imize risk to patients. The negotiation of additional long-term grant support can pose serious time problems in such instances.

Funds from the pharmaceutical industry are available in small amounts for specific studies, and are unquestionably useful in covering the expense of some investigations. Such funds do not, however, provide a sound continuing base from which to obtain salaries for trained investigators or for research assistants.

Many clinical pharmacology units have entered the initial stage of their development. With small staffs (often one man) they are making a modest beginning in meeting the needs in the area of predoctoral and postgraduate teaching of clinical pharmacology, the recruiting and training of well qualified clinical pharmacologists, and research on drug action, comparative efficacy, mechanism of action, structure-activity relationships, toxicity, and pharmacologic interactions in man. Most urgently needed at this time is the type of support which will facilitate the development of more adequate staffs in those university clinical pharmacology units which have demonstrated potential in their training and research activities.

By bringing additional well trained and capable faculty members into these groups, the clinical pharmacologist could give more attention to such things as his function as an interdepartmental catalyst, mechanisms of drug toxicity, and the investigation of drug action in depth. Only through effective teaching programs and the impact of investigative programs which attract students and house staff can clinical pharmacology exert maximal appeal and recruit talented people.

There is a recognized need for more well trained clinical pharmacologists to meet the current demands of teaching and research, to develop programs in the many medical schools currently without them, and to staff future centers, such as the proposed regional complexes which are charged with bringing research advances more effectively and safely to therapeutic application.

To meet these needs, the most fruitful approach at this time might well be to foster the development of well staffed clinical pharmacology units to attract capable people and to train them effectively. Despite the sources now contributing toward this goal, additional support is clearly required. Funds are needed for the stable support of senior faculty positions in those clinical pharmacology units which have demonstrated potential in their training and research programs. *The lack of such funds is the single greatest limitation in the next stage of the development of clinical pharmacology.* In addition, support for young clinical pharmacologists at the immediate post-trainee level is often lacking, and many of the research functions of the clinical pharmacology unit are not readily supported by long-range research grants. Funds for new studies are generally available from the pharmaceutical industry only if the interests of the firm in question and of the investigator coincide. Support is also not readily available for the important service functions provided by the clinical pharmacology unit. A special type of unit or program support would be extremely helpful to provide funds for such activities on a continuing basis.

The location of space for the laboratories, offices, and clinical research units needed by clinical pharmacology groups differs considerably from institution to institution. Many groups have research space available within the department of pharmacology or in an area immediately adjoining the research space of the pharmacology department. The ideal location of space for a clinical pharmacology unit would be close to both the department of pharmacology and the research area related to clinical investigation. Clinical facilities are obviously of great importance, and in selecting the site for such facilities, consideration should be given both to the needs of the investigator and the physical and psychological comfort of patients.

Some units have inadequate space for their current programs, and most units would find the expansion of their faculty sharply limited by the shortage of space and facilities for additional investigators.

Space for specific clinical research projects is primarily available at the present time in categoric disease-oriented clinical research units (such as those for cancer chemotherapy) or in the multidisciplinary clinical research areas. Where such facilities are not available, they will have to be provided.

Because of the interdepartmental nature of clinical pharmacology it is suggested that responsibility for development of space for such groups be a function of the dean of the medical school in cooperation with the chairmen of the department of pharmacology and of the clinical department or departments most directly involved. *It is suggested that those groups interested in fostering the development of clinical pharmacology recognize that lack of space currently limits the adequate staffing of most clinical pharmacology units.*

If one accepts the general philosophy and specific needs described above, it is difficult to avoid the conclusion that the welfare of the American public demands that means be found to expand clinical pharmacology. There are two major sources of available funds: the government and the pharmaceutical industry. Both sources are now making contributions, but grossly inadequate ones. The cost of establishing clinical pharmacology units in all U. S. schools would not be high, and the potential benefits would be immeasurable.

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Notes

1. Daniel L. Azarnoff, U. of Kansas; Paul Calabresi, Yale; Edward A. Carr, Jr., U. of Michigan; Thomas C. Chalmers, Jr., Tufts; J. Richard Crout, U. of Texas, Southwestern Medical School; Thomas E. Gaffney, U. of Cincinnati; Leon I. Goldberg, Emory; Glenn W. Irwin, Indiana U.; Harris Isbell, U. of Kentucky; Hershel Jick, Tufts; Walter M. Kirkendall, Iowa U.; Louis Lasagna, Johns Hopkins; John A. Oates, Vanderbilt; John A. Owen, Jr., U. of Virginia; Lawrence G. Raisz, U. of Rochester; Alvin P. Shapiro, U. of Pittsburgh; William R. Wilson, U. of Iowa.
2. This report has been examined and is endorsed by the Council and the Clinical Pharmacology Committee of the American Society for Pharmacology and Experimental Therapeutics.

Aging

The biological aspects of aging were discussed at a symposium held at the Salk Institute for Biological Studies, San Diego, California, 4–6 November 1965. Speakers included gerontologists from the United States and England.

Maynard Smith (University of Sussex, England) provided a general introduction to theories of aging. In his opinion it was unlikely that there was any such thing as *the* aging process but only a series of aging processes which natural selection would tend to synchronize even if the causes were physiologically independent. He emphasized the impossibility of deciding

anything about the responses and capacities of the individuals who make up a group from a study of the life table of the group. He also emphasized the advantages of *Drosophila* in studies on aging processes. His studies indicate that irradiation causes accelerated rather than precocious aging.

He pointed out the importance of proteins in aging changes, and reported that the incorporation of leucine in flies increases with age. Since the experimental flies were in a steady state, the finding implied either that protein is denatured more rapidly or that more protein becomes enzymatically inactive.

Smith discussed in detail the importance of somatic mutation in aging especially in relation to the part which radiation may play in mimicking the process. He concluded that while somatic mutations clearly occur it is much more doubtful whether they occur sufficiently often. It is even more doubtful whether such mutations can be responsible for the aging changes which are induced by x-irradiation.

Curtis (Brookhaven National Laboratory), speaking on chromosome breakage, radiation, and aging, agreed with Smith in that there is no one cause of aging. He emphasized more strongly that somatic mutation and irradiation are more closely linked and relevant to the problem of aging. His supporting evidence was derived from his own studies on the frequency of chromosomal aberrations in the livers of long- and short-lived mouse strains. Some participants questioned the validity of the experimental method because some of the underlying assumptions had not been verified. A verdict of not proven was perhaps the final outcome of the whole discussion on somatic mutation.

Sharp divisions were evident between Puck (University of Colorado) and Hayflick (University of Pennsylvania) on the aging of cells in tissue culture. Both participants agreed that the original work by Carrel on which so much theorizing about the potential immortality of undifferentiated cells had been based could not nowadays be fully accepted because of technical inadequacies. Hayflick, on the other hand, described his careful and well controlled experiments which seemingly show that human cells in tissue culture can only support a limited number of replications before they die out or take on characteristics of malignancy. He also believes that cultures derived from aged human material reach failure point after fewer multiplications than did cultures from embryonic tissue. However, this thesis that cells in culture do not behave like bacterial cultures, but have limited life spans, was immediately questioned by Puck. He emphasized the undoubted fact that the potentialities of cells for prolonged survival in tissue-culture conditions have progressively developed as our expertise in compounding media and controlling the environment has improved. Puck saw no reason for believing that technical improvements were coming to an end; he indicated that cultures in his own laboratory had continued for more than 500 replications without visible chromosomal change.

Relevant to this issue were Krohn's (University of Birmingham, England) attempts to see for how long an organized tissue, such as skin, as opposed to individual cells, can be serially transferred from one host to another (within an inbred strain of mice). Here, too, technical difficulties had to be overcome, but the age of some pieces of transplanted skin had already exceeded twice the known recorded maximum life span of any mouse. But, like Puck, Krohn could see no satisfying end to such experiments about which someone might always say—if only you had gone on a little longer. The general discussion emphasized repeatedly how important it would be to acquire more understanding of the activities of stem cells and ways of identifying them, whether they lie amongst the basal layers of the skin or the intestinal epithelium or, as in the experiments Till (Ontario Cancer Institute) described, in the bone marrow or spleen. What makes stem cells divide and what brings their reproductive life spans to an end—if anything does—are problems of great concern to all gerontologists.

Krohn described how transplantation techniques can be used to create situations in which tissues of one age can be examined in the environment provided by an animal of another age. Such heterochronic grafts can be used to indicate whether aging changes in a tissue are dependent on inbuilt controls within the tissue itself or are brought about by changes in the surrounding environment. One series of experiments in serial transplantation has already been mentioned and two other examples were given. In the first, Krohn described the age changes in reproductive performance of the female mouse and showed that it is in the uterus rather than in the ovary that the major deterioration occurs. Second, he showed that declining metabolic activity in the skin of mice with increasing age is a function of the tissue itself rather than of the age of a host mouse to which the skin had been transplanted.

Discussions on aging in insects (Rockstein, University of Miami) and aging in bacteria (Glaser, University of California, Berkeley) provided new information on the relevance of such aging to the problems of mammalian aging.

A group of shorter papers which concluded the meeting indicated the diversity of possible approaches to the overall problem. Thus Brandes (Johns Hopkins, Baltimore) emphasized the importance of internal self-destructive processes related to the activity of lysosomes and the formation of pigment within cells; Saunders (Marquette University, Milwaukee) demonstrated how something akin to aging or at least "programmed death" is a characteristic of some parts of embryological development; and Walford (University of California, Los Angeles) emphasized autoimmunity as a mechanism responsible for aging.

All participants must have been convinced from the discussions that studies of how the passage of time affects cells, organs, and organisms are part of fundamental biology. They must have been impressed too by the way in which specialists from other fields can recognize the relevance to aging of their own particular studies and can contribute usefully to a specialist symposium. What we seem to need is more awareness of the intellectual stimulus that the study of aging can provide and of the ways in which the parameter of age can be introduced as an important facet in all sorts of studies by many biologists who would not ordinarily call themselves gerontologists.

The meeting was supported by the National Institute of Child Health and Human Development of the National Institutes of Health (PH43-65-581) and, in the early days of its planning, had owed much to the interest which the late Leo Szilard, Senior Fellow of the Salk Institute, had shown in the subject. The penetrating

and skeptical comments which Szilard would certainly have brought to the meetings were sadly missed by the members of the symposium.

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Solvay Conference

The first Solvay conference took place in 1911 in Belgium, and was organized by Ernest Solvay, a Belgian industrialist and philanthropist. The purpose of the first, and succeeding conferences, was to discuss a new scientific theory or development. Attendance is always limited to invited guests plus a small number of scientists at the Université Libre de Bruxelles.

The thirteenth Solvay Conference of Chemistry took place in Brussels during the week of 24 October 1965. The subject of the conference was the reactivity of excited organic molecules. Nine invited papers were presented; the last day was devoted entirely to discussion. Somewhat more than 50 scientists attended this conference.

C. A. Coulson (Oxford, England) discussed the present state of theoretical knowledge of the excited electronic states of molecules. The present model of molecular electronic configuration is that of single molecular orbitals computed, in the most favorable cases, by a Hartree Fock method. Those excited states, well represented by excitation of a single electron from one of the orbitals which are filled in the ground configuration, lend themselves to certain qualitative predictions concerning their nature. For instance, one can frequently predict that their lowest potential configurations will be with certain bonds between constituent atoms either lengthened or shortened, and either weakened or strengthened. Quantitative statements of the extent of these effects are in the distant future, if ever. For certain excited states which consist of a resonance mixture of various single electronic excitations even qualitative predictions are now impractical.

R. Daudel (Paris) reported on the predicted nature of the lowest excited electronic state of various conjugated aromatic molecules. Daudel has made progress in predicting the location of reaction in photoexcited aromatic molecules.

G. Porter (Sheffield, England) discussed theoretical and experimental work on photochemical reactions of aromatic molecules. The usual sequence of events is that first discussed by G. N. Lewis: photoexcitation to an excited singlet state, followed by radiationless conversion to the lower-lying metastable triplet, which may either react, phosphoresce, or be deactivated by a radiationless transition. The primary-excited singlet, in some cases at least, appears to undergo quantitative conversion to the triplet. But even when such simplification exists the possible fates of the excited triplets makes exact interpretation of its reaction rate difficult. However, in individual cases by using a variety of techniques a complete mapping of the various processes has been achieved.

G. O. Schenk (Mulheim, Germany) and George Hammond (Cal Tech) presented papers on similar subjects but with some differences of interpretation. The lowest-excited (triplet), electronic state of ethylene has a minimum energy with a nuclear configuration in which the two CH_2 planes are at right angles, instead of parallel as they are in the ground state. Thus photoexcitation of substituted ethylenes results in transformation of cis to trans configurations and vice versa. The same reaction can be obtained by photoexcitation of an aromatic molecule in the same solution with the ethylenic compound, if the triplet aromatic excitation has equal or higher excitation energy than that of the ethylene derivative. The electronic excitation is then transferred from the aromatic molecule to the ethylene derivative. Many studies of these sensitized-transfer reactions have been made, especially in the laboratories of Hammond and of Schenk. The exact course of the details of some of these sensitized excitations is not completely clear, although my impression was that most of the ambiguity lay in the semantics.

Various photochemical reactions of relatively complicated organic molecular types were discussed by N. C. Yang (Chicago), W. C. Dauben (Berkeley), and E. Havinga (Leiden). The photochemistry of the solid state was reported on by C. M. J. Schmidt (Weizmann Institute, Israel).

To a physical chemist whose training in organic chemistry ceased almost 40 years ago, and whose contact with organic reaction kinetics has been only sporadic since then, the conference was enormously impressive. The detail with which the course of most complicated and diverse reactions are understood is amazing. Many of these reactions involve electronic photoexcitation of one molecule followed successively by internal conversion to a triplet state, transfer of the electronic excitation (and the spin) to a second molecule, and reaction of this molecule involving very great readjustments of atomic configurations and with the participation of other reactants. In many cases, the details of the succession of steps and a fair quantitative understanding of the efficiencies are known.

The proceedings of the conference including the very lengthy and valuable discussion will be published in the near future.

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Forthcoming Events

April

24. Society for **Clinical Ecology**, 1st annual mtg., Chicago, Ill. (T. G. Randolph, Human Ecology Research Foundation, 720 N. Michigan Ave., Chicago 11, Ill.)

24–26. American Assoc. of **Colleges of Pharmacy**, Dallas, Tex. (C. W. Bliven, 1507 M St., NW, Washington, D.C. 20005)

24–27. American Soc. of **Abdominal Surgeons**, Chicago, Ill. (B. F. Alfano, 663 Main St., Melrose 76, Mass.)

24–27. American **Oil Chemists'** Soc., Los Angeles, Calif. (C. H. Hauber, The Society, 35 E. Wacker Dr., Chicago, Ill. 60601)

24–28. **Infectious Pathology**, 4th intern. congr., Stuttgart, Germany. (G. Hoffman, Hugstetterstr. 55, 78 Frieburg im Briesgau, Germany)

24–29. American College of **Allergists**, 22nd annual congr., Chicago, Ill. (J. D. Gillespie, 2141 14th St., Boulder, Colo. 80302)

24–29. American Soc. of **Hospital Pharmacists**, annual mtg., Dallas, Tex. (J. A. Oddis, 2215 Constitution Ave., NW, Washington, D.C. 20037)

24–29. American **Pharmaceutical** Assoc., Dallas, Tex. (W. S. Apple, 2215 Constitution Ave., NW, Washington, D.C. 20037)

25–27. **Antidepressant Drugs**, symp., Milan, Italy. (S. Garattini, Inst. di Richerche Farmacologiche "Mario Negri," Via Eritrea, 62, Milan)

25–27. **National Acad. of Sciences**, 103rd annual mtg., Washington, D.C. (Home Secretary, NAS, 2101 Constitution Ave., NW, Washington, D.C. 20418)

25–27. American Acad. of **Pediatrics**, Montreal, P.Q., Canada. (E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill. 60204)