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TO : Files
THRU C. L. Dunham, M. D., Director
Division of Biology and Medicine
FROM : H. D. Bruner, M. D.
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Division of Biology and Medicine
SUBJECT: NOTES ON BNL ACBM MEETING - MARCH 13, 14, 1959

DATE: March 26, 1959

SYMBOL: BMM:HDB

An executive meeting from 9 to 9:30 before the program brought out the criticisms which have been leveled at the Medical and Biology Departments and the interpretations which have been made of the ACBM's reports; it was requested that these programs be reviewed in this light and the Committee's recommendations be made definite.

Lee Haworth introduced the general program of BNL and in effect discussed the charter of BNL relative to current activities. For example, he called attention to the 30 Bev accelerator; the effects of radiation on all kinds of systems together with study of the normal situation; the use of radiation as tools to study objects, masses, and atoms - neutron scatter, paramagnetic effects, and activation analysis; research that bears on efforts to improve the science of atomic energy in its various aspects; and lastly the practical aspects of making nuclear energy useful - solving problems of a pragmatic nature. A "complete-range" of outlook and approach to the problems of atomic energy was claimed and the special value of this elbow-rubbing was emphasized.

In response to a question he described most of the training and fellowship opportunities available to students and post-graduates. He then explained the rational of the fixed pattern of progression of the temporary and permanently appointed scientists.

Lee Farr reviewed briefly the professional status of the men being appointed for research at the Medical Department. They are career men and up for their Boards with about 3 years or more postgraduate experience. He claims they are getting the status more and more of a recognized center in that Boards are giving them credit for their work at BNL. They have had about 65 such people over the past 10 years. They have taken in others in the basic sciences oriented to medicine, but these have been of secondary concern. The research emphasis is on man and human processes and dimensions.

[illegible] (Attachment #1) falls in 4 categories.

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The environmental medicine refers to the problems of radiation effects in man and how man's diseases are affected by the increase in radiation in man's environment. He then made a strong pitch for a study of the radioepidemiology of leukemia in Suffolk County (500,000 population) but he has modified it to requesting the help of the New York State Board of Health with guidance by the Medical Staff.

He then talked much more generally about the other activities of the Medical Department. It was so general that it could hardly be reported except verbatim, but it involved a good bit of philosophy, hopes and history along with specific large parts of the program. He gave a special plug for Mn metabolism - there seems to be a relation between the Mn curve of disappearance and the ability to respond to an anti-Parkinsonian drug.

The items and separate subjects were largely along the lines set up at our December 1958 visit. (This could be used for the 189's).

Dr. Farr's discussion of and plea for neutron capture therapy, using a case history of an hemangiosarcoma in a child, was superb.

Gene Cronkite discussed the tritiated thymidine procedure. The T^3 goes on to position 3 of the thymidine base. It has become a world-wide standard procedure. At least 20 men at the BNL Medical Department are using it in one way or another to study their problems.

He agreed that DNA was a poor place to insert T^3 and reported empirical studies indicating that it was more damaging than HTO equivalent. However, 1.0 μc/gram gave good autoradiographs while 30 μc/gram of mouse gave no gross, clinically detectible effect. The problem of the spot disintegration of the T^3 is not understood or evaluated, certainly not in terms of rads. The recoil energy of the H^3 product is about 3 ev and hence barely enough to create even excitation and not enough to cause ionization. He gave an excellent summary of the overall metabolism of T^3 and thymidine. This should be published. He also has data on turnover of HTO in man and non-volatile T^3 excretion. Some 40-60% of injected tritiated thymidine goes into a form not identifiable as either HTO or non-volatile T^3 forms.

In HeLa cells 50 rad gave about the same effect on reproduction time (normally 24 hours and DNA synthesis time of 7 hours) as 0.2 μc of tritiated thymidine per ml of culture. Work is going on to learn whether there are effects on genetic processes, chromosome breakage, and carcinogenesis.

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He then described his own work on maturation time and generation number for bone marrow cells. He claims that the primitive cell does not show reproduction to any great extent prior to the erythroblast reproduction. This is in contradiction to Osgood who feels that there is little reproduction at the erythroblast stage. (A new basis for hematological argument seems to be forming).

His present experiments indicate that the granulocytes stay in the blood about 6 hours and maximum of 48 hours.

This line of study is being extended to human cancers. Peculiarly, his data suggest that neoplastic cells have a very slow doubling time compared to normal tissues. This means a slow cell turnover and growth for cancers, just the opposite of what has been assumed.

A tour of the reactor and a hospital unit followed.

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After lunch the Biology Department took over.

Dr. Curtis explained that they have not had many graduate students and don't expect to. The number of post-graduates, however, have been larger. Because much know-how is necessary, the post-doctorals have come on the basis of working with a staff member to solve a given problem. These arrangements have been irregular and not formalized. A number of foreign workers have been supported for various periods. There also have been a number of faculty members working here.

He described the bases for the program as being:
(1) Biological; (2) Something which can be done at BNL especially well; (3) That it be in the Forefront of Biology; and (4) That it have a tie-in University research program.

The program was divided into Radiation Effects (Radiobiology, Genetics and Molecular Biology) and Nuclear Techniques (Mammalian Physiology, Cellular Physiology and Biochemistry).

H. Quastler is interested in the mathematics of the cell reproduction systems of the body from birth to death. But even the very simple 5 compartment system of the gut epithelium has 40 rate constants or components which have to be determined. He used counts of the gut wall and villi to support this concept. He was loathe to compute the time rates for the irradiated gut wall using T^3-thymidine to check the sequence of replacements.

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Dan Koshland reviewed his studies on protein structure and function relative to space-position of enzyme groupings - the active sites.

When chymotrypsin reacts with DFP, the enzyme is blocked and it was found that the DFP was on the serine although it should have gone on the histidine. They have worked on phosphoglucotransmutase and P^{32} to try to identify the active site. He found that the sequence of amino acids was the same for chymotrypsin and PGM. This and other activity showed the necessity for both serine and histidine at the active location. This led to the concept of the need for specificity of amino acid sequences as a component of the enzyme leading to bond breaking. The structure then will determine the properties and function of an enzyme, determine what substrates it will relate to. Antibodies may have this property of amino-acid specificities to a high degree. The gene may be another form of amino acid specific location structure. There is a repetitition of this basic amino acid structure in other enzymes as well.

Dr. P. S. Woods reviewed the early work on labeled thymidine relative to the chromosome. They have also gone to salivary gland chromosomes of Drosophila. Their thesis is that the giant chromosomes of Drosophila are the result of failure to split longitudinally. They have also used T^3-cytidine for growing root tips of Vicia. Here with cytidine (which goes to RNA) the activity was in the nucleolus and from the nucleolus into the cytoplasm, the function of the nucleolus apparently being to produce RNA for cytoplasmic function.

Dr. R. C. Fuller has been trying to link up structure and function in the photochemical system used for photosynthesis. The process involves (1) Energy capture and transfer; (2) Energy conversion (Electromagnetic energy to chemical energy, specifically ATP); and (3) Energy storage and utilization. The chloroplast carries out all 3 of these functions.

The photosynthetic apparatus of certain bacteria is simpler because the photosynthetic pigments exist in a particulate form. They convert $H_2O + CO_2 + H_2S \xrightarrow{\Delta} CHOL + S + HOH$. These chromatophores can be isolated from the bacteria and employed in vitro for study. They contain chlorophyll and carotinoids and it can be shown that the carotinoids capture the light energy which is then transferred to the chlorophyll. This organism does not store CHO but converts it to amino acids, such as aspartic acid, glutamic acid, etc. This conversion is anaerobic and must have light, so that in this organism photosynthetic protein synthesis predominates.

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Dr. Steffensen pointed out that chromosome breakage is much greater when Ca^{++} and Mg^{++} are lacking or reduced in the medium. The rate is also temperature sensitive, increasing with rise of temperature. The effect of X-rays is independent of the pO_2 or pN_2.

He described current ideas about the structure of genes: Eight layers thick with each layer being composed of 4 DNA molecules having protein between the two surfaces of DNA. The point here is that the components of the genes are precisely lined up and yet breaks don't seem to do as much damage as one might expect. He currently is using Ca^{45} to study the subsequent history of eggs fertilized by radiation damaged sperm.

Howard Curtis discussed why premature aging occurs and what does it consist of. Several ideas were considered.

(a) The accumulation of insults. He tested this idea by comparing an LD_{50} with mice treated with typhoid vaccine and nitrogen mustard against untreated controls.

The experiment was repeated using these insults repeated every 14 weeks. The survival in all these cases was not different from controls. Hence the multiple insult theory is not true.

(b) Accumulated somatic mutations. This was tested using nitrogen mustard by multiple injections, but the rates were not increased so that this concept (as tested) did not pan out.

Hence, a new theory is needed which will explain both the somatic and/or biochemical relations.

Dr. Sparrow described his work on inducing genetic changes in plants. Different plants have very different rates of mutation, but show the same basic phenomena.

Tritiated thymidine was used to expose plant seeds; there was evidence of chromosome breaks proportional to time of exposure.

He finds that plants with large chromosomes and the smallest chromosome number have the highest sensitivity to radiation.

Tumors are easily produced in plants by chemicals or by radiation.

Werner Heis (a new member) discussed his work dealing with protein structure. He appears to be the one who worked out the structure of ribo-nuclease; M.W. = 14,000. He will work further on this at BNL.

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Saturday morning the program was by the Instruments Division (and Health Physics) by J.B.H. Kuper. The work here will increase by virtue of the reopening of the Cosmotron, the Medical Research Reactor and before long the "Big Ring."

They expect to have to get into more and more sophisticated machines as time goes on and these machines have to be kept operating - e.g., 100 channel analyzers and the large digital computer.

They have had a small but steady flow of foreign and local men in Nuclear Instruments - about 5 per year. In Health Physics there has been a larger effort and a steadier flow of students, both foreign and local.

The meteorology group was a large, practical-operation group designed to monitor the argon from the stack. As the problem became better known the group has switched to research of various kinds and for other people as well such as Army, etc.

The need for a building for the Department was mentioned.

Lee Gemmil (Health Physics) spoke for Fred Cowan and pointed out that the research done in this area was by 12 of the total staff of 45 health physicists. Some of the work has been on laundry and cleaning; air, dust, and water monitoring; control of waste water; instruments for these purposes; and, finally, waste disposal.

The reloading of the pile with new enriched fuel has made new problems and much more work.

Dr. Carsten, speaking for their training activities, dwelt mostly on the Radiological Health Physics program in which they take the 10 to 30 people from the UR course for practical work. There are now 167 graduates.

Will Higginbotham for the Instrument Division noted that he had 55 people including glass blowers, calibrators, repair men, computer builders, valve-tube builders, electronic engineers and builders, etc. They are also building the computers for the Medical Division for compartment-diffusion analysis.

Mr. Smith, Meteorology, said that they do some service work and forecasting, but most of their work is in evaluation of the reactors and a study of atmospheric pollution relative to air-cooled reactor operation; i.e. safe operation of a reactor. Their research interests lie in "diffusion" of materials in air at distances of 50 to 100 miles from the source of the materials, as for example, a smoke or a reactor.