

lay the abortion. It is possible that the saline kills the cells of the placenta and interferes with the production of progesterone and thus leads to the initiation of labor by releasing the brake. Alternatively, the saline may enter the maternal blood stream, making it hypertonic and stimulating the release of both antidiuretic hormone and oxytocin from the pituitary. It is known that women feel very thirsty during the treatment.

Louis Holm (University of California, Davis) described an interesting situation in which the fetus itself plays a role in the initiation of labor. In one strain of Holstein-Friesian cows the fetus is not delivered at the normal time but may remain inside the mother for months beyond the normal time of delivery. A variety of methods have been tried but all were unsuccessful in inducing labor in these cows. The newborn, if delivered by cesarian section, will die of hypoglycemia in 6 to 8 hours but will survive if treated with the appropriate adrenal corticoids. It appears that an inherited alteration in the pituitary-adrenal axis in some way prevents the fetus from signaling to the maternal organism that labor should begin. The fetal pituitary at term is only two-thirds normal weight and has a reduced number of acidophil cells. Somewhat similar conditions in other breeds of cattle and in sheep were described and it was noted that reciprocal crosses of horses and donkeys do not have the same gestational age.

John Biggers (University of Pennsylvania) described experiments in which one ovary of the mouse was removed. The other ovary then undergoes hypertrophy and produces a large number of eggs. After fertilization all of these blastocysts implant in a single horn because there is no connection between the two horns of the uterus in the mouse. The average length of gestation in the mice, each of whom had one ovary, was 19 days instead of the usual 20 days. Further experiments showed that the shortened gestation is due not to crowding in the one horn but to the overcrowding in the mother as a whole.

Jonathan Lanman (State University of New York, Brooklyn) reviewed the concept that the placenta initiates a homograft response in the mother and that rejection of the homograft initiates labor. After pointing out that if this were true a member of an inbred

strain could not deliver its young, he described a beautiful series of experiments demonstrating that this phenomenon is not involved. It appears that trophoblastic cells are not antigenic. Perhaps an important factor is that the placenta, in contrast to grafts, has its own blood supply.

The clinical circumstances which may initiate labor were reviewed by James Walker (University of St. Andrews, Scotland). He showed that it is difficult to relate certain of these factors to the general concept that oxytocin initiates and progesterone inhibits labor itself. Zander had described a decrease in the concentration of progesterone in the blood in the week preceding labor, but Walker could detect no general pattern in the concentration of progesterone before labor. At term the concentration of progesterone is much greater in the uterine vein than in the maternal peripheral veins. Analyses of the amount present in peripheral blood do not provide a reliable index of the progesterone secreted by the placenta.

In the final session the physiologic findings of the conference were summarized by Ernst Knobil (University of Pittsburgh) and the clinical findings were summarized by Ernest Page (University of California, San Francisco). Other participants in the general discussion were Willard Allen (Washington University), Richard Blandau (University of Washington), Geoffrey Dawes (Cambridge University), Rune Eliasson (Karolinska Institute), Frank Fremont-Smith (AIBS), Fritz Fuchs (University of Copenhagen), Harry Gordon (Albert Einstein), Carl Hartman (Margaret Sanger Research Bureau), Eileen Haselmeyer (NIH), Evelyn Johnsen (NIH), Elsa Keiles (NIH), William Little (NIH), Franz Rosa (NIH), Kenneth Ryan (Western Reserve University), Sydney Segal (University of British Columbia), and Margaret Thomas (Children's Bureau).

The meeting, under the chairmanship of Claude A. Villee, was sponsored by the National Institute of Child Health and Human Development.

The transcript of the discussion will be published with Jean Marshall as scientific editor.

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## Prenatal Irradiation: Effects on the Development of the Central Nervous System and Postnatal Behavior

The effects of prenatal irradiation on the central nervous system and postnatal behavior were discussed at a workshop conference held in Washington, D.C., 4-6 October 1963. The discussions were devoted exclusively to American and Russian research in this field.

The opening session was chaired by E. Furchtgott (University of Tennessee), who reviewed the Soviet literature on this subject; additional material was prepared by W. R. Stahl (Oregon State University). A major portion of the Soviet presentations concentrated on the recently translated book by I. A. Piontkovskoy, *Effects of Ionizing Radiation on the Functions of the Higher Nervous System of Progeny* [Medzig, Moscow, 1961 (AEC-tr-5553)].

In this review of this work, the similarities and divergencies between the American and Soviet approaches to this area of research became apparent. This was made evident, in the Russian research, by the use of behavioral variables reflecting Pavlovian types of performance processes. Unfortunately, their omission of detailed descriptions of research methodology, including those pertaining to control of stimulus parameters, radiation dosimetry, nature of subjects, and so forth, made critical appraisal difficult. However, their research has demonstrated a variety of alterations on the central nervous system with dosage levels as low as 1r per day for a 20-day period. In addition, they, more than we, have utilized interdisciplinary approaches to this problem and have integrated results at the behavioral, anatomical, and physiological levels. However, they also have not found clear dose-response relation at the low dosage levels used, and have also observed differential effects on male and female progeny after prenatal irradiation. The Russians appear to have the same difficulty that we have in trying to explain those results. It was the consensus among the scientists attending this conference that although Soviet accomplishments were comparable to ours, there was a definite need for us to foster a greater emphasis in interdisciplinary research for this important research area.

K. R. Brizzee (University of Nebraska) served as chairman of the ses-

sion devoted to evaluation of effects on developing central nervous system morphology. In providing a historical perspective to the research data in this field, S. P. Hicks (University of Michigan) presented the most systematic descriptions of a calendar of histopathological events occurring in the nervous system in response to prenatal irradiation at dosage levels of 150 to 200 r. With the increased interest of effects at lower dosage levels, Brizzee and Jacobs (University of Utah) reported on their own work and described some of the procedures and results obtained by using techniques of quantitative histopathology and cellular morphology. In this discussion of morphological alterations, the question was raised about the effects of prenatal irradiation on organ systems other than the central nervous system which may indirectly alter the central nervous system or behavioral processes.

Throughout the previous discussions and the entire conference, emphasis was placed on possible genetic interactions operating through germinal or somatic mutations, and effects on the central nervous system, development, and behavior after prenatal radiation exposure. R. L. Brent (Jefferson Medical College) described the results of cytogenetic studies in which chromosomal aberrations were observed following early irradiation of the differentiating fertilized cell. Invariably, these chromosomal aberrations involved nervous system anomalies. S. P. Hicks theorized that alterations of maturation (anatomical, physiological, or behavioral) at any developmental age may be the result of somatic mutations following prenatal irradiation. The opinion prevailed that this area of research could be best served by utilizing more rigorous control over the experimental populations studied by selecting more homogeneous rather than heterogeneous animal strains. In addition, the need was stressed for cytogenetic investigations to give direct evidence for somatic mutations, and for studies to be undertaken of successive generations for evidence of germinal mutations affecting the function of the nervous system and behavior, as had been recently reported by the group from Texas Technological College.

The session devoted to neurophysiological and neurochemical correlates of prenatal irradiation was led by S. P. Hicks. It was of great interest to note that these areas have received almost

no attention. It has been only in the last year that several reports became available describing cortical and subcortical electrographic alterations (seizure activity) from animals whose cerebral cortex could be described as "disorganized" but whose external appearance and behavior looked "normal." This direct evidence of neurophysiological impairment corroborates previous descriptions of convulsive phenomena occurring spontaneously and induced by appropriate stimulation after prenatal radiation exposure. There is no available literature on neurochemical changes, although several laboratories are currently investigating the problem. These areas together with descriptions of autonomic nervous system function need extensive elaboration.

The discussion of postnatal behavioral changes after prenatal irradiation generated intensive discussion. This session was chaired by J. C. Sharp (Walter Reed Army Institute of Research) who reported on his own work in addition to organizing the relevant material into areas of our current knowledge. It was the consensus that the behavioral data represented too much of an effort to catalog the types or varieties of postnatal behavioral changes after prenatal irradiation, with too little emphasis placed on developing a calendar of changes corresponding to what is available in the neuroanatomical area. In addition, it was felt that behavioral scientists have tended to work alone with little attempt to integrate or collaborate their data with other biological disciplines. R. K. White (Texas Technological College) argued strongly for multivariate research designs utilizing factor analytic methods in order to cope with the tremendous amount of available data in experiments of this type. One research problem that received special attention was the consideration of sensory deficits following the prenatal irradiation as measured by operant conditioning methods. Sharp reported visual and auditory sensory thresholds were not impaired, and J. Falk (University of Michigan) found both brightness and pattern discrimination remained functional in rats, with prenatal irradiation on days 15, 17, or 19, whose visual cortex was severely impaired.

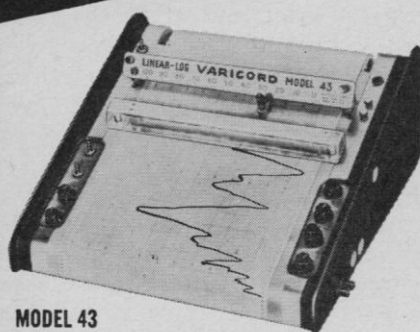
Recent research has shown that extremely low dosages of irradiation could have both anatomical (gross and cellular) and behavioral effects if administered during the first 36 hours

following fertilization (S. J. Kaplan, Peace Corps). Although this phenomenon cannot yet be explained, it was felt that there may be mediating biochemical mechanisms to account for these changes. J. Havlena (Wayne State University) presented recent data which partially supported the behavioral changes reported by S. J. Kaplan and R. Rugh (Columbia University).

G. W. Meier (National Institute of Neurological Diseases and Blindness) spoke on the question of mechanisms mediating the prenatal irradiation effects. He noted the necessity of considering (i) the direct effects of the prenatal irradiation on the central nervous system and other organ systems altering behavior, and (ii) the indirect effects through the maternal environment altering the development of the fetal central nervous system and thus resulting in behavioral changes. Several experimental solutions were suggested as a means of exploring these approaches. One concerns the use of continuous, rather than acute, radiation exposures because the indirect effects through the mother may persist for more time than that required in a single exposure. In addition, it would be desirable to study, through the techniques of acute preparation, simultaneous physiological recording of both mother and fetus during radiation exposure in order to determine if there were physiological changes concurrent in either one or both with radiation exposure.

A summary of the conference highlights and future research prospects was prepared by D. J. Kimeldorf (U.S. Naval Radiological Defense Laboratory) and J. Werboff (The Jackson Laboratory). Kimeldorf referred to the group many pertinent questions related to neuronal radiosensitivity, types of radiation, radiation dosimetry, and other parameters of radiation that are so crucial in other biological experiments utilizing radiation as the major manipulative tool. It was apparent that we are still far from developing the answers to these questions. Werboff, in his summary, suggested the grave importance of this area of research, in that low levels of prenatal radiation exposure may be altering a variety of biological and behavioral systems that may become evident late in the individual's lifetime. Under these circumstances it becomes too easy to relate his difficulty to concurrent life situations rather than to causes occurring

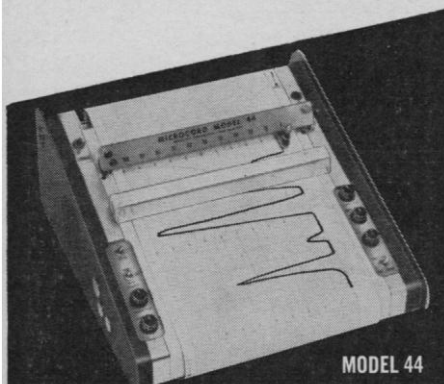
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prior to birth. Our concern for ourselves, our progeny, and our national welfare forces us to continue and expand this important area of research with particular emphasis placed on the development of systematic and integrative research into the biological and behavioral concomitants of prenatal irradiation.

Other participants in the conference were C. D'Amato (University of Michigan), E. Harvey and P. S. Henshaw (U.S. Atomic Energy Commission), G. Shaber (Jefferson Medical College), M. R. Sikov (Wayne State University), and J. N. Yamazaki (University of California, Los Angeles). This conference was held under the auspices of the American Institute of Biological Sciences, with support from the U.S. Atomic Energy Commission, contract No. AT-(49-7)-1287. The proceedings of the conference were completely transcribed, and after they are edited they will be available to interested scientists who may obtain them by writing to the address shown here.

J. WERBOFF

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## Forthcoming Events

### April

9-11. American Assoc. for **Cancer Research**, annual, Chicago, Ill. (H. J. Crech, AACR, Institute for Cancer Research, Fox Chase, Philadelphia 11, Pa.)

9-11. Association of **Clinical Pathologists**, spring meeting, London, England. (G. Cunningham, Dept. of Pathology, 47 Lincoln's Inn Fields, London, W.C.2)

9-11. **Geological Soc. of America**, southeastern section, Baton Rouge, La. (R. J. Martin, 1426 Harvard Rd., NE, Atlanta, Ga.)

9-11. Southwestern **Psychological Assoc.**, annual, San Antonio, Tex. (C. C. Cleland, 2104 Meadowbrook Dr., Austin, Tex. 78703)

9-13. **Roentgen Congr.**, German, Wiesbaden, Germany. (H. Lossen, Deutscher Röntgenkongress, Fichterplatz 20 III, Mainz, Germany)

10. **Natural Phenolic Compounds**, symp., Tokyo, Japan. (M. Shimokoriyama, Dept. of Botany, Univ. of Tokyo, Hongo, Tokyo)

10-11. American **Laryngological Assoc.**, San Francisco, Calif. (L. G. Richards, 12 Clovelly Rd., Wellesley Hills 82, Mass.)

10-11. Association of **Physicians of Great Britain and Ireland**, annual, Oxford, England. (G. de J. Lee, Dept. of Medicine, Radcliffe Infirmary, Oxford)

11. **Paleontological Research Inst.**, Ithaca, N.Y. (R. S. Harris, 109 Dearborn Place, Ithaca)

11-12. **Histochemical Soc.**, 15th annual, Chicago, Ill. (A. D. Deitch, Dept. of

Microbiology, Columbia Univ., 630 W. 168 St., New York 32)

12. **Industrial Fibers**, European inst., Milan, Italy. (F. Tommy-Martin, 40 rue du Stand, Geneva, Switzerland)

12-13. American Soc. for **Artificial Internal Organs**, Chicago, Ill. (B. K. Kuserow, Dept. of Pathology, Univ. of Vermont College of Medicine, Burlington)

12-17. Federation of American Societies for **Experimental Biology**, Chicago, Ill. (H. B. Lemp, The Federation, 9650 Wisconsin Ave., NW., Washington, D.C.)

12-17. Society of **Motion Picture and Television Engineers**, semiannual technical conf., Los Angeles, Calif. (J. M. Waner, Eastman Kodak Co., 6706 Santa Monica Blvd., Hollywood 38, Calif.)

12-18. Chemistry of **Natural Products**, intern. symp., Kyoto, Japan. (Science Council of Japan, Ueno Park, Tokyo, Japan)

13-15. Institute of **Environmental Sciences**, annual, Philadelphia, Pa. (J. Breen, RCA Bldg., 10-1-2, Camden 2, N.J.)

13-15. **Microelectronics**, 3rd annual symp., St. Louis, Mo. (T. F. Murtha, P.O. Box 4104, St. Louis, Mo. 63136)

13-16. American Acad. of **General Practice**, Atlantic City, N.J. (M. F. Cahal, Volker Blvd. at Brookside, Kansas City 12, Mo.)

13-16. **Industrial Health**, conf., Pittsburgh, Pa. (American Industrial Health Conf., 55 E. Washington St., Chicago, Ill.)

13-16. **Industrial Medical Assoc.** and American Assoc. of **Industrial Nurses**, Pittsburgh, Pa. (C. D. Bridges, 55 E. Washington St., Chicago, Ill. 60602)

13-16. American **Radium Soc.**, White Sulphur Springs, W. Va. (J. J. Stein, U.C.L.A. Medical Center, Los Angeles 24, Calif.)

13-17. **Fluid Power**, intern. conf. and exhibition, London, England. (Secretary of the Conference, The Tower, 229-243 Shepherds Bush Rd., Hammersmith, London, W.6)

14-16. **Power Conf.**, Chicago, Ill. (W. A. Lewis, Illinois Inst. of Technology, Chicago)

14-18. Primary Disorders of **Heart Muscle** (by invitation), CIBA Foundation symp., London, England (CIBA, 41 Portland Pl., London, W.1)

14-18. **Mathematical Logic**, conf., Oberwolfach, Germany. (M. Barner, Mathematisches Forschungs-institut, Hebelstr. 29, 78 Freiburg im Breisgau, Germany)

15-17. **High Energy Physics**, conf., Chilton, England. (Inst. of Physics and the Physical Soc., 47 Belgrave Sq., London S.W.1, England)

15-17. **Ophthalmological Soc.** of the United Kingdom, annual, Dublin, Ireland. (Secretariat, 47 Lincoln's Inn Fields, London, W.C.2, England)

15-18. British **Paediatric Assoc.**, annual, Scarborough, England. (E. W. Hart, Inst. of Child Health, Hospital for Sick Children, Great Ormond St., London, W.C.1)

15-18. American Soc. for **Public Administration**, natl. conf., New York, N.Y. (ASPA, 6042 Kimbark Ave., Chicago, Ill.)

15-18. **International Scientific Radio Union (URSI)**, spring meeting, Washington, D.C. (M. G. Morgan, U.S. Natl. Committee, URSI, Dartmouth College, Hanover, N.H.)