

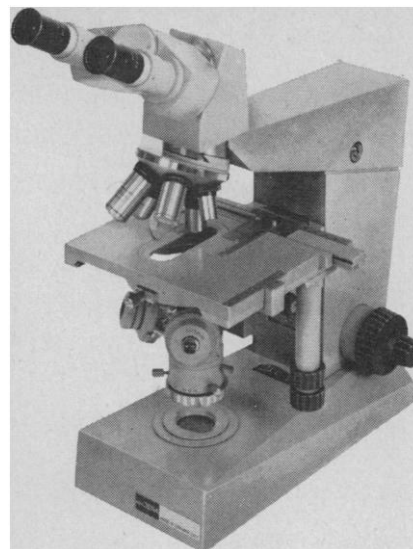
Human Histocompatibility Antigens and Susceptibility to Disease

A cooperative seminar on human histocompatibility antigens and susceptibility to disease was held in Santa Barbara, California, on 4 to 6 October 1972 under the U.S.-Japanese Agreement in Science. Those in attendance included ten scientists from the United States, eight from Japan, and two from India. In addition to being expert in transplantation immunology and tissue typing, the participants offered representation of the disciplines of genetics, epidemiology, computer technology, pathology, and surgery. The objectives of the seminar were to consider appropriate international studies of the relations of HL-A to disease and to improve the reagent facilities of the countries involved.

The initial half-day session was devoted to a survey of the general significance and problems of histocompatibility testing, with special emphasis on the HL-A system—reviewing data on the comparison of HL-A specificities in Japanese and Caucasians and on the relation between HL-A specificities and several disease conditions. R. Payne (Stanford University) began by identifying the two segregant series of the HL-A system with its total of at least 30 specificities. The effectiveness of HL-A typing in increasing graft survival in transplants between siblings was emphasized, but it was pointed out that other, possibly independent, genetic loci (that of mixed lymphocyte interaction) are also important in graft rejection. The complexity of the known genetic linkages in both mice and man was pointed out by B. Amos (Duke University). The MLC locus in mice lies between the K and D regions of H-2, being close to the Ir loci and to the Ss and Slp loci as well. Although disease-associated phenomena are only partially understood, it was emphasized that one of the genes conferring susceptibility or resistance to Gross leukemia virus is associated with certain alleles of the K region of the H-2 complex. The complexity of the HL-A system in man is less well understood than is the H-2 locus in mice; but it seems likely that the K region in mice is analogous to the second segregant series of man and that the HL-A system is closely linked to the MLC locus in man. There is some evidence for a locus controlling immunoglobulin levels and hypersensitivity reactions in this genetic region. P.

Terasaki (UCLA) continued the discussion, with emphasis on racial and disease-associated HL-A factors in man. Specificities HL-A 1, 3, 8, and W14 are lacking in Japanese, and Japanese and Caucasians differ in the relative rate of occurrence of a variety of other histocompatibility specificities. The clearest example of a disease-histocompatibility relationship seems to be psoriasis, in which HL-A 13 and W17 are increased and HL-A 12 is decreased as compared to the normal Caucasian population. Others pointed out that there may be decreases of certain HL-A specificities with age and during the course of severe, debilitating disorders.

The second session was concerned with a detailed discussion of typing techniques, procurement of reagents, methods of data analysis, and reports from the Japanese delegates on studies of HL-A specificities in their populations. The major technique used in typing is complement-mediated cellular lysis by selected alloantisera. The micromethods used by Japanese and U.S. investigators were similar. A major difference is that in the United States it is usual to find more than one method used in each laboratory for detection of membrane antigens. A discussion of procurement of appropriate reagents was led by E. Yunis (University of Minnesota). Since most antisera in use today have been obtained from postpartum mothers, serum is collected on the third postpartum day and screened for antibody activity. If such activity is found at a titer of 1:4 or greater, two units of plasma are collected in an anticoagulant by plasmaphoresis. Serum prepared from this with calcium chloride is then dispensed in vials for later use. Since the specificity of antisera collected at different intervals postpartum varies, it has been found useful to retest serum from these donors several times during a 9-month postpartum period. It was estimated that a minimum of 24 separate cell preparations are required for screening antisera, and it was pointed out that cell preparations may be preserved in dimethylsulfoxide, fetal calf serum, and minimum essential medium in liquid nitrogen or for shorter periods on the bottom of a mechanical freezer where the temperature is maintained at -70°C or lower. Although computer analysis has now become an in-



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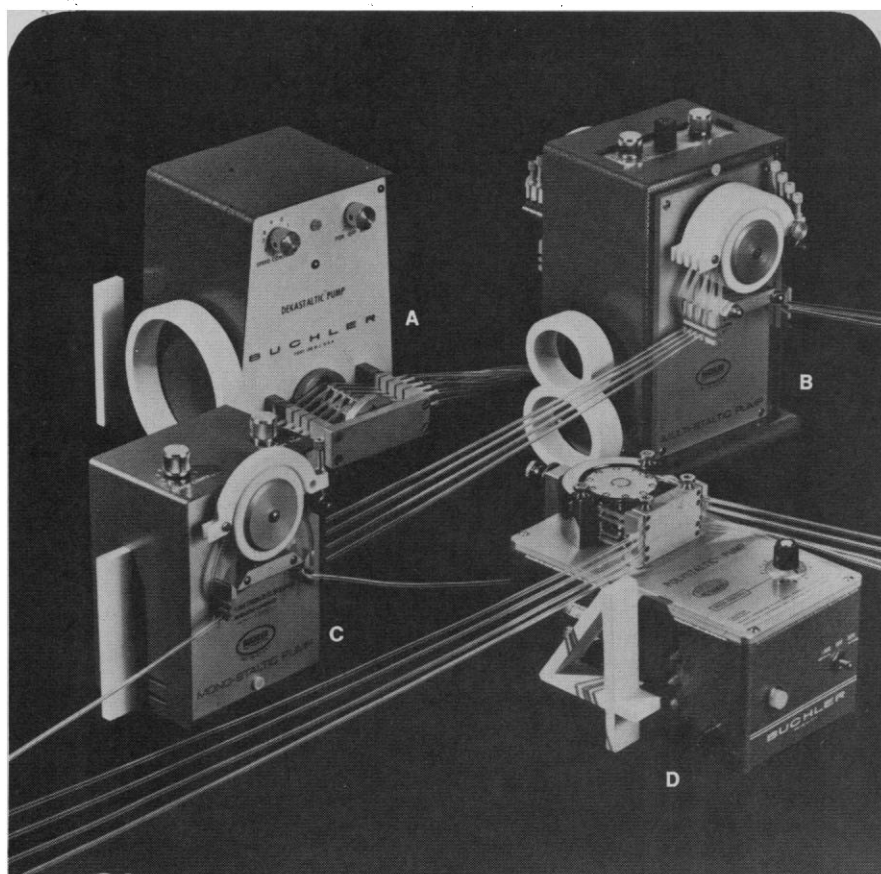
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tegral part of tissue typing, the programs used vary from laboratory to laboratory and visual inspection of data remains an important laboratory tool. K. Tsuji (Keio University) and Y. Iwasaki (Chiba University) offered reports of HL-A typing among native Japanese and M. Yokoyama (Honolulu) reported similar data on Japanese living in Hawaii. These data were generally similar to the results obtained by Terasaki described earlier. Because of the large proportion of blanks or unidentified specificities apparent in the genotyping of each of these series, it is to be expected that serums obtained from multiparous Japanese women will provide the international scientific community with significant additional identifiable serologic specificities.

The third session continued the discussion of HL-A in different populations, the role of HL-A typing in transplantation, and the potential of application of legal fingerprinting (dermatoglyphics) techniques to tissue typing. K. Balakrishnan (India) presented data concerning the HL-A typing of members of various castes in India. There was no recognizable difference between members of each of the four castes studied. These individuals were close to Caucasians in the distribution of their HL-A antigens and differed from the distribution of HL-A antigens evident in Japanese. There was a difference in distribution of HL-A antigens when northern and southern Indians were compared. The discussion of tissue typing and transplantation was brief, but centered on the fact that identify for four antigens ("full-house" matches) permitted improved survival of organ grafts. T. Inou and M. Matsukura (Tokyo University) presented data on the reclassification of dermatoglyphics and their potential use in compatibility testing. Although the data were interesting the thought was expressed that a correlation was not what would be predicted because of the multifactorial determinants of fingerprints.

The fourth session was concerned with HL-A typing and susceptibility to disease. A. Lilienfeld (Johns Hopkins University) began the discussion by reviewing the reported occurrences of neoplasm with an increased family incidence. This was followed by a discussion of the relationships of HL-A specificities and disease. The clearest examples of such as association seemed to be psoriasis and celiac disease. In the former, an increase in W-17 was most marked in patients with a family

history of psoriasis and HL-A 13 was most prominent when a family history of psoriasis could not be elicited. K. Orita (Okayama University), K. Tsuji, and T. Yoshida (Aichi Cancer Center) discussed results of Japanese investigators with respect to their studies of susceptibility to cancer and HL-A typing with special emphasis on gastric cancer. M. Aizawa (Hokkaido University) reported a study of the relation between HL-A typing and the occurrence of Australian antigen. K. Nomoto (Kyushu University) closed the discussion by reviewing the possibility of relating HL-A typing with certain defects in the ability of hosts to efficiently handle certain bacterial agents such as BCG.

The fifth and final session was concerned with a discussion of the ways in which international cooperation between the countries involved in this seminar might effectively increase our knowledge of the relation between cell surface markers and immune responsiveness or disease. The first order of business seems to be to provide up-to-date information on available serums, to train Japanese investigators in techniques in use in the United States, and to standardize methods for use in the various countries. It was felt that these objectives could be achieved in part by establishing a serum bank in Japan and having local and international workshops. With the availability of these facilities and maintenance of the lines of communication developed during this seminar, it should be possible to begin critical investigations of the relation of HL-A specificities to various disorders that have different geographic rates of occurrence.

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Forthcoming Events

November

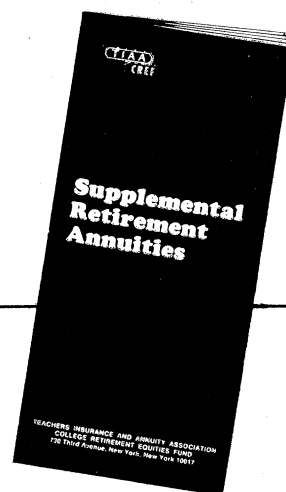
11-16. American Nuclear Soc., San Francisco, Calif. (O. J. DuTemple, ANS, 244 E. Ogden Ave., Hinsdale, Ill. 60521)

12-14. Geochemical Soc., Dallas, Tex. (E. E. Angino, Dept. of Geology, Univ. of Kansas, Lawrence 66044)

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