregular area which has no radioactivity. Of tests on 185 patients, two were falsely positives and one was falsely negative.

Study of the parathyroid gland by means of radioisotopes is limited because of the small size and the variable anatomical location of the gland. E. James Potchen (Peter Bent Brigham Hospital) presented in the final lecture his experience in developing a technique of examining this organ. The tracer used is Se^{75}-labeled SeMe. For this technique to be successful, the activity of the thyroid gland must be suppressed. This is accomplished by administering cytomel 4 days prior to scanning. For proper interpretation of the results, four successive scans should be made and then integrated by superimposition. The results of this procedure have been encouraging.

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Bioclimatology

Eight American and 11 Japanese physiologists, meeting at Sapporo, Japan, 4–7 November 1964, discussed bioclimatology and the possibility of joint investigations of some of its problems. The seminar was sponsored by the U.S.–Japan Cooperative Science Program and accommodated by the Hokkaido University School of Medicine.

In the first session, on fundamental concepts, F. Sargent (University of Illinois) discussed the thesis that bioclimatological theory as applied to humans must be developed from the ecological viewpoint; the fundamental concept is that of fitness of the ecosystem, an extension of L. J. Henderson's "fitness of the environment." He suggested that circadian and seasonal variations of human physiology are instances of biological fitness. Examining the problems of seasonal variation in illness, he advanced the hypothesis that there is a "normative ecosystem"; departures from this system explain seasonal variation of illness and elucidate problems of "environmental health." Sargent suggested that racial variation in physiological adaptations likewise accord with this ecological concept.

D. H. K. Lee (U.S. Public Health Service) developed the ecological