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MINUTES

139th MEETING

ADVISORY COMMITTEE FOR BIOLOGY AND MEDICINE

U. S. ATOMIC ENERGY COMMISSION

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September 10, 1971 - AEC HQ
September 11, 1971 - "H" St. Office

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The 139th meeting of the Advisory Committee for Biology and Medicine was held September 10-11, 1971, at AEC Headquarters and the "H" Street Office. The members present were Drs. R. D. Moseley, Jr. (Chairman), Stout (Vice-Chairman), Finch, Haagen-Smit, Laughlin, and Miss Rosemary Elmo (Executive Secretary). Dr. Schull and Dr. Storer (Scientific Secretary) were unable to attend. Dr. H. D. Bruner, Assistant Director, DBM, acted as DBM representative during the morning session in the absence of Dr. John Totter, Director. Dr. Totter attended the afternoon session on the 10th and the executive session on the 11th.

The Committee was briefed on the following items:

CALVERT CLIFFS LITIGATION. Mr. Marcus A. Rowden, Office of the General Counsel, and Mr. Lester Rogers, Director, Division of Radiological and Environmental Protection, briefed the Committee on the holdings of the Court of Appeals in the Calvert Cliffs case and the steps the Commission had undertaken and contemplated in implementation of that decision. Mr. Rogers discussed the impact on the Regulatory program of the implementation of the Calvert Cliffs Court decision regarding the National Environmental Policy Act. The AEC issued on September 9, 1971, revised regulations to implement the Court decision. The effect of the new regulations is to make the AEC directly responsible for evaluating the total environmental impact, including thermal effects, of nuclear power plants and assessing this impact in terms of the available alternatives and the need for electric power.

Mr. Rogers stated that the Court decision affects some 65 construction and operating license applications involving 97 nuclear power units. In addition, 5 nuclear power reactors for which operating licenses were issued after January 1, 1970, are affected as well as 3 fuel reprocessing facilities. All of these applicants must prepare environmental reports and the AEC must prepare environmental statements that will be used in licensing proceedings on these cases.

Mr. John Whitnah, Assistant Director for Administration, DBM, discussed the effect of environmental impact statements on the DBM research programs. He said that at the request of the AEC, Argonne National Laboratory identified a total of approximately 23 man-years which could be redirected from biology and medicine research programs to the preparation of environmental impact statements during the balance of FY 1972. Most of this effort has been engaged in fresh water environmental studies, particularly in the thermal effects area. There will also be a significant input from radiological and health physics studies, particularly at Oak Ridge. The dollar magnitude of the research programs affected is approximately 900 thousand dollars during the current fiscal year.

ICONS PROGRAM, LOS ALAMOS SCIENTIFIC LABORATORY. Dr. John Kirby-Smith, Assistant Director for Biological Sciences, DBM, reported on the current status of the ICONS (Isotopic, Carbon, Oxygen, Nitrogen and Sulfur) production at Los Alamos indicating that Carbon-13 continues to be produced in the existing two columns at a rate in excess of 6 kilo per year. The rebuilt NO column at the DP West site is expected to be in operation by November 1971 with an expected production rate of approximately 1.5 kilo/yr of ^{15}N and 450 kilo/yr. of ^{14}N. Engineering design is continuing for the new isotope facility to be built at Los Alamos for the integrated production of all the stable isotopes of carbon, nitrogen and oxygen. Contracts for the drilling of holes to contain the first of these ICONS distillation columns are to be let in the near future.

Dr. D. C. Borg, DBM, discussed the plans for clinical studies at LASL. He reported on a meeting that was held at LASL on 14 January 1971 to explore the possibility of inter-laboratory collaboration on a ^{13}C clinical demonstration program. The meeting was informal in character and grew out of the express need of LASL and of DBM to establish a firm market for ^{13}C-labeled products. Clinical use of carbon-13 had appeared most promising as a "market" for volume use of the isotope that would be most accessible at an early time.

Shreeve of BNL prepared for the meeting a list of possible clinical diagnostic applications of ^{13}C that served as the nucleus for discussion. The group concluded that a clinical test was feasible, and preliminary plans were made for a pilot study, which is now in the process of being set up. Oxidation of orally administered glucose-1-^{13}C as a sensitive screening test for diabetes was selected for the initial carbon-13 clinical demonstration after weighing a number of considerations. These included patient availability, prior documentation with ^{14}C studies, diagnostic usefulness, a high incidence of the clinical condition being studied, the availability of an appropriate ^{13}C labeled material for a loading study, the efficiency of utilization of the ^{13}C label, and the ease and facility of obtaining samples for detection.

Shreeve proposed to carry out preliminary clinical tests during the first half of 1972, when he would be a visiting scientist at LASL. Further studies would be carried out with a patient group obtained from his present clinical program at BNL or his affiliations with the Meadowbrook Hospital on Long Island. Each patient would undergo parallel studies with ^{14}C-labeled glucose, and intravenous glucose tolerance tests and other documentations would also be carried out to insure the greatest possible clinical relevance of the limited number of ^{13}C studies that could be done, using 1-^{13}C-glucose prepared by Ott and Gregg, of LASL. Primary ^{13}C measurements on alkaline samples containing expired $^{13}CO_2$ from patients would be made with a gas chromotograph/mass spectrograph (GC/MS) apparatus in Klein's laboratory at ANL. Modifications to increase the sensitivity of separating mass ratios 44 and 45 would be undertaken directly by Klein, and if preliminary tests indicate that significant gains in detection sensitivity may be confidently expected, development of an inexpensive (less than $20,000) prototype GC/MS instrument for routine stable isotope determination in clinical laboratories would be undertaken.

AERIAL SURVEY PROGRAM. Mr. L. J. Deal, Chief, Civil Effects Branch, DBM, brought the group up to date on developments in the joint AEC-OEP study on Federal response to an accident involving a nuclear site. In August, a detailed document describing the organization directly responsible for protective actions and identifying the AEC capability will be available. He then described the Aerial Radiological Measuring System which is available to respond to accidents at any nuclear site. He also described the work under the Division of Military Application auspices for responding to weapons accidents and its possible application to ARMS program for using aerial measuring techniques to monitors for Pu-239.

FINDINGS OF ATOMIC BOMB CASUALTY COMMISSION. Dr. Seymour Jablon, Associate Director of the Follow-up Agency, Division of Medical Sciences of the National Research Council, and Chief, Department of Statistics, when in residence at the Atomic Bomb Casualty Commission, Japan, reported chiefly the most recent mortality data derived from the 1966-1970 collection cycle. He concentrated on the Life Span Study which involves the survivors themselves rather than to studies of the offspring of the survivors which are also going forward.

In general, there seems to be developing an increased risk of cancer in those surviving the higher dose levels, whereas the morbidity for other diseases such as tuberculosis, stroke, or other circulatory diseases is not increasing at present. The morbidity data in the two cities do not always coincide perfectly. The patterns of morbidity and mortality are continuing to evolve as the population ages.

Since very few of these current observations have been previously reported, a precis of Dr. Jablon's presentation is included as an Annex. Since the presentation was made with reference to tabular data on slides, the observations have condensed into brief, possibly overly categorical statements evident in the numerical data.

Dr. M. A. Bender, Biology Branch,DBM, discussed the proposed genetic studies at ABCC. He briefly reviewed previous attempts to measure radiation-induced mutation rates in the offspring of the ABCC -populations exposed at Hiroshima and Nagasaki. He then outlined a new proposal by J. V. Neel and W. J. Schull of the Department of Genetics of the University of Michigan Medical School to initiate a new study in collaboration with ABCC. The proposed study will search for newly arisen protein variants among the F_1, presumably due to mutations induced in the germ live cells of the exposed parents. Neel and Schull propose to screen a battery of some 25 suitable serum and erythrocyte proteins, augmented by additional proteins as methods become available. They estimate that at a minimum some 11,000 children of "exposed" parents and about 22,000 children of "unexposed" control parents can be studied. Making conservative estimates of the human spontaneous mutation rate and the mean parental radiation doses, they feel that they can probably demonstrate a statistically significant radiation-induced increase

if the doubling dose is of the order of 60r or less. Even if no increase can be demonstrated, however, an estimate can be made of the minimum value for the human mutation doubling dose. Neel and Schull propose an initial "R and D" year followed by a four-year sampling program at ABCC and a final two-year data analysis period. The proposal has been approved by the BM Research Committee and by the National Academy of Sciences, but Japanese approval remains to be negotiated.

CLEAN-UP OF BIKINI ATOLL. Dr. N. F. Barr, Assistant Director for Radiological Physics, DBM, and Mr. T. McGraw, Division of Operational Safety, presented a report on the status of the Bikini resettlement program. The results of surveys conducted in 1969 and 1970 are consistent with those of earlier surveys and support the conclusions and recommendations of the ad hoc committee which in 1968 assessed the radiological hazards of resettlement of Bikini. DOS and DBM staff will meet on September 14 with contractors and representatives of the Department of Interior and Environmental Protection Agency to discuss future monitoring and research activities.

PU EXPOSURE AT ROCKY FLATS. Mr. Robert J. Catlin, Assistant Director for Health Protection, Division of Operational Safety, reviewed in some detail the circumstances of the Rocky Flats incident of August 22, 1971, which led to receipt of substantial lung burdens of Plutonium-239 by two radiation workers at Rocky Flats. He discussed the decline in lung burdens over a period of time, resulting from elimination of plutonium through the feces and urine, and for one individual by three lavage procedures. The lavage was successful in removing approximately 10% of the estimated lung burden. DTPA was administered to both individuals. Direct measurements of Plutonium-239 in the lungs indicated that the lung burdens estimated (based upon measuring Americium-241 and assuming a Plutonium to Americium ratio) might be too high by a factor of two.

Dr. Joseph Goldstein, Chief, Medical Branch, DBM, presented medical progress highlights on the Rocky Flats accident. Areas of importance to the care of the two internally exposed individuals, and the chronological clinical course during the period August 22 to September 8, 1971, inclusive, were reviewed. The initial lung ^{239}Pu burdens were reported as approximately 9 Maximum Permissible Lung Burdens (0.16 nanocuries of ^{239}Pu = 1 MPLB) for Mr. Smith and 28 MPLB's for Mr. Olveda. Both values were derived indirectly from measurements of ^{241}Am. On August 22 both individuals refused DTPA intravenous treatment. This was not pressed by the physician in charge because he was informed that they were exposed to oxides which are not responsive to DTPA. Subsequently, it was learned that plutonium chloride was a constituent of the aerosol. These daily DTPA treatments were given Mr. Smith beginning August 30. His urinary excretion of plutonium increased from .05 to about 2.5 nci/day after the initial DTPA injection. On September 8 he had 7.3 MPLB of ^{239}Pu.

In the interim, after conferring with Dr. D. Hylton, of Rocky Flats, Dr. Roger McClellan, of Lovelace Foundation, and with Drs. Kylstra and Hall, of Duke University, who are experienced in performing lung lavage on humans, Mr. Olveda agreed to a lavage. On August 29, in Albuquerque, his measured lung burden was 426 nanocuries, compared with 450 nci observed at Rocky Flats on August 22. Complete lung function tests and other preparatory tests on August 28-29 were normal. On August 30, under a general anesthesia, his right lung was lavaged with 25.5 liters of saline. This was repeated on his left lung on September 3. On September 8 his right lung was washed again with 12 liters of saline. These three sessions were uneventful with full subjective recovery in several hours. Preliminary estimates of ^{239}Pu in the three "wash fluids" were 31, 9 and 4 nanocuries, respectively. In addition, Mr. Olveda also received DTPA daily during August 30-September 9. On September 6 at Lovelace he had a lung burden of 7.2 nanocuries of ^{241}Am which provided an estimate of 285 nanocuries of ^{239}Pu. The uncertainty of the assumed Pu-Am ratio was introduced by measurements taken at LASL on September 7 which gave 7.8 nanocuries of ^{241}Am but only 160 nanocuries of ^{239}Pu by direct measurement.

Despite these measurement discrepancies, which may be significantly modified by subsequent measurements of Mr. Olveda and Mr. Smith at the three aforementioned institutions, it appears that the lavage was to the distinct advantage of the patient especially when the risk of the procedure in a healthy individual is considered to be no more than that of the general anesthetic. Further, this incident will be covered in such detail that it may contribute significantly to an accepted treatment guidance that would include improved appraisal of such accident situations and promulgation of good and common medical practices. A review of current practices is planned for September 30 at Hanford.

RECENT DEVELOPMENTS IN NUCLEAR POWER PLANT HEARINGS. Dr. W. R. Bibb, Medical Branch, DBM, informed the ACBM of the scope of the participation by DBM staff in hearings on nuclear power plants. Specifically, staff participation in the hearings on the Palisades, Davis-Besse, and Shoreham plants was discussed as well as the nature of the testimony offered in opposition to these plants. The ACBM was also briefed on DBM staff participation in hearings conducted before various state legislative bodies and citizens' groups. Finally, anticipated DBM participation in the pending legal action to prevent further testing on the Nevada Test Site was reviewed. A short discussion by members of the ACBM on the nature of the public's concern about the environmental effects of radioactivity followed.

At the executive session on November 13 the Minutes of the previous meeting were approved.

Dr. Moseley requested the secretary of the ACBM to advise Mr. Eason that Dr. Lincoln should be appointed to the ACBM subcommittee to assist the AEC in its review of present radiation exposure record-keeping practices. Dr. Moseley and Dr. Laughlin are the other subcommittee members.

Dr. Totter discussed the difficulty of getting data from ABCC. He said that the data belongs to the Japanese and requires back and forth translation to make certain it is correct. Because of the load on the computer the entry of the data into the computer takes about one year.

The real ABCC problem seems to be the change in the value of the yen and rapid increase of costs in Japan. The cost ranges from 3.6 million three years ago to what will probably be 5.6 million in 1972. The Japanes government will be urged to go into the program with additional funds. Dr. Dunham, of the National Academy of Sciences, has asked the National Cancer Institute if they want to "buy into" the ABCC program. The suggestion was cordially received and they will probably agree to do this. Dr. Finch inquired how the scientific merit of the program was evaluated in comparison to the cost. Dr. Totter replied that he regards the program as totally essential regardless of cost. Dr. Laughlin commented that this is a unique opportunity to get valuable data, and he thinks the ABCC program should be strongly supported. He thought it unusual that it has been possible to conduct this program even with Japanese aid. Dr. Finch asked if the Committee could suggest that some opinion be developed anticipating criticism or suggesting limitations of the operation. He suggested that a paper be developed more formally indicating what has been accomplished and the potential value in the next decade from the standpoint of cancer.

The Committee considered possible candidates to fill the vacancy existing on the ACBM. In view of the emphasis to appoint women to committees the following names were suggested: Dr. Mary T. Bunting, Dr. Edythalene Tompkins, Dr. Mildred Cohn, Dr. Marian Koshland, Dr. Rosalind Yalow and Dr. Mary Ellen Jones. Background information on these individuals will be furnished to the ACBM.

The next ACBM meeting will be held November 12-13, 1971, at the Health and Safety Laboratory, New York Operations Office.

The meeting was adjourned at 11:30 A.M.

Respectfully submitted,

Rosemary Elmo

Rosemary Elmo, Executive Secretary
Advisory Committee for Biology
and Medicine

ANNEX - REPORT OF SOME RECENT
OBSERVATIONS OF THE ATOMIC BOMB CASUALTY COMMISSION

Seymour Jablon

The core of the ABCC research program consists of the Life Span Study which traces the mortality of a cohort of about 109,000 Japanese of Hiroshima and Nagasaki including survivors who were located near and at varying distances from the hypocenters. The controls consist of persons who immigrated into the cities after the bursts or were in the city beyond range of the weapon effects. Additional control mortality information is obtained from entry into the conventional Japanese National Vital Statistics reporting system with the assistance of the Japanese National Institute of Health. The population comprising the Life Span Study is a "floating" cohort as the youngest members are 26 years old; this age structure occasions unusual epidemiological treatment.

The Life Span Study is backed up by two major programs which are equally critical to the overall mission of ABCC. They are: 1) The Autopsy Pathology Studies program which has obtained autopsies on 40% of deceased members of the Life Span Study. In view of the Japanese custom of cremation or other disposal within 24 hours of death, the program has been phenomenally successful; 2) The Adult Health Study conducts biennial physical examinations on a sub-cohort of 20,000 persons drawn from the larger Life Span Study cohort. Its procedures supply information on the biomedical and epidemiologic changes occurring as the exposed population ages. It has the added value of diagnosing the onset of possibly lethal disease in time to institute proper medical care.

A new analysis of mortality through 1970 in the Life Span Study has recently been completed, and highlights from this were presented. Analyses were made with reference to the so-called T-65 radiation dose estimates, the dosimetry system devised by John Auxier and staff of the Health Physics Division of the Oak Ridge National Laboratory.

1. The mortality ratios (ratio of actual number of deaths to the number expected from Japanese national death rates) from all diseases were very high for survivors whose doses were estimated to exceed 200 rads and who were children under 10 at the time of the bombings (ATB). The mortality ratios declined with increasing age at time of exposure, but were slightly elevated even among those aged 50 or more ATB.

2. Mortality from leukemia among the survivors has been declining since 1950-54, but was still more than 15 gimes expectation in 1965-70 among high dose survivors (200 + rads).

3. In terms of age ATB, sensitivity to radiation leukemogenesis was greatest among children under 10 years of age, least among those 10 to 19, and then rose with increasing age.

4. Mortality from cancer (excluding leukemia) in 1966-70 was sharply elevated among children under 10 years of age ATB exposed to more than 100 rads. Sensitivity to radiation carcinogenesis was a declining function of age at exposure when measured in terms of relative risk.

5. Study of lung cancer, specifically, is complicated by the fact that mortality ratios for this disease have been increasing very rapidly in these cities over the 20-year period studied.

6. Mortality from breast cancer was sharply elevated in 1965-70 among female survivors with doses exceeding 50 rads. The effect was strongest among those 10-19 years old ATB, and then declined with increasing age. No cases occurred among children under 10 ATB, but these children may not yet be old enough to show an effect.

7. Relative risks for the 200 + rad broup, compared with the 0-9 rad group, for the entire 20-year period varied widely for different diseases. Significant elevations were apparent for leukemia, other cancer, neoplasms of unspecified malignancy and possibly "other disease," but not significantly elevated for tuberculosis, stroke, or other cirulatory system disease.

8. There is some observed variation in the relative risks with reference to the specific sites for cancer. However, the variation, although large, is not statistically significant, because some of the numbers are small. With the additional data that will become available in future years the picture will become clarified as either the various risks draw together or, alternatively, the differences become statistically significant.

9. Leukemia mortality during the entire period 1950-70 was very nearly a linear function of total dose in rads.

10. Excluding leukemia, the relationship of cancer mortality to dose looks approximately linear, except for a sharp dip in the region 100-199 rads; the dip results wholly from an unexplained aberration in the Nagasaki data.

11. In Hiroshima, the mortality ratios for cancer in the 200+ rad group increased constantly from 1950-54 to 1965-70, with an accelerated increase from 1960-64 to 1965-70. In Nagasaki, by contrast, the ratio was very high in 1950-54, declined during 1960-64, and then increased, in parallel with Hiroshima, in 1965-70.

12. With reference to the differences between Hiroshima and Nagasaki and a possible relationship to the RBE of neutrons as compared with gamma radiation for leukemia, the response in Hiroshima is very nearly a linear function of dose from the smallest to the largest dose levels. In Nagasaki, on the other hand, no response is visible below 100 rads, but above 100 rads the response appears linear and parallel to Hiroshima,

but at a lower level. /The neutron dose contribution at Nagasaki was smaller than at Hiroshima./

If an RBE dose in REM, using an RBE value of 5 is inserted instead of Total Dose (neutrons plus gamma radiation in rads) the Hiroshima and Nagasaki leukemia curves come very much closer together. In both cities, however, the response then becomes distinctly non-linear with pronounced concavity.

13. In Hiroshima the curve of mortality from cancer excluding leukemia versus total dose is nearly linear whereas in Nagasaki there is an enormous dip in the 100-199 rad range and the response at the highest doses is much smaller than in Hiroshima.

14. In terms of the RBE dose, the curves for mortality from cancer excluding leukemia for the two cities are not brought together as well at the highest dose levels as they were in the case of leukemia. It appears that an RBE of 6 or even 7 might be required to bring the two cities into agreement. At the lower dose levels agreement remains poor, since no amount of numeric manipulation will compensate for the deficit of cases in Nagasaki in the 100-199 rad (largely gamma rays) range. Further, when an RBE of 5 is used, the Hiroshima regression of mortality on dose, which is very nearly linear using Total Dose, becomes concave using the RBE dose.

15. As time has passed, there has been a shift in the excess mortality in the high dose survivors from leukemia to other cancer. In 1950-54, the excess leukemia deaths were about twice as numerous as those from all other cancer; by 1965-70, the excess from other cancer has come to be three times that from leukemia.