azide. Clemmons postulated that the depression of aerobic metabolism would limit the availability of essentials in collagen synthesis that may be derived from the citric acid cycle. Also considered were glutamic semialdehyde, aspartic semialdehyde, and the aldehyde derived from the oxidative deamination of lysine. These unusual amino acids, according to Clemmons, may be part of the crosslinking mechanism, pyrrolidine structures, or desmosine-like structures. This inhibition of the cytochrome oxidases must be considered in terms of the complex biochemical alterations and their effects on collagen synthesis. R. S. Bhatnagar (Philadelphia General Hospital), in describing the effects of AAN on collagen synthesis of the tibiae from chick embryos in a synthetic medium, found an increase in both protein synthesis and the utilization of glucose. He also demonstrated an increase in collagen synthesis and an increased specific activity of newly synthesized collagen in the lathyritic bones, by using proline-C^{14} in the medium. The increase in soluble collagens and the increase in free and peptide-bound hydroxyproline liberated into the medium were proportional to the AAN concentration. AAN failed to solubilize prelabeled collagen, a finding which differs from that of Nimni with penicillamine.

V. Matukas and J. L. Orbison (University of Rochester) studied the dense granules found in cartilage matrix of normal animals. These granules disappear from the matrix of 14- to 16-day-old chick embryos 48 hours after injection of BAPN. Modification of histochemical techniques for electron microscopy showed the granules to react with colloidal iron, to be removed by hyaluronidase and trypsin, and not to react with methenamine silver. Loss of sulfate in the areas containing the granules followed the loss of these granules. These results are consistent with the interpretation of the granules as protein-polysaccharide complexes. Their rapid disappearance following BAPN is thought to add new evidence for a defect in protein-polysaccharide metabolism as a major alteration in lathyrism.

I feel that the workshop was an unqualified success in accomplishing its aim, namely, to promote the exchange of ideas and to examine the various hypotheses in the light of a variety of experimental results. As the reader must realize from this summary, no single hypothesis emerged as being the most reasonable one. This reflects the complexity of the problem. The many approaches taken in investigating the phenomenon of lathyrism are a credit to the independent thinking of the investigators.

The questions raised by such a workshop are as important as the answers which were obtained on the basis of the data. Below are listed some of the questions which came to my mind as a result of this conference:

1) What is the nature of the relationship between lathyrogenic activity and the lathyrogens as carbonyl-reacting reagents?

2) Do the lathyrogens affect specific enzyme systems and, if so, which ones and by what mechanisms?

3) Is there any direct effect of the altered carbohydrate metabolism on the chemistry of the collagen?

4) What is the nature of the aldehydes in acid-soluble collagen?

5) Are both neutral-salt-soluble and acid-soluble collagens precursors of insoluble collagen?

6) Why do the different lathyrogens produce different pathologies in the same or different in vivo systems?

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Behavioral Sciences: Vocabulary

The breakdown of precise boundaries between scientific disciplines is reflected in the need for indexing and retrieval vocabularies that describe new conceptual frontiers. The behavioral sciences in particular are hard pressed to intercommunicate with impinging disciplines, as well as among themselves. The development of a biomedical thesaurus of behavioral sciences was discussed by psychiatrists, psychologists, sociologists, and anthropologists meeting with representatives of groups concerned with information exchange in these areas. Held at the National Library of Medicine, the meeting was the first step of a task force to update the Library's medical subject headings (MeSH) in behavioral sciences on which the Medical Literature Analysis and Retrieval System (MEDLARS) and Index Medicus are based.

Martin Cummings (National Library of Medicine) emphasized that only scientists with specialized knowledge can develop vocabularies capable of giving access to information of direct importance as well as providing serendipitous exposure to peripheral material. Paul T. Wilson (American Psychiatric Association) described dangers besetting the development of vocabularies, especially the human factor in term selection. Jonathan Cole (National Institutes of Health) noted that the major problem in interdisciplinary communication is lack of understanding of concepts. The importance of conceptual control, mediated by scientists, rather than formal vocabulary control was emphasized by David Hersey (Smithsonian Institution); he pointed out that term compatibility of itself does not guarantee consistency in usage. Discussion brought out an unanswered educational question, whether it is more efficient to train the individual scientist to communicate effectively outside his immediate field, or to educate a cadre of scientist-communicators within specialties to "translate" from one field to another.

Formulation and use of vocabularies were briefly described by some of the organizations that process behavioral science information. The vocabulary needs of the indexing and search sections of the National Library of Medicine served as a mandate for the task force. George Saslow (University of Oregon Medical School) summarized three points to be kept in mind: (i) It is impossible to eliminate variability in indexing and retrieval due to human differences in understanding; (ii) a means of spot checking how well a vocabulary is being used must be devised for quality control; and (iii) scientists at the frontier of concept development must be able to maintain contact with vocabulary users. Thomas A. Sebeok (Indiana University, Bloomington) pointed out that whereas selection of terms might be done easily, their satisfactory definition would be a time-consuming problem of consensus where, in fact, none may exist. The necessity of relating vocabulary selection (for example, in anthropology) to the kind of literature described (for example, biomedical) was stressed by Clellan Ford (Yale). Indexers tend toward generalization when they are uncertain, and Clifford T. Morgan (University of California, Santa Barbara) emphasized that term

definitions should facilitate discrimination between meanings. Howard Freeman (Brandeis) indicated that a sophisticated and authoritative thesaurus could have application beyond that of MEDLARS. The meeting accomplished its twofold purpose of bringing together a few of those who generate and use information in biomedical behavioral sciences and those who convey it, and of formulating guidelines toward developing a useful and imaginative communication tool. The five members of the task force are hopeful that their colleagues will communicate to them any comments or suggestions for improving biomedical literature analysis in behavioral sciences.

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Structure of Cell Membranes at the Molecular Level

At the City of Hope Medical Center, Duarte, California, 9–11 December 1965, about 60 scientists from the Los Angeles–San Diego–San Francisco area met at a conference held by the Center's Institute for Advanced Learning in the Medical Sciences. The conference featured three formal presentations by F. A. Vandenheuval (Canadian Department of Agriculture) on "Lipid constituents of membranes"; D. T. Warner (Institute Fellow at the City of Hope, on leave from The Upjohn Company) on "Proposed structures for the protein components of membranes"; and O. Hechter (Worcester Foundation for Experimental Biology) on "The lipoprotein arrangements of mitochondrial membranes." These formal presentations were followed by open discussions and short presentations by other participants, including Lars Elfvin (U.C.L.A.), T. Kakefuda (City of Hope), Sidney Fleischer (Vanderbilt University), and D. Branton and R. Park (University of California, Berkeley).

F. A. Vandenheuvel reported on his study of the lipid constituents of cell membranes by the use of molecular models. Most of this work was done by making projection photographs of the appropriate Dreiding stereomodels and then drawing in the space-filling characteristics of the various atoms using full Vander Waal's radii. In this way he has examined in considerable detail the space-filling shape and volume of various lipid components and their possible arrangement in a lipid layer or bilayer. The average cross-sectional size and length of each of the most common components have been determined with accuracy by his procedure. These dimensions have then been compared with the known measurements for lipid layers as determined by x-ray methods or electron microscopy. The organization of the polar groups of lipid components with relation to a water lattice or inserted ionic components in such a lattice was also illustrated with projection photographs of the Dreiding stereomodels. Vandenheuvel has extended the studies to the proteins, examining again the space-filling characteristics for the side chains of the individual peptide moieties of a hypothetical primary sequence based on the approximate amino acid composition of the myelin sheath. He also presented an actual model (Dreiding set) of a portion of the sequence fitted onto a water lattice, and demonstrated with this model the contact of the various polar groups and some of the peptide oxygens with the oxygen positions in water. In his concept a so-called layer of protein would be a single peptide chain in thickness. As the chain coils around a central origin the peptide oxygens lie either above or below the plane which is generated by the coil. This would constitute the primary layer of structural protein. Molecules of functional protein, such as enzymes, attached to this primary layer would then constitute the membrane superstructure. Arguments for the existence of unit lipoprotein particles in membranes were presented, and the forces governing membrane stability and lipid turnover were discussed.

D. T. Warner presented a proposed conformation for the membrane proteins based on studies with molecular models, beginning with simple antibiotics and ending with a suggested model of the entire cytochrome *C* sequence. This proposed conformation, designated for simplicity as the "hexagonal conformation," has the peptide chain so arranged that the peptide carbonyl oxygens lie in a uniform hexagonal array. Thus a cyclic hexapeptide forms one hexagon of peptide oxygens, a cyclic decapeptide forms two fused hexagons, and a continuous protein subunit chain generates an expanding spiral of peptide oxygens whose continuing hexagonal pattern builds a honeycomb network. An intriguing property of this peptide network is its similarity to the hexagonal "second neighbor" oxygen pattern of the ice lattice; this similarity introduces the possibility of a precise collinear hydrogen bond contact between a water layer and a peptide layer. This lamination could introduce stabilizing features as well as proton transfer properties into the system. Individual protein subunits in the "hexagonal" conformation could also conceivably interact with each other through their respective hydrophobic (that is, side chain) surfaces to form peptide bilayers. Fundamentally such a peptide bilayer would be like a lipid bilayer, but the protein analogue would have a thickness of about 6.9 angstroms compared with 45 angstroms for the usual lipid bilayer. The outer surfaces of such a protein bilayer in this model would both be coated with water. Under suitable conditions of temperature and *p*H, Warner suggested the possibility that the water could serve as a cement between the various bilayers, producing rods as in the case of protein from tobacco mosaic virus or layers in membrane structures.

O. Hechter outlined the development of a conceptual model for biological membranes, starting from the idea that one protein coat of a membrane must serve as the fundamental scaffold in membrane construction, which dictates the arrangement of the lipids and water structures. Using principles for packing protein subunits and lipids developed in the first two discussions, Hechter considered the protein scaffold to be built of modular protein subunits in hexagonal conformation, interlocked equatorially primarily as hexamers, but including some pentamers as well. The protein subunits are interlocked at "hydrophobic" surfaces, forming a protein bilayer or "sandwich." The hydrophobic surfaces of the subunits of the "sandwich" arrangement are considered to have complimentary surfaces; non-covalent and covalent bonding interactions between complimentary groups are invoked to provide stability to the interdigitated assembly of protein subunits.