Meetings

Congenital Malformations and Cancer: United States–Japan Cooperative Science Program

Epidemiologic research into the origins of cancer and congenital malformations was discussed at a meeting in Tokyo, 1–5 November 1965. This conference was part of the U.S.–Japan Cooperative Science Program, administered by the Japan Society for the Promotion of Science and the National Science Foundation.

R. W. Miller (National Institutes of Health) outlined Japan's exceptional data resources for epidemiologic research, and the need to train scientists and to secure financial support to make the most of the opportunities which these resources provide. T. Yanase (Tokyo Medical and Dental University) and T. Soda (Institute of Public Health) described the family registry system (*koseki*), which can serve as a low-cost follow-up system for prospective studies of live births, marriages, divorces, and deaths, and for ascertaining family relationships. About 7 percent of all marriages in Japan are consanguineous; half of them involve first cousins. Thus, the effect of rare recessive genes on growth, development, and disease can be evaluated. W. J. Schull (University of Michigan) reviewed the methods for study of consanguinity effects, the results obtained to date in Japan, the new questions and problems which have arisen in consequence, and the prospects for extending current knowledge. He observed that as research moves from questions about the presence or absence of particular genetic phenomena to estimates of their frequencies with the greatest precision possible, it is increasingly realized that these estimates are not entirely reliable unless active steps are taken to control, in particular, the socioeconomic variability. H. B. Hamilton (Atomic Bomb Casualty Commission) described hematologic surveys which showed geographic and ethnic clustering of persons with hypocatalasia. Such individuals are carriers of acatalasia, a disorder first recognized in Japan and caused by a rare recessive gene. All but one of the Japanese with acatalasia were of consanguineous parentage.

M. Yamaguchi (National Institute of Industrial Health, Kawasaki) and K. Tsuchiya (Keio University) described the industrial medical records required by the Labor Standard Law of 1947, and the feasibility of using the data collected to determine the effects of occupational exposures on the occurrence of cancer and on reproductive performance. The Law requires that in all industries with more than 50 employees there be standard medical records maintained by certified health supervisors. With the cooperation of the employer it is possible to conduct epidemiologic research into industrial hazards not only on the workers but also on their offspring, and to couple data from occupational histories with those of the *koseki* records. Tsuchiya also cited as a potential source of epidemiologic data the annual published summaries of all autopsies in Japan. The possibility of relating cancer or congenital malformations to exposures in home industries was raised by T. Hirayama (National Cancer Center, Tokyo).

H. Nishimura (Kyoto University) described legal and ethical circumstances which limit the study of human conceptuses in Japan. Because of the respect with which the Japanese regard the unborn child lost by abortion, whether spontaneous or induced, it is necessary in Japan that international collaborative studies involving these specimens be carried out where appropriate regard for the human material used will be shown. From a study of early embryos obtained by induced abortion, Nishimura concluded that there is a considerable variation in Streeter's horizons for a given gestational age and that certain malformations (cyclopia, spina bifida, and polydactyly) are more frequently observed in early embryos than in newborn infants. Sex-chromatin studies were not made because of limitations in personnel and facilities. Cytogenetic studies are planned. R. J. Blandau (University of Washington) urged that special attention be given to information collected on environmental factors in the pre-implantation period and that, if possible, the placenta be studied along with the embryo. R. L. Brent (Jefferson Medical College) evaluated the opportunities for immunologic study of conceptuses. He concluded that fluorescent-labeling techniques of all types can be applied to the embryo and trophoblast to determine the presence of antigens and specific antibodies; tissues and cells from the embryo can be transplanted to non-human hosts or to tissue-culture media to measure the development of the embryonic humoral antibody system and cellular competence; and blood serum can be obtained from the mother to correlate with data obtained from the embryo. It may also be possible to perform safe and accepted immunologic and vaccination procedures just before induced abortion to evaluate placental transfer and the ability of embryos to respond at various stages of gestation.

T. Takai (Osaka City University) discussed (i) the enzymatic development of normal and malformed human fetuses, and (ii) the mass screening of children for inborn errors of metabolism. Schull suggested the application of inventiveness in the Japanese electronics industry to the automation of mass medical screening procedures which could measure simultaneously numerous biochemical constituents of body fluids. I. Hayashi (Nagasaki University) described his autopsy studies on endocrine pathology as related to congenital malformations.

T. Takatsu (Tokyo University) presented the results of the Tokyo metropolitan area registry of childhood cancer since its inception 18 months ago. Among the 187 cases registered, there appeared to be an excess of hepatoblastoma and a deficiency of Wilms's tumor as compared with the frequency in the United States. Beginning 6 months ago, special attention has been given to the occurrence in the same child of congenital malformations and cancer. Dubois's sign, commonly found in Down's

syndrome but not in normal persons, appeared to occur more often than usual among children with leukemia. Miller reviewed clinical and epidemiologic evidence for the excessive occurrence of childhood cancer and congenital defects in the same person, family, or community. Through such concurrences, one may be able to recognize common agents or mechanisms in the genesis of the associated diseases.

W. M. Haenszel (National Institutes of Health) described retrospective epidemiologic studies in progress concerning cancer of the stomach and lung in Japanese migrants to Hawaii and California as compared with the experience in Japan. Differences in the histories obtained in the three locales may be of etiologic significance. Hirayama presented the rates for causes of death in the converse situation, namely, among foreigners in Japan in contrast to the native population. K. G. Johnson (Atomic Bomb Casualty Commission) told of clinical cardiovascular studies on cohorts of Japanese in Hiroshima for comparison with issei and nisei in Honolulu.

M. Segi (Tohoku University) noted the variations in cancer rates within Japan and compared the rates for all Japan with those of other countries. Most notable was the very high Japanese rates for stomach cancer, the occurrence of which was particularly frequent in certain prefectures, such as Nara.

E. Matsunaga (National Institute of Genetics) showed that certain epidemiologic characteristics of Down's syndrome were the same in Japan as in Western countries, and that new observations from study of the *koseki* record indicate an association between the syndrome and (i) birth order and (ii) pregnancy-free interval between succeeding livebirths—an association which may suggest a hormonal means for suppressing chromosomal aberrations. M. Hayashi (Toho University) reported on the frequency in Japan of congenital malformations in the newborn (0.73 percent of 83,988 deliveries in 1961) and some epidemiologic data on phocomelia that was induced by thalidomide.

P. Kotin (National Institutes of Health) spoke of the interaction between epidemiologic and laboratory research, and of the problems and techniques common to oncology and teratology. He stressed that observations from either discipline may well apply to the other.

Several participants urged that steps be taken to standardize methods, terminology, and definitions to improve international comparisons of results from medical research. Blandau noted the exceptional opportunity in Japan for the study of the development of the normal human embryo. J. Warkany (University of Cincinnati) suggested the establishment of informal small groups of scientists in the United States and Japan through which questions about oncology and teratology (literature and resources) in the two countries could be channeled. There was some concern on the Japanese side that the function of these groups might conflict with that of existing organizations. Soda cited the Atomic Bomb Casualty Commission in Hiroshima and Nagasaki as an exceptional resource for epidemiologic competence and for a wide spectrum of research on human development and disease.

It was suggested that U.S. embryologists, teratologists, epidemiologists, and biostatisticians be encouraged to work at Japanese universities and institutes under the sponsorship of the U.S.–Japan Cooperative Science Program. A series of recommendations was also made to facilitate cooperative research between the two nations in embryology, teratology, and cancer epidemiology. It was emphasized that there was no intent to alter the current administration or funding of research in these fields.

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Seaweed

Marine algae are important because of their applications in agriculture and also as a possible source of food for man. In order to foster original research, both fundamental and applied, in the field of marine algae, the 5th International Seaweed Symposium was held in Halifax, Nova Scotia, 25–28 August. The topics at this symposium were evenly divided among botanical, chemical, and applied aspects. A symposium within a symposium developed on the subject of algal polysaccharides.

In discussing the seaweed industry of the future, F. N. Woodward (Scotland) stressed the possibilities of mass culture as a source of protein; the cultivation of areas for selected species, as in Japan; and the great need for mechanization in harvesting and drying. He also noted the possibilities of further applications of the unique algal polysaccharides in agriculture, industry, and medicine. The use of mustard, *Sinapis alba*, as a test plant with which to assess growth response to seaweed extracts was described by Challen and Hemingway (United Kingdom). Stephenson (United Kingdom) reported specific effects from the use of liquid seaweed fertilizer; the use of such fertilizer increased the resistance of some field crops to frost, to pathological fungi, such as *Botrytis*, on strawberries, and to animal parasites, such as aphids, on beans and sugar beets.

Recent studies by Araki (Japan) on the polysaccharides of agarophytes, revealed the chemical constitution of agarose and agaropectin. Sulfate groups as half-esters were established in agaropectin only. The remarkable finding of variable, but appreciable, amounts (1 to 20 percent) of 6-*O*-methyl-D-galactose in agarose was reported. Pyruvic acid was confirmed as a constituent of only two agaropectins. In agarose the molar ratio of D-galactose + 6-*O*-methyl-D-galactose to 3,6-anhydro-L-galactose was always unity.

Anderson and Rees (Scotland) have found that carrabiose units account for 88 to 99 percent of the molecule of κ and λ carrageenans based on the products after methanolysis of native and alkali-treated material. A new, widely distributed, sulfated heteroglycan, isolated first from *Ascophyllum*, has been discovered by Larsen and Haug (Norway) and named ascophyllan. It contains fucose, xylose, and a uronic acid. The uneven distribution of mannuronic and guluronic acids in the main chain of alginic acid was postulated by Haug and Larsen (Norway) from studies of partial hydrolysis with oxalic acid. The isolation of specific κ and λ carrageenases from *Pseudomonas carrageenovora* was reported by Yaphe and co-workers (Canada).

The finding of pure poly-*N*-acetylglucosamine as the only constituent of the extracellular fibers of the diatom, *Thalassiosera fluviatilis*, by McLachlan,