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REPORT OF
BROOKHAVEN NATIONAL LABORATORY'S
MEDICAL DEPARTMENT
VISITING COMMITTEE
MAY 8-9, 1980

David V. Bates, Chairman
James V. Neel
Clement A. Finch
Elizabeth C. Miller
Stanley J. Adelstein
Hans L. Falk (absent)
Ronald G. Crystal
David Nathan

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BROOKHAVEN VISITING COMMITTEE

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REVIEW OF SPECIFIC PROJECT AREAS

1. THE GENETICS CLUSTER (Drs. Carsten, Bender and Tice)

The work of this group was reviewed by Drs. Miller and Neel. Dr. Carsten's work on the genetic and somatic effects of tritium appeared well planned and executed, and should meet the question of tritium effects for the foreseeable future. One could wish for a better genetic endpoint than dominant lethals, but the necessary funding was apparently not available. Dr. Tice presented his recent work on the ability of inhaled benzene to produce Sister Chromatid Exchanges (SCE's) and chromosomal aberrations and to affect cellular proliferation kinetics in bone marrow. At the exposures used, there was an increase in SCE's but not in chromosomal damage. However, with the simultaneous administration of phenobarbital, a well known inducer of tissue enzymes, chromosomal damage was documented. The findings extend our knowledge of another potential environmental mutagen-carcinogen, and also illustrate the complexity of these effects, since the sex differences and phenobarbital effect suggests the observed results may be due to the action of benzene metabolites. Dr. Bender directed most of his remarks to collaborative work with Dr. Ishii which extends his very longstanding interest in specific kinds of DNA lesions and their enzymatic repair systems. Specifically, he presented rather elaborate observations on the effects of inhibitors of DNA synthesis (such as hydroxyurea, novobiocin, cyclohexamide and others) in spontaneous and ultraviolet induced SCE's in Chinese hamster cells. Out of the pattern of observed responses comes the suggestion that SCE production (which is still poorly understood) may involve a DNA-gyrase like enzyme. This suggestion should lead to further experimentation.

The reviewers find this work of generally good quality, characteristic of universities with active research programs in these fields. The productivity of all these investigators, especially in view of the relatively small financial support for Bender and Tice, seemed more than adequate.

The discussion of future plans largely revolved around Dr. Carsten's use of millipore filter chambers and Bender's (and Setlow's) in vitro studies of variations in DNA repair capabilities of lymphocytes from a normal human population after a variety of exogenous insults. The former are of interest because they constitute a system for the study of host mediated (mouse) effects on human cells, using cytogenetic endpoints. The cells bring the study of agent effects a step closer to the human, although the location of the cells within the peritoneal cavity may provide only limited contact with tissue metabolism of interest. Dr. Bender and Dr. Setlow's program calls for quantitative analyses of Sister Chromatid Exchange and DNA repair in lymphocytes from apparently normal persons from the general population after challenge by one of four agents, U.V. light, ionizing radiation, mitomycin C., or N-Methyl N-Nitroso Urea. Each of these challenges will be made either alone or in combination with bromodeoxyuridine (essential for studies of SCE). The data will be analyzed to determine the distribution of the activities of members of the "normal population" and for identification of those individuals with

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levels of SCE or DNA repair outside the normal range. Once these individuals are identified, analyses of family members and more detailed genetic studies can be undertaken.

The results from such a study should be of value to DOE and other regulatory agencies as they consider the range of possible responses in the general population to environmental contaminants.

These three scientists were very concerned about the impact of DOE's budgetary process (with its possibility of precipitate decisions on drastic changes in funding of specific areas) on the stability of their research funds and planning of continuing productive research.

2. REVIEW OF CELLULAR TOXICOLOGY AND HEMATOLOGY GROUP (Drs. Cronkite, Commerford, and Miller) by Dr. Finch and Dr. Nathan

The Hematology Program under the distinguished leadership of Gene Cronkite has undergone a major shift in the content of its EPA supported activities. The Dexter type marrow cell culture technique has been adapted to the evaluation of noxious effects of environmental pollutants on stem cells. Interesting preliminary observations on benzene damage were presented. This experimental model has the capability of quantitating the proliferative capacity of the stem cell population and perhaps of detecting malignant change. A second ingenious test system permits the experimenter to determine whether substances penetrate the outer membrane of the stem cell and therefore are in a position to effect the proliferative behavior of that cell. Isotopically labelled compounds are first allowed to enter the body. At a later time, marrow is withdrawn and frozen for a period of time and then studied for colony forming capacity. Any decrease observed is a function of the amount of radiation to the cell nucleus which in turn is a function of the penetration of the compound into the cell. Other projects include an evaluation of the presence of contaminating endotoxins in components of the cell culture media used to evaluate colony formation. Efforts are also being made to isolate stem cells in higher concentration. All of these studies benefit by the extensive background of Dr. Cronkite and studies of cellular proliferation.

Additional studies undertaken by Dr. Miller and supported by the NIH are concerned with the role of erythropoietin in regulating erythropoiesis in animals and man. Of particular interest is the lack of an identifiable response with minor degrees of hypoxia in rats. A sensitive radioimmunometric assay was employed and agreed rather closely with the polycythemic mouse bioassay, so that methodology appears reasonably secure. Her work has been carefully performed and the results are of considerable interest. Detailed studies of erythropoietin levels in man are in progress. Of interest is the stability of the erythropoietin level in normal subjects during the 24-hour period. The studies in patients with chronic pulmonary disease may present difficulties in interpretation because of the multiple variables. Kinetic studies of erythropoietin would be of interest.

In summary, it is encouraging to see the adaptation of this laboratory's activities to the needs of the Environmental Protection Agency. Dr. Cronkite and his associates have made continued important contributions to our knowledge of blood cell physiology and would seem to represent a valuable resource for the total Brookhaven program. Additional studies carried out under other support than the EPA will increase the attractiveness of the total program for visiting scientists.

3. REVIEW OF PROPOSED COAL WORKERS STUDY (proposed by Drs. Avacedo, Susskind and others) reviewed by Dr. Bates and Dr. Crystal

This protocol involves a beginning feasibility study of bringing a group of retired coal workers from Virginia to the clinical facility for five days study. The program has been planned together with Marshall university at West Virginia and the intent is to pursue a somewhat abbreviated protocol to explore the feasibility of more detailed studies. The basic purpose of the study is to relate pulmonary function tests to x-ray appearances and clinical studies. The same group of miners will be studied at the university in Philadelphia by Dr. Robinson and Friedman by the technique of pneumomagneto-graphy.

At Brookhaven the intention is to do ordinary pulmonary function tests, a complete work history and illness history, contemporary studies of ventilation and perfusion distribution using krypton and xenon by the technique already published by this group of workers, and by the use of gallium to study evidence of an existing inflammatory component. There is also an intent later to use the total body counter to study particulate clearance involving polystyrene particles with Strontium 85.

The miners will be selected in Virginia, in West Virginia, will all be over the age of 35, and are expected to have moderately severe disease but not very severe incapacity. The reviewers felt that the study was on the whole useful since it would bring to bear on a small sample of miners the kinds of techniques only available at Brookhaven. We had three suggestions to the group to increase the value as whole:

- A. The final objective should be not to study retired miners with the kind of advanced disease these men are likely to have, but to study a group of smokers and non-smokers each exposed for a relatively short time (about five years) of underground work in the mine. Efforts should be made now to secure the collaboration of management and unions for that study which is likely to be of much more interest than the attempt to correlate different methods of measuring incapacity in a group of men already partially disabled. The real need in this field, in our opinion is to examine critically and with newly devised tools the impact of five years of underground work on men who both smoke and do not smoke.

- B. The method of ventilation perfusion measurement devised by the workers of Brookhaven is interesting and theoretically sound but it would be very important that at the same time as it was being applied to this sample of men, simultaneous measurements were made using the technique of Wagner and West devised at San Diego involving the gas chromatographic analysis of blood and air after a bolus containing dissolved gases. This method is without hazard and doesn't involve additional radiation dosage. It is a relatively simple technique being widely used for clinical investigation. There are two reasons why this group of investigators should from the beginning use this method in parallel with their own using the isotopes. The first reason is that the validity of their described method of measuring ventilation perfusion ratio has not yet been established nor compared with other methods, and the second reason is that the comparison of the two methods is a point of major scientific importance in its own right, regardless of which group of patients were to be studied.
- C. We also felt that it would be as well to obtain the collaboration of the Department of Mine Safety to determine average dust levels in the specific mines in which the group of miners had worked, together with chemical analyses of the coal to which they had been exposed. It would be as well to collect this information at the start of the study.

With these suggested modifications in mind we think the study should be actively encouraged since it will show whether or not the clinical facility at Brookhaven can be easily used for this kind of investigation in the future. In addition the clinical correlations they are likely to be able to draw will be of interest and have value on their own account.

4. PULMONARY TOXICOLOGY GROUP (Drs. Drew, Chanana, Joel, and others) reviewed by Dr. Bates and Dr. Crystal

The reviewers visited the barn to look at the resources available for the method being developed by Dr. Chanana to collect continuously thoracic duct lymph from adult sheep. This barn now has a facility for making measurements of ventilation perfusion distribution in the living sheep, and the sheep are being exposed to noxious agents such as nitrogen dioxide at the present time. We heard considerable discussion of this preparation and the work projected for it. Dr. Joel described his work on particle absorption and also the work he is currently doing concerned with the immunological reaction in the isolated lobe of the sheep in collaboration with Dr. Chanana. This involves instillation of foreign red cells into the lobe of the lung with the study of the subsequent reactions. The group was joined by Dr. Elliott Shaw at this point to describe the possible use of this animal preparation for the pursuit of his enzyme studies concerned with elastase and collagenase in the sheep. The visitors found a number of points to criticize in the current work in progress with the sheep. To some extent this looked like a surgical technique in search of a problem, rather than a well planned and carefully thought out scientific program to answer certain specific questions. It seemed clear to us that neither of the principle investigators, Dr. Chanana and Dr. Joel, had a sufficiently broad or prolonged background in the kinds of

studies they were pursuing to be able to make a very convincing case for the kind of work which they currently have in hand. Thus the surgical preparation being used by Dr. Chanana seems to involve familiarity necessarily with the very large literature on pulmonary edema and factors which influence lymph flow and composition, but the preparation has not been designed to answer specific questions which have been identified as not being tackled by previous investigators. Much the same might be said about the study of the response of lung to the instillation of foreign material. On the other hand, the scientific originality and capability of Dr. Shaw is beyond question and if the preparation provides him with a useful additional method for his work, it could probably be justified on that basis alone.

We then briefly toured the inhalational toxicology unit and were glad to find this in full productive work under the leadership of Dr. Drew. We examined the project being done in collaboration with the Thermal Insulation Manufacturers, in which glass fibers of two different sizes are inhaled by rats, and a subsequent electronmicroscopy study of the lungs reveals how the macrophages are attempting to deal with these fibers. Very elegant pictures have been produced showing that with large fibers four or five macrophages attach themselves to the length of the fiber, much like a "shish-kebab", whereas if the fibers are very much smaller the macrophages ingest them and they look like a bundle of sticks of firewood inside the cell.

We also examined work recently completed on the effects of different gases on normal rats and rats from the hypertensive colony (which revealed interesting differences in response not wholly explained) and also benzene work done in collaboration with Dr. Tice. It is proposed to work with coal dust in future work and to try and induce lesions comparable to those of coal workers pneumoconiosis in different animals. It is also intended to study acrolein exposure and silica exposure. It is also felt necessary to repeat some earlier studies done by Dr. Drew on the interaction of sulfur dioxide and benzpyrene since with modern technology it is felt that a better approach can now be made to this problem than was possible ten years ago when the work was first done.

The visitors noted that the involvement of Dr. Kushner has in fact been minimal in this work, since he has been to the laboratory no more than twice in the last two years. It was our view that the Pulmonary Inhalation Toxicology Program had got off to an excellent start and is already doing important and highly relevant work. It is obviously directly within the mandate of the supporting agencies and hopefully will command a basis of strong support. We were very much less impressed with the work on the sheep preparation because the background knowledge of the investigators in that project on the lung in general seemed to us to be not at a sufficiently profound level to ensure that useful information is obtained. This group as a whole does not have any existing need for the use of the clinical facility.

5. REVIEW OF NUCLEAR MEDICAL GROUP by Drs. Adelstein and Sweet

There are four sub-groups in this division and each will be described in turn.

A. Medical Physics Group (Dr. Cohn)

This group has been developing the total body neutron activation analysis facility. This has been an excellent program and the work is very relevant to in vivo noninvasive measurements of metal content of tissues. It has already been successfully applied to cadmium and to iron and there are other aspects which are being discussed which would be important. The reviewers noted there was perhaps insufficient correlative work going on in relation to other dysfunctions related to metal content discovered but there is no doubt of the value of the technique being developed and its probable future usefulness. There is also a useful program on nitrogen balance in neoplasia but this is somewhat in a vacuum and the visitors felt that there was a need for outside collaboration possibly with an organization such as Sloan Kettering. There are certainly considerable strengths in this area at Brookhaven, but collaborative activities need to be actively sought and worked on.

The total body neutron activation analysis facility and whole body counter are ideal instruments for support of the general clinical research center either to be used in collaboration with Stony Brook or with other internal and external clinical investigators. The facility at present is used primarily for the evaluation of treatment in primary osteoporosis, for changes in bone calcium secondary to chronic renal disease, and for the analysis of total body nitrogen in cancer patients (by prompt gamma analysis) for the development of protein sparing diets in cachectic individuals. One wonders if this methodology could be extended with benefit to spinal cord injury patients, raising particularly the possibility of Veterans Administration support.

Among other methodologies, Dr. Cohn's group has developed a nuclear resonance technique for measuring iron content in the heart and liver and are applying this to the problem of iron overload in thalassemia. We did not have any indication as to whether or not the measured levels would be correlated with cardiac and liver function studies.

In terms of occupational exposure, they have developed a mobile facility which can be used for measuring cadmium. They are working on other methods which can be employed for measuring the organ contents of iron and silicon. It strikes me that it is important for them to develop exposure-concentration relationships along with an understanding of those activities which might modify such relationships (for example, smoking and diet). If these exposure-concentration relationships are non-linear, then they might form the basis for setting exposure limits, either on the basis of absolute exposure values or on the basis of measured organ concentrations, the latter allowing for biologic

variability. In addition, one would also like to see this group develop concentration-response relationships; for example, the relationship of cadmium exposure to cadmium uptake in liver and kidney and the relationship of cadmium uptake in liver and kidney to renal function; alternatively, the relationship of welding activities to iron concentrations in the lung and the relationship of iron concentration in the lung to pulmonary function could be explored.

This group has focused considerably on the development of technology and they could, with profit, now concern themselves with an increased effort in data gathering, particularly in conjunction with colleagues in the Medical Department who could help with functional measurements. It would be too bad if opportunities were missed here to develop the kinds of information that are need for occupational limit-setting and are now demanded by a risk-conscious society.

B. The Radionuclide Production Program (Dr. Richards)

This program is headed by P. Richards and formerly was located in the Division of Applied Sciences. It consists of a number of activities:

- a) the use of the BLIP facility for the production of radionuclides;
- b) the pursuit of radiopharmaceutical research especially with regard to the development of ruthenium-97 radiopharmaceuticals; and
- c) the study of the chemistry of technetium-tin radiopharmaceuticals.

The BLIP program has had several interruptions but seems now to be settling down in terms of its activities, although funding is insecure beyond 1981. Some of the radionuclides are intended for use outside of the Brookhaven National Laboratories, but transportation problems have demonstrated that these must be of sufficiently long half-life for their export to be practical. Some of the radionuclides can be used most profitably within the Brookhaven Laboratory including the large rubidium-81-krypton-81M generators and short-lived iron-52, while others lend themselves to outside research collaboration. It would appear that this program would be helped by more formal outside advice. For this reason we suggest that a medical radionuclide advisory group be established to meet twice a year to review all the Brookhaven radionuclide production programs and to help with suggestions as to the best use of the isotope production facility.

With regard to the research program concerned with ruthenium-97, this isotope is not likely to allow studies of a kind not done at present but could be marginally and perhaps even significantly better than radiopharmaceuticals now labeled with gallium-67, indium-111 and technetium-99M for the same purposes. It is important that the rate of development of these radiopharmaceuticals parallel in intensity what is considered state-of-art in terms of development and diffusion. It is also essential that clinical trials begin as speedily as possible and that outside collaboration be employed if the population mix at the Medical Department at Brookhaven is an impediment for the testing and diffusion of these new radiopharmaceuticals. For example: collaboration with a pediatric group for the study of Ru-HIDA; the possible establishment of a multi-institutional study for Ru-transferrin in tumor and abscess detection

such as was done with gallium-67; and the participation with a neurological group such as Dr. Moore's at Stony Brook or Dr. Katzman's at Einstein for the evaluation of RuDPTA for CSF fluid dynamics.

With the general retrenchment taking place in the department, the group should concentrate its efforts in areas that are unique to the Brookhaven Laboratory such as the development of radiopharmaceuticals with isotopes uniquely produced by the BLIP facility.

C. Clinical Nuclear Medicine Program (Dr. Brill)

This program is now under the direction of Dr. A.B. Brill who, during the year, replaced Dr. Hal Atkins. Dr. Atkins has moved to Stony Brook but spends one or two days a week in the Brookhaven Medical Department.

The program is in a period of transition, and first we reviewed Dr. Atkins' former program which included a number of projects which, although of merit, do not reflect optimal utilization of particular Brookhaven strengths. Exceptions are the use of the rubidium-krypton generator for pulmonary function studies in the pneumoconioses (see Pulmonary report) and the use of manganese-52M in conjunction with the Pett-3/6 instrumentation.

Conversely, Dr. Brill's report on the new directions he sees for his group seem to address approaches that are more specifically designed to engage the BNL facilities, especially:

- a) positron emitting chemistry group;
- b) the computational facilities so strong within BNL; and
- c) collaborative efforts with medical physics and the instrumentation divisions.

Dr. Brill's strong background in the physical sciences makes him a natural leader for this group and we look forward with interest to next year's review when we can see which of these programs has been implemented. In any event, it is my belief that he has started the nuclear medicine group in a new direction which it has sorely needed.

We wish to commend Dr. Brill's intention to strengthen the ties between his group and that of Dr. A. P. Wolfe in the Department of Chemistry. Dr. Wolfe's work in the development of positron-emitting radioindicators is of the first rank, and he has had to turn, in some instances, outside of the Laboratory for proper collaboration. This has been possible using fluoride-18 but will not be possible in the case of carbon-11, nitrogen-13 and oxygen-15 because of their very short half-lives. It is therefore important that the Laboratory acquire a state of the art ring-detection device, and I am pleased to learn that the PETT 6 device will be available in about a year. The availability of this device in conjunction with the cyclotron produced material should not only strengthen the collaboration between Dr. Brill and Dr. Wolfe but also will provide opportunities for clinical investigators from AUI and other medical centers to cooperate in the types of collaborative research

programs that have been so successful in the Departments of Physics and Chemistry in the past. If such relationships can be built up with first-rate clinical investigators in the medical schools that relate to Brookhaven, it would go a long way to improving the intellectual environment and the quality of work done in the Laboratory.

D. The Radiation Therapy Group (Dr. Bennett and Dr. Fairchild)

The Boron capture neutron therapy group (under R. G. Fairchild) has embarked on new approaches that might obviate former difficulties. For example, use of epithermal neutrons and new agents with substantially improved tumor-to-blood ratios. They have also begun to explore approaches to tumors outside of the central nervous system (for example, malignant melanomas using borated chlorpromazine). As the effectiveness of this melanoma treatment may be a function of the tumor cells' melanin content, there may be some problems in treating the general population of melanoma patients; but the necessity of a better treatment of melanoma and the usefulness of tumor models for boron capture therapy justifies the effort in my opinion.

The Proton Therapy group is under the direction of Dr. G. W. Bennett. Their activities can be divided into two categories. First is the establishment of a facility for the treatment of intercranial tumors which is being constructed in conjunction with N.Y.U and the Nassau County Medical Center. This will permit the use of the proton beam for treatment as has been the case at the Harvard Cyclotron. Second, the use of positron activation analysis for producing oxygen-15 and carbon-11 in vivo is being explored. This method can be used to determine regional blood flow in tumors by following the washout of water labeled with oxygen-15. In addition, with appropriate instrumentation, it might allow the planning of the positron radiation fields in conjunction with transverse tomographic imaging. An exciting variation of this has been proposed by Dr. Brill which is to administer stable isotope precursors which could be activated by the external beam in situ, thus irradiating tumor cells without damaging normal tissue that might take up the tracer but lie outside of the radiation field.

These programs are sufficiently innovative and exciting, that they should be encouraged as unique features of the Brookhaven efforts.

A question arose as to the rationale for having radiation therapy programs in a DOE sponsored laboratory. We believe that the reasons have been stated before, namely that these methods are spin-offs from the technology developed as part of the energy program at the Laboratory, and it is extremely cost-effective to have them applied to medical treatment purposes.

COMMITTEE RESPONSE TO MAJOR GENERAL AND POLICY QUESTIONS

Dr. Borg's survey of problems dealing with supporting agencies and his review on the morning of the 9th of May of the future possibilities were actively considered by the Committee in its discussion with individual investigators. Although we did not have an opportunity as a full committee to discuss the many questions raised in Dr. Borg's presentations in detail, we did have an opportunity to discuss certain aspects of these problems. In the hope that these suggestions may be useful we therefore list them under the various headings in which they were raised.

1. FINANCING OF THE CLINICAL BED FACILITY

This is a problem which the Visiting Committee has addressed each year. We did not consider it in detail this year but it is clear to us that there is inevitably a "competition" between the resources necessarily devoted to keeping this facility open in its present form and the necessary secure funding which will be needed to keep the best members of the research group on a secure foundation. We feel that it's important that an outside committee should look specifically at this question at this point of time, when it should be possible to define very precisely the future role of Stonybrook in relation to the clinical facility. That medical school should now have developed its programs to a sufficient extent, and to have generally completed its faculty recruitment so that the whole question can now be addressed again. We recommend that the trustees establish an ad hoc advisory committee only on the clinical facility at Brookhaven and its future funding and use. We would recommend that such a committee should include a senior administrator of a major and research hospital on the eastern seaboard, a Brookhaven trustee, a member of the Visiting Committee (we would recommend Professor David Nathan for this position) and two other distinguished clinical investigators with experience in the management of research clinical beds. A number of possibilities of people come to mind in this latter category and possibly Professor Tosteson who worked at Brookhaven at one point might be considered a suitable choice. The mandate would be to advise the Trustees on the future use of the clinical facility at Brookhaven.

In our opinion it would be necessary to convene a meeting of the Medical Research Group at Brookhaven with the heads of departments at Stonybrook or divisions of departments for a full preliminary discussion of identified opportunities, existing collaboration, and possible future use. We found no evidence that that kind of far ranging discussion had so far occurred. We feel that it is essential that discussion should be structured with the Brookhaven group on the one hand and the Stonybrook group on the other in advance of the meeting of the advisory committee which we have recommended. There are reasons to suggest that the future collaborative use of the Brookhaven facility might indeed be expanded; however it is essential to establish policy lines to determine whether this really involves the provision of an accredited hospital

at Brookhaven, or whether some simpler style of facility might not meet the needs of the existing research group and possibly also the Stonybrook group as well.

2. THE INVOLVEMENT OF BROOKHAVEN IN ENVIRONMENTAL HEALTH PROJECTS AND THE ESTABLISHMENT OF MAJOR ENVIRONMENTAL HEALTH SCIENCE CENTER

Dr. Borg explained to the committee his problem in raising funding to get a core grant for the Brookhaven Department and establish the relevant research groups as an environmental center. It was the general view of the Visiting Committee that, although this might eventually become a more feasible objective, it was extremely difficult to pursue it as a singleminded objective at this point of time. It is clear from our review of the individual projects that some strong areas naturally fall directly into such a project development. We agree that the strong sections of this research should be developed as much as possible as it would be good policy to expand and develop the middle strength of the quality scientific work in areas closely related to the declared mandates of the agencies. We doubt however that it will prove feasible to establish, (through the core grant process) an environmental health sciences center until the environmental work has been better established. It is also essential in our view to recognize that the work of some groups, in particular amongst the work reviewed by Dr. Cronkite, be protected and funded regardless of whether or not it seems to fit well into such an overall concept. Perhaps a more profitable approach would be to request that the agencies, particularly the Department of Energy, should throw major support behind certain new lines of research at Brookhaven. The core funds available through such a major application would serve the purpose Dr. Borg identified as being needed to consolidate the program as a whole. This possibility is explored in the next section.

3. OCCUPATIONAL HEALTH RESEARCH

It may be helpful to emphasize that there is a world of scientific laboratory research, scientific journal publication, etc. on the one hand, and a world of Workers' Compensation Boards, working environment, and industrial and union experience in relation to actual conditions, on the other. It is difficult to form a bridge between those two worlds. This might be achieved through a structured approach by the members of the Brookhaven group to departments such as the one at Mt. Sinai in New York which specialize in the field work of Occupational Health Medicine, and have extensive and experienced epidemiological backup. It seems to be too difficult for Brookhaven to establish the large group of people required for the "within industry" footwork required to do active research in that segment, but on the other hand the resources now being deployed at Brookhaven might be extremely well utilized with continuous consultation with those doing the field work who know where the problems are.

A typical example of this kind of opportunity is provided by careful reading of the review of the Department of Energy 'Research on Human Health

Effects of Low Doses of Ionizing Radiation' published by the National Research Council. This recent review (1980) by a distinguished committee of the National Academy of Science of the DOE Research Program emphasized that the principle objectives of the total research program "include the determination of risks from exposure to external radiation from internally deposited radionuclids and the use of this information in the development of standards to protect the health of nuclear workers at DOE and related facilities and of the population at large". In their review of the only project funded by DOE which bears directly on the problem of uranium miner mortality (see pp. 39 - 41 of this report) they are critical of the fact that there is very little coordinated research on the health of uranium miners. It seems to the Chairman of the Committee that Brookhaven has a unique opportunity to contribute to this by studying the effects of inhaled radon daughters on carcinogenesis in rats in the new pulmonary inhalation facility. Dr. Drew stated that he would easily be able to do this work which requires exposure facilities out of the range of most university departments. The only rat exposure data available at the present time is a result of a research program conducted by the French Nuclear Energy Authority. It is quite clear that this work must be greatly extended and has direct relevance to the standard setting process for radon daughters which is the main underground carcinogenic hazard encountered by miners. Our suggestion here would be the following aggressive approach to DOE:

- A. To point out in strong, blunt terms that the review published by DOE indicates the need for major expansion of that work in relation to radon daughters.
 - B. That only Brookhaven can quickly establish that work and get it started.
 - C. That the work should command major longterm support for the pulmonary inhalational capability and that this support should be immediately forthcoming. The essential philosophy here is to identify very clearly a weakness in the Department of Energy's research program as a whole (or use a weakness identified by its reviewing committee as here) and then seek to punch a major research effort through this deficiency. The accruing funds, which certainly should be major, could be used for the kinds of purposes for which the core grant concept is sought by Dr. Borg. In other words, an alternative strategy to trying to develop a coherent philosophy in the absence of a strong scientific protocol, would be to identify weakness and deficiencies in the Department of Energy's program and design a punch into those deficiencies with very strong financial backing.
4. We have indicated in this report certain individual areas where Brookhaven in our view should take the initiative in structuring contact between its workers and others in the field. A useful way of doing this is to sponsor workshops on specific topics with a planned series of presentations by those at Brookhaven and by those outside to display the possible interdigitation between them. This would be a useful step but care would have to be exercised that these were in areas not already suffering from a surfeit of conferences, symposia, task forces, etc. It is our general view that the Brookhaven group

must seek mechanisms for such more effective interrelationship and take initiative to foster them rather than expect them to occur by accident or naturally. We think this kind of program should be an active concern of the Director of the Medical Department.

5. We would like to draw to the attention of the Trustees that this year the Visiting Committee followed a rather different program as compared to previous years, which enabled individual members of the Committee to meet with individual investigators for long enough to obtain considerable insight into the potential and objectives of the research program in those areas. We would like to stress that this may or may not be an appropriate method of progress in future years. However, it is an important aspect of planning the year to consult with the Chairman of the Medical Department a couple of months in advance of the meeting of the Committee so that they may decide the program which would best fulfill the objectives of the Visiting Committee, the Department, and the Trustees in any individual year. Members of the Committee generally found this year that the experience of the visit was more satisfactory for them than had been the case in the past, but it will be necessary to vary the format in different years in relation to the problems or objectives which are identified.

It was of singular help to the Chairman to be made aware in March of the problems which the Department was confronting this year and the efforts being made by Dr. Borg to deal with these issues. The Visiting Committee would like to emphasize the particularly difficult situation with which Dr. Borg has had to deal, and the difficulties of reorienting the work of the Department in the light of the interagency complexities which are now confronted and the problem of longterm budget security. We hope that the various comments we have been able to make this year may be of some assistance to him in dealing with these problems. All the Committee is very indebted to Dr. Borg and to individual members of his Department for the frankness and freedom with which they discussed their research programs and the work of the Department as a whole. Without the opportunity for such exchanges between the Committee and the active research workers in the Department it is unlikely that the advice of the Visiting Committee can be of much value to the Department as a whole or to the Trustees.

6. This report has been edited and reviewed by all members of the Committee. All of their proposals for change have been incorporated in this final draft.

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D. V. BATES,
CHAIRMAN