"Preliminary Copy"

THE ACTIVITIES OF THE ADMINISTRATIVE OFFICE

714085

J. H. Harmon

In the spring of 1955 the Medical Division directed a major effort toward preparations for the Geneva Conference on the Peaceful Uses of Atomic Energy. Upon an invitation from the United Nations, eight papers were presented for review and possible acceptance for oral presentation at the conference. Four of the papers were accepted for publication and each paper was then retyped for direct reproduction. The design, fabrication, and purchase of equipment for exhibits added appreciably to the administrative effort.

During the year the Division received a total of 376 visitors. Many of these were at the hospital for more than one day and the estimated visitor day averaged approximately 2 per work day. Approximately 87 of the visitors were from foreign countries. In addition to these casual visitors, 11 other foreign visitors worked at the Medical Division facilities for an accumulated total of 225 man weeks. Four of this number were employed as resident physicians, and the remaining seven obtained their support from other sources.

During June, July, and August ten visiting scientists availed themselves of the Medical Division's research facilities. The majority of these people were Research Participants assigned to this division by the University Relations Division of the Institute. The Medical Division paid no salaries but did provide laboratory facilities, equipment, materials, and supplies.

During this calendar year the Division has been in a construction program. The year saw the completion of the clinical research and out-patient facilities, which contain rooms for 6 hospital beds, 4 offices, a patient recreation room, a cobalt 60 teletherapy room, and a medical physics room. The capital projects budget was so limited that it was necessary to use operating funds to complete these facilities. This procedure created a number of budgetary problems in FY-55 and FY-56. During the summer and fall plans were developed for a clinical training building of approximately 2,200 square feet. This building will contain special equipment and facilities for the training of visiting medical personnel. The plans and specifications were announced for construction bids in late December; every effort will be made to complete and equip this unit in time for the third week of the advanced medical course.

During the year the research program required the use of 25 radioisotopes or a total of 12.2 curies of radioactive materials. The teletherapy program required 1.5 curies and the balance of radioisotopes were used in basic research and in patient care and treatment programs.

During the year 81 patients were admitted to the research hospital and 153 former patients were readmitted. The average daily patient census was 12.5. The first admission patients came from 12 states as follows:

State	In-Patients	Out-Patients
Ohio	1	
North Carolina	19	2
Florida	8	
South Carolina	2	
Tennessee	39	10
Virginia	4	
Kentucky	1	

State	In-Patients	Out-Patients
Alabama	3	
Michigan		1
West Virginia	1	
Georgia	2	
Mississippi	1	

The volume of records on patients has grown to such an extent that file references and cross-indexing methods had to be examined and a new system established. This new system will require a major effort of the medical records section during the first part of 1956.

The Medical Division staff remained at about the same level as for 1954. The total employees averaged 67 for the year and this represented an average of 61 regular employees; 3 residents, and postresidents in radiology; one part-time employee; and two temporary employees. In the fall of this year an extensive recruitment program was necessary to replace Dr. Ralph Kniseley, Pathologist, who resigned to accept another position. An unsucessful effort was made to employ a clinician to fill the position left vacant when Dr. Malcolm Tyor resigned in June 1954 to enter private practice.

During the year there was an average of 88 purchases per month for equipment material and supplies. In addition to these purchases there was an average of 79 issues per month from the ORINS warehouse. There was a total of 125 shop orders for technical services.

During the fiscal year ending June 30 of this year the Division spent more than the authorized budget ceiling. The authorized operating budget for FY-56 has a fixed ceiling. At the end of November the Division had spent more than the budgeted expenditure for the 5 month's period. The over-expenditure resulted from expenses connected with the Geneva Conference and extraordinary expenses from the Technical Services Department in completing the clinical research and out-patient facilities. In order to recover this overexpenditure, it will be necessary to maintain a lower than usual average monthly cost ceiling for the remaining seven months of this fiscal year.

And administrative reorganization plan for the Division was presented at the fall meeting of the Board of Directors. This plan was designed to relieve the division chairman of many routine administrative details and to redefine the areas of responsibilities. This plan provides for a Chief of Clinical Services; Chief of Laboratory Research; Chief of Biomedical Research; and Chief of Medical Physics. The general organization chart has been completed and the detailed chart is now in preparation.

PROCEEDINGS OF THE SECOND ADVANCED COURSE IN THE USE OF ISOTOPES IN MEDICINE

Elizabeth B. Anderson

The Proceedings of the second advanced course in the use of isotopes in medicine is at the Government Printing Office in the final stages of publication. The title is "Radioisotopes in Medicine", and the editors are Gould A. Andrews, Marshall Brucer, and Elizabeth B. Anderson. Forty-two speakers have contributed 45 chapters. The other three chapters are the three evening clinics. The discussions of the talks have been grouped into 18 discussion sections.

The 804 two-column, 8" x 10" pages are illustrated with 569 line drawings and half tones. In addition to the lists of references at the ends of chapters, a general bibliography arranged in what we believe to be workable categories has been included. From abcesses to zinc 65 the book has been indexed in considerable detail.

In order to keep the price from being completely beyond the reach of most isotope users, we have consented to a paper back. It is of sturdy construction, however, and may be bound in hard covers if the ownder wishes to send it to a bindery. Announcements will be made when the price is set and publication is complete. It will be available from the Superintendent of Documents, Washington 25, D. C.

LIST OF PUBLICATIONS OF THE MEDICAL DIVISION
RECEIVED BETWEEN JULY 1 - DECEMBER 31, 1955

Bahner, Carl Tabb

Effect of Compounds Related to 4-(p-Dimethylaminostyryl) quinoline Methiodide on Lymphoma 8. Cancer Research 15, 588-592, October 1955.

Brucer, Marshall

Teletherapy Devices with Radioactive Isotopes. International Conference on the Peaceful Uses of Atomic Energy. A/CONF.8/P/179, USA, June 23, 1955.

Brucer, Marshall, Eldridge, James, and Trombka, Jack

Thyroid Radioiodine Uptake Calibration. International Conference on the Peaceful Uses of Atomic Energy. A/CONF.8/P/196, USA, June 23, 1955.

Comar, C L.

Radioisotopes in Animal Physiology and Nutrition - Mineral Metabolism. International Conference on the Peaceful Uses of Atomic Energy. A/CONF.8/P/90, USA, July 1, 1955.

Andrews, Gould A., Kniseley, Ralph M., Palmer, Etna L., and Kretchmar, Arthur L.

Therapeutic Usefulness of Radioactive Colloids: Comparative Value of Gold 198, Chromic Phosphate (P 32), Yttrium 90, and Lutecium 177. A/CONF.8/P/184, USA, June 23, 1955.

Harris, Norman O. and Hayes, R. L.

A Tracer Study of the Effect of Acute and Chronic Exposure to Sodium Fluoride on the Thyroid Iodine Metabolism of Rats. Journal of Dental Research 34, 470-477, August 1955.

Hayes, R. L., Brucer, Marshall, and Arakawa, Edward

Some Integral Dose Relationships in Co 60 Teletherapy. Abstract 64. Radiation Research 3, October 1955.

Brucer, Marshall

Special Report of the Medical Division on Teletherapy Design Problems. I. Cs 137. TID-5086 (2nd Rev.) May 15, 1955. Available from the Office of Technical Services, Department of Commerce, Washington 25, D. C. Price: 40 cents.

Brucer, Marshall, Kerman, Herbert D., and Richardson, Jasper E.

Teletherapy Design Problems II. Cobalt 60 Teletherapy Unit. ORO-109. 1953. For sale by the Superintendent of Documents, United States Government Printing Office, Washington 25, D. C. Price: 35 cents. Second printing.

Brucer, Marshall and many others

Teletherapy Design Problems III, with supplement: Proceedings of the Third Industrial Conference on Teletherapy. ORO-127 and ORO-127 (Suppl.)1954 . For sale by the Superintendent of Documents, United States Government Printing Office, Washington 25, D. C. Price: 50 cents and 35 cents. Second printing.

Brucer, Marshall

Teletherapy Design Problems IV. Isodose Charts for the Co 60 Hecto-curie Teletherapy Machine. ORINS-10, March 15, 1955. Available from the Office of Technical Services, Department of Commerce, Washington 25, D. C. Price: 75 cents.

CLINICAL STUDIES

G. A. Andrews
Etna L. Palmer
A. L. Kretchmar
Betty M. Cooper
R. M. Kniseley*

STUDIES WITH I 131

Previously reported studies on the destruction of the thyroid gland with I 131 are being continued. A series of new histologic specimens is available on patients with multiple myeloma who are given large doses of I 131 and whose thyroid glands showed varying degrees of radiation damage.

The long range study of thyroid carcinoma continues, with increased use of the scintiscanner and improved external counting methods in an effort to understand more clearly the behavior and distribution of radioiodine. Histologic specimens and autoradiograms showing the distribution of the isotope in the lesions are obtained wherever possible. Two unusual cases of thyroid carcinoma in children showing a peculiar clear cell transformation after removal of the normal thyroid have been carefully studied and a report on them is in preparation.

Selected patients with hyperthyroidism and with heart disease are being treated with radioiodine. Several types of special studies have been done on these patients. One of these is to follow the protein-bound radioiodine in the plasma at daily intervals for periods of 10 days after each tracer and therapeutic dose. This is being done in an effort to determine whether or not the therapeutic dose will produce a significant abnormal release of protein-bound iodine material and, if so, whether the quantity of this material released into the blood stream can be used as an index of the effectiveness of the therapeutic dose.

A series of patients having received radioiodine were studied for the salivary iodine excretion over a period of many days after each dose; this program was chiefly carried by Dr. Zeth Gabrielsen, a visiting resident from Norway. The concentration of the isotope in the saliva was compared with the free and protein-bound isotope in the plasma. All of the data, which are being prepared for publication, indicate that the concentration of the isotope in the saliva derives entirely from the unbound form in the plasma. No evidence has been produced to support the theory that the salivaries play an important role in breaking down iodine-containing organic compounds.

The effort to treat multiple myeloma with large doses of radioiodine has in general been unsuccessful. Slight temporary improvement in some patients has been seen but has not been considered to be of sufficient degree or duration to justify recommendation of this form of treatment. Detailed autopsy studies on several patients with radioassays and autoradiograms has failed to indicate any tendency for the myeloma lesions to concentrate the radioiodine. It appears that any benefit obtained is a result of the rather generalized radiation produced.

Special external counting studies (see section on Medical Physics) on the thyroid with the scintiscanner and with various uptake measuring devices have

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* Present address: Department of Pathology, Eden Hospital, Castro Valley, California.

been continued. The old type of scintiscanner with a simple cylindrical collimation and a small crystal has proved to be of distinct value in studying certain types of isotope distribution pattern. Perhaps its greatest single usefulness has been in evaluating the location of areas of functioning tissue in the neck of patients with thyroid carcinoma. The scintiscanner has frequently made it possible to differentiate between residual normal and areas of carcinoma. We have been unable to confirm, however, the reports of success in delineating small hyper- and hypofunctioning lesions in the thyroid gland. It appears to us that the old type of scintiscanner is considerably less discriminating than it has been reported to be. We have seen examples of adenomas showing distinct differences in function from normal tissue but not detected by the scintiscanner. There has been some success in delineating the criteria for evaluation of scintiscan records, and describing the cause of artifacts. The instrument has been found useful in many isotopes other than radioiodine.

An improved scintiscanner developed by P. R. Bell, J. E. Francis, Jr., and C. C. Harris has been given limited trial and shows great promise. Its chief virtues are a high degree of sensitivity, relative freedom from inverse square law effect, and fine discrimination.

Another instrument developed largely by P. R. Bell and the group working with him is a probe counter for surgical procedures. This has been found to be of distinct value chiefly with radioiodine.

ROSE BENGAL TAGGED WITH I 131

Work has begun, and is continuing, on the evaluation of Rose Bengal tagged with I 131 as a liver function test. This program is being carried out by Dr. Warren Glaser and other members of the staff. The experiment has been divided into two parallel and simultaneous determinations.

1. The first part of the work has involved (a) injecting Rose Bengal I 131 intravenously into selected patients admitted to the clinical service. The surface of the liver has then been surveyed with the medical spectrometer and a permanent record has been obtained on a Brown or Esterline-Angus recorder. (b) The data obtained are correlated with the liver chemistries and the clinical condition of the patient at the time of testing.

2. The second part of the work involved injecting Rose Bengal I 131 into adult rats and sacrificing them at appropriate intervals. The livers are then assayed for I 131 activity and gross and microscopic autoradiograms are made. Other tissues such as the gastrointestinal tract and spleen are also assayed.

At this time it is too early to attempt to make a direct correlation between the curves obtained on liver survey and the various diseases of the liver. There are, however, definite indications that the shape of the curve (time necessary to reach maximum activity, the absolute height of the curve, the plateau and slope of the excretion portion) is altered by both intrinsic and extrinsic hepatic disease.

The technique for microscopic autoradiography of the liver is still to be refined. However, preliminary data suggest that the radioactivity does diffusely locate in the hepatic cells and is not concentrated in the Kupfer cells. More careful resolution is necessary before a final evaluation can be made.

BONE-SEEKING ISOTOPES AND OSTEOGENIC SARCOMA

A study of osteogenic sarcoma has been continued and a considerable number of patients have been followed throughout the course of the disease. The use of gallium has not been continued during the last six months but P 32 and other isotopes have been given for the purpose of the study of their distribution in lesions. Several patients have been subjected to repeated surgical procedures by Dr. George Minor of the University of Virginia for removal of pulmonary metastases although this appears to be a rather discouraging therapeutic approach. Because of the multiplicity of metastases in most cases, several patients have shown evidence of significant palliation and further study of the operation appears worth while. One of the unusual findings in this group of currently studied patients is that metastases in the chest wall occur rather frequently. The mechanism of their production is obscure.

STUDY OF COLLOIDS AND RARE EARTH ELEMENTS

A continuous study has been made of patients having fluid accumulations as a result of metastatic neoplasms. Efforts have been made to determine the therapeutic usefulness of yttrium 90 and lutecium 177 as isotopes for intracavitary injection, in close cooperation with Dr. Kyker and other members of the staff working with basic biochemical and animal studies. Complete evidence has been collected indicating that these isotopes remain well localized in the region of the cavity and from a point of view of metabolism and distribution are highly suitable for this type of therapy. It is not yet possible to state their relative merits in comparison with colloidal gold 198 or chromic phosphate (P 32). Neither do we know the doses of yttrium and lutecium necessary to produce an adequate radiation effect. Continued studies on this problem are in progress.

Studies of plasma disappearance and distribution after intravenous administration of these materials have also been performed. A preliminary report on this work was given at the Rare-Earth Conference.

STUDY AND TREATMENT OF HEMATOLOGIC DISORDERS

In addition to continued use P 32 for certain patients with polycythemia vera and the continued study of intravenous colloidal gold 198 in chronic granulocytic leukemia, certain selected patients have been studied with iron 59 and chromium 51 in an effort to gather more information about isolated clinical cases of interesting blood disorders. One of these patients, studied in great detail, is a man with aplasia of the erythrogenic elements of the marrow, without much disturbance of granulopoiesis or thrombocyte formation.

TRAINING PROGRAM

The clinical staff of the Medical Division continued to assist in the teaching of the basic courses given by the Training Division of the Institute. During most of the one-month basic isotopes technique courses a clinical program

involving three or four afternoons plus one lecture was carried out. There were also special lectures in other parts of the Training Division Program including a regular lecture in the courses for veterinarians given by Dr. Kretchmar.

The clinical staff of the Medical Division continued to maintain an active training program. For the first time the one-year approved residency in internal medicine (experimental clinical medicine) has been filled. There are now two residents on this program, one who began in July and one who began in October.

The short-term three and four months residencies were filled by a variable number of individuals during the year; usually one or two persons were working in this category at any one time on the Medical Division Program.

A medical student who had finished his junior year was employed during the summer as an extern. The training opportunities in this relationship were also emphasized. A postresident assistant in radiology worked with a division of time, 50 per cent with the Oak Ridge Hospital and 50 per cent with the Medical Division. This position was filled by two individuals during the past year.

These training activities are carried on in a very informal way. The regular ward rounds are held three days a week, with emphasis upon the discussion of clinical problems and application of research techniques involving isotopes. In addition, a regular Thursday night conference was held as has been done from the beginning of the Medical Division Program. Informal teaching with resident groups was carried on in connection with isotope procedures on patients, outpatients problems, diagnostic problems, and special laboratory experiments.

GENEVA EXHIBITS

The clinical staff of the Medical Division along with other members of the Division participated in the preparation of a group of special exhibits to be sent to the Geneva Conference to be used in various teaching programs. These exhibits consisted chiefly of series of 35 millimeter slides arranged for automatic projection. Each subject was presented in a group of 48 slides. A total of 15 exhibits, with 48 slides each, was prepared by the Medical Division. The slides involved the use of material of various types of teaching material including pictures of patients, equipment, colored photomicrographs, blood smears, and X rays. These were grouped into a coherent presentation of subject by means of carefully worded labels on each slide plus occasional complete slides given over to textual material. Among the exhibits that involved the clinical staff of the program were the following:

1. Clinical use of colloids in rare earths in cancer therapy.
2. The effect of radiation on the thyroid gland.
3. The facilities of the Medical Division for investigation with radioisotopes of experimental medicine in the study of cancer.
4. Radioisotope techniques in the pathology department of the hospital.
5. Microscopic autoradiography.
6. Techniques for gross autoradiography.
7. Clinical use of the scintiscanner.

These exhibits have proved to be of considerable interest and have been shown repeatedly since they were prepared, sometimes being sent out as self-explanatory teaching material and at other times used totally or in part by members of the Division, as illustrated material for lectures.

OUTPATIENT PROGRAM

An increasing number of studies mainly of hematological diseases, is being made on an outpatient basis chiefly under the direction of Dr. Etna L. Palmer, with visits scheduled on Tuesday and Thursday mornings. Some of the polycythemia patients are treated entirely as outpatients. The others and the leukemia patients are admitted for treatment and are followed as outpatients. Certain anemias, Hodgkin's disease, lymphosarcoma, and some bone and thyroid cancers can be followed on an outpatient basis. A few consultations are done routinely.

Between December 15, 1954 and December 15, 1955, a total of 57 persons were seen as outpatients with a total of 357 outpatient visits. This averages almost 30 visits per month. Outpatients are mainly from Oak Ridge and the surrounding counties but some patients come from a distance. Twelve persons with leukemia were seen, 11 with polycythemia, 4 with cancer of the thyroid, 2 with bone cancer, 1 with multiple myeloma, 1 with infectious mononucleosis, and 1 with cirrhosis. Many others were routine consultations and follow-up visits on patients previously treated in the hospital.

VASCULAR PATTERN OF THE BONE MARROW

During 1955 Dr. Chiyeko Okawa completed her work with the Medical Division and returned to Japan. She had spent about two years with us on a Damon Runyon Fellowship. She had previously been in Oak Ridge as a short-term resident from the University of Alabama where she took a period of residency training under the sponsorship of a church organization. Following her work in Alabama she had returned to Japan for a brief period and then came back to the United States to fulfill her Damon Runyon Fellowship program. Her chief research interest was in the study of the vascular pattern of bone marrow by microangiographic techniques. This proved to be a difficult research problem because of the complications in dealing with the bony cortex in such a way that adequate specimens of the marrow areas could be obtained. She used a number of different techniques and with the help of Dr. Raymond Hayes, was able to develop a preparation of barium sulphate that had a very fine particle size and was suitable for showing the smaller capillaries and sinusoids. During most of her work she collaborated with Jack Trombka who had had previous experience with microangiographic techniques, particularly in connection with the choice of energy, development of exposure techniques, and choice of film.

Other methods were employed involving routine histologic techniques, special staining preparations, and the preparation of metal and latex casts of the larger vessels. Most of the studies were done on the femur of the rabbit, and a good deal of information on the vascular pattern of the marrow cavity was obtained. In addition to studies on the normal marrow pattern, some experiments were done to demonstrate the changes associated with irradiation, leukemia, and severe anemia.

AUTORADIOGRAPHY

During 1955 an active autoradiographic program was in progress. The autoradiographic work was done chiefly by William D. Gibbs and William C. Fields who worked in cooperation with many different members of the basic and clinical staffs.

During the year, 550 gross autoradiograms and 800 microscopic autoradiograms were prepared. The staff also lectured to six basic isotopes courses at ORINS Special Training Division. In October and November, Dr. Thomas Shockley, a professor from Meharry Medical College spent six weeks at the Medical Division learning autoradiographic techniques and interpretations.

The autoradiograms continued to prove extremely valuable in demonstrating radioisotope distribution. Some consideration was given to the comparison of autoradiographic information and radioassay information of isotope localization. Analysis of a group of gross autoradiograms obtained at autopsies, in comparison with radioassays on the same tissues, demonstrated that the radioassays are subject to a great deal of error and misinterpretation if they are not supported by autoradiographic data. This is particularly true when the distribution is uneven and when there are wide differences in isotope concentration within small areas of the tissue. It becomes apparent that the size of the sample used for radioassay may determine the results obtained and the values may be very misleading if in analyzing radioassay reports one tends to consider that the activity was uniformly distributed to the specimen assayed.

In the studies of radioactive colloids, particularly yttrium 90 and lutecium 177, the autoradiograms again proved their usefulness and contributed in a major way to the current research effort.

Preliminary work on a project to determine relative sensitivities of some films commonly used for gross autoradiography has recently been completed. The purpose of these experiments is to determine which film is most sensitive to the energy and type of radiation emitted from any given isotope.

PATHOLOGY

During 1955 the Medical Division lost one of its most valuable staff members when Dr. Ralph Kniseley resigned to take a position as associate pathologist in Eden Hospital, Castro Valley, California. During his period with the Medical Division, an interval of about four years, Dr. Kniseley did some excellent research, maintained a high level of service functions, and contributed greatly to the enthusiasm of the staff members. His mature viewpoint and sound judgment were important reasons for the pleasant relationships that existed between staff members during the time that he was in Oak Ridge. His research encompassed several varied projects. He was particularly interested in the histologic effects of radioactive colloids and also in changes produced in the thyroid gland and tumor tissue by radioiodine.

Dr. Kniseley was very active in autoradiography. During his period in Oak Ridge much information was amassed, particularly based on gross autoradiographic studies in patients who had been given radioisotopes and who came to autopsy. Much of this gross autoradiographic information has yet to be published.

Microscopic autoradiographic techniques were also studied actively and have been increasingly satisfactory technically and increasingly useful in the research program.

Dr. Harold Steffee has joined the Medical Division and the Oak Ridge Hospital to replace Dr. Kniseley. Dr. Steffee comes to Oak Ridge from the National Institute of Health and has been interested in research on carcinoma of the lung.

LABORATORY RESEARCH

RARE-EARTH STUDIES

INTRODUCTION

Granvil C. Kyker

Studies using radioisotopes of the lanthanons and yttrium have continued throughout the period of this report. The work has aimed mainly at extending the objectives included in the preceding Semiannual Progress Report (ORINS, Medical Division, period ending December 31, 1954, pp 1-12). The principal objectives include (1) the effects of the nature and the quantity of rare-earth carriers on the mobilization of radioactivity and (2) the comparative biochemical properties of various elements in the series.

INTRAVENOUS STUDIES OF RARE EARTHS IN DOGS

Granvil C. Kyker
John Rafter
Edgar Cress
Lewis Warren
Nelson Stevens

Three radioisotopes of the rare earth elements - lutecium 177, holmium 166, and neodymium 147 - have been compared in about twenty-five dogs. Each isotope was produced by activation of the natural rare-earth oxide with a similar procedure for processing (Semiannual Progress Report, Dec. 31, 1954, pp. 9-10). The radioactive product gave a preparation of the rare-earth chloride, rendered isotonic with additional sodium chloride, and adjusted to a pH slightly less than 4.0 for stability. The preparation was standardized by a beta-counting procedure.

The ionic preparations of radioactive rare-earth chlorides were administered intravenously to adult mongrel dogs. Blood samples were drawn at five minutes and at increasing intervals up to three times the half life of the isotope. Measurements by hematocrit and of radioactivity in whole blood and in plasma were made. Finally various tissues including bone, liver, spleen, lung, heart, and kidney were examined by gross autoradiography.

Carrier-free preparations of the isotopes were not available. The total dose was, however, varied from 10^{-7} to 10^{-4} moles per kilogram by production of the radioisotopes in the Low Intensity Test Reactor or the Oak Ridge Graphite Reactor (flux approximately 10^{13} and 10^{11}, respectively) or by the addition of stable carrier. In general, there appears to be an increased amount of radioactivity that circulates longer with increased chemical doses. An occasional exception occurs. Animals that received similar chemical doses showed a similar degree of duplicability. The localization seen in the autoradiograms of various tissues is consistent with reticuloendothelial mobilization. These records also reflect to some degree an effect of dose in which large aggregates of radioactivity are seen best at intermediate levels of rare-earth dose. Further analysis of the data is in progress.

A critical experiment in the comparison of different isotopes and different levels of dose is the simultaneous administration of two or more to the same subject. The methodology for this purpose has been studied and preliminary experiments have begun with radioholmium and radiolutecium.

RARE EARTH RADIOISOTOPES WITH HETEROGENEOUS CARRIERS

Granvil C. Kyker
Edgar Cress
John Rafter
Nelson Stevens

Previous reports have included specific studies of a radioisotope of one rare earth and stable isotope of another rare earth as carrier. There is much similarity in the effect of total rare earth dose to be seen among the various combinations that we have studied. For more conclusive evidence of the general nature of this effect we have chosen a commercial grade of mixed rare earth chloride (No. 340, Lindsay Chemical Company) as carrier. Convenient availability and half life influenced the selection of yttrium 91 over various isotopes of the lanthanons as the radioactive tracer. In five groups of mice the intraperitoneal dose of rare earth was varied from carrier-free yttrium 91 (less than 10^{-10} moles per kilogram) up to the limiting toxic dose (approximately 10^{-4} moles per kilogram). Similar to earlier results with specific cases, mobilization is sharply decreased with increasing chemical dose so that with the largest doses the radioactivity is almost completely confined to the injected cavity.

INTRAMAMMARY STUDY OF RADIOLUTECIUM IN DOGS

Granvil C. Kyker
W.M. Christopherson
H.F. Berg
Marshall Brucer

Previous results indicate that radiolutecium administered interstitially into the superior mammary gland of dogs is mobilized largely by regional lymph nodes with very little radiocontamination of adjacent tissue. By comparison, the intranodal distribution, although usually uneven, is at least as good as that seen for radiocolloidal gold 198. Also the lutecium appears to be tolerated better at the primary site of administration.

These studies are being continued in order to evaluate other factors that may improve the intranodal pattern of distribution. Factors under current evaluation are other levels of chemical dose and weak complexing agents. Further experiments are necessary to afford conclusions.

RARE EARTH RADIOISOTOPES AND TISSUE METABOLISM

Edgar A. Cress
Granvil C. Kyker

The similar internal behavior of different rare earth radioisotopes under the influence of the same heterogeneous rare-earth carrier affords a unique tool for studying the effects of different radiation characteristics at the cellular stage. With a carrier dose of 3 milligrams per kilogram, a large tracer dose of radioisotope will be less than 10^{-5} per cent of the total rare earth administered. Different radioisotopes representing different emitted radiations and different rates of decay can therefore be incorporated into the mixture with carrier without significantly changing the composition of the dose. The various combinations

that have been studied strongly suggest similar patterns of localization of radioactivity. Methodology is established and preliminary experiments are in progress to evaluate the effect of stable and radioactive isotopes of rare earth elements on the metabolic rate and capacity of rat liver following intravenous administration.

SELECTIVE IRRADIATION OF LYMPH NODES BY RADIOLUTECIUM (LU 177)*

Granvil C. Kyker
W.M. Christopherson
H.F. Berg
Marshall Brucer

The article presents chemical and physical properties, and radiation characteristics of lutecium 177. Dosimetric considerations provide a basis for its comparison with other radioisotopes of current medical interest. The preparation of the isotope in a reactor and its radiochemical processing to yield preparations for biological use are described.

The results of interstitial studies in the canine mammary gland afford certain conclusions. When a soluble salt of the radioisotope is injected interstitially, formation of the insoluble hydroxide occurs. With the amounts of carrier used, it behaves largely as a colloid and is mobilized to the reticuloendothelial system. When injected into the right superior mammary gland of dogs, it concentrates in the regional lymph nodes within a few hours. Its ionizing radiation is confined largely to these nodes. The radiation characteristics indicate that no appreciable radiation of other organs occurs. The concentration and dispersion of Lu 177 throughout a lymph node is at least as satisfactory as the concentration and dispersion of colloidal Au 198. The distribution observed with tracer doses and the dosimetric comparison of Lu 177 with other isotopes in medical use have suggested further studies of tissue damage by larger doses.

RARE EARTHS AND AMINO ACIDS

The circulating fraction of a dose of the various rare earths we have studied is regularly observed to be present in the plasma. This is true both soon and late following intravenous doses containing either large or small amounts of stable carrier. Soon after large carrier doses it is probable that a considerable amount of the rare earth is present as an aggregate of hydroxide resembling the dispersed phase of a colloid. After rapid removal of colloid by reticuloendothelial uptake, the small fraction that continues to circulate is probably combined in a soluble form. At both stages the rare earth, as traced by its radioisotope, remains stable in plasma during centrifuging. Binding of the metal could be either by protein or by simpler constituents. Stability constants of rare earth chelates reported for a few lanthanons indicates significant binding by certain amino acids. Two experimental approaches to this question have been pursued: (1) column chromatography and (2) paper electrophoresis.

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* Cancer, In press.

(1) AMINO ACID STUDIES USING COLUMN CHROMATOGRAPHY

Granvil C. Kyker
Martha Stewart

By means of a column of weakly acidic cationic exchange resin (Amberlite IRC-50 (H)) approximately 11 x 140 mm, approximately 5 micrograms of lutecium chloride containing Lu 177 tracer was studied with various elutriants, including acids, chelating agents, and amino acids. The radioactivity in 5 ml fractions of the eluate was measured. The minimal concentration of hydrogen ion that was observed to elute the lutecium stands between pH 2.8 and pH 2.6. This critical range of pH was observed for hydrochloric, lactic, and acetic acids. Similarly, acetate-veronal buffer at pH 2.87 failed to remove the lutecium from the resin. The chelating agents were used at 0.001 M. Both versene and versenol in acetate-veronal at pH 3.2 gave quite rapid removal, the rates being almost equal or slightly faster for versene. Citrate was much slower and antipyrine was almost ineffective. Three acidic, three basic, and six intermediate amino acids in 0.001 M solutions buffered at pH 2.87 (acetate), pH 5.5 (acetate), and pH 7.32 (veronal) were tried. Fast removal occurred with arginine, slow with histidine, and none with any of the others. At higher concentrations (0.01 M and 0.05 M), aspartic acid and lysine at pH 2.87 also removed the activity.

(2) AMINO ACID STUDIES USING PAPER ELECTROPHORESIS

Renaat Loos*
Gould A. Andrews
Granvil C. Kyker

Part of the radicactivity in ascitic and body fluids of patients having received radiolutecium undergoes electrophoretic transport in veronal buffer at pH 8.6. The nature of the transporting agent is unknown and it became of interest to survey the amino acids under these conditions. The following amino acids were used: DL-alanine, beta alanine, L-arginine, L-asparagine, DL-aspartic acid, L-cystine, DL-glutamic acid, glycine, L-histidine, L-leucine, DL-isoleucine, L-lysine, DL-methionine, DL-serine, DL-tryptophane, L-tyrosine, 3,5-diiodotyrosine, and DL-valine. The horizontal strip method of paper electrophoresis was used. DL-Aspartic acid showed transporting action. Further experiments show this action to be due to an unidentified impurity present (less than 0.1 per cent) in commercial aspartic acid. The highest complexing activity observed for the unknown substance showed that two parts from one preparation transported one part of lutecium. Further study continues toward the identification of the complexing agent. In contrast with the conditions on exchange resins at pH 2.9, in parallel studies, the basic amino acids showed no transporting action.

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RARE EARTHS AND PLASMA PROTEINS

Renaat Loos*
Granvil C. Kyker

Other experiments with various examples of the rare earth elements have shown that the circulating fraction of the dose regularly appears as a constituent of plasma. Current interpretations of this biochemical behavior assume a combination in some manner with the proteins in plasma. The specific nature of such an interaction is not known. Neither is it known whether different rare earths behave the same or may reflect the slight scale of differences that are typical of their more important chemical properties. An experimental comparison of lutecium, holmium, and neodymium tagged with Lu 177, Ho 166, and Nd 147, respectively, is under way using paper electrophoresis on plasma taken at various times after varying intravenous doses to dogs and other animals. The present early stage of the work does not permit rigid conclusions but the results do suggest close similarity between elements, association of radioactivity mainly with globulin, and some evidence of the effect of time on the association of the element with specific protein fractions.

AMINO ACID METABOLISM UNDER CORTICAL HORMONE STRESS

Arthur L. Kretchmar
Granvil C. Kyker

The study proposes to measure amino acid levels in lymphoid and various other soft tissues under conditions of known adrenal cortical hormonal levels in order to provide more adequate interpretation of protein metabolism under these conditions. The extent to which levels of amino acids in plasma reflects changes in their level in tissue as a result of hormonal or nutritional stresses remains unanswered. Although proteins have been among the most extensively investigated of the chemical systems of tissues, reports are not available that record simultaneously changes in plasma amino nitrogen and tissue amino nitrogen and their correlation with excreted nitrogen.

In order to make such measurements on the same experimental subject, extensive methodology is required. Included among the procedures that called for critical evaluation are:

1) adrenal demedullation and subsequent regeneration as an index of exogenous cortical hormonal levels.

2) design and construction of a continuous multiple injection apparatus.

3) measurement of blood volume and of blood in tissue by the use of red blood cells tagged with chromium 51.

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4) Chemical methods including the micro-determination of total, amino acid, and urea nitrogen and of sodium and potassium by flame photometry to follow metabolic interrelationships of protein and minerals.

Following the establishment of the necessary procedures, preliminary experiments using rats have included:

a) measurement of the rate of regeneration of adrenal cortex following medullectomy.

b) satisfactory immobilization of animals and their continuous intravenous injection for twenty-four hours.

c) measurement of the residual blood in liver, spleen, kidney, lung, intestine, and muscle of exsanguinated animals.

d) effect of perfusion of the animal on the wet weight / dry weight ratio of these organs.

e) comparison of amino nitrogen in plasma with liver and thymus using homogenates prepared with picric acid and with boiling water.

Also a stock of the ten essential amino acids to be used in the continuous perfusion of experimental animals has been verified by determinations of their content of total carbon, total nitrogen, and amino nitrogen.

POTASSIUM AND RUBIDIUM IN DOGS

M.K. Berkut*
Granvil C. Kyker

Preliminary reports (ORINS Quarterly Progress Report, April 1 - June 30, 1955, p. 16; Semiannual Progress Report, period ending December 31, 1954, pp. 11-12) indicate interest in the possible use of Rb 86 as a substitute tracer of potassium. Twenty dogs were used in the present study in order to compare the relative rates of excretion of potassium and rubidium. Isotopes of both elements were administered simultaneously. A well-type scintillation counter was used to measure both isotopes. The rubidium 86 (19.0 days) was measured by difference in counting before and again after decay of potassium 42 (12.4 hr). The data indicate very rapid mobilization of both isotopes and somewhat slower renal excretion of rubidium than of potassium. Other conclusions must await the further analysis of the data, now in progress.

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* Research Participant from the University of North Carolina, Chapel Hill, North Carolina.

THE FATTY ACID METABOLISM OF SPICARIA VIOLACEA ABBOTT

George T. Johnson*

A study was made of the fatty acid metabolism of Spicaria violacea Abbott, a mold previously found to grow with certain long chain fatty acids as the sole carbon source. The optimum conditions for respiratory studies on this mold by means of standard manometric techniques were ascertained. The long chain fatty acids were found to have specific biological effects under the conditions tested, with some stimulating and some inhibiting oxygen uptake by the organism. Tracer experiments were carried out on several fatty acids labeled with carbon 14. This work was oriented toward elucidating the mechanism of fatty acid oxidation by the mold. Preliminary results indicate some possible differences between the pattern in this mold and that normally found in mammalian cells.

(An abstract of a paper presented September 14, 1955, in Minneapolis to the Division of Biological Chemistry, American Chemical Society.)

HOLMIUM 166 WITH RARE-EARTH CARRIERS

Granvil C. Kyker
John Rafter

The characteristics of holmium 166 suggest its potential usefulness internally. Its half life is 27.3 hours and it decays by beta emissions to erbium. The decay scheme shows energies of 1.84 and 1.76 Mev for approximately one-fourth and three-fourths of the disintegrations, respectively; the latter undergoes 80 kev gamma transition. Production of the radioisotope in a reactor is convenient from holmium oxide. The product is converted to the chloride in sodium chloride at pH 4 before administration.

The isotope prepared in this manner has been studied following intravenous or intraperitoneal injection in approximately 150 animals including mice, rats, and dogs. The amount of holmium in the dose greatly influences the mobilization of radioactivity. Intravenous doses are largely deposited in the liver. Intraperitoneal doses are almost completely retained intracavitarily when the dose of rare earth is 10^{-4} moles per kg or more. Two other rare earths, yttrium and lanthanum, similarly immobilized radioholmium. Mediastinal tissue was regularly very radioactive following intraperitoneal doses; this suggests lymphatic deposition. The early pattern of radioactivity showed little redistribution with time.

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* Research Participant from the University of Arkansas, Fayetteville, Arkansas.

(Abstract of paper presented April 15, 1955, in San Francisco at the annual meeting of the American Society of Biological Chemists.)

INTERSTITIAL YTTRIUM IN PROSTATE AND PARAMETRIUM

Granvil C. Kyker
Julio Toriello
Ralph M. Kniseley

We have previously emphasized the availability and potential usefulness for internal radiation of several radionuclides of the rare earths and have reported on certain biochemical similarities among elements in this group. Their study with yttrium offers advantages since this element is readily available, offers suitable radioisotopes, and conveniently delineates the metabolic pattern of the heavy lanthanides. Two milliliters of 0.01 M yttrium chloride adjusted to pH 4.0 in isotonic sodium chloride and containing approximately 125 microcuries of radioyttrium 91 (half life, 57 days; beta, 1.54 Mev) /ml liter was injected in the prostate and parametrium of 5 male and 5 female dogs. Three of each sex were killed at 3 days and the remaining 4 animals at 7 days. The mobilization of the dose was determined by radioassay of the tracer in 10 tissues remote to the injected area and in approximately 30 samples from autoradiographically mapped retroperitoneal tissues. A rather similar lymphatic pattern near the site of injection was observed in each animal. Some nodes within 5 to 10 cm showed a concentration of yttrium approaching that in the primary site of injection and 1000 times that of immediately adjacent tissue. Microautoradiography of representative specimens showed a diffuse but somewhat irregular distribution of yttrium in the parametrium. The pattern in iliac and para-aortic nodes was not uniform. Variations in the prostate appeared to indicate localization in injected lobules and interstitial tissue.

(Reference to an abstract of a paper on the program of the American Society for Cancer Research, April 15, 1955, San Francisco.)

Preliminary Studies of Yttrium 90 in Man.
Gould A. Andrews, Granvil C. Kyker, Ralph M. Kniseley, and Etna L. Palmer. Proc. Amer. Assoc. Cancer Res. 2 (1), 1, (1955).

RARE-EARTH ROUND TABLE AND CONFERENCE

Two programs were organized on the subject of Rare Earths in Biochemical and Medical Research. The first was a round-table session in San Francisco on April 14 arranged in conjunction with the annual meeting of the Federation of American Societies for Experimental Biology. The session also drew interest from some attending the concurrent meetings of the American Society for Cancer Research. The discussions were led by speakers from the scientific staff of (1) Crocker Laboratory, University of California, (2) Montefiore Hospital and Polytechnic Institute of Brooklyn, New York, (3) Argonne National Laboratory, and (4) Oak Ridge Institute of Nuclear Studies. The response to the meeting called for the organization of a conference on the subject.

Following the preliminary meeting, a program for a conference was organized. The conference was held in Oak Ridge on October 27, 28, and 29, 1955. Twenty-seven speakers contributed papers. These were organized to emphasize chemical, pharmacological, biochemical, metabolic, and dosimetric considerations of the rare-earth elements and their radioisotopes, and also their potential medical application. Approximately sixty in addition to the speakers registered for the conference. Following the scientific program, ways to provide continuity of the group for the purpose of exchanging information and arranging future conferences were considered.

The collection of manuscripts, editing of recorded discussions, and preparation of an index are in progress. A Proceedings of the conference is expected to appear early in 1956. These meetings and a Proceedings constitute new material for the subject.

MEDICAL DIVISION EXHIBIT

RARE EARTH RADIOISOTOPES OF MEDICAL INTEREST

A series of forty-eight slides was arranged for automatic projection. The subject is treated in three parts. The first deals with the selection of radioisotopes of potential medical usefulness. This focuses special attention on the rare-earth elements. The second part deals with the production of the desired radioisotopes from the natural stable isotopes and with radiochemical procedures that yield suitable preparations for biological study. The last part of the exhibit uses typical results from studies in animals to illustrate the importance of dose in the controlled localization of radioactivity and metabolism of these elements.

(Recorded radio program produced by Moyra Youds, British Broadcasting Corporation.)

Atomic Energy and Medicine, Marshall Brucer, Gould A. Andrews, Granvil C. Kyker, and Ralph M. Kniseley. Program No. 6 in New World, Extension Division of the University of Alabama, Vol. 13 (No. 2) August, 1955.

SOUTHEASTERN SECTION OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE

The annual program of the Section was arranged at Emory University, Atlanta, for November 18, 1955. The program consisted of sixteen scientific papers presented during the morning and afternoon sessions, and a business meeting. The speakers represented five of the eight major institutions comprising the Section. Approximately fifty registered for the meeting.

Representing the Southeastern Section, the national meetings of sectional secretaries and of the council were attended, April 11, 1955, in San Francisco.

SIXTH CONGRESS OF MEDICINE OF GUATEMALA
November 28 - December 4, 1955

Five days of the program were devoted to the scientific program consisting of eleven sessions with a total of eighty-five reports and more than one hundred authors. As invited guests of the Congress, Dr. Gould A. Andrews and I collaborated to present a session on the use of radioisotopes in basic research and in clinical medicine. An outline of topics included in the session follows:

I. Introduction

- A. Objectives of ORINS and the Medical Division
- B. Clinical Program of the Medical Division

II. Exhibit of Medical Division Facilities

III. Radioisotopes as Investigative Tools

- A. Basic Concepts and Properties
- B. Isotopes in Medicine

IV. Studies and Applications

- A. Therapeutic Use of Radioactive Colloids
- B. The Rare Earths: Isotopes of Interest; Animal Studies
- C. Useful Methodology: Autoradiography; Scintiscanner

V. Discussion and Summary

BIOMEDICAL RESEARCH

C. L. Comar

INTRODUCTION

Attention has been given to studies of alkaline earth metabolism in man. There has been emphasis on (a) magnitude of and factors affecting absorption, (b) fate of elements in the body, (c) route of endogenous excretion, (d) results of daily administration versus single dose technique, (e) extrapolation of animal data to man, and (f) radiation dosage to the gastrointestinal tract from ingested radioactivity. This approach is of interest from the standpoint of possible therapeutic and diagnostic application, the residual effects of such usage, the role of calcification in certain malignancies, patient management under conditions of hormonal imbalance, and health physics considerations.

Newer developments in instrumentation are being explored to determine situations in biomedical research where there are real advantages from the more refined methods and increased sensitivities available.

Surveys have been initiated and are being continued for the amounts of radioactivity present in man and animals as correlated with atomic bomb tests.

Training and educational duties have taken considerable time and effort - in particular, the biological aspects of the basic Special Training Division course, the Veterinary Radiological Health course, organization of symposia, and participation in scientific meetings. A combined training and research project of considerable interest has been concerned with the nature of avian coccidial immunity.

METABOLISM OF STRONTIUM 85 IN HUMAN BEINGS

C. L. Comar
W. E. Lotz*
R. H. Wasserman
Joe Gray
J. S. Eldridge

Studies in man that were not heretofore practical have been made possible by the recent availability of cyclotron-produced strontium 85. Strontium 90 is not suitable for such studies because of its long half life; carrier-free strontium 89 has varying amounts of strontium 90 contamination that precludes its use; pile-produced strontium 89 has no long-lived contamination but does not have a high enough specific activity for most purposes. Strontium 85 has a 65-day half life, a 0.8 Mev gamma ray, K-electron capture, and is produced in carrier-free state by bombardment of rubidium. The main disadvantage is the relatively high cost, $200 per millicurie.

Studies have been completed on 4 patients. In 2 individuals the Sr 85 was administered orally 3 times a day for 20 days. The excretions and blood were assayed. At steady state the average fecal excretion was 60 per cent of the intake, the urinary excretion was 6 per cent, and the level in the blood was about 2.5 per cent of the daily intake. When the dosage was stopped, the excretion fell to a very low value, in agreement with data from animal experiments that indicate tenacious retention of such alkaline earth radioisotopes.

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Of particular interest are the relationships between the known body burden, the level of excretion, and the blood content after the dosage has been stopped.

One patient received a single oral dose, of which 86 per cent was excreted in the feces and 3 per cent in the urine. Another patient received a single intravenous injection. This patient was in terminal condition and the excretions were so low as to reflect the abnormal metabolism. Autoradiograms of bone and tissue distribution data were obtained at autopsy from two individuals.

The results from these experiments permit logical extrapolation to behavior in human beings from a large body of animal data now available.

THE COMPARATIVE EXCRETION OF CALCIUM AND STRONTIUM INTO THE GASTROINTESTINAL TRACT

Leon Singer*
A. B. Medlin**
M. Maqsood†
M. M. Nold††
C. L. Comar

Forty-six mature mongrel dogs were used to study the comparative excretion of Ca 45 and Sr 89 into the various segments of the gastrointestinal tract. Both single and double isotope studies were done. In some experiments the dogs were prepared by tying off segments of the gastrointestinal tract, injecting the radioisotope intravenously, and collecting the contents of the segments a short time later (about 30 minutes) for radioassay. With seven animals the bile duct was cannulated to allow direct estimation of the biliary contribution to the intestinal content of injected Ca 45 and Sr 89.

Both radioisotopes were secreted into all parts of the gastrointestinal tract. The comparative secretion rates can be noted from the following condensed table:

Table I

Percentage of Excreted Dose in Gastrointestinal Tract of Dogs

	Ca 45	Sr 89
Stomach	6	3
Small Intestine	45	78
Large Intestine	49	19

It can be seen that compared to Ca 45, there was more Sr 89 excreted into the small intestine and less into the large. In terms of amounts, there

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* Research Participant from the University of Minnesota, Minneapolis, Minnesota.
** Research Participant from the A and M College of Texas, College Station, Texas.
† Visiting Investigator from Lahore, Pakistan.
†† United States Air Force Veterinary Corps, Oak Ridge, Tennessee.

was about three times as much Sr 89 excreted into the gut as Ca 45. A partial explanation is derived from the bile collection experiment which is summarized in Table 2:

Table 2

Percentage of Injected Dose Appearing in Bile Collected at Different Times. (Double Isotope Study in Dogs)

Time (min)	Ca 45	Sr 89	Sr 89/Ca 45
0-60	0.037	0.150	4.0
60-120	0.018	0.086	4.7
120-180	0.027	0.060	2.3
180-240	0.026	0.056	2.2
240-360	0.032	0.066	2.0
Total	0.140	0.418	

Apparently, Sr 85 is preferentially secreted into the bile as compared with Ca 45 and this preferential secretion is accentuated at the early times after dosage. Again, there appears to be a three-fold preferential excretion of Sr 89 as compared with Ca 45.

A preliminary study indicated that calcium and strontium are bound to an equal degree with plasma proteins. This experiment was done by using an ultrafiltrate obtained by centrifugation techniques with a semipermeable collodion membrane.

In both man and animals estimates have previously been made of total digestive juice calcium based on the assumption of equal absorption of blood calcium and digestive juice calcium from the gut. The data presented in this report indicate that significant amounts of digestive juice calcium enter the lower parts of the tract. Thus, the previous values are probably in considerable error on the high side. It had been hoped that some quantitative estimate of the error would be obtained from this study; however, further data are needed.

EFFECTS OF CORTISONE AND PARATHYROID EXTRACT ON CA 45, SR 89, AND P 32 BEHAVIOR IN THE RAT

W. E. Lotz*
C. L. Comar

It is well known that parathyroid extract will cause removal of calcium and phosphate from bone, increased urinary excretion of phosphate, and marked calcification of the kidneys. It was recently reported that administration of cortisone to patients suffering from hypoparathyroidism interfered with calcium metabolism and intensified an already hypocalcemic state. Also, cortisone has been shown to restrain the growth of one type of osteolytic breast cancer. Experiments were undertaken to investigate the possible interaction of cortisone

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and parathyroid extract in the rat by observation of effects on behavior of P 32 and Ca 45; studies were also made with Sr 89 because of the general similarity of calcium and strontium metabolism and the differences in renal clearance of these two elements. Special attention has been given to urinary excretions because the rate of calcium excretion has been shown to be related to progress of disease in patients with osteolytic metastases.

Parathyroid treatment produced the expected results: high blood calcium, high kidney Ca 45, removal of Ca 45 from bone, increased urinary P 32 excretion. Cortisone treatment had no measurable effects except for a decreased Ca 45 urinary excretion. In animals receiving both cortisone and parathyroid, the most significant finding was the low kidney Ca 45 as compared with the parathyroid animals; the blood calcium and urinary P 32 excretion was the same as in the parathyroid animals.

The effects of parathyroid extract and cortisone treatment on Sr 89 was much the same as for Ca 45 except that cortisone by itself did not decrease the urinary excretion of Sr 89.

The control of kidney calcification by cortisone treatment may be of clinical value. Study of all the data indicates no direct interaction between the hormones, but rather a degree of competing action on the kidney.

FACTORS AFFECTING UTILIZATION OF ALKALINE EARTHS

R. H. Wasserman
C. L. Comar
M. M. Nold*

The role of various amino acids and organic compounds in promoting the gastrointestinal absorption of calcium has been investigated; corollary information has been obtained on the comparative metabolism of calcium and strontium. In double-tracer experiments, Ca 45 and Sr 89 were orally administered to rats along with the test substance. The amount of radioisotope found in the bone at a standard time later was used as a measure of utilization. Sufficient numbers of rats were used in each trial to permit assignment of statistical significance to differences observed. The results may be summarized by a listing of the substances tested in decreasing order of response.

Series A: lysine $\cong$ arginine > tryptophane > leucine > histidine > isoleucine > methionine $\cong$ valine $\cong$ threonine $\cong$ phenylalanine $\cong$ control

Series B: lysine >> aspartic acid > glutamic acid $\cong$ hydroxy proline > tyrosine > serine $\cong$ glycine > alanine $\cong$ proline $\cong$ control

Series C: lactose > lysine $\cong$ arginine >> leucine $\cong$ gluconate > methionine > lactate > citrate $\cong$ B vitamins $\cong$ control

Further experiments have shown that the foregoing effects are primarily related to increase of absorption from the gastrointestinal tract. Preliminary studies have led to suggested modes of action and relationships with vitamin D.

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* United States Air Force Veterinary Corps, Special Training Division, ORINS.

The differences between controls and the most effective agents are large enough to be of therapeutic and nutritional significance.

In general, Ca 45 was preferentially absorbed from the gut by a factor of about 1.6 over Sr 89. In all cases, substances that promoted Ca 45 absorption were even slightly more effective in promoting Sr 89 absorption. It appears that calcium and strontium are to some extent independently absorbed; however, the absorptive processes are probably similar in that both minerals compete for the same site in the active transport mechanism across the intestinal barrier.

CITRIC ACID AND CALCIFICATION PROCESSES

J. C. Schooley*
R. H. Wasserman
C. L. Comar

Bone is a rich source of citric acid, containing about 70 per cent of that contained in the whole body. Tumor tissue usually, though not invariably, contains much citric acid.

The enzyme, citrogenase, necessary for production of a high citric acid level in bone has been characterized. It is known that parathyroid and vitamin D will raise blood citric acid and that vitamin D will also raise bone citric acid. Also, parathyroidectomy has been shown to decrease bone citrogenase. The metabolic pattern, and function of citric acid in bone is not understood.

As a first step in the present study, methods have been established and tested for determination of blood citric acid, bone citric acid, and bone citrogenase. Chromatographic methods are being developed for separation of citric acid from other organic constituents of bone.

One preliminary experiment has been done with rats in an attempt to localize the vitamin D action; this was based on the use of fluoroacetate, which is known to block the degradation of citric acid. The results were equivocal. Carbon 14-labeled citric acid and C 14-labeled acetate have been obtained and will be used to estimate the rates of synthesis and turnover of citric acid. An experiment is also planned to see whether there is a direct relationship between vitamin D action and citrogenase.

LOW-LEVEL COUNTING FACILITIES

C. L. Comar
J. I. Trombka

Highly sensitive counting methods are needed because they will permit metabolic studies in patients with lower amounts of administered radioisotopes. This will lead to better utilization of expensive radioisotope preparations, the

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* United States Department of Defense.

possibility of obtaining more data with hazardous radioactivities, and the opportunity of studies with more normal subjects. The increasing trend to detailed study of separated biological components(e.g. thyroid hormones or protein fractions) also places greater demand on sensitivity of radioassay.

Gamma counting is accomplished by use of a 3-inch crystal, heavy lead shielding with a cadmium copper liner, and single or multiple channel instrumentation. Beta counting equipment is being assembled that relies primarily upon heavy shielding and anticoincidence tube arrangements. An important part of the over-all technique is the avoidance of contamination.

The sensitivities are known for most radioisotopes as measured with ordinary counting assemblies such as the thin mica window Geiger tube, the internal counter and the one-inch scintillation crystal. The advantages in biological work offered by the more refined methods will be evaluated in terms of added costs or increased difficulty of measurement.

THYROID COLLECTION PROGRAM

C. L. Comar
M. Brucer
J. C. Schooley
Collaborating Pathologists*

In 1954 it was reported that nuclear detonations had produced radioactive materials (presumably I 131) that were accumulated and detectable in the thyroid glands of cattle in the United States. This raised the question concerning how much I 131 was present in human thyroids, whether this would interfere with present-day diagnostic tests of thyroid function using I 131, and finally the extent of any radiation hazard.

Arrangements were made with pathologists in varying parts of the country to send to Oak Ridge thyroid glands taken at autopsy. These glands were processed in Oak Ridge and counted for gamma activity by means of highly sensitive scintillation equipment. The sampling started in March, 1955, to coincide with the continental spring tests and has been continued to date. So far over 600 thyroid glands have been analyzed. A meeting was held July 8, 1955, for presentation of results to the pathologists and discussion of sampling problems.

The results may be summarized as follows:

1) From March to June, 1955, the thyroid values ranged from 0.5 to 18×10^{-5} microcuries per total gland. Highest values were found in the Salt Lake City area with more or less even distribution over the rest of the country. Since the end of July the values have been below detectable levels (0.5×10^{-5} microcuries per gland).

2) Human glands contained 1/10 to 1/50 the amounts of radioactivity found in comparable cattle thyroids.

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* Listed on following page.

3) Detectable amounts of I 131 did reach the human population from the 1955 continental spring tests; the levels were so low as to constitute no hazard or interference in diagnostic tests.

It is suggested that most of the radioactivity is acquired by inhalation.

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FALLOUT SURVEY PROGRAM WITH LIVESTOCK

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B. F. Trum*
M. M. Nold**
J. N. Shively*
U. S. G. Kuhn III**
J. C. Schooley†

In late 1954 the Armed Forces Special Weapons Project inaugurated a survey of environmental radioactive contamination with the Veterinary Corps of the Army and Air Force being responsible for the sampling of animal populations. The Institute has cooperated in this program in assuming responsibility for development of procedures because of special facilities such as the 20-channel gamma-ray spectrometer and low-level counting facilities.

Thyroid gland, milk, and bone samples have been collected from cattle throughout the continental United States and overseas during a period covering the 1955 continental atomic bomb tests. Procedures based on ion exchange separation were developed for I 131 detection in milk; however, samples were not generally large enough to permit measurements. Several bone samples were analyzed for Sr 90 through the courtesy of Dr. Kulp of Lamont Observatories. Values were of the order of one hundredth to one thousandth of the maximum permissible body burden. At the conclusion of the spring tests the sampling was stopped except for thyroid samples from 2 stations in the United States. To date, over 600 thyroids have been analyzed.

The results are summarized as follows: The test shots caused measurable increases in the I 131 contents of the cattle thyroids. The highest values were from the Nevada - Southern Utah area; the highest individual value observed was 0.4 microcuries in the total thyroid. Over the rest of the country most of the values fell between 10 to 1000 $\times 10^{-5}$ microcuries per thyroid; abroad, the values were considerably lower. The pattern was generally similar to that reported for gummed-paper collections of fallout. Near the end of July 1955, the values had fallen to nondetectable levels. There was a slight increase in animals from the San Francisco area, in the latter part of November; this was probably caused by the reported Russian test.

Cattle values were 10 to 50 times higher than comparable human or dog values. From a study of thyroid glands from cattle on pasture as compared with barn-fed animals it is suggested that at least 75 per cent of the I 131 in cattle comes from ingestion.

Facilities and training in radiochemical procedures have been provided for an Armed Forces veterinarian assigned to the Santa Fe operations. Bone, thyroid, and stomach contents have been processed from deer and livestock that have lived most of their life near the Nevada test site.

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† United States Department of Defense.

IRRADIATION OF THE GASTROINTESTINAL TRACT BY INGESTED RADIOACTIVITY

M. M. Nold*
H. Kakehi**
R. H. Wasserman
R. L. Hayes
C. L. Comar

There is interest in the radiation dose received by the intestinal mucosa from passage of radioactive materials through the tract. This will be a factor in diagnostic or therapeutic use of radioisotopes administered by the oral route; also, there are health physics aspects of importance.

Glass dosimeters are now available that are small enough to be implanted in tissues to be studied. These dosimeters are now being calibrated for the radiation of interest, and implantation techniques in dogs are being worked out. The initial experiments are planned to show the relative radiation dose received by different parts of the gastrointestinal tract when insoluble beta emitters of different energies are fed. Absolute dosages will also be estimated insofar as possible. These results will be correlated with histological observations.

CELLULAR IMMUNITY IN AVIAN COCCIDIOSIS

P. P. Levene†
C. L. Comar

Numerous attempts were made to label coccidial oocysts with various radioisotopes. Oocysts were soaked in solutions of P 32, I 131, Se 75, and Ca 45. There was considerable nonmetabolic absorption of Sr 75 and P 32. The following radioisotopes were fed to fowls in an effort to label the oocysts in vivo: P 32, Cr 51, Se 75, Ca 45, Y 91, C 14-glycine and Rb 86. Significant tagging occurred only with Se 75, but even then not sufficiently to permit tracing the tagged oocysts after they had been injected into another animal.

Detailed studies were carried out to clarify the nature of coccidial immunity in poultry. The approaches were as follows: a) massive treatment of a bird with serum from immune birds, followed by a challenging infection; b) immunizing one cecal horn while the other was protected from infection, followed by a challenging infection to the previously protected cecal horn; c) immunizing the ceca with sexual forms of coccidia followed by a challenge with asexual forms; d) immunizing the ceca with sexual forms followed by a challenge to the small intestine with asexual forms; e) examination of labeled blood and tissue proteins by paper electrophoresis for differences between immune and nonimmune birds. The above experiments required development of special surgical techniques as well as production and isolation methods for the infective agents.

The results suggest that there are no circulating humoral antibodies but rather that there is a localized tissue immunity.

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MEDICAL PHYSICS

Marshall Brucer

CESIUM 137 TELETHERAPY MACHINE

During the past year the cesium teletherapy machine has been installed and put into operation. The teletherapy room was redesigned during the early months of 1955, and because of the construction of the new building much of the work was stopped during the first four months. With the completion of the new construction, a new tile floor and sound proofing was added to the teletherapy room. A new "touch guard" system was added to the variable field diaphragm. This is the one point on the machine that does protrude, and in case of malfunction it is possible that the 4 1/2 tons of steel could injure a patient lying on the table under the cesium beam. The touch guard was installed so that with a few ounces of pressure at the protruding nose, the machine will stop all of the motors and freeze the motion.

A considerable amount of difficulty was encountered in balancing out various components of the electronic controls. These, however, have been balanced and during the past few months have worked satisfactorily. The automatic isodose plotter has been set up in one corner of the cesium teletherapy room and routine isodose curve studies are now in progress with various collimator and field size settings. Depth dose curves as shown in Fig. 1* indicate that the central axis depth dose is about as predicted from the 250 kv and the cobalt central axis depth dose curves. One of the major problems in the use of cesium will be concerned with the question of source size. It has been found already that with the minimum collimation there is an appreciable increase in the penumbra as was expected. However, it appears from preliminary studies that the amount of collimation possible with a telescoping collimator reduces the penumbra from the large source so that it is almost equivalent to that of the cobalt source. This has verified the assumption that larger source sizes can be used with cesium provided there is an additional length of collimation.

An open house for scientific and professional people in Oak Ridge was held on December 1, at which time the characteristics of the cesium machine were demonstrated in their final form. It is expected that the machine will be available for use on patients as soon as a number of the basic isodose curves are completed.

COBALT 60 TELETHERAPY MACHINE

During the construction of the new building, the cobalt 60 teletherapy machine was moved into the mechanical equipment room. The conditions of this room were not such that definitive work could be done, but the machine was kept in operation so that a certain number of patients could be treated, although this was done under difficulties. The new construction included a separate room for the cobalt machine, and in June it was installed in the new room. The cobalt machine is now being used for routine treatments of patients and it has been used to test a new variable field diaphragm which has been constructed by the W. F. and John Barnes Company. An illustration of the protection characteristics of the variable field diaphragm is shown in Fig. 2. The machine is also being

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* The figures will be published in the ORINS Semiannual Progress Report for the period ending December 31, 1955.

used at the present time by Dr. Mewissen, a visiting scientist from Belgium, who is making a study of tumor production with and without radiation protection agents in mice.

VARIABLE FIELD DIAPHRAGM

One of the irritating things about the cobalt 60 hectocurie teletherapy machine has been the constant replacement of cones during treatment. Approximately 30 of the hectocurie units are now installed and in use throughout the United States. A large number of prototype cones were developed in cooperation with the W. F. and John Barnes Company and were sent to the Medical Division for tests. With these cones a complete set of isodose curves at 35 and 50 cm source skin distance (SSD) has been measured and published as Teletherapy Design Problems IV. A large number of these cones have been sent to various members of the Teletherapy Evaluation Program who have hectocurie machines in operation. The experience with these cones is that although they are perfectly adequate for therapy they are unhandy to use because of their weight and the necessity for constant replacement. For the past two years this problem has been realized and an attempt has been made to design various kinds of variable field collimators that could be used instead of replaceable cones. One design made by the W. F. and John Barnes Company has been tested and has been found adequate. It has been the feeling of many of the people who are working on the project that the inside edge of any cone must follow the visual line of projection of the beam. This means that a simple four block system of collimating the beam is not sufficient but that the block or leaves of a variable field diaphragm must follow the shape of the beam. In order to accomplish this shaping of the beam, it becomes necessary either to make the cone excessively long or excessively large. Many other variable field diaphragms have been proposed throughout the world and each one has been a compromise solution to the problem. One of the preponderant drawbacks to most of the solutions so far proposed has been the excessive cost of making a complex mechanical device.

During 1955 a contract was negotiated with the Westinghouse Electric Corporation to produce a new type teletherapy machine. Although this machine emphasizes three factors not related to the variable field diaphragm, within this contract another compromise solution has been suggested. The suggested compromise is to make a series of 12 to 15 cones as a part of the primary shield of the teletherapy head itself, and to wrap these 12 or 15 cones around the machine; it is felt that this compromise will do away with the common complaint of the unhandiness of replaceable cones and will also decrease the cost of a coning system.

NEW WESTINGHOUSE TELETHERAPY CONTRACT

During the year 1955 a contract was negotiated with the Westinghouse Electric Corporation to develop and produce a new teletherapy machine. This machine will concentrate on the development of solutions for three other problems that have been found to be of prime importance in the practical use of teletherapy throughout the country. A study has been made of many of the machines that have been installed by various Teletherapy Evaluation Program members. A preliminary report on this survey was presented and will be published as a part of the International Conference on the Peaceful Uses of Atomic Energy held in Geneva, Switzerland, August 1955. In this report it is pointed out that one of the

primary difficulties in the installation of teletherapy machines has been the problem of protection and the design of teletherapy rooms. Therefore, the new development with the Westinghouse Electric Corporation will emphasize the development of a machine that has an inherent protection.

Another one of the major problems that is still present in the teletherapy field is the production, distribution, and acquisition of cobalt 60 sources. The production problems of cobalt 60 are such that it promises to continue to be in short supply and to be very expensive. Since the cost of cobalt 60 is almost exponential with increasing specific activity, it is felt that some arrangement should be made to design equipment that can be used with either low specific activity cobalt or with worn out sources no longer useful in other teletherapy machines. The one solution that is apparent is the use of multiple headed machines. Therefore, the Westinghouse contract will emphasize the development of a double headed cobalt machine. Concomitant with this problem is the problem of rotational therapy. The history of rotational therapy has been one of ever increasing interest throughout the past 50 years. With the development of isotope sources it is now possible to produce mechanically adequate rotating rotational equipment. Therefore, combined with the double headed machine idea is the problem of rotational therapy. The first machine to be developed under the Westinghouse contract will emphasize only the simplest and most practical of the rotational therapy ideas.

An ever present problem in the design of teletherapy equipment is the economic problem in using the machine. The Medical Division has participated in a number of Teletherapy Industrial Conferences at which many of these questions were discussed. Many of the economic problems are described in the minutes of the first three industrial conferences, and in the minutes, now in press, of the fourth Teletherapy Industrial Conference. One of the major problems has turned out to be the amount of time that is used not in the treatment per day but in the setting up of patients. Patient handling is therefore of fundamental importance in the design of teletherapy equipment. This problem is being emphasized in the new machine being developed under the Westinghouse contract.

THYROID UPTAKE CALIBRATION PROGRAM

For a number of years it has been realized that radioiodine uptake measurements, as performed by many different techniques over the world, are highly variable. This point of view was brought out and emphasized in the 1953 second advanced medical course. Following this meeting, an attempt was made to develop a program that would help correct this situation. When in vivo studies are made, a host of unknown correction factors for absorption, scatter, body background, geometry, and instrument sensitivity are necessary. It was felt that in order to calibrate the results of many laboratories, it would be necessary to have a full-sized phantom closely duplicating the upper half of the human torso complete with appropriate radioactive organs. Such an expensive construction would not be warranted if the model must be frequently refilled with short-lived material such as I 131. The calibration of repeated fillings would be open to question. Before such a model could be developed it was necessary to find a radioactive iodine gamma ray standard that imitated sufficiently closely the spectrum of radioiodine that the standard could, under all conditions, be used in place of radioiodine.

An investigation of a number of standards was carried out during 1954 and

it was found that a mixture of barium 133 and cesium 137 in suitable proportions would yield a combined gamma-ray spectrum that closely resembles that of iodine 131. This mixture has been manufactured and it is now called mock-iodine. A program of calibration of mock-iodine has been carried out with the National Bureau of Standards, the National Physical Laboratories of England, and the National Physical Laboratories in Germany. Further calibrations are in process. All of these laboratories indicate that mock-iodine is an adequate substitute for iodine. The three radioisotopes, barium 133, cesium 137, and iodine 131, were assayed in a high pressure ionization chamber to find their absolute strength in millicuries based on assumed energy distributions. Since the decay scheme of barium 133 is unknown, a barium calibration kit has been prepared that defines the barium 133 millicurie based upon these assumptions. This arbitrarily defined millicurie is being used in all sample preparations and has been loaned to a number of the national physical laboratories for check. A whole series of other calibration kits has been prepared and will be made available to various laboratories that want to do their own studies on mock-iodine.

Since the primary reasons for developing a long-lived iodine 131 substitute was to construct phantoms that simulated the geometry of clinical situations, it was necessary to find a way of dispersing the mock-iodine in a uniform manner in various strengths through large and small sources of variable shapes. The dispersion medium had to have a soft-tissue-like effective atomic number; its density had to be close to unity, and for practical reasons it had to be non-corrosive; for safety reasons it had to bind the long-lived isotope tightly. Many materials were investigated and discarded that did not meet one or another of the necessary criteria. An ion exchange resin, Dowex 50, was found to be an ideal dispersion medium.

Dowex 50 is a cation exchange resin consisting of polymerized hydrocarbon-containing substituent sulfonic acid groups. The hydrocarbon chain is cross-linked to form a 3-dimensional network. The large hydrocarbon molecules are combined and the final product is prepared in the form of small spheres that can be separated into size groups by sieving. Resin particles in the size group 50 to 100 mesh are suitable for mock-iodine sources.

Extended sources of radioactive materials are made by passing the isotope in solution through the resin in ion exchange columns. Mixed activity resins can then be obtained by mechanically mixing the proper quantity of resins that have been labeled with the respective isotopes and with inactive resins. The barium-cesium mixed resin is made by combining and mixing a barium 133 labeled resin with a cesium 137 labeled resin in the proper proportions. Another way of obtaining the mixed resin is to mix the barium 133 and cesium 137 solution in the proper proportion and then to pass the mixed solution through a column of resin. After drying, the resin is mixed to give a uniform dispersion of the two isotopes.

After the long-lived substitute was found to represent iodine 131 reasonably well, a set of phantoms was constructed incorporating discrete sources to represent the thyroid gland or metastatic lesions containing iodine 131 together with a weaker filling material to represent the body background and other organs.

As shown in Fig. 3, the phantom is the upper torso of a plastic store mannequin complete with head and detachable upper halves of each arm. The plastic shell, which is 3 to 4 mm thick, and its contained resin were considered sufficient filter for the excess of low energy radiation and the containers for the thyroid were made of aluminum. The first series of phantoms, made with aluminum thyroid glands, were found to allow the escape of slightly too much low energy radiation. All of these mannequins are being repaired and the new

mannequins will be made with babbitt thyroids. On investigation the repaired mannequins have been shown to have the same iodine spectrum as that of many patients.

To carry on the survey and calibration, a Thyroid Uptake Calibration Committee has been formed with seven cooperating medical schools. In October 1955, at the second meeting of this Thyroid Uptake Calibration Committee, the first results of the survey were shown. The variation in measurements from laboratory to laboratory was much larger than had been expected. Immediately after the Geneva Conference one of the mannequins was taken to 14 different hospitals in England and an English survey was made. In this case also the results showed a wider variation than was expected. The Thyroid Uptake Calibration Committee is now actively engaged in making plans for further surveys. A set of minutes of the first meetings of the Thyroid Uptake Calibration Committee has been distributed to all of those who have participated in the tests.

Because of the great and immediate importance of the thyroid uptake calibration program, plans are under way to present this material in an advanced medical course specifically designed around the problem of external radioisotope measurements. The Medical Division has already in its possession the first clinical radioisotope instrument that was developed in the early 1940's by S.M. Seidlin and L.D. Marinelli of New York. We also have in operation a New York system counter with attachments that allow us to reproduce almost all of the glass wall Geiger-Muller tube counting systems. The Fluharty counter is similar to an end-window counting system and this is already in operation. A rotational counting system and a triple-headed bed counting system are being developed. This is expected to be finished early in 1956. A training table consisting of an end-window counter system, a medical spectrometer system, and a scintillation counter system is being returned from the Geneva Exhibit. This will be in operation early in 1956. A number of other counting systems are already in operation. With all of these counting systems, it is expected that the Medical Division will be able to set up a complete historical demonstration-type program that will allow residents and participants in the advanced medical course to do radioactive iodine uptake counting on all available systems to see the faults and advantages of each. With the development of this set of equipment, the Thyroid Uptake Calibration Committee will attempt to make recommendations on the procedures that can be followed in a future radioiodine uptake calibration program.

SCINTILLATION SCANNING PROGRAM

Along with the Oak Ridge National Laboratory Instrumentation Division, and particularly with the help of P.R. Bell, J.E. Francis, Jr., and C.C. Harris, there has been developed a number of ideas on the various scanning devices. The problem of thyroid scanning has become increasingly important in the clinical use of radioiodine not only from the standpoint of the usual uses in thyroid carcinoma and hyperthyroidism, but also in many other clinical applications. The scanning problem is an exceedingly complex one, both from the instrumentation and from the clinical viewpoint. With this available scanner, an exhibit on the clinical scanning problem has been completed. This equipment has lately been changed to include a number of focused-field collimators with both 2- and 3- inch crystals, and a program is currently developing on the general problem of the external localization of internal sources of activity.

Evaluation Program in conjunction with an advanced course in teletherapy during the summer months of 1956. It is hoped to be able to coordinate this meeting with the Eighth International Congress of Radiology which is to be held in Mexico City and to invite a number of foreign speakers to this course.

DOSIMETRY

Raymond L. Hayes
Edward Arakawa

A preliminary study of the dose received by patients undergoing clinical treatment with the TEP hectocurie Co 60 teletherapy machine has been completed and an empirical formula has been derived, the use of which will permit calculation of the dose received by a particular patient under various treatment conditions. This information has in turn been compiled in graphical form. Use of these graphs by radiologists using the TEP hectocurie machine should make it possible for them to make rapid and easy estimations of the average tumor dose and the integral or total body dose received by patients undergoing treatment. Factors that can be taken into account are the distance from the source to the tumor, the size of the tumor, the size of the patient, and the position of the tumor in the patient under conditions of stationary or rotational treatment (rotation of the patient about the central axis of the tumor).

The results of this study serve to emphasize the rather serious treatment handicaps produced by the penumbra effects associated with the use of extended source teletherapy machines. They further tend to point up the desirability of a greater emphasis on dose relationships as opposed to the economic factors involved in future teletherapy design.

A study has been initiated of the potential clinical usefulness of the Naval Research Laboratory's silver phosphate glass dosimeter needles. This type of dosimeter is quite small in size and should find considerable use in certain types of dosage problems. Initial studies will be concerned with the evaluation of their limits of usefulness for the various types of radioisotopes now in clinical use at the Medical Division.

PHENOL DETERMINATION IN CHEMICAL DOSIMETRY WITH THE BENZOIC ACID SYSTEM

Marion T. Clark*
R. L. Hayes

4-Aminoantipyrine (1-phenyl-2,3-dimethyl-4-aminopyrazolone-5) is a sensitive reagent for the detection of phenols. A method using this reagent for the quantitative determination of p-hydroxybenzoic acid is being developed at the Medical Division at the present time. p-Hydroxybenzoic acid is one of the several products produced by the action of ionizing radiation on the benzoic acid dosimeter system. In the presence of a suitable oxidant, 4-aminoantipyrine reacts with p-hydroxybenzoic acid to form a chloroform-extractable quinone-imine type of dye. The other hydroxybenzoic acids formed during the irradiation of the benzoic acid dosimeter system do not form chloroform extractable dyes with 4-aminoantipyrine; hence use of this reagent should make it possible to determine

* Summer Research Participant from Emory University, Emory University, Georgia.

quantitatively p-hydroxybenzoic acid in the presence of both o- and m-hydroxybenzoic acid.

Although 4-aminoantipyrine, as stated, is quite sensitive as a detector for phenols, it would be desirable to have available a reagent of this type that was even more sensitive. One possible method of improving the sensitivity is by the introduction of color intensifying groups into the basic 4-aminoantipyrine structure. A review of the literature revealed that no such alteration of 4-aminoantipyrine for this purpose had been attempted. Accordingly a project involving the synthesis and analytical evaluation of a number of phenyl substituted 4-aminoantipyrines and other similar 4-aminopyrazolone-5 types of compounds was initiated during the summer of 1955 while one of the authors (M.T.C.) was a research participant with the Medical Division. This project is being continued on a cooperative basis with the main portion of the synthetic work being carried out at Emory University under the direction of M.T.C.

ISORESPONSE CURVES FROM EXTERNAL COUNTING EQUIPMENT

D. A. Ross*
Hirotake Kakehi**
M. Brucer

Along with the problem of the external measurement of internal sources, studies are being made on the isoresponse curves around the "standard" flat field collimating system, and this is being continued as a study of the isoresponse curves at various energies around one particular type of counter. The isoresponse curves at four different radioactive iodine energy levels in air, in an infinite water phantom, and in a finite neck-sized phantom are being measured. It has been found already that the isoresponse curves are totally different at the different energies and that the problem of collimation is one of the big factors in the errors encountered in the thyroid uptake calibration survey.

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* Research Participant from the University of Tennessee Medical School, Memphis
** Fulbright Fellow from Chiba University, Japan

CHEMICAL PROTECTIVE AGENTS AND X-RAY INDUCED LEUKEMIAS

Jean Mewissen, M.D.*

Survival after X irradiation is strikingly influenced by some protective chemical agents. Becaptan or B mercaptoethylamine has been recently shown to protect mice against early radiation deaths. Whether Becaptan will also lessen the likelihood of Lymphoid-Tumor inductions and development in irradiated mice. is being investigated.

This experiment is designed to study the dose response pattern for lymphoid tumor induction in γ irradiated mice protected by Becaptan. A total of approximately 800 C 57 BL mice was used and assigned to different treatment groups receiving 4 different total doses according to a graded sequence, each dose being the product of $e^{0.3}$ and the next lower dose. The irradiation source was provided by a Cobalt 60 Teletherapy Unit. In addition to providing data on the protective action of Becaptan against γ radiation, the experiment is aimed to investigate the mechanism of lymphoid tumor induction by γ radiation.

EXHIBITS

The Medical Division, in preparation for the Geneva meetings in the summer of 1955, prepared a series of 14 exhibits. Each of these exhibits consists of 48 slides that are shown on an automatic projector and describe one phase of the use of radioactive isotopes in medicine. Four of these exhibits were shown at the Geneva Conference and the others are being used in the Medical Division and are being distributed to various participating medical schools. A cobalt 60 installation exhibit describes the problems that have been solved by persons who already have installed cobalt 60 machines. This exhibit has been sent to a number of schools that are contemplating the installation of a cobalt machine.

An exhibit on the use of radioisotopes in the field of pathology and some of the modifications necessary during the postmortem examination of radioactive patients has been prepared. This exhibit was shown at two meetings of pathologists and now has been distributed to a number of universities for use in their training programs for residents in pathology. All of the other exhibits have found many uses besides the original one intended and they have become very important training aids. Further exhibits of this type are planned for the future.

THE INTERNATIONAL CONFERENCE ON THE PEACETIME USES OF ATOMIC ENERGY
Geneva, Switzerland, 1955

The Medical Division prepared a portion of the exhibit that was shown at the International Congress on Atomic Energy held in Geneva, Switzerland. Drs. Brucer and Comar of the Medical Division presented oral papers before the Congress

* School of Medicine, University of Liege, Leige, Belgium

and four of the papers have been accepted which will be printed in the Proceedings of the Congress.

Brucer, M. Teletherapy Devices with Radioactive Isotopes.

Comar, C.L. Radioisotopes in Animal Physiology and Nutrition - Mineral Metabolism.

Brucer, M., Eldridge, J., and Trombka, J. Thyroid Radioiodine Uptake Calibration.

Andrews, G.A., Kniseley, R.M., Palmer, Etna L., and Kretchmar, A. L. Therapeutic Usefulness of Radioactive Colloids: Comparative Value of Gold 198, Chromic Phosphate (P 32), Yttrium 90 and Lutecium 177.

The first two papers were presented orally and all four were published.

A number of official reports have been prepared for the Atomic Energy Commission on the Medical Division's participation in the Congress. An informal mimeographed report on the meetings has been distributed.

SIXTH MEDICAL CONGRESS IN GUATEMALA

November 28 - December 4, 1955

MEETING HIGHLIGHTS

84 scientific papers with representation of 105 authors.
Approximately 600 doctors in Guatemala a large percentage of whom are members of the College of Medicine.
Twenty-two members of the college presided at scientific sessions.
Organizing committee for the Sixth Congress was composed of 12 doctors.

The School of Medicine is under the administration of the University of San Carlos (except for University of Peru, the oldest university of the western hemisphere). The faculty affiliations are different from those typical of medical schools in the states. Much of the teaching is done by practicing physicians who give lectures rather than by full-time faculty.

A break-down of the topics composing the program shows a wide scope of scientific medicine. About forty papers dealt with internal medicine, including: alcoholism (3), anemia (1), angiography (1), anesthesiology (1), cancer (2), electrocardiography (1), electroencephalography (1), epilepsy (1), hydrocephaly (1), malaria (2), neurology and neuropsychiatry (5), poliomyelitis (1), rehabilitation (3), skeletal disorders (4), and other miscellaneous medical problems (12). Among the specialties, surgery was represented by about 15 papers as follows: general (3), thoracic (3), skeletal (2), colostomy (1), gastrectomy (1), hernia (1), thyroidectomy (1), and sympathectomy (1). The scope of other medical and surgical problems that were discussed included cardiology (4), gastroenterology (6), and nutrition (5). The importance of public health and preventive medicine in Guatemala was reflected by several reports dealing with cancer (1), sanitation (1), epidemiology (1), and tuberculosis (5). One specially arranged session of the program dealt with the use of radioisotopes in basic research and in clinical medicine (8).

CLINICAL PROGRAM OF MEDICAL DIVISION OF ORINS

Gould A. Andrews

The clinical program of the Medical Division attempts to fill three needs - 1) an active research project 2) advanced training facilities for physicians, and 3) clinical care for a small group of patients.

The research program emphasizes the therapeutic use of unfamiliar radioisotopes. With this chief objective it is possible to make maximum use of the various facilities of the program. These facilities are such that we are able to study each isotope from many viewpoints - radiation characteristics, biochemistry, pharmacology, distribution in animals, and finally, trials in patients.

There are also in progress experiments of a more basic nature, not directed toward actual therapeutic use of isotopes, but utilizing isotopes

and new techniques.

The educational program includes residency experiences for physicians who are taking advanced training in radiology, medicine, surgery, and other specialties. Most of the training programs extend from 3 months to one year. In addition there are special brief clinical courses for practicing physicians.

The patient care program involves the use of various clinical, X-ray, and laboratory methods to evaluate the effects of the isotopes given. In addition, all necessary forms of treatment are available for the care and comfort of the small group of research patients, most of whom have malignant neoplasms.

These remarks will indicate something of the breath of our activities and may suggest some opportunities of interest to the medical profession of Guatemala.

SLIDES USED FROM EXHIBITS IN GUATEMALAN MEETINGS

Medical Division Facilities		Rare Earths	Gross Autoradiography	Clinical Colloids	Scintiscanner
1	27	3	7	1	5
3	11	4	9	4	9
39	37	5	10	5	12
47	18	7	11	6	7
48	19	10	12	7	6
33	41	12	15	11	32
32	42	13	39	13	15
25	43	18	43	16	29
5	44	22	42	18	30
24	46	23	45	21	39
15		28	37	22	37
12		29		25	
13		31		33	
14		33		37	
34		34		40	
16		36		41	
8		37		42	
9		41		43	
10				44	
28				45	
29				46	
26				47	

9:20 - 9:25 REMARKS BY VISITORS IN RESPONSE TO INTRODUCTIONS

(Kyker and Andrews)

(Kyker's part) Facilidades general de la division medica del instituto.

Dr. Molina, Dr. Romeo de Leon, Los Doctores y las Doctoras de Guatemala, Las Senoras, y Otras personas: Primero, permitanme decirles que es honor especial y un privilegio participar en el programa de su congreso. Fueron bondadosos en invitarnos dada nuestras dificultades en el idioma. Con la asistencia generosa de Dr. Toriello, esperamos exponerles algo de interes y valor. Empezamos con el bosquejo corto del programa del instituto en Oak Ridge - no porque sea hacer este typo de trabajo del laboratorio, sino para orientarles en el origen de nuestros resultados.

El instituto de Estudios Nucleares es una corporación no lucrativa perteneciente a treinticuatro universidades del sur. La organización es subvencionada para AEC en casi todas susgastas. El instituto esta organizada en cuarto divisiones: primera, adiestramiento especial; segunda, relaciones con las universidades; tercera, museo; y cuarta, division médica. La primera enseña varios cursos basicos y especiales durante el año. La segunda apadrina investigaciones y estudios graduados en Oak Ridge y en varias universidades por los miembros de la facultad y estudiantes graduados en ellas. La tercera se dedica a la education publica en energia atomica.

La cuarta, la division médica, tiene dos objectivos uno, investigaciones cientificas y, dos, adiestramiento. El primero objectivo consiste en estudios internos y externos de los radioisótopos para diagnosis y terapie. El doctor Andrews describirá la parte clinica del programa. Nuestras facilidades dan énfasis tambien a los estudios básicos de los isótopos radioactivos útiles antes de emplearlos en el trabajo clinico. El segundo objectivo - adiestramiento - se consigna a las universidades maternas y al publico cientifico a traves de: uno, contratos con numerosos consultantes de facultades y con otras especialistas; dos, conferencias dictados por los miembros del cuerpo de la división médica; y tres, a traves de cursos especiales y reuniones. Como ejemplos de los ultimos, el mes pasado conducimos una reunión especial sobre las tierras raras en investigación bioquímica y médica. Durante la ultima semana de diciembre de este año, habrá una reunión de cuatro dias sobre Enérgia Atómica y Agricultura en Atlanta. Tengo algunas copias de estes programas conmigo para quien tengan interés. De interés especial a los doctores de Guatemala, es un curso especial sobre el uso de isótopos radioactivos en medicina durante cuatro semanas del año proximo, que será anunciado mas tarde por el instituto.

El doctor Andrews se dirigirá ahora a ustedes.

RADIOISOTOPES IN RESEARCH AND MEDICINE

Symposium offered to the Sixth Congress of
Physicians and Surgeons
Thursday Morning, Dec. 1, 1955
Guatemala City
Gould A. Andrews, Granvil C. Kyker, and Julio Toriello*

1. General Chairman - Opening remarks
2. Dr. Toriello - General remarks about symposium
3. Brief remarks by visitors

   (Kyker - General Program of Institute and Medical Division;
   Andrews - Clinical Program of Medical Division)
4. Exhibit on Medical Division Facilities (Andrews and Kyker)
5. Basic Concepts Concerning Radioisotopes (Kyker)
6. Isotopes in Medicine (Andrews)

-INTERMISSION-

7. Clinical Colloids (Andrews)
8. Rare Earths: (A) Radioisotopes of Interest (Kyker)

   (B) General Results in Animals (Kyker)

   (C) Radioyttrium in Prostate and Parametrium (Toriello)
9. Useful Methods in the Use of Radioisotopes

   (A) Autoradiography (Andrews)

   (B) The Scintiscanner in I 131 Studies (Andrews and Toriello)
10. General discussion and summary (Andrews)

*Dr. Toriello translated brief summaries into Spanish at the end of paragraphs and sections of material presented by Drs. Andrews and Kyker.

SIXTH CONGRESS OF THE COLLEGE OF MEDICINE OF GUATEMALA

Guatemala City, Guatemala

Granvil C. Kyker
Gould A. Andrews

From Monday, November 28, 1955 through Sunday, December 4, 1955

Outline of Scientific and Social Program

	Morning 9:00 - 12:00	Luncheon 1:00 - 2:30	Afternoon 5:00 - 7:00	Cocktail 7:00 - 9:00	Evening 9:00 - 10:30
Monday	_____	_____	_____	_____	*Inaugural Session
Tuesday	First	Las Palmas	Second	_____	Third
Wednesday	Fourth	Las Palmas	Fifth	*Courtesy of Mead Johnson	
Thursday	Sixth	Las Palmas	Seventh	_____	Eighth
Friday	Ninth	Las Palmas	Tenth	*Courtesy of Labs. Bonin	
Saturday	Eleventh	_____	_____	_____	*Dinner Dance
Sunday	_____	*Picnic	_____	_____	

*Wives Invited

SOME BASIC CONCEPTS CONCERNING RADIOISOTOPES

Granvil C. Kyker

List of items to be mentioned briefly as an introduction to the session.

1. Number of elements in universe.
2. Isotope examples of hydrogen.
3. Current concept of the structure of an atom.
4. Total number of isotopes.
5. Stable and unstable; natural and artificial isotopes.
6. A nuclear reactor.
7. Characteristic decay.
8. Half life.
9. $\alpha\ \beta\ \gamma$ radiation.
10. Sensitivity of detection.
11. Multiple detection.
12. Applications: tracer studies
    radiation sources

1. The chemist and physicist tell us that all material in all of the universe is composed of a relatively small number of elements. The number usually stated until recent years was ninety-two. More recently certain new ones have been produced by transmutation so that presently more than 100 have been examined.

2. Many of these elements exist naturally as atoms of different weight. For example hydrogen was thought to be a simple arrangement of one proton constituting its nucleus and one electron floating in an orbit about this nucleus. Then about a generation ago heavy hydrogen was discovered. This heavy hydrogen also had one planetary electron but in the nucleus there was a difference. The nucleus of both regular and heavy hydrogen had the same electrical charge but the weight of the latter was twice as heavy. This additional weight without electrical property was named a neutron.

3. The current concepts of atomic structure state therefore that the weight of an atom is almost completely located in the nucleus. Two primary particles compose the nucleus: - neutrons, possessing mass but no charge - protons, possessing mass, and also electrical charge equal and opposite to that of electrons.

   The electrons, possessing electrical properties but almost negligible mass, are in remote orbits. All chemical properties of an atom are attributable to the number and arrangement of the electrons.

   Therefore regular hydrogen and heavy hydrogen are isotopes of the same element with identical chemical properties; different mass, identical chemistry.

4. If we consider the total number of isotopes of all the elements, there are more than 1,000. This means that numerous isotopes are known for many elements. A large portion of the total are artificial and for the most part are produced in nuclear reactors.

5. The isotopes are classified into two groups: stable and unstable. The latter emit some form of energy when the nucleus undergoes a change and these are known as radioisotopes. Both stable and radioactive isotopes occur in artificial and natural materials. Examples of naturally radioactive isotopes are: radium, potassium, uranium, and rubidium. We have therefore developed physiologically in an environment of at least some radioactivity.

6. A nuclear reactor is a device that provides an atmosphere of neutrons the concentration of which can be controlled. By placing a stable isotope in this environment, some of the neutrons will collide with its nucleus and be absorbed. The product is another isotope.

7. The most characteristic property of a radioisotope is the rate at which its radioactivity disappears or decays. Nothing has ever been observed to alter this inherent rate: temperature, pressure, chemical reactions, electrical fields, etc. are without effect.

8. The rate of decay is exponential; that is to say that if one starts with a certain amount of radioisotope one half of it will decay in a certain time; of the 50 per cent remaining, one half of it (or 25 per cent of the original amount) will decay in another interval of time of equal length. The interval necessary for half of a given quantity of radioisotope to decay is known as its half life.

9. Whenever the nucleus of a radioisotope undergoes its characteristic change, some extra energy is released and is radiated. This energy is associated with the nuclear change as an emitted alpha, beta, or gamma ray. The gamma ray is similar to X rays and has great range of penetration. The β ray has relatively shallow penetration, and alpha rays are completely stopped by extremely thin layers of material. All three have apparently the same effect on matter in which their energy is absorbed. That is, each would in comparable amounts produce radiation injury similar to that produced by X-rays. Inside the body, however, alpha radiation can not be detected by external instruments, and beta radiation can be detected only if the isotope is near the surface, whereas proper instruments enable detection of gamma radiation at even great distances from the body.

10. One of the most striking characteristics of a radioisotope is the sensitivity that is possible in its detection. For example, if you could divide equally one milligram of a pure radioisotope such as radioactive gold among every inhabitant on the face of the earth, each inhabitant would possess a detectable amount.

11. An additional convenience in detection and measurement is afforded by recently designed apparatus for separately measuring each of several radioisotopes present in the same specimen of tissue or other material.

12. The practical usefulness of radioisotopes in present day scientific work relates to two applications: one is in tracer studies in which an exceedingly small amount of radioisotope mixed with a physiological amount of stable isotope of the same element enables one to determine its rate and pattern throughout a complex living system. The other relates to medical therapy in which the emitted energy is used to affect or destroy tissue in the same way that X ray and radium have proved useful tools for the physician.

CONCLUDING REMARKS

Gould A. Andrews

In conclusion, I would like to emphasize the great need for cooperation in the use of isotopes. There is, perhaps, no other diagnostic or therapeutic agent, or procedure, in the whole of medicine, which so urgently requires close collaboration of specialists from the different disciplines. This is true not only in research, but also in practical clinical applications. The following outline indicates this need.

BASIC ISOTOPE TECHNIQUES

Procedure	Specialist Needed
Preparation of stable material	- Inorganic chemist
Production of isotope	- Physicist
Determination of radiation characteristics	- Physicist
Preparation of special labeled compounds	- Organic chemist
Metabolic study, animal distribution	- Biochemist, pharmacologist
Instrumentation	- Electronics expert

CLINICAL ISOTOPE PROCEDURES

	Specialist		
	Radiotherapist	Internist	Surgeon
Tracer studies & Diagnostic tests	*	*	*
Blood diseases		*	
Thyroid disorders	*	*	*
Intracavitary therapy	*	*	*
Implantation of fixed sources	*		
Teletherapy	*		

The success of this cooperation has, in some institutions, been the most striking aspect of the isotope program, and sometimes has yielded benefits extending far beyond the original purpose of the collaboration.

TRIPS AND TALKS
CALENDAR YEAR 1955

January 4 — Funeral services for Dr. Samuel M. Seidlin, New York, New York. M. Brucer.

January 5 — Mt. Sinai Hospital, New York, New York. Talks with Dr. Norman Simon on brachytherapy problems. M. Brucer

January 21,22 — Bio-Medical Director's Meeting, Rochester, New York. M. Brucer. 1

January 23-25 — Medical School, University of Tennessee, Memphis, Tennessee. Talk to Department of Medicine. (Traveling Lecture Program of ORINS University Relations Division.) R.M. Kniseley

January 24-26 — Mt. Sinai Hospital, New York, New York. Talks with Robert Loevinger on beta dosimetry. American Cancer Society. Talks with J. Edward Spike, Jr. M. Brucer. 2

January 26 — Medical School, University of Tennessee, Memphis, Tennessee. Talk to Department of Medicine. (Traveling Lecture Program of ORINS University Relations Division.) G.A. Andrews.

February 14 — Cedars of Lebanon Hospital, Los Angeles, California. Dedication of Cobalt 60 teletherapy unit. M. Brucer. 3

February 22-23 — University of Arkansas, Little Rock, Arkansas. (Traveling Lecture Program of ORINS University Relations Division.) Lecture to faculty and graduate students of the School of Medicine. "Skeletal metabolism with particular reference to the bone-seeking radioisotopes." C.L. Comar. (1)

March 1,2 — Cancer Symposium, Johnstown, Pennsylvania. "Cancer research with radioisotopes." M. Brucer. 4

March 1-3 — Argonne National Laboratories, Chicago, Illinois and Michigan State University of Agriculture and Applied Science, East Lansing, Michigan. Organizational meeting on two forthcoming symposia dealing with atomic energy and agriculture. C.L. Comar. (2)

March 3,4 — Teletherapy Evaluation Program, Annual Meeting, Detroit, Michigan. M. Brucer, J.H. Harmon, and Nelda Edwards. 5

March 8,9 — Discussions with the Rockefeller Foundation regarding symposia and general programs; with New York AEC and the Army Medical Service regarding survey program. New York, New York, and Washington, D.C. C.L. Comar. (3)

March 17 — American Chemical Society, Cincinnati, Ohio. "Some recent developments in bone and nutritional studies." C.L. Comar. (4)

March 29-April 1	American Chemical Society, Cincinnati, Ohio. R.L. Hayes.
April 1	Consultation with photographic processor relative to Geneva exhibits, Atlanta, Georgia. M. Brucer and G.A. Andrews.
April 1	Cancer Research Laboratory, University of Florida, Gainesville, Florida. (Traveling Lecture Program of ORINS University Relations Division.) "Biochemical studies with certain rare earth radioisotopes." G.C. Kyker.
April 5	Stable Isotopes Division Seminar, Oak Ridge National Laboratory, Oak Ridge, Tennessee. "Use of cyclotron-produced isotopes." M. Brucer.
April 11	National Meetings of Sectional Secretaries and of the Council of the Society for Experimental Biology and Medicine, San Francisco, California. G.C. Kyker.
April 11-15	Federation Meetings, San Francisco, California. G.A. Andrews, G.C. Kyker, C.L. Comar, and A.L. Kretchmar. Rare Earth Round Table. "Dose effects and bone patterns in rare-earth metabolism." G.C. Kyker and C.L. Comar. Program arranged by G.C. Kyker. American Society of Biological Chemists. "Interstitial yttrium in prostate and parametrium." G.C. Kyker, J. Toriello, and R.M. Kniseley. Presented by G.C. Kyker. General Meeting. "Comparative metabolism of calcium and strontium." C.L. Comar.
April 15-17	American Association for Cancer Research. San Francisco, California. "Preliminary studies of yttrium 90 in man." G.A. Andrews, G.C. Kyker, R.M. Kniseley, E.L. Palmer. Presented by G.A. Andrews.
April 18-22	Symposium on Amino Acid Biogenesis and Protein Synthesis, University of California at Los Angeles. A.L. Kretchmar.
April 19	University of North Dakota, Grand Forks, North Dakota. (Traveling Lecture Program of ORINS University Relations Division.) "Metabolic properties of rare earth radioisotopes of medical interest." G.C. Kyker
April 24	V Congreso Inter-Americano de Radiologia, Washington, D.C. Conferences on the scintiscanner. M. Brucer.
April 30-May 2	Medical Association of Georgia, Augusta, Georgia. "Uses of radioisotopes in medical research." G.A. Andrews.

May 4,5	University of Michigan, Ann Arbor, Michigan. Talk to Medical Staff. "Clinical use of radioactive colloids." G.A. Andrews.
May 6,7	Program presented for Biomedical General Advisory Committee, Oak Ridge, Tennessee. M. Brucer and staff.
May 15-19	Radiation Research Society, New York, New York. "Some integral dose relationships in Co 60 teletherapy." R.L. Hayes.
May 24	Consultation with Office for International Conference relative to Geneva Conference, Washington, D.C. M. Brucer. 8
May 25	University of Tennessee, Memphis, Tennessee. (Traveling Lecture Program of ORINS University Relations Division.) "Rare earths in biochemical and medical research." G.C. Kyker.
May 26,27	Dedication of the Armed Forces Institute of Pathology, Washington, D.C. R.M. Kniseley.
June 1	City of Hope Medical Center, Duarte, California. Dedication of cobalt 60 teletherapy unit. M. Brucer. 9
June 2	Bio-Medical Director's Meeting, Los Alamos, New Mexico. M. Brucer.
June 3-5	A.M.A. Meetings and American Therapeutic Society, Atlantic City, New Jersey. G.A. Andrews, R.M. Kniseley. Gold Exhibit. Symposium on diagnostic and therapeutic uses of radioisotopes. "The future uses of radioisotopes in therapy." G.A. Andrews.
June 13,14	Bellevue Hospital, "Cobalt teletherapy installations." Conferences with the International Nickel Company on brachy-therapy devices, New York, New York. M. Brucer. 10
June 13-17	Postgraduate Course No. 8. Fundamental Advances in Internal Medicine. University of Colorado School of Medicine, Denver, Colorado. Etna L. Palmer.
June 14,15	Lexington, Kentucky. Talk to Medical Society. G.A. Andrews.
June 21-23	McCollum-Pratt Symposium on Inorganic Nitrogen Metabolism. Baltimore, Maryland. "Function of molybdenum in xanthine oxidase." C.L. Comar. (7)
June 22	Physicians' visit to the ORINS Medical Division, Oak Ridge, Tennessee.

"The program of the Medical Division." M. Brucer
"The use of isotopes in therapy." G.A. Andrews
"Iodine clearance problems." A.L. Kretchmar
"Thyroid uptake calibration." J.S. Eldridge
"The biochemistry of rare earths." G.C. Kyker
"Autoradiography." R.M. Kniseley
"Dosimetry measurement." R.L. Hayes
"The teletherapy and brachytherapy programs." M. Brucer
Tour through Medical Division facilities. J.H. Harmon

July 8 — Brachytherapy Committee. Oak Ridge, Tennessee. M. Brucer, J.S. Eldridge, Elizabeth B. Anderson.

July 8 — Meeting of pathologists cooperating in the Thyroid Collection Program, Oak Ridge, Tennessee. C.L. Comar, G.A. Andrews, R.M. Kniseley, J.H. Harmon, M. Brucer.

July 15-18 — University of Louisville Medical School, Louisville, Kentucky. Talks on thyroid uptake, cobalt 60, and lutecium 177. M. Brucer, G.A. Andrews, G.C. Kyker. 11

August 1-5 — Gordon Research Conference on "Structure, Chemistry, and Physiology of Bones and Teeth." Chairman of Session, C.L. Comar. (8)

August 3-9 — Thyroid Uptake Survey.
Spartanburg General Hospital, Spartanburg, South Carolina.
Charlotte Memorial Hospital, Mercy Hospital, and Malle Clinic, Charlotte, North Carolina.
Veterans Administration Hospital and Watts Hospital, Durham, North Carolina.
University of North Carolina Medical School, Chapel Hill, North Carolina.
Depaul Hospital, Norfolk, Virginia.
Medical College of Virginia, Richmond, Virginia.
University of Virginia Medical School, Charlottesville, Virginia.
Kings Daughter's Hospital, Staunton, Virginia.
J.S. Eldridge.

August 8-20 — International Conference on the Peaceful Uses of Atomic Energy, Geneva, Switzerland. "Teletherapy devices with radioactive isotopes." M. Brucer. "Radioisotopes in animal physiology and nutrition." C.L. Comar. (9)

August 24-September 8 — Thyroid uptake calibration surveys in England. 12
Royal South Hants Hospital, Southampton, England.
Bristol Royal Infirmary, Bristol, England.
Christie Hospital and Holt Radium Institute, Manchester, England.

Leeds Royal Infirmary, Leeds, England.
Sheffield National Cancer Center for Radiotherapy, Sheffield, England.
Nottingham Royal Infirmary, Nottingham, England.
Leicester Royal Infirmary, Leicester, England.
The University of Cambridge, Cambridge, England.
Addenbrooke's Hospital, Cambridge, England.
Royal Cancer Hospital, London, England.
Marsden Hospital, London, England.
New End Hospital, London, England.
Middlesex Hospital, London, England.
University of London, London, England.
Hammersmith Hospital, London, England.
Talks on cobalt installations, cesium 137, teletherapy, thyroid uptake calibration, scintiscanner. M. Brucer.

August 29 — Medical Research Council, Harwell, England. "Metabolism of bone-seeking radioisotopes." C.L. Comar.

August 30,31 — Visit to Agricultural Research Council's Field Station, Compton, England. C.L. Comar.

August 31-September 2 — Thyroid Uptake Survey.
Vanderbilt University School of Medicine, Veterans Hospital, and Meharry Medical College, Nashville, Tennessee.
Baptist Memorial Hospital, Kennedy Veterans Hospital, and University of Tennessee Medical School, Memphis, Tennessee.
J.S. Eldridge.

September 12-15 — American Chemical Society, Minneapolis, Minnesota. "Iodine 131 content of the human population: low level methods." C.L. Comar. American Society of Biological Chemists. "Holmium 166 with rare-earth carriers." G.C. Kyker and John Rafter. Presented by G.C. Kyker.

September 19 — Meeting of public health nurses of Cocke, Hamlin, Sevier, Roane, Anderson, Jefferson, and Loudon counties, Oak Ridge, Tennessee. "Nursing techniques in relation to radioisotope therapy." Mary Sutliff. "Psychological problems of patients and their families during terminal care." Etna L. Palmer.

September 19-23 — American Hospital Association, Atlantic City, New Jersey. J.H. Harmon.

13

September 19-23 — American Roentgen Ray Society, Chicago, Illinois. "An automatic controlled pattern cesium teletherapy machine." M. Brucer. Also in attendance F. Comas.

September 20-22 — Thyroid Uptake Survey.
Emory University Hospital, Veterans Administration Hospital, Piedmont Hospital, and Georgia Baptist Hospital, Atlanta, Georgia.

Maxwell Air Force Base Hospital, Maxwell Air Force Base, Alabama.
Veterans Administration Hospital and University of Alabama Medical Center, Birmingham, Alabama.
Holy Name of Jesus Hospital, Gadsden, Alabama.
Baroness-Erlanger Hospital, Chattanooga, Tennessee.
J.S. Eldridge

(10)

September 22 — Eighth Industrial Health Conference, Houston, Texas. "Atomic energy contribution to agriculture." C.L. Comar.

September 25-October 4 — Recalibration of the Keleket-Barnes hectocurie unit at Wayne University, Detroit, Michigan. J.I. Trombka.

September 30-October 1 — American Medical Writer's Association, St. Louis, Missouri. Elizabeth B. Anderson.

October 3,4 — Industrial Teletherapy Conference, Ottawa, Canada. M. Brucer.

14

October 7 — Berea Symposium on Atomic Energy, Berea, Kentucky. "Application of atomic energy to agriculture and biology." C.L. Comar.

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October 10 — 25th Annual Scientific Assembly of the Medical Society of the District of Columbia, Washington, D.C. Talk by G.A. Andrews.

October 11,13 — American Society for Clinical Pathologists. Pathology exhibit. R.M. Kniseley and G.A. Andrews.

October 14 — Thyroid Uptake Calibration Committee, Oak Ridge, Tennessee. M. Brucer, G.A. Andrews, Etna L. Palmer, A.L. Kretchmar, J.S. Eldridge, J.H. Harmon, Elizabeth B. Anderson.

October 20 — Tracerlab Symposium on Applications of Radioactivity in the Food and Food Processing Industries, Boston, Massachusetts. "Radioisotopes in nutritional research." C.L. Comar.

(12)

October 20-November 2 — Exhibit, "Man, the atom, and the future." On behalf of the Carnegie Endowment for International Peace, the Atomic Industrial Forum, and the Fund for Peaceful Atomic Development, New York, New York. A.L. Kretchmar and Warren Glaser.

October 22 — Talks with a Milwaukee industrial group on teletherapy design problems. M. Brucer.

15

October 24,25 — Bio-Medical Director's Meeting, Cleveland, Ohio. M. Brucer.

October 26 — Department of Radiology, Wayne University, Detroit, Michigan. Talks on teletherapy and brachytherapy. M. Brucer.

16

October 27-29	Conference on Rare Earths in Biochemical Research. Oak Ridge, Tennessee. Program arranged by G.C. Kyker. "Electrophoretic studies with amino acids." R. Loos. "Skeletal patterns of small intravenous doses." C.L. Comar. "Effect of dose on mobilization." G.C. Kyker and G.A. Andrews. "Dosimetry calculations and conference summary." M. Brucer.
October 28-November 2	American Society of Anesthesiologists, Boston, Massachusetts. Betty M. Cooper.

November 4	Organization meeting of the University of Michigan for the East Lansing conference on the use of isotopes in agriculture scheduled for January 12-14, 1956. C.L. Comar. (13)
November 5,6	Subcommittee on Human Applications, Oak Ridge, Tennessee. M. Brucer and G.C. Kyker.
November 17	Meeting of public health nurses of Knox, Anderson, Blount, Morgan, Claiborne, and Union counties, Oak Ridge, Tennessee. "Home nursing problems in relation to terminal cancer patients." Mary Sutliff. "The role of the public health nurse in the early detection of cancer." Etna L. Palmer.
November 17	Thyroid Uptake Survey. Veterans Administration Hospital and Emory University Hospital, Atlanta, Georgia. J.S. Eldridge.
November 18	Southeastern Section of the Society for Experimental Biology and Medicine, Atlanta, Georgia. "Some fundamentals of autoradiography - an illustrated lecture." W.D. Gibbs. "Gamma-ray spectrometry in radiochemical and medical research." J.I. Trombka. "The thyroid uptake survey of the Medical Division of ORINS." J.S. Eldridge. Sectional secretary and in charge of the annual meeting, G.C. Kyker.
28-30 de Noviembre-1-3 de Diciembre	Congreso Nacional de Medicina de Guatemala. "Isotopas en medicina." "Uso terapeutico de los coloides radioactivos." "Uso terapeutico del iodo radioactivo." "Conceptos leasicos en los estudios con indicadores radioisotopicos." "Tierras raras radioisotopicos." "Investigacion en animales de isotopos de interes medico." Desarrollo de los temas a cargo de los invitados de honor, Doctores Gould A. Andrews y Granvil C. Kyker. Traduccion y Resumen, a cargo del Dr. Julio Toriello.

December 1	Seventh Annual Nuclear Sciences Seminar. U.S. Naval Reserve, Oak Ridge, Tennessee. "Medical aspects of atomic Energy." M. Brucer.

December 5,6 — Westinghouse Corporation, Baltimore, Maryland. Talks on moving field therapy. M. Brucer.

December 6 — T.V.A. Association of General Practitioners, Knoxville, Tennessee. "Radioisotopes in medicine." Warren Glaser.

December 10-12 — Radiological Society of North America, Chicago, Illinois. M. Brucer.

December 11 — Brachytherapy Committee, Chicago, Illinois. M. Brucer.

December 12 — Teletherapy Evaluation Program, Chicago, Illinois. M. Brucer.

December 13 — Forsyth County Medical Society, Winston-Salem, North Carolina. "Some general considerations in the treatment of patients with incurable neoplasms." G.A. Andrews.

December 15 — Cancer Seminar Group, Cancer Research Laboratory, University of Florida, Gainesville, Florida. "Uses of radioisotopes in medical research." G.A. Andrews.

December 27-30 — American Association for the Advancement of Science, Atlanta, Georgia. M. Brucer, C.L. Comar, G.C. Kyker, R.H. Wasserman. The National Academy of Economics and Political Science, The Oak Ridge Institute of Nuclear Studies, Section on Social and Economic Sciences of the AAAS, and the National Social Science Honor Society. Program on "Some peaceful uses of atomic energy." M. Brucer, presiding. Physics Section. "Radioactive measurements in clinical diagnosis." M. Brucer. Pharmacy Section. "Developments in radioactive pharmaceuticals." M. Brucer.

Symposium on Atomic Energy and Agriculture. Program arranged by C.L. Comar.
Session 1 - Soil-plant relations.
Session 2 - Plant metabolism and crop improvement.
Session 3 - Animal metabolism.
Session 4 - Food sterilization.

In addition to these talks, numerous lectures by various members of the Medical Division staff were given for the courses of the ORINS Special Training Division.