Meetings

Cholera Research: United States–Japan Cooperative Medical Science Program

The United States–Japan Cooperative Medical Science Program was established in 1965, by agreement between President Johnson and Premier Sato, with the objective of stimulating cooperative medical research programs designed to improve the health of the peoples of Asia. As a part of this program, American and Japanese scientific panels were appointed in six areas including tuberculosis, leprosy, cholera, parasitic diseases, malnutrition, and viral diseases. The objectives of these panels have been to develop integrated research programs designed to solve major practical problems in their respective areas and to stimulate research.

At the initiation of the U.S.–Japan Program, the Joint Cholera Panel emphasized the following points. Despite the fact that a consistently effective regimen with intravenous fluids for cholera has been developed, the overall mortality rate during the current cholera pandemic has been greater than 20 percent. The continued cholera toll has resulted from the fact that a large proportion of cholera cases have occurred in impoverished rural areas, where adequate and appropriate therapy with intravenous fluids are not available. It is unlikely that prompt and adequate intravenous fluid therapy can be made available to a large proportion of affected patients in rural Asia in the near future. It is also unlikely that the sanitary measures essential to the ultimate eradication of cholera can be carried out in cholera endemic areas within the next two decades. In view of these considerations, the Cholera Panel adopted the following primary research goals: (i) the development of an effective means of conferring long-term immunity against cholera, and (ii) the precise delineation of pathophysiologic mechanisms in cholera, with the object of developing a pharmacologic means of rapidly reversing the gut physiologic alterations responsible for the disease.

A Symposium on Cholera Research, sponsored by the U.S.–Japan Cooperative Medical Science Program, was held in Palo Alto, California, in July 1967. At this time, recent advances in cholera research were reviewed, and current research needs, especially in the areas of immunology and pathophysiology, were emphasized.

In the area of immunology, H. W. Mosley (Pakistan-SEATO Cholera Research Laboratory) described recent field trials which indicated that available whole-cell and fractionated antigen cholera vaccines conferred only limited immunity for a relatively short period (3 to 6 months). In these field trials, a significant correlation was demonstrated, for the first time, between the vibriocidal antibody titer and immunity. A causal relation between vibriocidal antibody and immunity was not, however, established. In the ensuing discussion, both Japanese and American participants emphasized the dearth of knowledge of basic immunologic mechanisms in cholera, and the great need for further studies of antibodies directed against both *Vibrio cholerae* and the heat-labile exotoxin produced by this organism.

In the area of pathophysiology, investigators from Johns Hopkins reported that experimental cholera, duplicating the major clinical and physiologic features of the naturally occurring disease, can be produced in the dog by challenge with either virulent *V. cholerae* or sterile filtrates of broth cultures of *V. cholerae*. Studies on this experimental cholera model have indicated that (i) almost all the diarrheal fluid originates in the small bowel; (ii) the fluid secreted by each segment of small bowel after stimulation by exotoxin has the electrolyte pattern characteristic of spontaneous secretions from that segment of bowel; and (iii) the exotoxin-induced hypersecretion of fluid and electrolyte is not accompanied by evidence (on electron microscopy) of damage to either mucosal epithelial or capillary endothelial cells. It is felt that the dog may serve as an adequate model for defining the mechanism by which the cholera exotoxin causes hypersecretion of electrolyte by the small bowel mucosal cells.

Representatives of the SEATO Cholera Laboratory in Dacca and the Johns Hopkins University group in Calcutta reported independent studies which demonstrated that active gut absorption of glucose, and the sodium associated with it, remains essentially normal in actively purging cholera patients. The two groups of investigators further reported that glucose-associated sodium absorption can counterbalance the cholera-induced electrolyte secretion into the gut lumen. Thus, electrolyte balance can be maintained, during severe cholera, by oral administration of electrolyte solutions containing glucose. These observations lead to the hope that an effective oral therapy of cholera may prove a practical solution in the treatment of a large proportion of cholera patients in rural areas of developing countries.

At the conclusion of the symposium, it was pointed out that neither of the primary research goals of the Cholera Panel has been achieved. Several factors, however, make it possible that these goals may be attained in the foreseeable future.

1) Funds have been set aside for support of research directed toward development of an effective immunizing agent against cholera and for more precisely defining the pathophysiologic mechanisms in cholera.

2) Commercial production of crude cholera exotoxin has been initiated; limited amounts of the crude exotoxin will be made available to qualified investigators for cholera research.

3) The recently described canine model of cholera should facilitate pathophysiologic and long-term immunologic studies of this disease.

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Paleolimnology

Paleolimnologists aspire to interpret past conditions and processes in lakes by comparison with the present and thereby also to gain a better understanding of the present by knowing its genesis. The raw materials of paleolimnology are the accumulated sediments and the geomorphology of their basins. The kinds of primary materials deposited are controlled by regional geology, climate, and by an array

of biological processes occurring both in the lake itself and in its watershed. These primary sediments may subsequently be modified by secondary transport and by a variety of biological activities. The chemistry, mineralogy, and structure of the sediments reflect the depositional environment. The morphological and biochemical remains of organisms in the sediments give insight into past communities and ecosystems and their development.

The first international meeting on the history and developmental processes of inland water bodies was held at the Biological Research Institute in Tihany, Hungary, 28 to 31 August 1967. Altogether 80 persons from 20 different countries attended. Approximately half the participants were from the socialistic countries—chiefly the Soviet Union, Poland, and Hungary —and the remainder were from western Europe, North America, Senegal, and Japan.

The first day was devoted mainly to geology, physics, and chemistry. The second day was concerned primarily with biological topics. On the third day the participants went by boat to Keszthely at the west end of Lake Balaton. An intermediate stop was made at Balatonszemes to learn about the efforts of the VITUKI laboratory which studies and manages the hydrologic regime of the lake. At Keszthely there were lecture-demonstrations of the geology of the region and the geological history of Lake Balaton, the pioneer work of L. Lóczy in studying Balaton, and the cultural archeology of the region. The fourth day was devoted primarily to integrating subjects, including many-sided collaborative studies on particular lakes.

The Russians have been making extensive studies of their large lakes in Asia. G. A. Dmitriev reported that Lake Baikal is approximately 30 million years old, and that since the basin is only about two-thirds filled with sediments, it should enjoy another 15 million years at present process rates. Lake Issyk-Kul, as reported by V. V. Aleshinskaya, is known to have experienced two major transgressions, corresponding to the last two glacial ages, during which times the lake drained to the west. It is now a closed basin and also was closed during the last interglacial, dated at $110 \pm 40 \times 10^3$ year by uranium isotopes. In more recent times the Aral Sea has had a fluctuating water level, as reported by A. V. Shnitnikov, with three periods during the past 5000 years, including the cold period from 1300 to 1500 A.D., when the water level was high enough to establish a connection with the Caspian Sea. Studies indicate that all these large lakes presently with closed basins experienced concurrent transgressions and regressions of size and lake level, brought about by major climatic changes. Such throughflow connections in the past are believed by F. D. Mordukhay-Boltovskoy to be the means whereby the distinctive Ponto-Caspian fauna attained its present distribution.

D. A. Livingstone (U.S.A.) reported that at least in Kenya and Uganda the pluvial periods were out of phase with the glacial ages, unlike the situation in the Great Basin region of the United States. H. Faure (Senegal) reached the same conclusion concerning the paleohydrology of the Sahara region.

Quite a number of persons (M. Kabailiene, U.S.S.R.; M. Ralska-Jasiewiczowa and K. Wieçkowski, Poland) were concerned with thermokarst relationships of northern lakes, particularly the fact that the peat that formed over the top of the unmelted ice block eventually arrived at the anomalous position of being at the bottom of the lake when the ice block melted, usually during the Alleröd. Wieçkowski reported such deposits as much as 60 meters below present water surfaces.

D. D. Kvasov (U.S.S.R.) reported on the extensive proglacial lakes in eastern Europe during the Würm Glacial, their changing aspects during the various stadials and interstadials, and the fact that they exerted dominant control over the hydrology and periglacial processes at this time.

Remains of various groups of organisms occur abundantly enough in the sediments to be used for interpreting past conditions. Pollen and spores, diatoms, Cladocera, ostracods, midge larvae, beetles, and mollusks, including glochidia, were reported on. Diatoms not only are usually abundant in sediments but also are good indicators of temperature, salinity, water level, and other conditions. Persons actively working with diatoms (R. Margalef, Spain; M. Kabailiene, U.S.S.R.; J. Meriläinen, Finland; K. Crabtree, England; B. Marciniak, Poland; Z. Reháková, Czechoslovakia; J. L. Richardson, United States; and others) used this opportunity to get together informally to talk over mutual problems.

Persons interested in the animal fossils, particularly the Cladocera (W. T. Edmondson, E. S. Deevey, R. O. Megard, J. DeCosta, C. E. Goulden, D. G. Frey, and M. C. Whiteside, U.S.A.; D. Flössner, East Germany; H. Müller, West Germany; H. Löffler, Austria; J. Rzoska, England; O. Sebestyén, Hungary; and J. Hrbaček, Czechoslovakia) also convened for an informal discussion. The chydorid Cladocera seem to be almost uniquely favorable for studying adjustments of communities to changing environmental conditions. The species-abundance relationships of a stable chydorid population correspond almost precisely to those predicted by the MacArthur Type I distribution. Major disturbances, by man or volcanic eruptions, create immediate imbalances, which may require an average of about 200 years for complete restoration (Goulden). Departures from the predicted distributions can be used to assess the degree of imbalance in community organization.

Some of the newer statistical techniques are also being applied to palynology in an attempt to make more sophisticated interpretation of past conditions. J. G. Ogden (U.S.A.) has been using the Spearman rank-correlation coefficient to determine the closest agreement between a fossil pollen spectrum and all the available present-day pollen spectra from different major vegetational types. As more present-day spectra are accumulated, the method should become a major tool in the interpretation of past vegetations, their successions, and disturbances.

L. Ronai (Hungary) has such an impressive geological section in the Balaton region that G. Lüttig (West Germany) suggested it might be presented for consideration as a substitute type locality for the Pliocene-Pleistocene boundary.

W. Tutin (England) agreed with conclusions reached earlier by Mackereth that the changing stratigraphy of sediments in lakes of the English Lake District does not reflect changing levels of productivity in these lakes but rather changing rates of erosion in their watersheds, brought about by man through deforestation and subsequent use for agriculture of the lands cleared. Other persons in rebuttal suggested that although much of the material in the English lakes may have been derived from their watersheds rather than from the lakes themselves, this relationship cannot be extrapolated to all lakes.

Nevertheless, lakes are sensitively re-

sponsive to changes in watershed conditions. It is likely that the sedimentary record in lakes, which is an historical record as well, will be useful not only for interpreting precultural events and conditions but also the degenerative changes in waters resulting from man's more recent activities. Studies of Lake Washington (W. T. Edmondson, U.S.A.) and Lake Zürich (E. A. Thomas, Switzerland) indicate that sediments hold great promise.

Scientists in the Soviet Union have already recognized the importance of paleolimnology by having held two large symposia at Minsk and Leningrad on the paleolimnology of the northwestern European portion of the U.S.S.R. A third meeting is planned for Vilnius in a couple of years.

The symposium was sponsored by the International Association of Limnology and the Biology Department of the Hungarian Academy of Sciences, with support of the International Union of Biological Sciences and Section PF of the International Biological Program.

The proceedings of this symposium will be published in the Mitteilungen series of the International Association of Limnology (T. T. Macan, Secretary).

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Calendar of Events

Courses

Histochemistry, Vanderbilt University, 28 July–17 August. For college and university teachers of zoology. Applicant must be member of faculty of an accredited college or university and teach at least one course in some area of zoology. In addition, he must be interested in histochemistry, either in teaching and/or in research. Living and travel expenses for 20 selected participants will be funded by a grant from the National Science Foundation. *Deadline for applications: 1 May.* (Dr. Burton J. Bogitsh, Box 1733, Station B, Vanderbilt University, Nashville, Tennessee 37203)

Advanced Study in Gerontology, University of Southern California, 17 June–29 July. For graduate students and professional people in the aging field. The institute will be conducted in three 2-week sessions. Students may attend for 2, 4, or 6 weeks. The first 2-week session will consist of a general survey course on concepts and issues in gerontology; the second will cover human physiology and aging, aging and personality, urban ecology and aging, and introduction to scientific computing; the third will cover implications of urban ecology for architecture, behavior, brain, and aging, aging and the family,