405124

UNIVERSITY OF CALIFORNIA SCHOOL OF MEDICINE

San Francisco

203

RADIOLOGICAL LABORATORY

Robert S. Stone, M.D., Director
Gail D. Adams, Ph.D., Associate Director

PROGRESS REPORT

April 1, 1950 - December 31, 1951

ATOMIC ENERGY COMMISSION CONTRACT
No. AT-11-1-GEN-10, Project #2

Submitted March 28, 1952

Orig. - Dr. Shields Warren
Washington, D.C.
4 copies - A.E.C. Area Mgr's Office
Berkeley, Calif.
2 copies - File - Radiological Laboratory
San Francisco, Calif.

RADIOLOGICAL LABORATORY

April 1950 - December 31, 1951

INDEX

ORGANIZATION CHART

DIRECTOR Robert S. Stone, M.D.

ASSOCIATE DIRECTOR Gail D. Adams, Ph.D.

ADMINISTRATIVE SECTION — Personnel as of March 15, 1952

Administrative Assistant	Robert F. Jenkins, Jr.
Secretary	Mrs. Alice M. Trissell
Stenographer	Miss Lois Castellanos
Sr. Typist Clerk	Ray J. Morris

HEMATOLOGY SECTION

Chief of Section	B. V. Low-Beer, M.D.
Consultant	Paul M. Aggeler, M.D.
Sr. Laboratory Technician	Dorothy Carey
Laboratory Technician	Colleen Rohder

RADIOIODINE SECTION

Chief of Section	Earl R. Miller, M.D.
Consultant	Morris E. Bailey, M.D.
Scientist	John H. Simonton, M.D.
Jr. Scientist	Herman E. Seufield
Laboratory Technician	Ann B. Raitt
Laboratory Technician	Archie D. Prestridge

PHYSICS SECTION

Chief of Section	Gail D. Adams, Ph.D.
Jr. Scientist	David B. McClellan
Sr. Accelerator Technician	Donald E. Riesen
Sr. Laboratory Mechanician	Henry D. Stair

BIOLOGY SECTION

Chief of Section	Henry I. Kohn, M.D.
Scientist	Shirley E. Gunter, Ph.D.
Scientist	Robert F. Kallman, Ph.D.
Sr. Laboratory Technician	Carol N. Baier
Laboratory Technician	Vernon E. Wilder
Animal Caretaker	Walter Hicks
Laboratory Helper	Margaret R. Leonard

CLINICAL SECTION

Chief of Section	Robert S. Stone, M.D.
Scientist	??
Visiting Scientist	John W. Beland, M.D.

RADIOLOGICAL LABORATORY

PROGRESS REPORT
April 1950 - December 31, 1951

SUMMARY OF SCOPE AND PURPOSE

The scope of the Radiological Laboratory has been determined by its historical development. The original task at the University of California School of Medicine was a study of the effects produced on the blood of patients by total body irradiation. The work was started in 1942 using x-rays and was expanded in 1945 to include the use of beta rays from intravenously injected radiophosphorus. Also in 1945, the program of evaluating the clinical usefulness of radioiodine was initiated. In 1947, the problem of investigating the physical characteristics, biological effects, and clinical usefulness of multimillion volt radiations was added. While these various activities have been grouped under titles varying somewhat from year to year, they are now all included in the title "Radiological Laboratory" which operates under Contract AT-11-1-GEN-10, Project #2.

The primary purpose of the Radiological Laboratory is the improvement of radiation therapy of cancer. This purpose is being pursued at present, by investigating the radiations from a 70 Mev synchrotron, by continuing the study of how best to use radioiodine on patients, and by trying to determine better the effects of radiations on the blood of patients.

ADMINISTRATIVE SECTION

Robert S. Stone, M.D., Director

The Radiological Laboratory Building, which was built by contract through the Radiation Laboratory, was finally accepted by the University on September 18, 1951 and the process of moving in the furnishings and equipment

was started very shortly thereafter. Orders were placed at once for such equipment as could not be accepted for delivery until the building was ready. The synchrotron had arrived on August 26, 1951 and its installation was started at once. X-rays were first produced on November 9, but as of December 31 the instrument had not been accepted from the General Electric Company.

Administratively, we have had difficulties in arranging for such alterations in the building as were found necessary when we began to use it. The problems were those of the source of finances and the responsibility for the work, since the building was constructed under the Radiation Laboratory's contract, but is operated under contract with the School of Medicine, the financing was all coming from the Atomic Energy Commission but through the two channels. With the cooperation of all concerned, these problems seem to have been satisfactorily solved.

STAFF

On May 12, 1950, Dr. Gail Adams, Ph.D. was appointed a Lecturer and Consultant. Dr. Adams was at the time, working with Dr. Kerst at the University of Illinois. He joined the staff, full time, as of January 1, 1951, in charge of the Physics Section and, as of October 1, 1951, was appointed Associate Director of the Radiological Laboratory. His staff now consists of Mr. Donald Riesen, Sr. Accelerator Technician, appointed July 1, 1951; Mr. David B. McClellan, Jr. Research Physicist, Grade I, appointed August 27, 1951; and Mr. Henry J. Steier, Sr. Laboratory Mechanician, appointed September 4, 1951.

In our last progress report it was mentioned that Dr. Henry I. Kohn, Sr. Surgeon in the U. S. Public Health Service, was helping with

the planning of the Biology Section of the Radiological Laboratory. As of January 1, 1951, he was appointed Chief of the Biology Section. He is still on assignment from the U. S. Public Health Service. He has assembled a staff consisting of the following: Dr. Shirley E. A. Gunter, Ph.D., Jr. Research Biologist (microbiology), appointed October 15, 1951; Dr. Robert F. Kallman, Ph.D., was appointed Lecturer on December 17, 1951 after an agreement had been reached to appoint him as Jr. Research Scientist to take charge of the mammalian exposure problems; Mrs. Carol N. Baier, Sr. Laboratory Technician, was appointed August 8, 1951; Mr. James L. Campbell, Laboratory Technician, was appointed September 4, 1951 (terminated January 31, 1952); Miss Beverly Birk, Laboratory Technician, was appointed July 1, 1951 (terminated October 31, 1951); Mr. Walter Hicks, Animal Caretaker, was appointed October 27, 1951.

The Hematology Section was started with Dr. Low-Beer's help and operated under his direction. While Dr. Low-Beer was away on sabbatical leave for the first six months of 1951, Dr. Paul M. Aggeler was in charge. Miss Corey, the Sr. Laboratory Technician, and Miss Rehder, the Laboratory Technician, have continued to serve this section throughout this reporting period.

The Radioiodine Section has been continuously under the direction of Dr. Earl R. Miller, who started it in 1945. During the current report period, he was helped until June of 1950 by Dr. George L. Alexander; from July 1, 1950 to February 14, 1951 by Dr. Glenn Sheline; and from July 1, 1951 to December 31, 1951 by Dr. John H. Simonton. Dr. Morris E. Dailey, who had been doing some clinical work with thyroid diseases, became Consultant on February 1, 1951 and is still continuing in that capacity. There has been considerable turn-over in the technical staff. Mrs. Marian

Feigenbaum, who joined the project as Laboratory Technician in August 1949, severed her connection on June 10, 1950. Miss Mary-Ann Hirsch, Laboratory Technician, who started on January 3, 1950, left on May 19, 1950. Mrs. Louise Prestidge was employed as Laboratory Technician in May of 1950 and terminated in September 1951; she was replaced by Mrs. Lonette Rappoport who only worked from September 1 to November 9, 1951. Mrs. Ann Raitt was employed as Laboratory Technician on March 21, 1951 and is still with the Section. Mr. Arch D. Prestridge was appointed as Laboratory Technician on November 20, 1951 and is still with the Section. Mr. Norman Scoffield who is employed elsewhere in the University, works part time as a Technical Physicist, and has been serving the Section since January 3, 1951.

The Clinical Section cannot become very active until the synchrotron is available for treatments. However, Dr. John W. Boland, M.D. has been with us since October 1951 and has devoted some time to planning methods of treatment and some time to assisting in the Biology Section. He is a British-American Exchange Fellow of the American Cancer Society (Research Fellow in Radiology, School of Medicine).

In the direct administration of the project, Dr. Stone was classed as "in charge" until October 1, 1951 when he was appointed Director. Dr. Gail D. Adams helped with the administration of the project from January 1951 and was appointed Associate Director in October 1951. Mrs. Alice Trissell was the Secretary and only secretarial help with the project until July 1951, at which time she took a leave of absence until September 1951. With the expanding program in the new building, Mr. Robert F. Jenkins, Jr. was appointed Administrative Assistant on July 2, 1951, and Miss Lois Castellanos was appointed

Stenographer and Receptionist on July 11, 1951. Mr. Roy J. Norris who is listed on the Organization Chart as a Sr. Typist Clerk, was employed as of January 24, 1952.

PERSONNEL PROBLEMS

We have had some personnel problems that arose from the difficulty of establishing, in some instances, what is "recognized University policy". This has affected us mainly in connection with removal expenses, where the contract reads that our policy "shall be determined in accordance with established University policy", and the University policy states that "research personnel appointed under University contracts may be reimbursed for removal expenses where provision for payment is an allowable cost under the contract and up to the limit permitted in the contract". We feel that it is very necessary for us to be able to pay the removal expenses of scientific personnel, in order to procure people from the East and mid-West, since our salaries are often lower than are offered elsewhere, particularly at the National Laboratories sponsored by the Atomic Energy Commission.

People employed in the Radiological Laboratory on a full-time research basis do not have the degree of security that goes along with academic University appointments. It is therefore necessary that the rules of the University be interpreted somewhat more leniently in connection with the salaries, travel, removal expenses, etc., than is necessary for those having academic tenure. In other words, it is very difficult to operate a research project on "established University policy" when that policy is established for Faculty members with tenure rather than research personnel on annual contracts.

It should be pointed out that non-academic personnel also feel less secure on research contract jobs than on regular University appointments. Many non-academic people are willing to accept a slightly lower salary rate from the University than from many non-University jobs because of a sense of security in the permanance of the University. This does not apply to employment on contract projects under the University where the job will terminate when the contract ends.

Another problem that is facing us is how to procure physicians on the salaries available under University rules. Anyone with an M.D. degree is able to make so much more money in the private or even salaried practice of medicine that the salaries offered by the University on the basis of that needed for other academic staff, are not sufficiently high to attract physicians of the caliber we want. The University permits physicians on the School of Medicine staff to supplement their income by practicing their profession for limited periods of time. This is difficult to arrange in connection with men at the Radiological Laboratory.

FINANCIAL MATTERS

The completion of the Radiological Laboratory building has permitted the planned growth of the project. More space and more equipment have made possible some progress, but budgets have had to be projected into the future and we have, up to the present, always anticipated completion dates ahead of those actually experienced. Because of these delays our expenditures have not equalled the budgetted allotments. In the present year, as in previous ones, the expenditures for the first half of the year do not equal those anticipated for the second half of the year. Because of this necessarily slow expansion, we have had our financial problems, both with

the University and with the Atomic Energy Commission. The latter organization, repeatedly through each year, questions the need for the funds that were agreed upon in the contract supplement, because the apparent rate of expenditure for the earlier quarters is smaller than the calculated rate. The University on the other hand, has insisted that a definite contract was signed for definite funds and that we should not feel in any way handicapped by presumed withdrawing of funds. We now anticipate that the authorized steady state will be reached during Fiscal 1953 and that then many of our present financial problems will diminish. However, increased personnel will be required when the clinical work is activated and we may have to replace personnel now financed by the U. S. Public Health Service and the American Cancer Society with people on our own payroll.

The necessary lag between the initial request for purchase of an item by the Radiological Laboratory and the actual reimbursement to the University by the Atomic Energy Commission, creates a problem during the period of expansion because the Atomic Energy Commission records reflect a rate of expenditure that is not current. The expenditures as they appear to the Atomic Energy Commission throughout most of the year, are much below the actual expenditures as we know them to be from our own books. Let us illustrate this point by current figures. From the claimed expenditures, as of December 31, 1951, it would appear that our yearly operations budget for Fiscal 1952 would be in the neighborhood of $129,000.00, whereas, with our knowledge of encumbrances, increases in salary rolls, etc., we estimate that the year's expenditures will be between $159,000.00 minimum and $175,000.00 maximum. We, on our part, will attempt to keep the Berkeley Atomic Energy Commission office better informed of our current financial

status from month to month, so that they in their turn can keep the Chicago Operations office up to date on our financial needs.

Our needs for funds for equipment continue to be rather great. It seems difficult for many people to understand why we need money for equipment when we have just moved into an "equipped" new building. It is true that the basic equipment for producing radiations with energies up to 70 Mev has been provided; and the basic essentials for the biological, clinical and physical laboratories have been installed. However, we are a research laboratory and as with any research program, it will be possible to determine the equipment needed only as the program unfolds.

We already know of the function to be performed by some equipment while the equipment has yet to be planned. For example, we know that we will need some apparatus to put and keep the patients in proper alignment with the beam of radiation, but we are not yet decided as to just what structural arrangment will be best.

Before concluding this discussion, I wish to say that while there are many administrative problems, the spirit of cooperation and the desire to help solve the problems has been so great on the part of the Atomic Energy Commission's representatives and those from the University's administrative offices that we look forward to fewer and fewer difficulties in the future.

HEMATOLOGY SECTION

April 15, 1950 - February 15, 1952

Written by Dr. Paul Aggeler
B.V. Low-Beer, M.D. - Chief of Section

A. Studies on Platelet Enumeration:

This study has been concerned with the development of accurate platelet counting methods for whole blood, plasma and platelet suspensions. The evolution of the problem has been as follows:

1. In March 1950, five direct venous blood platelet counts were done using the standard Spencer Bright Line counting chamber (depth 100 microns), Tocantins modification of the Rees and Ecker counting fluid, high dry (430x) magnification and bright field illumination. The results of these counts done by our technician were compared with counts on the same specimens done by another competent observer. The results varied widely. By careful cross checking it was determined that the difference in the counts obtained by the two technicians was due almost entirely to classification. It was decided by the author that he himself could not decide whether one technician was counting too high because she was including artefacts or whether the other technician was counting too low because she was excluding small platelets. It was therefore decided to attempt to devise a method of platelet counting in which better visualization of the platelets could be attained.

2. Five platelet counts using the Petroff-Hausser bacterial counting chamber (depth 20 microns), high dry (44x) apochromatic objective, 0.95NA condenser and 12x and 20x, periplan eyepieces attached to a Leitz microscope with 1.6x magnification in the prism of the binocular were done. The magnification in this system was 850 (12x eyepieces) and 1400x (20x

eyepieces). The results were unsatisfactory because of the poor resolving power of the lens system for unstained material.

3. The method of Scheff and Ralph (Am. J. Clin. Path. 19,1113, 1949) for the elution of platelets from venous blood was adopted and modified. The platelet suspensions so obtained were counted in the Petroff-Hausser chamber with oil immersion (970x) magnification and medium dark contrast phase lighting. Visualization of the platelets was excellent. In this work 29 eluent specimens were prepared and on them 50 direct chamber platelet counts and 41 dry smear indirect platelet counts were done. Seventeen standard erythrocyte counts were done on the parent venous blood specimens. From evidence obtained from the dry smears it was decided that the elution method removed approximately 95% of the platelets from the venous blood specimen. However, it was decided that the Petroff-Hausser counting chamber was unsatisfactory because of the following defects: the chamber rulings were chipped and inaccurately ruled; coverslip drag occurred when the oil immersion objective was used; the limitation of the working area, imposed by the plastic rim of the coverslip, often made it impossible to view the entire central ruled area of the chamber; only one counting area was provided in each chamber. Since that time a number of specially constructed chambers have been provided for our use through the courtesy of Mr. C. E. Guellich of the American Optical Company.

4. We then used phase contrast lighting, oil immersion magnification (970x) and a specially constructed chamber made of crown glass with a thickness of 1.25 mm and depth of 20 microns but in other respects similar to the standard Spencer Bright Line hemacytometer. A venous blood specimen was obtained from each of 30 normal individuals. An erythrocyte count

using standard methods, duplicate eluent platelet counts and dry slide platelet counts before and after elution were done. From this work it was determined that the means of the dry slide platelet counts and eluent platelet counts agreed, but that there was wide variation between the results of the two methods on individual counts. The previous observation that approximately 95% of the platelets were removed from the venous blood specimen, (as determined by the dry slide method) was confirmed.

5. An attempt was made to adopt the above shallow chamber method to direct platelet counts. It was immediately discovered that although the visualization of the platelets was excellent and their differentiation from artefacts easy, the distribution of the erythrocytes and platelets in the chamber was greatly altered. In an attempt to produce normal distribution in the chamber by the use of various types of diluting fluids for the platelets and various surface tension reducing agents on the chamber 154 erythrocyte counts and 16 platelet counts were done in the 20 micron chamber and 69 erythrocyte counts were done on the standard 100 micron chamber. On the basis of this work a method for treating the 20 micron chamber and coverslip with benzalkonium chloride to reduce surface tension was developed.

6. Venous blood specimens were obtained from 30 normal individuals and on each the following counts were done in duplicates: direct erythrocyte and platelet counts in the 20 micron chamber, indirect dry smear platelet counts, platelet counts by the elution method, indirect wet preparation slide platelet counts using phase contrast lighting and oil immersion magnification, indirect dry slide platelet counts on the residuum of the elution and erythrocyte counts in the standard 100 micron hemacytometer using Hayems and Tocantins solutions. It was found that the average

erythrocyte count in the 20 micron chamber agreed with that obtained by standard methods and that the average platelet count was the same by all four methods employed. However, it was shown that there was wide variation between the results obtained by different methods on the same blood specimen and there was much greater spread in the distribution of the results in the two methods which employed the 20 micron chamber (direct and elution) than in the two methods which did not (wet and dry indirect counts).

7. In order to establish the degree of variation in the platelet counts and the degree of correlation between erythrocyte and platelet concentration in counts done by the above method, and also to improve conditions, 109 platelet counts and 109 erythrocyte counts were done in duplicate in the 20 micron chamber. In addition, 82 duplicate erythrocyte counts were done in the standard 100 micron chamber.

As a result of these investigations it was determined that the results of platelet counts done with this method were unreliable.

8. In the previous experiments, tests of reliability were based on counts done only in the counting area of the chamber. In order to investigate the distribution and concentration per unit area more thoroughly a reticule for the eyepiece of the microscope was obtained and 155 erythrocyte counts of consecutive fields from end to end and/or side to side of the chamber platform were done under varying experimental conditions, including:

a) 20μ crown glass, metallic coated platform chamber, 0.2 mm crown glass coverslip, both cleaned with water and alcohol;

b) chamber as in (a) with circular quartz coverslip;

c) all conditions as in (a) except coverslip treated with varying

concentrations of benzalkonium chloride;

d) all conditions as in (a) except both coverslip and chamber treated with varying concentrations of benzalkonium chloride;

e) various combinations of crown glass metallic coated, crown glass without metallic coating and pyrex with metallic coating chambers and crown glass, quartz or vycor coverslips all chemically cleaned by soaking in potassium dichromate sulfuric acid cleaning solution and steaming over boiling potassium permanganate solution;

f) conditions as in (e) with variations of type of diluting fluid and dilution of blood;

g) standard 100μ chamber and standard coverslip counts for comparison with above;

h) comparative erythrocyte and platelet counts in the same areas at various locations on the platform.

We have made two main observations from this work with shallow chambers (20 to 40μ).

a) A gradient in RBC, increasing from mounting end to far end is present. It may vary from slight to pronounced. The number of cells in counting area may be close to standard count — usually a little low.

b) An occasional count is obtained which is as low as one-half or as high as twice that of the standard.

The present working hypothesis is: There are two reasons for obtaining counts which differ from those obtained with the standard 100μ hemacytometer and 0.44 mm coverslip. They have the same cause, i.e., the shallowness of the chamber, and are interrelated but for the purpose of

clarification and investigation will be considered separately.

a) Chemical: Surface phenomena such as adsorption of protein, prevent even distribution of cells in chamber and probably account for abnormally high counts by allowing the coverslip to be floated, thus increasing the volume of the chamber.

b) Physical: Flexibility of coverslip allows it to bend downward when a chemically clean chamber is loaded which results in a reduction in volume and abnormally low counts.

Experimental Evidence:

a) It is possible to influence both distribution of cells and overall count by coating chamber and/or coverslip with various chemicals.

b) Substances, such as grease or silicone which prohibit wetting of the glass surface, produce very high counts, apparently by floating the coverslip.

c) "Undermounting" shallow chamber with thin coverslip produces very low counts with a high degree of reproducibility. The concentration of RBC is greatest at the sides and lowest in the middle. This result has never been obtained with the standard coverslip and shallow chamber.

d) In 8 out of 10 times, with a chemically cleaned double chamber, the platform mounted second had the lower count. This is probably caused by downward bending of the coverslip over the empty chamber while loading the opposite side.

e) Using a chemically cleaned chamber, the thin coverslip was observed to be bent with increasing upward concavity during

loading of the chamber by visualising diffraction fringes between the coverslip and the chamber shoulders.

It was decided that the lateral shoulders should be moved as close as possible to the edges of the platform and that an additional shoulder should be placed between the two platforms in order to provide maximum support for the coverslip and thereby minimize downward bending of the coverslip. It was also decided that the material should be pyrex since it was observed that the calcium in crown glass leached out in the cleaning process, and that quarts and vycor did not have suitable optical properties for phase microscopy. Specifications for a new chamber incorporating these features are attached, (see appendix).

9. In order to evaluate the reliability of indirect platelet count methods which are in current use in our laboratory, and in order to provide a body of data for comparison with a more absolute value which we hope to attain with the direct method described above, 400 platelet counts were done (number of platelets per 1000 arthrocytes) by dry smear and wet preparation methods.

B. Ultrasonic Vibration of Platelets:

This work was undertaken in an effort to determine whether there are differences between the mechanical fragility of platelets in individuals with various diseases and in the same individual before and after irradiation. Preliminary experiments using an ultrasonic vibrator at the Laboratory of Experimental Oncology showed that the method was feasible. A General Electric Ultrasonic Vibrator was purchased for our laboratory in August 1950.

1. Experiments using heparinized blood showed that the method of

temperature control (dry ice) used in the preliminary experiments was unsatisfactory. A new method of continuous water cooling was devised.

2. Methods for making platelet suspensions previously used were adapted to the equipment available in this laboratory using six 500 cc units of blood obtained from the Irwin Memorial Blood Bank.

3. Eight platelet suspensions from the blood of normal subjects were prepared and vibrated for periods up to 90 minutes. Platelet counts were done at 15 minute intervals. Ninety-six platelet counts using the 20 micron chamber method were done. A variable reduction in the platelet count after vibration was observed. Considerable discrepancy between duplicate counts was sometimes observed and further work on this project is being held in abeyance pending further improvement of the platelet counting method.

C. Hematological Effects of Total Body Irradiation:

1. External irradiation - 52 complete blood counts were done on six patients in continuing follow-up studies of patients previously reported.
2. Radioactive phosphorus - 85 complete blood counts were done on eleven patients in continuing follow-up studies of patients previously reported.
3. Three hundred and fifteen complete blood counts were done on thirty-three patients, and 29 sternal bone marrow studies were done on twelve patients under study in the radioactive Iodine Program.
4. Three hundred and ninety-nine hematocrit studies and sedimentation rates were done on various members of the above three groups.
5. Fifty-three complete blood counts were done on employees.

SPECIFICAT ONS FOR SPECIAL HEMOCYTOMETER

1. Pyrex glass.

2. Thickness (distance from bottom to top of shoulders) 1.2 to 1.7 mm.

3. Flat bottom.

4. Two platforms, flat, parallel to the shoulders and situated at a depth of 20 microns below level of the shoulders. The tolerance on flatness, parallelism and depth must not exceed 1 micron.

5. Dimensions of platforms 13 x 7 mm.

6. Each platform to be separated from surrounding shoulders by a moat 3/4 mm wide and 1/2 mm deep.

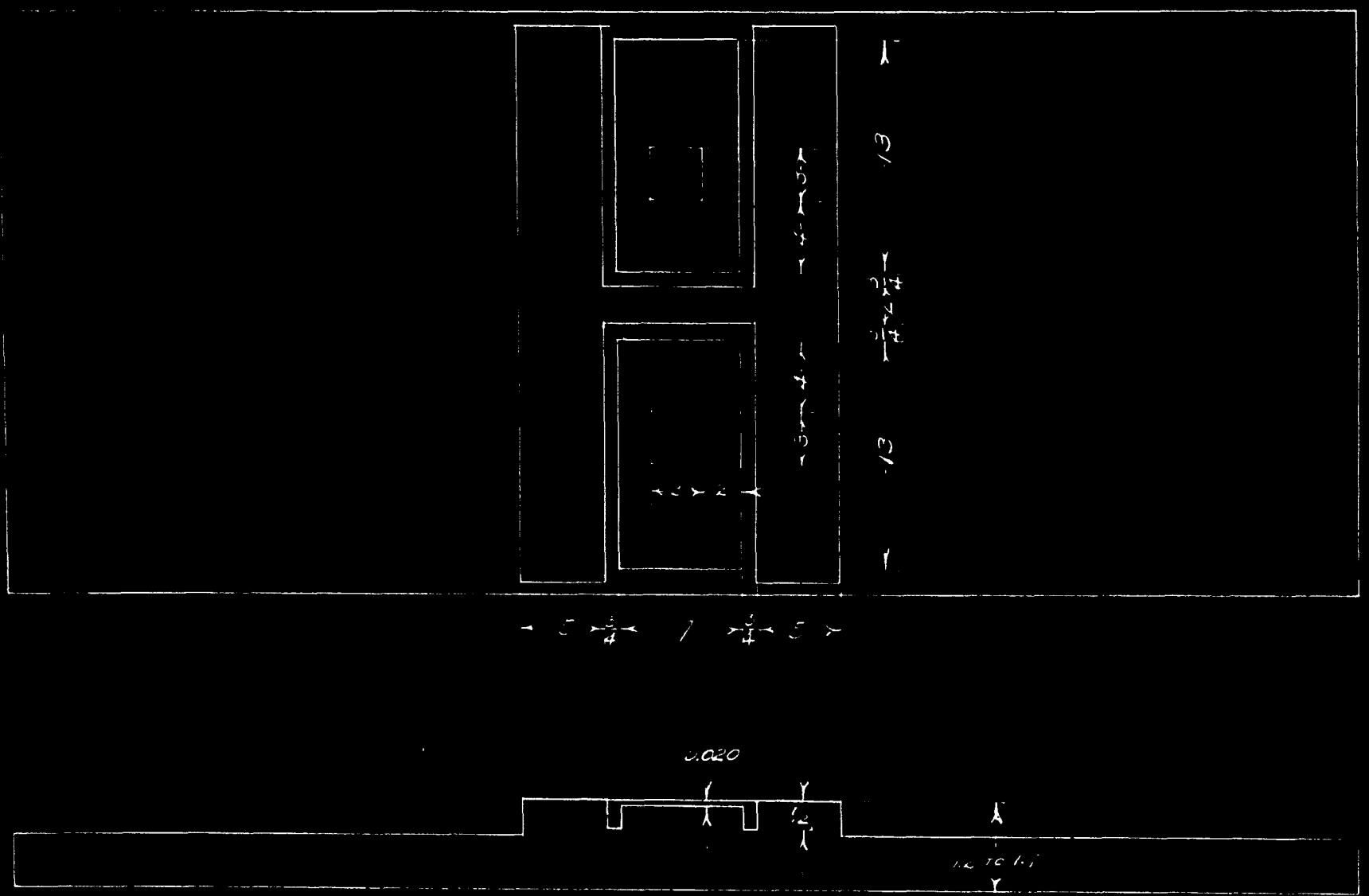
7. Lateral shoulders to be 5 to 6 mm wide.

8. Central shoulder joining the two lateral shoulders and separating the two platforms to be 2 mm wide.

9. NO metallic coating on the platforms.

10. Improved Neubauer rulings.* The center of the 3 mm square ruled area to be located 5 1/2 mm from the central edge of the platform and 3 1/2 mm from each lateral edge.

* If it is impossible to make accurate rulings without a metallic coating on the chamber we would consider bids for unruled chambers meeting all other specifications.



20 MICRON PYREX HAEMOCYTOMETER.

ALL DIMENSIONS IN MM. VERTICAL SECTION NOT TO SCALE.

RADIOIODINE SECTION

April 1950 to December 31, 1951

Earl R. Miller, M.D. - Chief of Section

The activities and purposes of the Radioiodine Program are:

a. The study of radiation effects produced by I^{131},

b. The evaluation of thyroid function in primary thyroid disease and other disease states,

c. The treatment of patients with benign and malignant thyroid disease,

d. The study of myxedema,

e. The follow-up of patients to whom I^{131} has been given,

f. The continued development of apparatus for more accurate and efficient counting and scanning of patients who have received radioiodine.

(See appendix for summaries of published papers on "Studies with Radioiodine")

a. The study of radiation effects produced by I^{131}.

The "normal" human is relatively resistent to acute effects of ingested I^{131}. In these, 25 mc of I^{131} or more is required to produce myxedema; 75 μc x 5 within about five months did not produce detectable changes in thyroid function; and no other organs studied (blood, kidney, liver) showed effects from doses as high as 50 mc. (See ref. 1 and 2 for effects of small doses; see ref. 3 for effects of large doses.)

Clinical and histological evidence of acute thyroiditis has been obtained from one patient to whom 75 mc of I^{131} was given when the patient was in the euthyroid state. This dose was given to the patient to destroy his remaining thyroid in preparation for possible treatment of the cancer of his thyroid. Other material obtained at operation and from autopsies

of patients to whom radioiodine was given has been and is being studied. These observations will be reported later.

Radioautographs were made on tissue from 123 patients between April 1950 and December 31, 1951, using the "tissue on NTB plate" technique in all but nine patients. These studies were performed on patients who were operated upon for non-toxic nodular goiters or carcinoma of the thyroid, and in certain cases of patients who had received I^{131} and who underwent autopsy before all the iodine had been excreted or had decayed. The studies were carried out for the purpose of determining where the I^{131} deposited in the various nodular goiters, in the normal thyroid tissue and in the carcinomatous tissue; and to study the effects of the radiations from I^{131} on the thyroid. This method was originally brought out by Titus Evans and was put into action on our program by Dr. Glenn Sheline. The method is used routinely now on all radioautographic studies with success. The NTB plates are calibrated for blackening and development by a white light exposure of four intensities on one end of the slide.

In the hyperthyroid patient, approximately 120 to 200 μc I^{131} administered by mouth per estimated gram of thyroid gland brought these patients out of their hyperthyroid state usually within a period of two to six months (4) (Appendix II).

In the patients with cancer of the thyroid, doses of 300 to 600 mc of I^{131} by mouth produced profound myxedema, hematologic effects, notably a marked reduction in platelet counts, no detectable changes in liver, kidney or gonadal function, while producing carcinostasis in several patients (5).

b. The evaluation of thyroid function in primary thyroid disease and in other disease states.

The clinician's evaluation of a patient's history, symptoms, and signs, plus his evaluation of the results of certain correlative laboratory procedures, constitutes the only available "measure" of thyroid function. The rate of I^{131} uptake in the thyroid in the first few hours after its administration was studied in a number of patients for some time before and after April 1950 and the results correlated with the clinical evaluation of their thyroid function. There is a good correlation between high early uptake and the presence of hyperthyroidism. The results of these studies were published. (6) (Appendix, I)

Studies of the RBC/plasma ratio of I^{131} as a function of time after I^{131} administration were undertaken with Dr. Kenneth G. Scott in patients with various thyroid diseases. This procedure is another test whose results have a high correlation with the clinical evaluation of thyroid function. The results of these procedures will be published.

Considerable thought has been directed toward the analysis of the problem and basis of the evaluation of thyroid function. The present clinical "measure" is uncertain and really deals only with the effect on the patient of the thyroid hormone and with conditions that mimic various thyroid states. There is no universally accepted sine qua non of the disease. All laboratory procedures however precise and accurate can, at best, have correlative significance with the uncertain clinical "measure". It is hoped that ultimately some combination of the more precise laboratory results will give us a statement of thyroid function. It would then be necessary only to determine from the symptoms and signs of the patient,

whether this level of thyroid function was "proper" for this patient or was producing "disease", rather than having to decide that (a) the patient is suffering from an abnormal thyroid and (b) that the abnormality is great enough to require therapy.

One or more evaluations of thyroid function were made on 87 patients between April 1950 and December 31, 1951 as the sole reason for our seeing the patient. The thyroid function evaluation is carried out by the independent clinical examination of the patient by a minimum of two physicians (usually three or four physicians do this) and the evaluation of the results of certain correlative laboratory procedures such as BMR, PBI, I^{131} uptake, and RBC/plasma ratio of I^{131} as a function of time after its administration. With the exception of the patients with non-toxic nodular goiters, most of whom had only radioautographic studies, the following new patients have had one or more evaluations of their thyroid function:

Thyroid evaluation only	87
Hyperthyroidism evaluation and treatment	50
Carcinoma of the thyroid, studied but not treated	29
? Carcinoma of the thyroid, studied but not treated	6
Carcinoma of the thyroid, autopsy specimen studied	3
Carcinoma of the thyroid, treated	12
Study and I^{131} thyroid destruction in patients with carcinoma of the thyroid	5
Non-toxic nodular goiter	55
Toxic nodular goiter	1
Thyroiditis	8

Miscellaneous studies

Obesity	11
Substernal goiter	7
Non-thyroid tumors	5
Non-toxic goiters	4
Myxedema	3
Others	5
	291

In addition, a number of patients accepted for study before April 1, 1950 had thyroid evaluations during the interval being reported upon, so that a total of 816 doses of I^{131} were administered to patients between April 1, 1950 and December 31, 1951. Each of these doses were followed by studies of the patient.

c. The treatment of patients with benign and malignant thyroid disease.

Treatment of patients with I^{131} is limited in this program to those with hyperthyroidism (in patients who do not have nodules in the thyroid) and to those with proved cancer of the thyroid.

The treatment of hyperthyroidism has been carried out since September 1946 in the present program. Between April 1950 and December 31, 1951, 50 patients have been given I^{131} for hyperthyroidism. The results of this method of treatment in the first 100 consecutive cases was published in August 1951 (4) (Appendix, II). The problem of dose of I^{131} for patients with hyperthyroidism was published in November 1951 (7) (Appendix, III). Before the studies leading up to the last paper were completed, patients were studied for a week, then treated with I^{131} if they needed it, and then studied again for a week. Since the dose studies were

completed, patients were seen in the morning, studied for the day, treated in the afternoon if they needed it and were permitted to return home in the afternoon. Complete reevaluation and retreatment, if necessary, is carried out 8 weeks, 16 weeks, 24 weeks, etc., after the treatment dose. The patients with hyperthyroidism are given 120 μc of I^{131} by mouth per estimated gram of thyroid. The results obtained with this method seem to be as satisfactory as were those which followed the longer and more complicated study.

Between April 1, 1950 and December 31, 1951, forty-nine patients, with proved carcinoma of the thyroid, have been seen and studied. Of these, 12 underwent treatment of their tumors with I^{131}. In addition, 6 patients with tumors possibly of thyroid origin were studied.

Of the 12 patients who were treated

3 are dead

4 were improved and still alive

3 were questionably improved

2 were not helped but are still alive.

Patients with proved carcinoma of the thyroid whose disease has spread beyond hope of surgical cure and who have objective evidence of the disease are accepted for treatment. Our present method of handling these patients can be outlined as follows: The patient is given 2 mc of I^{131} as a test dose. The uptake in the thyroid and in any obvious lesions and the urinary output of I^{131} is studied for 48 hours. At the 48 hour time a "scan" of the patient is made for more detailed information about the uptake of I^{131} in the neck and over any known lesions. Usually the chest is scanned in any case. During the 48 hour I^{131} study, the following determinations and procedures are carried out: Blood count, BMR, PBI, BSP,

bone marrow, Addis count, thymol turbity, uric acid, creatinine clearance, photograph, necessary x-rays usually including a chest, and clinical examination of the patient. At 48 hours a biopsy is obtained if possible in order to obtain radioautographic studies of the tumor. This biopsy is frequently obtained at the time of as complete a removal of the thyroid as possible. The patient is then given 25 to 100 mc of I^{131} depending upon circumstances. The patient is completely reevaluated each month as above (with the exception of bone marrow studies which are done every 2 months, and biopsy which is done as often as feasible). The treatment schedule is continued on a monthly basis of 100 mc of I^{131} by mouth as long as (a) there is evidence of uptake in the lesions and (b) there is evidence of no alarming symptoms or signs or laboratory evidence of abnormality severe enough to make us stop treatment. After conclusion of treatment, the patient is made and kept euthyroid by thyroid medication. Several patients have shown marked blood count changes. The platelets particularly have shown remarkable reduction after therapy. Discontinuance of therapy, time, and the administration of thyroid substance with the consequent loss of myxedema, and in some cases, transfusion have in all cases restored the blood picture to nearly normal limits. For awhile, 50 mc of I^{131} was given every two weeks to patients with carcinoma of the thyroid. The most marked blood count changes were seen with this regimen. For the last few months, the 100 mc dose once a month schedule has been resumed. Not enough time has passed to permit us to see the effects of this change in regimen. The data on our patients with carcinoma of the thyroid are being studied and two papers are in preparation dealing with them. They will be published in Radiology when the studies are completed (3, 5).

d. The study of myxedema.

The need for the further study of myxedema grew out of the problems connected with the handling of p tients who are being treated for carcinoma of the thyroid with I^{131}. All of these patients become profoundly myxedematous. The blood changes, the metabolism of I^{131}, and the effects of myxedema, per se, on the tumor are all of interest and of major importance. Blood and I^{131} studies are being carried out on hypothyroid and myxedematous patients who have not been tr ated with I^{131} in order to see if the effects of myxedema can be separated from the radiation effects of I^{131}.

e. The follow-up of patients to whom I^{131} has been given.

Since the beginning of the pres nt I^{131} program in September 1945, 618 different patients have been seen. Of this number, those with hyperthyroidism and carcinoma present a follow-up problem. It is our custom to see patients who have had hyperthyroidism every 3 months for a year after they have become euthyroid and about yearly thereafter, and major effort of the Thyroid Clinic is directed toward this end. Dr. Dailey and Mrs. Louw have done a fine job with this.

f. The continued development of apparatus for more accurate and efficient counting and scanning of patients who have received radioiodine.

Scintillation counters have been in use in the program since the beginning of April 1950. These are about 30 times as efficient as the Geiger Counters previously used. A scintillation counter is mounted on a scanning unit which is in turn mounted upon an x-ray tube stand. The scintillation counter is connected to a scaling circuit which contains a count rate meter. The instantaneous count rate is recorded on a Speedomax recorder. The scanner carrying the scintillation

counter moves crossways over the patient at the rate of eight inches per minute. The Speedomax recorder paper moves at the same rate and in the same direction as the counter. The scaler has been rebuilt by Hugh D. Farnsworth and William Goldsworthy of James S. Norton's electronics group in the Radiation Laboratory in Berkeley, so that a single easily calibrated count rate meter is incorporated into it. The scaling factors of the scaler permit the use of various full scale readings from 3125 to 100,000 counts per minute with no significant variation from linearity throughout the scale. Three different time constants are available on the apparatus.

One other arrangement was tried before the present one was accepted. In this one, selsyn motors drove the scanner and the recorder paper at various equal rates. The system worked as expected, but the present system has greater flexibility and is therefore better.

The problem of collimating cones on the scintillation counters for use especially with the scanning device engaged our attention for a matter of several months. Several very efficient multichannel collimating cones have been made. Theoretical consideration of the multichannel collimators was undertaken by Dr. Robert R. Newell of Stanford. Work on these was carried out by Dr. William Saunders and the author. A paper has been prepared and is to be published soon in Nucleonics dealing with the design of multichanneled collimators. The present designs in use by Dr. Saunders and by us are highly efficient and very selective.

Summaries of published papers on "Studies with Radioiodine"

I. Function and Rate of I^{131} Uptake of Thyroid (6)

Data were collected on the I^{131} uptake in the thyroid during the first seven hours after its administration to five groups of patients. One group was considered clinically to have normal thyroid function and a second group was considered to be suffering from hyperthyroidism. An attempt was made to find a single quickly obtained value from the uptake curve in differentiating between these groups.

The uptake as given by the "%/hr." was tried first. It was calculated by taking the per cent of I^{131} collected by the thyroid during the first few hours after its administration and dividing it by the number of hours between administration and observation. Although this "%/hr." was dependent upon the time of measurement, it was as useful in these groups of patients as were the determinations of the basal metabolic rate, the protein-bound iodine, or the maximum uptake of I^{131} in the thyroid.

The absolute value of the uptake determined at any particular time between two and seven hours is of greater use than the "%/hr." in differentiating patients with hyperthyroidism from those without hyperthyroidism. This follows because of the variation of the "%/hr." with time. It has been found expedient to determine the uptake at one, three, and five hours and construct a curve with the data thus obtained. This provides three independent observations which serve as checks on one another and a curve which can be compared with the curve through the highest observations in the control group.

On the basis of the thyroid uptake during the first seven hours it was not possible to differentiate between euthyroid and hypothyroid individuals.

The results of the tests are unpredictable in patients with nodular goiters.

II. Treatment of Patients with Hyperthyroidism by I^{131} (4)

Data on the first 100 consecutive patients treated with radioactive iodine for hyperthyroidism at the University of California Hospital are presented. Methods of patient selection and treatment and the results of such treatment are given. The results of radioiodine therapy for hyperthyroidism in patients without nodular goiters are satisfactory. Follow-up studies of patients, up to five years in some cases, have shown a striking absence of recurrence. The number of patients rendered hypothyroid by this treatment is not more, and may be less, than following surgery. Further experience may permit us to reduce the incidence of this complication. No untoward effect of the treatment, except hypothyroidism, has become

evident in the follow-up of this group of patients.

The place of radioiodine in the therapy of hyperthyroidism is considered.

III. Problem of Dosage in the Treatment of Hyperthyroidism (7)

Since the treatment of hyperthyroidism by radioiodine is essentially radiation therapy of the abnormal thyroid, it would be advantageous if the proper radiation dose to the thyroid could be predetermined and could be expressed in roentgens. This paper deals with attempts to accomplish this. A test dose of I^{131} was given to the patient, the thyroid uptake curve was determined, the thyroid weight estimated, and the amount of I^{131} necessary to give the predetermined dose calculated. When this amount of radioiodine was given to each of a number of patients, it was found that the "preselected" radiation dose as calculated from the test dose uptake curve frequently differed from the "actual" radiation dose as calculated from the uptake curve of the therapeutic dose. These differences were dependent upon changes in effective half-life and maximum uptake between test dose and therapeutic dose.

A study of the results of treatment of hyperthyroidism by I^{131}, with the dose expressed in terms of microcuries per estimated gram of thyroid, showed that some remissions were achieved and that no hypothyroidism was produced by initial doses of 90 to 129 microcuries per gram. Treatment of a series of patients has accordingly been started with 120 microcuries per gram of thyroid as an initial dose. To date this dose of radioiodine seems satisfactory for the first treatment of hyperthyroidism in patients with diffuse toxic (not nodular) goiters. If necessary, subsequent doses of radioiodine are administered, their size being based on the response of the patient to the first dose.

BIBLIOGRAPHY

(1) Thyroid Function in Mental Disease; Am. J. of Psychiatry, Feb. 1950, Karl M. Bowman, M.D., Earl R. Miller, M.D., Morris E. Dailey, M.D., Alexander Simon, M.D., Berdeen Frankel, M.D.

(2) Thyroid Function in Mental Disease. A Multiple Test Survey; J. of Nervous and Mental Disease, Nov. 1950, Karl M. Bowman, M.D., Earl R. Miller, M.D., Morris Dailey, M.D., Alexander Simon, M.D., Berdeen Frankel, M.D.

(3) Paper in preparation.

(4) Studies with Radioiodine. II. Treatment of patients with Hyperthyroidism by I^{131}; Radiology, Vol. 57, Pages 227-33, Aug. 1951, Earl R. Miller, M.D., Morris E. Dailey, M.D., Mayo H. Soley, M.D., Nadine Foreman, M.D., A. V. Holmes, M.D., George L. Alexander, M.D., and Glenn E. Sheline, M.D.

(5) Paper in preparation on treatment of cancer of the thyroid with I^{131}.

(6) Studies with Radioiodine. I. Function and Rate of I^{131} Uptake of Thyroid; Radiology, Vol. 57, No. 1, Pages 37-46, July 1951, Earl R. Miller, M.D., Morris E. Dailey, M.D., A. V. Holmes, M.D., G. L. Alexander, M.D., G. E. Sheline, M.D.

(7) Studies with Radioiodine. III. Problem of Dosage in the Treatment of Hyperthyroidism; Radiology, Vol. 57, No. 5, Pages 720-28, Nov. 1951, Earl R. Miller, M.D., and Glenn E. Sheline, M.D.

PHYSICS SECTION

Report to December 31, 1951

Gail D. Adams, Ph.D. - Chief of Section

Since the Physics Section of Contract AT-11-1-GEN-10, Project #2 was not instituted at the time of the last progress report formulation, the following will be a complete history of activities and accomplishments of this Section from its inception to December 31, 1951. The 70 Mev synchrotron had been ordered and the Radiological Laboratory Building had been planned earlier.

Starting in May and continuing through December 31, 1950, the present Senior Investigator of this Section was employed in a consultative capacity without salary. In May and again in November, 1950, he was brought to San Francisco to assist in the formulation of plans for the occupation of the Radiological Laboratory Building, and for the detailed planning of the synchrotron program. During September, 1950 he also visited the General Electric Company at Schenectady, New York, for the purpose of understanding the design, construction, and operation of the 70 Mev synchrotron and of observing the current stage of completion. At that time, the magnet and pole laminations had been stacked, exciting coils fabricated, capacitor rack assembled, and the vacuum tube finished and tested. Other components were all at least started and in various stages of completion or testing. Those components subcontracted outside the General Electric Company had completion dates well in advance of the then target date for the start of overall tests (December 1, 1950). It is a matter of history that the actual testing started April 4, 1951.

During this period also, some of the program details were converted into lists of supplies and equipment which would be needed to

prosecute the program effectively. These lists were sent to San Francisco for issuance of purchase orders. Much of the equipment so listed could not be ordered for lack of a person in San Francisco who could assist in choosing among the offerings secured by the Purchasing Office.

The Senior Investigator was employed in a full time capacity in San Francisco as of January 1, 1951. He was then able to make procurement decisions and much time was so spent during the first half of 1951. In addition, many details of the synchrotron program were outlined. Specification and ordering of much of the furniture and the like for the building were also accomplished.

The Senior Investigator spent six weeks in Schenectady during the latter half of March and April, 1951, observing and assisting in the operation tests on the synchrotron. Particular attention was paid to the details of the magnetic field and other magnetic conditions relative to the operation of this device. Although not perfect, all magnetic characteristics appeared to be satisfactory, but some required corrections to be continuously applied and these were built into the machine. The last and overall test would be the production of x-rays. The first attempt resulted in the opening of a vacuum leak, apparently due to rigid coupling of magnet vibrations to the vacuum tube. It was apparent that the engineering required to minimize the rigidity of this coupling would take at least two weeks to design, fabricate, and test. In consequence, the Senior Investigator returned to San Francisco without witnessing x-ray production in Schenectady. The company planned to run the synchrotron with x-rays being produced for some 300 hours as proof testing before shipment. At least the majority of this test was witnessed by Mr. W. A. Rutz of the

Radiation Laboratory, Berkeley.

A Senior Accelerator Technician of considerable experience elsewhere was hired as of July 1, 1951. Being an engineer by training, his services have been invaluable in the design details of equipment to be fabricated in the laboratory shop. A Junior Physicist and a Senior Laboratory Mechanician were hired in August. The Mechanician has been able to convert the tools supplied into a working shop and has produced a number of components for use on the synchrotron and in the experimental programs of all sections of the project. Both physicists and the technician have observed and assisted in all stages of the synchrotron installation.

The synchrotron arrived in San Francisco August 27, 1951. The rigging and interconnection subcontracts were handled by the Radiation Laboratory, Mr. Ruts being the field supervisor. Mr. R. N. Edwards, synchrotron project engineer from Schenectady, arrived in San Francisco on about November 1, 1951 and x-rays were produced first on November 9. Very soon, two major problems appeared which have not been solved by December 31, 1951. These were (1) irregularities in the vacuum pumping control system and (2) destruction of injectors apparently caused by vibration coupled from the magnet to the vacuum system.

By November 21, 1951, the initial yield in the center of the beam as measured by a Victoreen thimble encased in a one-eighth inch lead had been increased to at least 1100 r per minute at one meter from the target. The filament of this first injector lasted 20 hours. All told, as of December 31, 1951, seven injectors have succumbed with a total filament life of 136 hours. Of these, three manufactured by the General Electric Company lasted a total of 64 hours and four made by the Radiation

Laboratory, Berkeley, lasted 72 hours. Although the average lifetimes are similar, the variations are large.

A critical examination of the vibration problem was made using first a light-beam magnifier and later a crystal accelerometer. The results, although not unequivocal, showed substantial vibration forces and amplitudes at the injector which were apparently coupled to the vacuum tube via the vacuum pump lead connection. Palliative measures were developed and installed. Their adequacy will not be known for some time to come.

Occasional use has been made of the x-rays produced. A preliminary test of x-ray films has shown that Eastman Industrial, Type M is nearly linear in blackening response to ionization delivered whereas Eastman No-Screen deviates appreciably from linearity. Ordinary medical x-ray film was shown to be very non-linear. There is no large-scale electron contamination of the x-ray beam. Using Industrial Type M and assuming precise linearity, the beam shape at 70 Mev was measured and found to have a full width at half maximum intensity of two degrees. From this beam shape and known absorption coefficients, a compensating filter has been designed and constructed. Because the aperture system as supplied with the synchrotron is not coaxial with the x-ray beam, it has not yet been possible to test this filter.

It appears that the maximum tissue dose available at one meter will be about 100 r per minute. The focal spot is about one millimeter high and is negligible in width. The light beam furnished with the synchrotron has been adjusted. It has been found useful for localizing the position to be occupied by the x-ray beam but requires the room to be

darkened. A few circuit modifications have been made to improve the overall operating characteristics of the synchrotron but otherwise the electrical behavior seems entirely satisfactory.

Various problems in the vacuum pumping system have consumed at least half of the man-hours since pumping started on October 25. By December 31, every valve had been revised at least once and then rebuilt. Certain anomalies in the control circuit require further revisions which have been designed and will be made when new parts are available. It is felt that the system is well designed but poorly engineered.

On December 31, the Physics Section finds itself with a presdwood phantom complete, a water phantom nearly complete, a vacuum calorimeter designed with construction to start soon, and means available and tested for counting induced activities as required by the program. In a word, this section is ready to start serious work but will not be able to start until the synchrotron operates well enough to be accepted from the manufacturer.

The members of this section have served all other sections of the laboratory in a consultative capacity, occasionally contributing calculations and techniques. A laboratory seminar has been instituted and the first series of lectures deals with the concepts and language of physics, pertaining particularly to radiations, both ionizing and otherwise.

An experimental program has been outlined in sufficient detail so that necessary groundwork will delay the start of irradiations of biological specimens as little as possible. No more than two months should elapse between acceptance of the synchrotron and the first biological irradiation. It is expected that the Physics Section will occupy about half of the synchrotron's operating time for the first year's operations.

BIOLOGY SECTION

Report for period ending December 31, 1951

Henry I. Kohn, M.D. - Chief of Section

The Biology Section of the Radiological Laboratory was formally established in February, 1951, but had no quarters until the Radiological Laboratory Building was read for occupancy late in September. The calendar year of 1951 was therefore chiefly one of planning and procurement.

To contribute to the radiological treatment of cancer is the objective of the Biology Section, and it's work is therefore oriented toward the clinical problems of the radiotherapist. During 1951, a research program for the next two years was elaborated in some detail. The first item on this program is to compare the effectiveness of the x-rays from the 70 million volt synchrotron with those from therapy machines now in general use. Such information will be helpful in deciding what dosage should be used in the clinical trials. The comparisons will be made using a variety of biological materials, including the normal and cancerous tissues of small laboratory animals, the chick embryo, and various microorganisms.

The equipment and supplies required for the initiation of this program are now on hand, including cages specially designed for the limited storage facilities available, a 250 kv x-ray machine and animal exposure cabinet, microscopes, glassware, chemicals, incubators, etc. Breeding stocks of rats especially suitable for cancer research have been obtained from the National Cancer Institute (Fisher No. 344) and from Professor W. F. Dunning of the University of Miami (A x C Line 9935). A breeding stock of mice has been established at the Cancer Research

Genetics Laboratory of the University in Berkeley. Lines C and A are being crossed, and the F-1 generation will be used in the first series of experiments. These genetically controlled lines are suitable for general laboratory work. In addition, since they show a low, relatively constant incidence of breast and pulmonary cancers, it will be possible to study the effect of radiation, and of other factors, upon the time of appearance and upon the incidence of these tumors. For the work with unicellular organisms, some 25 different species have been obtained, representing various degrees and kinds of metabolic specialization. The relative suitability of the members of this collection for radiation studies is now being determined.

Arrangements for collaboration have been made with members of several other departments of the University. Dr. Kenneth DeOme, head of the Cancer Research Genetics Laboratory at Berkeley, will serve as a consultant in genetics and will collaborate in the experiments relating radiation sensitivity to genetic type. In addition, Dr. DeOme's laboratory is supplying all of the mice to be used, and will care for those mice surviving exposure to radiation that are to be observed until death. Dr. Timothy Crocker, of the Department of Medicine, and Dr. John Boland, a visiting Cancer Society fellow from England in the Department of Radiology, will collaborate in experiments involving the radiation-sensitivity of the chick embryo and of certain mammalian tumors.