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*Dear Reinhardt  
file*

RADIOACTIVITY RESEARCH CENTER REPORT

January 1, 1962 to June 30, 1963

K. G. Scott, Ph.D., Director

I. Service

The use of radionuclides and the service offered by the Radioactivity Research Center continues to increase on this campus; 1,230 isotope shipments were received during the reporting period representing a two-fold increase over the previous eighteen months. This involved the handling of 18,005 Curies of labelled compounds and isotopes and 268.5 Curies of Tritium. This is a reduction from the total amount in curies received in the previous period and represents a trend toward more expensive and exotic radiochemicals ordered in smaller quantity, better delivery by manufacturers and less decay prior to use.

The isotopes mentioned above were used in research in 236 projects described in this report and as routine diagnostic tests and therapy. Such projects place a heavy demand upon the consultative time of the academic staff and upon the available equipment and technical staff. The work load upon the liquid scintillation and gamma ray spectrometers has been especially heavy and 101,305 samples were assayed for one or more radionuclides during the past eighteen months. Additional space and personnel are necessary if we are to continue to serve this campus adequately.

II Instruction in Bioradiology and Related Subjects

The teaching of medical students, residents and others, employs the combined facilities of the Radioactivity Research Center and Radiology and in some instances, also receives financial support from the School of Pharmacy and the Department of Emergency Medicine. Fifty freshmen medical students enrolled in Emergency Medicine 121-B and thirty six continued the course in the sophomore year to complete the laboratory exercises and qualify for certification. Twelve students, mostly at the graduate level in the basic sciences enrolled in Bioradiology 125. Three evening courses were offered through Continuing Education in order to offer to those in outlying areas, the opportunity to learn isotope technics. The first, a series of five 2-hour lectures had an enrollment of over one hundred and fifty. This was followed by a fall and spring laboratory work shop comprised of thirteen 2-hour sessions leading to Atomic Energy Commission or California State certification following a comprehensive examination. The course was over subscribed (40) with students coming from as far as Redding and Modesto.

A one month full time course in isotope fundamentals is also offered and is primarily taken by the resident staff but also by research fellows, visiting faculty and others enrolling in Continuing Education. A large number of these from foreign countries return to establish isotope research programs in their home land. Fifty six M.D.'s or Ph.D.'s and sixteen technicians took this course.

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### III Radiochemistry (C. T. Peng, Ph.D.)

The following radiochemicals were synthesized and purified: (1) Vitamin D<sub>2</sub> tritiated; 11 mc, specific activity 150  $\mu\text{c}/\text{mg}$ , (2) Dicumarol <sup>131</sup>I labelled, approximately 10  $\mu\text{c}$ ; (3) Warfarin, <sup>131</sup>I labelled, approximately 10  $\mu\text{c}$  (4) Myleran-2-<sup>3</sup>H, approximately 1.6 gm. specific activity 450  $\mu\text{c}/\text{mg}$ , (5) Myristic acid-<sup>3</sup>H-1-<sup>14</sup>C, high specific activity; (6) Stearic acid <sup>3</sup>H, high specific activity.

### IV Future Expansion

A. Neutron activation analysis: A neutron generator has recently been obtained and is being installed in order to initiate a program of activation analysis. With a fast flux of  $10^{10} \text{ n}/\text{cm}^2/\text{sec}$ , this method will make possible a sensitive method for the detection of a number of elements without exposing the subject to unwarranted radiation or sample degradation including isotopes of iodine, nitrogen, fluorine, oxygen and many of the trace elements which are biologically important. The measurement of such activated nuclides will involve the use of a programmer (rabbit) and a multichannel (400 or 512) spectrometer plus print out and other ancillary equipment. The total cost of this complex will be about \$18,000. We are approximately \$7,000 short in obtaining the complete unit.

B. Whole Body Counter: The acquisition of a whole body counter sufficiently shielded to eliminate the major contribution to background by cosmic ray radiation is most desirable, cost: \$300,000. A means of financing are being explored. The acquisition of the multi channel analyzer mentioned above plus the detector now in hand will make it possible to measure whole body fluxes of radioactivity in subjects with the same approximate precision of that at Donner Laboratory in Berkeley or the projected facility at San Francisco General Hospital.

C. Over the year, it has become apparent that the teaching of isotope technics and related biophysical principles will occupy a large part of the time of the academic and technical staff. In order to enhance the Center's teaching potential, we are applying for a National Institutes of Health teaching grant to obtain badly needed equipment such as dual channel probes, scintiscanners, a model hospital clinical isotope laboratory for instruction of new students and other items related to specialized training in this field.

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INVESTIGATOR AND DEPARTMENT

Glass, L.E. Ph.D.  
Anatomy

Glendening, M.B., Ph.D.  
Ob & Gyn

Gonzales, I.E., M.D.  
Pathology

Greenberg, D.M., Ph.D.  
Biochemistry

ISOTOPE AND PROJECT

<sup>131</sup>I: Labeling mouse serum proteins

Tritium: Tritium gas will be used by Dr. Peng in the Radioactivity Center to label approximately 500 mg. Estriol. The resulting product with a desired activity of 10 to 20 millicuries per milligram will then be purified and used in MS 206 in microgram amounts per experiment as a tracer during the extraction of tissue being analyzed for Estriol.

<sup>14</sup>C: Tracer amounts of radioactive histidine are added to plasma previously obtained from mothers and their babies, before deproteinization and chromatography of an ion exchange column in order to determine the recovery of histidine originally present in the plasma.

Tritium (cholesterol 7-<sup>3</sup>H; palmitic-9-10-<sup>3</sup>H acid) The aim of this project is to determine whether or not cholesterol and palmitic acid accumulate in the arteries of rabbits who have developed various types of arterial lesions. Approximately ten rabbits with known arterial lesions will be used. Five rabbits will receive one dose of 1-4 mc of cholesterol-7-<sup>3</sup>H intraperitoneally. Five other rabbits will receive one dose of 1-5 mc of palmitic-9-10-<sup>3</sup>H acid intraperitoneally. The animals will be sacrificed from one to seven days after the intraperitoneal injection and autoradiographs of the arteries will be made.

Tritium: <sup>3</sup>H Nucleosides and nucleotides to be used to study conversion of ribonucleotides to deoxyribonucleotides in vivo and in vitro. May also be used in experiments with lipids and amino acids. These are not yet projected. Dosage would be at small level as in the above.

<sup>14</sup>C: Metabolism of various compounds of biochemical interest. Different members of the group are studying the metabolism of <sup>14</sup>C labeled amino acids and carboxylic acids and other compounds of importance for the metabolism of the animal body. These problems are: 1) Biosynthesis of choline and thymine from <sup>14</sup>C-formaldehyde. 2) Biosynthesis of serine from glyceric acid-<sup>14</sup>C. 3) Synthesis of cholesterol from acetate-<sup>14</sup>C in tumors. 4) Phospholipid metabolism of tumor studies with choline-<sup>14</sup>C. 5) Biosynthesis of protein studied with <sup>14</sup>C-amino acids. 6) Tryptophan metabolism. 7) Histidine metabolism.

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INVESTIGATOR AND DEPARTMENT

Epstein, W.L., M.D.  
Dermatology

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Farquhar, M.G., M.D.  
Pathology

Gerguson, E.H., M.D.  
Dermatology

ISOTOPE AND PROJECT

$^{14}\text{C}$ ;  $^3\text{H}$ : An isotopically labeled corticosteroid and a potent antibiotic will be applied to localized areas of skin of older patients with malignancies and skin diseases. After 2 to 12 hrs., the surface material will be removed and skin biopsies performed. Localization of the drugs will be detected by radioautographs of the frozen sections.

$^{14}\text{C}$  (glycopyrralate);  $^{14}\text{C}$  (a fluorotriamcino-lone acetonide)  $^3\text{H}$  (triamcinolone acetonide): Isotopically labeled corticosteroids (2,3) and a potent anticholinergic drug (1) will be applied to localized areas of skin of older patients with psoriasis or malignancies. After 6-12 hrs., the surface material will be removed and skin biopsies performed. Localization of the drugs will be detected by autoradiographs of frozen sections.

$^3\text{H}$  Methionine;  $^3\text{H}$  Leucine: The use of radio-isotopes will be given intravenously to small laboratory animals. At selected intervals after their injection, the animals will be sacrificed and the tissues (primarily pituitary glands) will be fixed and embedded for electron microscopy. Thereafter sections will be prepared for autoradiography at both the light and electron microscope level utilizing thin films of Ilform emulsions according to the technique of Caro.

$^{131}\text{I}$ : The clearance of intradermally injected  $^{131}\text{I}$  will be determined following prior treatment of the skin with a number of physiological drugs including histamine, histamine-liberators, noradrenalin, serotonin, acetylcholine, pilocarpine, etc. The initial experiment will be carried out in guinea pigs in order to familiarize ourselves with the technique and safety factors. The results of these experiments will be compared to similar studies in humans.

$^{22}\text{Na}$ : The clearance of intradermally injected  $^{22}\text{Na}$  will be determined following prior treatment of the skin with a number of physiological drugs including histamine, histamine-liberators, noradrenalin, serotonin, acetylcholine, pilocarpine, etc. These experiments will be similar to  $^{131}\text{I}$  used with guinea pigs.

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INVESTIGATOR &  
DEPARTMENT

oontd.  
Grotsky, G., Ph.D.  
Metabolic Unit

ISOTOPE & PROCEDURE

$^{14}\text{C}$ : (cholesterol, palmitate, steroid hormone, androsterone, progesterone, etc.) In vitro studies involving metabolism of labeled intermediaries by tissue slices and homogenates. Tracer use for chromatographic localization.

$^{14}\text{C}$  Alanine and  $^{14}\text{C}$  Leucine: We are presently studying the effect of carbohydrates on insulin secretion in the isolated perfused pancreas of the rat. DeNovo protein synthesis will be simultaneously followed by measuring the incorporation of labeled amino acids into the pancreatic protein.

$^{131}\text{I}$ : Will be employed to label Lys-9-vasopressin and oxytocin for use in development of immunoassay.

$^{131}\text{I}$ : The iodide will be used for the synthesis of high specific activity  $^{131}\text{I}$  growth hormone and possibly ACTH (100uc/ $\mu\text{gm}$ ). Since only 5 mgm. of hormone will be used for each preparation, the final product will contain approximately 4-500uc after removal of excess iodide  $^{131}\text{I}$ . This product will be used for the immunological assay of growth hormone at the Metabolic Unit by techniques currently established for insulin.

$^{14}\text{C}$ -4 Dehydrepiandrosterone: Use of a tracer dose (approx.  $5 \times 10^3$  cpm) for double isotope technique in vitro. The isotope will be used to determine losses during purification by chromatography of dehydrepiandrosterone secretion rate and half time disappearance. The latter use of tritiated DHIA has been approved under application with Dr. Biglieri.

$^{14}\text{C}$  Testosterone-4;  $^3\text{H}$  Testosterone 1-2; The isotope will be used to locate chromatographically hydrolyzed urinary testosterone glucuronide. This exploratory work will be aimed at measuring recovery and secretion of testosterone.

$^{14}\text{C}$ ;  $^3\text{H}$ : These isotopes will be used in a double derivative isotope technique for the measurement of progesterone.

$^{90}\text{Sr}$ : The isotope is an integral part of the ionization detector of a gas chromatograph and will not be used in any other manner.

$^{14}\text{C}$ : A study into the causes of gout.

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Goldfien, A., M.D.  
OB-Gyn

Goodwin, L.D., M.D. 95  
Biochem.

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INVESTIGATOR &  
DEPARTMENT

ISOTOPE & PROJECT

Wissig, S.L., Ph.D. contd.  
Anatomy

fate in normal and hyperthyroid rats. This will be correlated with electromicroscopic observations on the same thyroid glands.

Witt, J.A., M.D.  
Neurological Surg.

<sup>32</sup>P: The <sup>32</sup>P is taken up on a resin-exchange bead which is sealed to the end of a wire 5 inches long, the wire being equivalent in size to a No. 22 needle. The entire needle and wire are then sealed in an aluminum shield 4 mils thick so that no chance exists that the <sup>32</sup>P resin-exchange bead can escape. Guide needles, 18 gauge, will be stereotactically inserted into the basal ganglion of dogs and fixed in place for chronic study. At the appropriate time, the <sup>32</sup>P sealed in the aluminum shield will be introduced through the guide needles, the bead protruding 5 mm. beyond the end of the guide needle. This will be left in place for periods ranging from 5 minutes to 2 1/2 hours, determined on the dose rate scale and the bead and its shield then removed. The animals will be allowed to survive varying periods of time, then sacrificed and serial sections done on the lesions thus produced in the basal ganglion to determine the characteristics as to size, configuration, etc. of the lesion thus produced by the beta particles emitted from the <sup>32</sup>P. This <sup>32</sup>P bead is sealed in its aluminum container and will be housed in a polyethylene shield of sufficient thickness to prevent any radiation hazard and the polyethylene shield is machined in such a way that insertion of the bead and its aluminum shield into the guide needle can be accomplished without removing the needle from its polyethylene shield. The application will be once only in each animal. The estimated activity of the resin exchange bead is 100 mc. and the one single bead will be obtained.

Yun-Chi, Ph.D.  
Biochemistry

<sup>14</sup>C; <sup>32</sup>P; <sup>3</sup>H: Yeast, *N. crassa*, and pigeon liver are incorporated in a medium containing the labeled compound. The nucleic acid from these organisms are examined to study the biosynthetic processes of a specific nucleotide from these radioisotopes.

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DEPARTMENT

Vogel, J.M., M.D. contd.  
Radioactivity  
Research Ctr.

Ware, Wm.H., DDS  
Dentistry

Way, W.L., M.D.  
Pharmacology

Way, E.Leong, Ph.D.  
Pharmacology

Wellington, J.S., M.D.  
Pathology

Wissig, S.L., Ph.D.  
Anatomy

ISOTOPE & PROJECT

determinations of the samples will be carried out at the Radioisotope Laboratory of the USPHS Hospital, San Francisco. Dogs will be utilized for the experiment. A specific surgical preparation is involved and will be carried out in the animal lab of the USPHS Hospital.

<sup>35</sup>S: Inorganic sulfate will be given parenterally in order to label cartilage growth centers sufficiently to obtain radioautographs. Doses are based on schedule reported in J. Lab. Inv. 8:149, '59. It has been estimated that in the order of 1% of the label gets into chondroitin sulfate. The monkeys to be used have already been operated unilaterally to transplant costo-chondral growth centers to the mandibular condyles. (These animals will be housed in the RRC in order to collect excreta for waste disposal).

<sup>14</sup>C: Labeled with heroin for drug metabolism studies.

<sup>3</sup>H Morphine: To study the metabolism of morphine.

<sup>14</sup>C: To synthesize radioactive heroin in order to follow its metabolic pathway. Labelled acetic anhydride will be prepared from BaC<sup>14</sup>O<sub>2</sub> and be used to acetylate both hydroxyl groups of morphine. The resulting diacetylmorphine (heroin) will be administered to mice and rats and its tissue distribution and urinary and fecal excretion will be studied. Attempts will be made to separate, isolate and characterize any radioactive products which might be formed.

<sup>3</sup>H: To activate normorphine and compare its physiologic disposition with morphine because normorphine has been postulated to be a metabolic product of morphine responsible for its analgetic and addictive properties.

<sup>51</sup>Cr: Tagging of chicken erythrocytes for the determination of survival time in auto and homo transfusions.

<sup>131</sup>I; <sup>3</sup>H Leucine 4,5: The isotopes will be used to study the site of protein synthesis (leucine) and thyroid hormone formation (<sup>131</sup>I) in the rat.

<sup>131</sup>I; <sup>3</sup>H Leucine. Rats will be injected with either isotope and sacrificed at various intervals after isotope administration. Radioautographs of thyroid glands will be prepared in order to determine the site of formation of protein (to be compared with the site of thyroglobulin formation) and its subsequent

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INVESTIGATOR &  
DEPARTMENT

Tarver, H., Ph.D. contd.  
Biochemistry

ISOTOPE & PROJECT

$^{131}\text{I}$  iodide;  $^{14}\text{C}$  benzoic acid & glycine;  $^{35}\text{S}$  labeled protein: The  $^{131}\text{I}$  will be used as an indicator in studies on thyroid metabolism in rats. The  $^{14}\text{C}$  will be used in studies on the formation of hippuric acid in rats. The  $^{35}\text{S}$  labeled protein will be used in turnover studies on plasma proteins in rats.

$^3\text{H}$  various amino acids & nucleotides;  $^{14}\text{C}$  nucleotides and  $\text{Ba CO}_3$ : The  $\text{Ba CO}_3$  will be used after conversion to  $\text{NaHCO}_3$  in media to grow organisms in order to produce labeled amino acids and nucleotides. Other amino acids and nucleotides will be purchased from commercial sources labeled with either tritium or  $^{14}\text{C}$ . These materials will be used on studies in protein and nucleic acid synthesis carried out for the most part in rats. On occasion, rabbits will be used.

$^{131}\text{I}$ : This isotope will be injected into rats, normal, hyperthyroid and hypothyroid, and the distribution of the isotope will be investigated after an hour.

$^{14}\text{C}$  amino acids;  $^3\text{H}$  amino acids: Study of protein metabolism with particular reference to methionine toxicity using labeled amino acids.

$^{14}\text{C}$ ;  $^3\text{H}$ : Study protein metabolism with particular reference to methionine toxicity using labeled amino acids. This work is a continuation of a project of Dr. Tarver's.

$^{14}\text{C}$ : 10mc. of palmitic acid 1- $^{14}\text{C}$  complexed to albumin will be administered intravenously to a pregnant patient undergoing therapeutic abortion and hysterectomy. The fetal tissues will be analyzed to assess transfer of a free fatty acid across the human placenta.

$^{14}\text{C}$ : The labeled palmitic acid will be injected into pregnant sheep and the time and rate of transfer across the placenta to the fetus will be determined. An attempt will be made to study fetal utilization of the  $^{14}\text{C}$  by assaying umbilical artery and vein samples. This work will be accomplished in collaboration with Drs. Holm & Parker at the UC Davis Campus, Veterinary Medicine.

$^{131}\text{I}$  insulin;  $^3\text{H}$  insulin: Insulin labeled with tritium and  $^{131}\text{I}$  will be utilized to study renal clearance for insulin and the role of the kidney in insulin metabolism and degradation. The preparation of the isotopic label in usable form will be carried out at the Radioactivity Research Center or purchased from Abbott. The animal experimentation and activity

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Trowbridge, H.O., Ph.D.  
Path. & Dentistry

Van Duyne, C., M.D.  
OB & Gyn

Vogel, J.M., M.D.  
Radioactivity Res.  
Center

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DEPARTMENT

Tarver, H., Ph.D.  
Biochemistry

ISOTOPE & PROJECT

<sup>131</sup>I: Plasma proteins (generally albumin) will be iodinated with the <sup>131</sup>I containing additional carrier. The iodinated proteins will be used to study the breakdown of proteins in the intact animal in order to try and determine the site or sites of breakdown. Activities of the order of 7 mc will be used only in the experiments with dogs, much less will be used in the experiments with rabbits and rats.

<sup>14</sup>C: The <sup>14</sup>C will be converted into organic form by growing *R. rubrum* on media containing the <sup>14</sup>C in the form of bicarbonate (10mc. or less). The organisms will be separated, and either individual amino acids will be isolated and used to label the proteins of animals or the whole bacteria will be fed to animals. Measurements will be made on rates of incorporation and release of the amino acids from proteins.

<sup>14</sup>C: These amino acids (leucine, valine, alanine and lysine) will be used to study the incorporation into, or the release of amino acids or their keto acid analogs from the proteins of plasma tissues.

<sup>14</sup>C: Acetate-1-<sup>14</sup>C, and -2-<sup>14</sup>C will be used in liver slices from rats to measure the incorporation into lipid when the slices are incubated under different conditions.

<sup>131</sup>I: The isotope will be injected into rats, normal, hyperthyroid and hypothyroid, and the distribution of the isotope will be investigated after an hour.

<sup>3</sup>H: The isotopes will be used first to label amino acids and then proteins. The proteins so labeled will be used in metabolic studies in rats and rabbits.

<sup>75</sup>Se: The isotope is to be incorporated into the proteins of yeast in which it will appear in the form of selenomethionine and selenocystine. These amino acid analogs will then be isolated from the yeast by conventional methods. Then, they will be used in studies on protein synthesis in rats.

<sup>14</sup>C acetate; <sup>14</sup>C malonate: Acetate-1-<sup>14</sup>C, acetate-2-<sup>14</sup>C, malonate-1-<sup>14</sup>C and malonate -2-<sup>14</sup>C will be used in studies on lipid synthesis in homogenates of various kinds prepared from liver.

<sup>75</sup>Se selenite & amino acids; <sup>131</sup>I iodide; <sup>32</sup>P: <sup>75</sup>Se selenite will be used to label amino acids in micro organisms for isolation and use in higher animals (rats). Selenated amino acid will be purchased as they become available. <sup>131</sup>I will be used to label various proteins for turnover studies in rats. <sup>32</sup>P will be used in studies on nucleic and metabolism in micro organisms and rats.

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Smyth, F.S., M.D.  
Pediatrics contd.

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Taub, Norman, M.D.  
CRI

Crauss, W.G., M.D.  
Medicine

Tarver, H., Ph.D.  
Biochemistry

ISOTOPE & PROJECT

and (2) its action on the reabsorption of phosphorus by the kidney tubule. These measurements are to be made after the oral ingestion of Vitamin D-<sup>3</sup>H by observing the disappearance of D-<sup>3</sup>H from the blood by counting it and its excretion in the urine and feces. Concurrently, the behavior of calcium and phosphorus will be measured chemically. This information will be of value in evaluating the clinical status of the patient and in determining his future therapy. A dosage of 3 microcuries per Kg of body weight will be employed which will result in a minimal whole body radiation exposure of 1.22 mr/day prior to the elimination of the Vitamin D or its metabolites.

<sup>51</sup>Cr; <sup>131</sup>I: To be used in the measurement of the pulmonary capillary hematocrit of the Chloralose anesthetized cat at rest and during exercise induced by electrical stimulation of the sciatic nerves.

<sup>133</sup>Xe: This is an established tool for the study of regional ventilation and perfusion in the lung. Its use has been mostly in man, but we plan to use it in dogs before and during the development of acute pulmonary edema. It will be given via a closed circuit airway system for ventilation studies. Almost all of it is expired since it is not very soluble. Some will be given in solution intravenously to measure regional blood flow in the lung. It is almost all expired via the airways. The half life is 5.27 days. We plan to give about 0.5mc per test and to record over the lungs using the dual recording rate meter set up in S-372. We have already used this device in practice tests and are familiar with it.

<sup>131</sup>I: <sup>131</sup>I tagged rattlesnake venom in order to follow its rate of absorption and tissue localization in mice and rabbits. Electrophoretic studies will also be made with the tagged venom.

<sup>131</sup>I cortisoloxin: Snake venom is to be labelled. The change in toxicity is to be evaluated in mice. Then, the disappearance time from an injected spot in a rabbit is to be measured.

<sup>35</sup>S: Yeast will be grown on media containing the radioactive sulfate; the yeast will be used either directly to label the proteins of experimental animals for turnover studies or else the yeast will be hydrolyzed, individual amino acids isolated, and used as such to label proteins. Methionine will be used to label plasma proteins in vitro using suitable chemical methods.

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INVESTIGATOR &  
DEPARTMENT

Sheline, G.E., M.D.  
Radiology

ISOTOPE & PROJECT

$^{203}\text{Hg}$ : Radioactive  $^{203}\text{Hg}$  Neohydrin has been shown to be the best substance available for selective location in brain cysts and tumors for external preoperative scintillation scanning localization techniques. Prior loading of kidneys with mercurhydrin reduces radiation dose to kidneys, with the larger doses needed for brain scanning techniques.

Smaller quantities given without prior mercurhydrin loading will remain in the kidneys long enough to allow external scintiscanning techniques in patients suspected of renal abnormalities.

$^{51}\text{Cr}$ : An occasional patient is encountered with repeated hemolytic episodes in whom no cause, such as spherocytosis or the other usual hemolytic etiologies, can be determined. These patients also exhibit very short survival times of their own  $^{51}\text{Cr}$  tagged red cells as well as those of compatible donor red cells. To help determine whether the hemolytic episodes are a manifestation of abnormalities in the red blood cells or in one of the other blood or vascular components, request is made to inject  $^{51}\text{Cr}$  tagged red cells from such patients into normal adult compatible recipients to determine survival time of the red cells in a normal environment. In each instance, the normal adult recipient will be a parent or sibling of the patient.

$^{131}\text{I}$ : It has been shown that Telopaque becomes attached to pigmented gall stones. Telopaque has been tagged with  $^{131}\text{I}$  and the present experiment is a continuation of the work. It is apparent that bile becomes free of the tagged substance within 48 hours and that one is then able to detect the radioactive material on the surface of stones with a counter at operation. This is potentially of great practical value to avoid overlooked stones. Attempts will be made to ascertain the quantities of radioactivity in gall bladder as well as common duct bile in addition to the stones. Telopaque  $^{131}\text{I}$  will not need to be ordered and will be available to us through the group at the University of Kentucky.

$^{14}\text{C}$ : Putting 50ug of  $^{14}\text{C}$  labeled Nicotine in pericardial sac of dogs, withdrawing and counting blood samples to determine speed of absorption of  $^{14}\text{C}$  Nicotine from pericardial sac. Acute experiments--dogs sacrificed after experiments.

$^3\text{H}$ : Pure Vitamin D will be labeled with  $^3\text{H}$  using the facilities of the Radioactivity Research Center which has been cleared for this study: Is is proposed to study metabolism of pure Vitamin D labeled with tritium in patients having D-resistant rickets and pseudo-hypoparathyroidism. Two actions of D are to be measured: (1) its absorption from the intestinal tract,

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len, Wm., M.D.  
Surgery, SFGH

Seight, P., Ph.D.  
CVRI

Smyth, F.S., M.D.  
Pediatrics

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INVESTIGATOR &  
DEPARTMENT

Sheline, G. E., M.D.  
Radiology

ISOTOPE & PROJECT

Any & all isotopes: For use in performing standardized, generally recognized diagnostic and therapeutic clinical methods as directed by the Section of Radiation Therapy.

<sup>24</sup>Na: To be used to study exchange rates of sodium from circulating blood to cerebrospinal fluid. This is part of an investigation to establish diffusion rates of electrolytes across the cerebrovascular barrier in cases of malignant tumors involving the brain or meninges.

<sup>131</sup>I: To be used to study exchange rates of iodine from circulating blood to cerebrospinal fluid. This is part of an investigation to establish diffusion rates of electrolytes across the cerebrovascular barrier in cases of malignant tumors involving the brain or meninges.

<sup>14</sup>C: To be used to measure diffusion rates of labeled metabolites from blood to cerebrospinal fluid. This is part of an investigation to establish diffusion rates of electrolytes across the cerebrovascular barrier in cases of malignant tumors involving the brain or meninges.

<sup>132</sup>I: The Tellurium 132 is to be used as a parent source for the <sup>132</sup>I. The <sup>132</sup>Te is a fission product to which carrier sodium Tellurite is added and adsorbed on alumina. The useful decay product (<sup>132</sup>I) is obtained by extraction with 0.01 M ammonia as is found in the system. Assay of the activity of <sup>132</sup>I before use will be conducted by Dr. Gail Adams. The <sup>132</sup>I has a very short half-life and could be used for short (less than 6 hr.) studies of thyroid function. The radiation exposure/microcurie ingested or injected would be a small fraction ( $\pm 1\%$ ) of the exposure from similar amounts of <sup>131</sup>I and would therefore be most useful in evaluating thyroid function in children and adolescents. It could be used whenever longer studies were not felt to be necessary.

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INVESTIGATOR &  
DEPARTMENT

Rubinstein, M., M.D.  
Neurology

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Ott, K.G., Ph.D.  
Radioactivity Re-  
search Center

ISOTOPE & PROJECT

$^{203}\text{Hg}$ . Neohydrin: This investigation is designed to label the pathologic lesion in experimental allergic encephalomyelitis with radioactive material and to obtain radioautographs of these lesions so as to delineate some of their characteristics. It is anticipated that a means of diagnosing demyelinating lesions of the CNS by radioisotopic techniques can be established. Studies on blood brain barrier in allergic encephalomyelitis will also be carried out.

$^{131}\text{I}$  (RISA) This investigation is designed to label the pathological lesion in experimental allergic encephalomyelitis with radioactive material and to obtain radioautographs of these lesions as to delineate some of their characteristics. It is anticipated that a means of diagnosing demyelinating lesions of the CNS by radioisotopic techniques can be established. Studies on blood brain barrier in allergic encephalomyelitis will also be carried out.

$^{131}\text{I}$ ;  $^{82}\text{Br}$ ;  $^{22}\text{Na}$ ;  $^{36}\text{Cl}$ ;  $^{86}\text{Rb}$ : Cancer research: Tumor Host relationship studies (continuous project since '48) to study the fate of iodinated compounds in normal and tumor-bearing animals.

$^{75}\text{Se}$ : The fate of  $^{75}\text{Se}$  as  $\text{H}_2\text{SeO}_3$  as well as Selenium substituted in the molecule in the sulphur containing amino acids will be investigated in rats.

$^{36}\text{Cl}$ : To investigate the action of lysergic acid derivatives on the intra-and extra-cellular fluid space of rats.

$^3\text{H}$  Water: Standardization of instruments at Radioactivity Research Center.

$^{32}\text{P}$ ;  $^{137}\text{Cs}$ : To calibrate instruments.

$^{86}\text{Rb}$ : Cancer Research: A study of the biological uptake of  $^{86}\text{Rb}$  in red cells from normal and tumor-bearing rats.

$^3\text{H}$ : Sealed source of tritium as hydride to be used as target for neutron generator, 3-5 curies per target. Half-life of target approximately 12 hours, one to twenty targets per year estimated use. Isotopes produced will be cleared in separate applications.

Any & all isotopes: For use in class in which principles and practices of radiation protection, radioactivity measurement standardization and monitoring techniques and instruments, mathematics and calculations basic to the use and measurement of radioactivity are taught and in which tracer studies are taught.

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INVESTIGATOR &  
DEPARTMENT

Pollycove, M., M.D.  
Radioisotope Unit  
SFGH

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raport, E., M.D.  
Medicine

Linhardt, W.O., M.D.  
Medicine

Edwell, V.W., Ph.D.  
Biochemistry

Esner, J., M.D.  
Metabolic Unit

ISOTOPE & PROJECT

<sup>14</sup>C: In order to study the effect of various pathologic states on glucose metabolism of the red blood cell. Whole blood from patients with various clinical states will be incubated in vitro with glucose -1 C<sup>14</sup> and the C<sup>14</sup>O<sub>2</sub> produced will be measured. For in vitro incubation with blood only; will not subsequently be administered to animal or man, not for human use.

Any & all isotopes: For use in performing standardized, generally recognized diagnostic and therapeutic clinical methods.

<sup>199</sup>Au: For diagnostic use in hepatic scintigrams.

<sup>198</sup>Au: For diagnostic use in hepatic scintigrams.

<sup>131</sup>I; <sup>51</sup>Cr: This is a request for renewal of approval given last year for use of these isotopes in the Cardiopulmonary Unit, SFGH. Because the Unit began as a new laboratory about two years ago, the work was late in getting started and only a very few experiments were carried out. Therefore, it is requested that the same approval given last year for use of these isotopes on patients for determination of red cell and plasma volumes, both total blood volumes and regional splanchnic blood volumes. In certain circumstances, they will also be used for the measurement of cardiac output and central blood volume for the measurement of cardiac output and central blood volume measurements following injection through a cardiac catheter and collection from rotating tubes via an indwelling arterial needle.

<sup>3</sup>H: Radiolabeling of ova from donor mice. Transplantation of ova into uteri of normal and x-irradiated mice, study of development of ova.

<sup>14</sup>C (mevalonic acid) <sup>14</sup>C (acetic acid): Isotopes will be used in experiments with bacterial extracts.

<sup>14</sup>C Progesterone-4; <sup>14</sup>C Testosterone-4; Delta 5; Pregnenolone 7a <sup>3</sup>H 17-a-hydroxy; <sup>14</sup>C Progesterone-4; In vitro tissue incubates will be enriched with the radioactive material and derivatives prepared by suitable chromatography. Only in vitro studies will be conducted with this material using excised testes and adrenals.

<sup>14</sup>C dehydroepiandrosterone; <sup>3</sup>H andros-4-ene-3,17-dione: To be used in vitro work, incubation of rabbit's testes, whole homogenate.

<sup>14</sup>C progesterone, <sup>3</sup>H pregnenolone: Progesterone-4-<sup>14</sup>C and pregnenolone <sup>3</sup>H-7a will be used as substrates for incubation of rabbit testes in vitro.

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INVESTIGATOR &  
DEPARTMENT

Petrakis, N.L., M.D.  
CRI

ISOTOPE & PROJECT

$^3\text{H}$ : In vitro studies only.

$^{131}\text{I}$ : To evaluate the effective blood flow in the bone marrow of patients with leukemia and neoplastic diseases and serious hematological disorders. A trace amount 1-5 $\mu\text{c}$  of  $^{131}\text{I}$  will be injected into the marrow cavity and its rate of clearance will be determined under a variety of pharmacologic conditions. Previous studies of this nature have been reported by the principle applicant.

Petrakis, Masouredis & Miller: The Local Blood Flow in Human Bone Marrow in Leukemia & Neoplastic Diseases As Determined By the Clearance Rate of  $^{131}\text{I}$ . J. Clin. Investig. 32:952, 1953. These are research tools used in studying cancer patients. There is no planned termination point for this study.

$^{51}\text{Cr}$ : Patients with hematologic disorders involving erythrocytes, leucocytes, and platelets, such as those associated with hemolytic anemias, purpuras, hypersplenism, lymphomata, leukemias, and carcinomas. Infections, etc., will be studied as to erythrocytic volume, red blood cell survival, and sites of deposition and destruction of tagged erythrocytes leucocytes and platelets. These are research tools used in studying cancer patients. There is no planned termination point for this study.

$^{59}\text{Fe}$ : To study the iron metabolism of erythrocytes in patients with serious hematological conditions and diseases, and in patients with leukemia, lymphomata, and other types of malignant neoplasms.  $^{59}\text{Fe}$  bound to plasma beta-globulin in vitro will be injected into patients to investigate the in vivo metabolism of iron with respect to rate and sites of erythrocyte and hemoglobin formation and destruction. These are research tools used in studying cancer patients. There is no planned termination point for this study. Patients are those having cancer or leukemia if under age of 40.

$^{131}\text{I}$ ,  $^{125}\text{I}$ :  $^{131}\text{I}$  Polyvinylpyrrolidone is to be used for routine diagnostic brain scans.  $^{125}\text{I}$  compounds to be used in performing standardized, generally recognized diagnostic clinical methods. The list of procedures & dosages as submitted Oct. 1962.

$^{14}\text{C}$ : In order to study the effect of various pathologic states on glucose metabolism of red blood cells. Whole blood from patients with various clinical states will be incubated in vitro with glucose- $^{14}\text{C}$  and the  $\text{C}^{14}\text{O}_2$  produced will be measured. For in vitro incubation with blood only, will not subsequently be administered to animal or man, not for human use.

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Mallycove, M., M.D.  
Radioisotope Unit  
SFGH

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INVESTIGATOR &  
DEPARTMENT

Eng. C.T., Ph.D.  
contd:

ISOTOPE & PROJECT

<sup>14</sup>C: In our study of the lipid metabolism and the metabolic fate of biological alkylating agents in normal and tumor-bearing rats and mice, labeled compounds will be used. These include various fatty acids, carcinostatic agents (chlorambucil, TEM, etc.) and some amino acids. These compounds will be either doubly labeled with <sup>14</sup>C and <sup>3</sup>H or labeled with <sup>14</sup>C at a given position in the molecule. At present, these labeled compounds are not commercially available.

<sup>35</sup>S: According to Robert & Warwick (Nature 183, 1509 '59) the in vivo mechanism of action of Myleran (Busulfan) is due to the formation with cysteine of a S-β alanyl tetrahydrothiophenium salt. However the identity of the compound was not firmly established except by analogy to in vitro reactions. We wish to follow up on this point by administering the alkylating agent labeled with tritium to normal and tumor bearing animals dosed with <sup>35</sup>S labeled cysteine or cystine. The urinary metabolites from these animals will be scanned for compounds containing both <sup>35</sup>S and tritium as labels in the molecule. Experiments will be repeated using other alkylating agents.

<sup>3</sup>H (gas); <sup>14</sup>C (BaC<sup>14</sup>O<sub>3</sub>) Preliminary study showed some significant differences in fatty acid composition of tissue lipids in normal and tumor bearing rats and mice, especially upon force-feeding. Therefore it is of interest to use labeled fatty acid esters to study the kinetics involved in the utilization of acid esters such as laurate, Myristate, palmitate, stearate oleate, etc. in these animals.

<sup>32</sup>P; <sup>32</sup>P as phosphate will be administered intraperitoneally to fasting normal and tumor-bearing mice. At varying time intervals following injection these animals will be sacrificed and the phospholipides from their organs will be extracted, radioassayed and fractionated by the technique of thin layer chromatography to determine their rate of formation.

<sup>3</sup>H (T<sub>2</sub> gas): Tritium will be used to synthesize Myleran (tetra methylene bismethane sulfonate) with tritium in the alkane moiety of the molecule. Approximately 8 to 10 g. of the tritiated material with high specific activity will be prepared. The tritiated Myleran will be sent to Helen Vodopick, MD, of the State Univ. of Iowa Hospital for use in clinical investigations under the guidance of Dr. Titus C. Evans. The project is undertaken as a joint effort of research.

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INVESTIGATOR &  
DEPARTMENT

Myers, H.M., DDS  
contd.

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Jarian, J.S., M.D.  
Gen. Surgery.

Olson, Marjorie M., Ph.D.  
Anatomy

Pengand, J.,  
Biochemistry

Rege, E.B., MD & Glen-  
ning, M.B., MD  
OB-Gyn.

Papac, Rose, M.D.  
Cancer Research

Peng, C.T., Ph.D.  
Radioactivity Res.Ctr.

ISOTOPE & PROCEDURE:

from the surface into the solution followed by precipitation of calcium F<sub>2</sub>. If the latter mechanism is true, labeled <sup>45</sup>Ca from the bulk solution should find its way into the microcrystals of calcium F<sub>2</sub>. Carrier free <sup>45</sup>Ca is needed to avoid exceeding the solubility product of calcium F<sub>2</sub> (3.67x 10<sup>-7</sup> at 22°C and pH 7.0) by inert carrier calcium which would be present in the less expensive <sup>45</sup>Ca over that of normal exchange reactions of the apatite will be a measure of the amount of calcium F<sub>2</sub> formation produced by the mechanism outlined.

<sup>35</sup>S: Labeled cysteine to be administered to normal and Vitamin A deficient rats. Taurine and SO<sub>4</sub> to be recovered from urine.

<sup>3</sup>H Thymidine: Project involves in vivo labeling of guinea pigs and mice with tritiated thymidine and passively transferring the labeled lymphoid cells obtained from the donors to recipient mice and guinea pigs. The recipient tissues are removed after appropriate intervals and labeled cells identified by autoradiography and/or quantitation of total tritium in tissues determined in a liquid scintillation counter.

<sup>3</sup>H: tritiated thymidine, cytidine, adenine: In vivo labeling of embryonic and placental tissues (rats).

<sup>14</sup>C; <sup>32</sup>P; <sup>35</sup>S; <sup>3</sup>H: In vivo labeling of compounds of interest for the study of protein synthesis; in vitro study of the purified enzyme systems involved with isotopic tracers.

<sup>3</sup>H: Tritium labeled estrone, estradiol, and estriol will be added to placental extracts and perfusates for the purpose of monitoring recoveries of these steroids from these preparations. Tritiated estrone and estradiol will be obtained commercially. Estriol will be tritiated by Dr. C.T. Peng of the Radioactivity Research Center. It is for this purpose that the 20 curies of tritium gas will be purchased. This will be handled only by Dr. Peng in the area of the RRC.

<sup>3</sup>H: To determine DNA synthetic times, turnover times, and resting phases of mitotic cycle in HeLa strain cells, and to determine alterations of these times in HeLa cells exposed to nitrogen mustard (varying concentrations of nitrogen mustard in times to exposure).

<sup>14</sup>C: Myristic-1-C<sup>14</sup> acid is to be given orally to normal and tumor-bearing mice to study the extent and the rate of its conversion to other fatty acids in tissue lipids in these animals.

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INVESTIGATOR &  
DEPARTMENT

Masouredis, S.P., M.D.  
contd.

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Cormack, K.R., M.D.  
Radiology

Myers, F.H., Ph.D.  
Pharmacology

Johnson, H., M.D.  
Pathology

Myers, H.M., DDS  
Dentistry

1159208

ISOTOPE & PROJECT

<sup>3</sup>H: <sup>3</sup>H labeled red cell isoantibodies will be prepared by polymerizing the corresponding labeled methionine to the antibody containing gamma globulin. The labeled antibodies will be reacted with red cells in vitro and radioautographic techniques will be used to study the binding of antibody to individual red cells.

<sup>59</sup>Fe: This will be used to study iron incorporation into red cell hemoglobin in patients with hematological disorders.

<sup>51</sup>Cr; <sup>131</sup>I: Serial blood volume determinations are to be made on five dogs by simultaneous use of <sup>51</sup>Cr-tagged red blood cells. <sup>131</sup>I-tagged serum gamma globulins, and T 1824-tagged albumin. The major purpose is to check the plasma volume space as determined by the globulin volume as compared to the albumin volume and that obtained from the red cell volume and venous hematocrit.

<sup>3</sup>H: Digitoxin, a representative cardiac glycoside, has a long duration of effect biologically but is chemically very short lived. This fact is established by several types of studies including the use of <sup>14</sup>C labeled digitoxin. The urinary excretion products have been shown by embryo duck heart assay to be cardioactive. Characterization of these active metabolites is the problem that we propose to study by using tritiated digitoxin. We propose to work with dogs with rabbit liver homogenate in which preparation we have already demonstrated the presence of enzyme that causes the disappearance of digitoxin.

<sup>3</sup>H Thymidine: <sup>3</sup>H Cytidine: Tissue cultures will be grown in medium 199 to which the tritiated substances are added. The uptake of the radiochemicals would be determined by autoradiology (Pele-The Stripping-film Technique of Autoradiography": Intern. J. Applied Rad. & Isotopes; 1956-57; 1-2: 172 (1) and determinations of specific activity by the method of Kahan (Purification & Measurement of Microgram Amounts of Radioactive Nucleic Acids & Proteins from Animal Cells in Tissue Culture; Analyt. Biochem. Sept. '60; 1(2):107-126).

<sup>45</sup>Ca: Treatment of hydroxyapatite or powdered tooth enamel with fluoride solutions varying from 300-30,000 ppm of fluoride and pH varying from 5-10 has revealed that calcium F<sub>2</sub> microcrystals are deposited on the surface of the apatite. It is postulated that the calcium F<sub>2</sub> is formed not by simple adsorption of the F<sup>-</sup> ions into Ca<sup>++</sup> ions of crystal surface but by dissolution of the Ca<sup>++</sup>

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DEPARTMENT

Ludowieg, J., Ph.D.  
contd.

Ludwig, F., M.D.  
Radiological Lab.

Maibach, H.I., M.D.  
Dermatology

Masouredis, S.P., M.D.  
CRI

ISOTOPE & PROJECT:

All the experiments concerning the incorporation of radioactive materials that will be handled in room MS 104 will have doses no greater than 0.1 mc.

$^{14}\text{C}$ : Radioactive incorporation in isolated in vitro systems (biochemical) which synthesize mucopolysaccharide intermediates.

$^3\text{H}$ ;  $^{14}\text{C}$ ;  $^{35}\text{S}$ : Above listed isotopes will be used during the period of one year in experiments involving the preparation on chemical compounds. The biological work will restrict the use of these compounds on cell-free systems with radioactive doses no larger than 0.1 mc. per mg. will be prepared in Dr. Peng's laboratory. The use and handling of these compounds will be in 104 of the old medical school.

$^{51}\text{Cr}$ : Ordinary and triple parabionts of male Sprague-Dawley rats. It is planned to inject intravenously in one of the parabionts one single time labeled erythrocytes and to determine when equilibrium between both partners is reached.

$^3\text{H}$ : For absorption study; external use only.

$^{131}\text{I}$ : This will be used to label plasma proteins and antibodies. The labeled proteins will be used primarily for in vitro immunochemical studies in the area of immunohematology.

Patients with the following disorders will be studied: 1) acute and chronic leukemias; 2) acquired hemolytic anemias, 3) multiple myelomas and other dysproteinemias. Practically all in category 3 and most in category 1 will be over 40 years of age. The acute leukemias and some of the patients in category 2 will be in the 25-40 yr. range because of the age incidence of these disorders.

$^{125}\text{I}$ : This will be used to label plasma proteins and antibodies. The labeled proteins will be used primarily for in vitro immunochemical studies in the area of immunohematology. Patients with the following disorders will be studied: 1) acute and chronic leukemia, 2) acquired hemolytic anemias and 3) multiple myelomas and other dysproteinemias. Practically all in category 3 and most in category 1 will be over 40 years of age. The acute leukemias and some of the patients in category 2 will be in the 25-40 year range because of the age incidence of these disorders.

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INVESTIGATOR &  
DEPARTMENT

Li, J.G., M.D.  
Medicine

oken, Hans F., M.D.  
Medicine

ongcope, C., M.D.  
Metabolic Unit

oran, Muriel R., Ph.D.  
Medicine

udowieg, Julio, Ph.D.  
Orthopedic Surg.

ISOTOPE & PROJECT

$^{60}\text{Co}$ : This experiment is designed to evaluate patients suffering from anemia in order to diagnose pernicious anemia and other macrocytic anemias.  $^{60}\text{Co}$  labeled  $\text{B}_{12}$  will be administered orally. The subsequent test will be essentially that of Schilling; urine and plasma samples will be measured for  $^{60}\text{Co}$ .

$^{47}\text{Ca}$ : All preparations of serum are done in Kalamazoo, Michigan by the Upjohn Co. Our part in the project is to separate serum proteins ultracentrifugally and determine ratio of bound to free  $^{47}\text{Ca}$ .

$^{14}\text{C}$  glucose;  $^{14}\text{C}$  cholesterol:  $^{14}\text{C}$  glucose will be used in vitro insulin assay utilizing rat adipose tissue and collection and measurement of  $\text{C}^{14}\text{O}_2$ .  $4\text{-C}^{14}$  cholesterol will be used in vitro studies of cholesterol esterification by homogenates of adrenal tissue.

$^3\text{H}$  Thymidine: Injection of single dose of  $1.5\mu\text{c}/\text{Gm}$ . intraperitoneally into rats and animals sacrificed after various intervals, intestine removed and tissues prepared for autoradiography. Animals to be used will be parabiotic pairs consisting of one control animal and one having had an intestinal resection.

$^3\text{H}$ : Administration of tritiated thymidine intraperitoneally in rats to be sacrificed at regular intervals to measure the turnover rate of the intestinal mucosa in normal rats and rats subjected to partial resection of the small intestine.

$^3\text{H}$ : Tritium incorporation into pyridine nucleotides. The reaction will be carried out in water solution, in "in vitro" experiments. Work will be done in a hood.

$^{14}\text{C}$ : Radioactive isotope incorporation into chemical compound. Experiments are to be performed with enzymatic systems "in vitro".

$^3\text{H}$ ; Sulphate-35: S-35 sulfate will be used to measure the rate of biosynthesis of sulfated compounds in embryonic cartilage extracts.

Tritium gas will be handled in the Radioactivity Research Center under the supervision of Dr. C. T. Peng. The purpose of this experiment is to tritiate uridine compounds in order to measure their incorporation in chondroitin sulfate present in embryonic cartilage.

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INVESTIGATOR &  
DEPARTMENT

Jergesen, F., M.D.  
contd.

Jones, M.D., M.D.  
Radiology

Katzung, B., M.D.  
Pharmacology

Preven, M.D.  
Preven. Med.

ISOTOPE & PROJECT

It is the purpose of this study to compare the uptake of  $^{51}\text{Cr}$  and  $^{32}\text{P}$  in osteoarthritic femoral heads that have been removed incidental to arthroplasty. The results will be correlated with microscopic examination of the removed bone.

$^{35}\text{S}$ : Two hundred microcuries per 100 grams body weight of Long-Evans' strain rats to be injected interperitoneally. Rats to be used will be males of 100, 300 and 400 gram weights, and females of 100, 200 and 300 gram weights. Two animals of each category will be utilized. Half of the group are to be sacrificed 24 hours after injection and the other half 72 hours after injection. Sections of mid and lower thoracic spine and upper and lower lumbar spine are to be prepared for radioautographs in order to assess the deposition of radioactive sulphur within the nucleus pulposus.

$^{45}\text{Ca}$ ;  $^{14}\text{C}$ : The effect of several maneuvers (effecting cardiac contractility in vitro) on calcium fluxes will be determined using  $^{45}\text{Ca}$  as the tracer material. Rat, guinea pig, and rabbit myocardium will be mounted in isolated tissue baths and exposed to physiologic saline solution containing  $^{45}\text{Ca}$  and then analyzed for uptake of calcium. Sucrose  $^{14}\text{C}$  will be utilized in a similar fashion to determine the extracellular space of the isolated tissue.

$^{131}\text{I}$ : To measure efficiency of fat absorption in rats subjected to various dietary situations by measuring the excretion of  $^{131}\text{I}$  in the feces after intragastric administration of  $^{131}\text{I}$  triolein.

$^3\text{H}$ : To study deposition of Vitamin A in the liver and to study mobilization of Vitamin A from the liver.

$^{14}\text{C}$ : To determine rate of synthesis of liver fat after various experimental treatments of the animals.

$^{14}\text{C}$  (acetate 1- $^{14}\text{C}$ ): To measure lipogenesis in calorie restricted rats.

$^{131}\text{I}$ : To be used to measure fat absorption in ad libitum and caloric-restricted rats.

$^{14}\text{C}$  (Acetate 1- $^{14}\text{C}$ ): The incorporation of acetate-1- $^{14}\text{C}$  into liver lipids will be measured in normal and starved rats.

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INVESTIGATOR &  
DEPARTMENT

Hopper, J., Jr., M.D.  
Medicine & CVRI

ISOTOPE & PROJECT

<sup>51</sup>Cr: contd. Tagged cells intravenously, 1-5x in patients, 1-2x in volunteers, intervals of 1 week or more in patients, no less than 4 weeks in volunteers.

<sup>59</sup>Fe: Studies contemplated in animals involve the measurement of blood volume by the <sup>59</sup>Fe red cell tag method, and of <sup>59</sup>Fe incorporation into the circulating RBC. These techniques are being used in connection with assay of erythropoietin. The <sup>59</sup>Fe red cell volume method being used is that of Contopoulous et al described in Endocrinology 55: 808, '54. The <sup>59</sup>Fe uptake method is that of Jacobson et al, described in the Jr. of Lab. & Clin. Med. 46:671, '55.

<sup>51</sup>Cr: Technique to be used is that of Sterling & Gray for the measurement of blood volume. Using sterile precautions, 10 to 15cc of blood removed from the patient whose blood volume is to be measured, is equilibrated with <sup>51</sup>Cr after washing three times with 0.9% saline solution, an appropriate aliquot will be injected into the patient, and another used to determine radioactivity of stock blood. Samples of blood will thereafter be taken from the patient at suitable intervals for the estimation of radioactivity and calculation of circulating blood volume.

<sup>3</sup>H Testosterone: The secretion rate of testosterone will be determined in selected cases illustrating various abnormalities in sexual development and adrenal disorders.

A tracer dose of 1-2µc of tritiated testosterone will be injected and urine collected for 24 hours. Testosterone will be enzymatically hydrolyzed from its glucuronide. The freed steroid will then be repeatedly chromatographed for separation, oxidized and specific activity determined.

<sup>14</sup>C cortisol: One µc of <sup>14</sup>C labeled cortisol is injected intravenously. Urine is collected and the metabolites of cortisol are separated chromatographically. Secretion rate can then be calculated.

<sup>32</sup>P: <sup>32</sup>P and <sup>51</sup>Cr have been used to evaluate the adequacy of circulation of the head of the femur (cf. Tucker, F.R., J. Bone & Jr. Surg. 32B: 100, '50). Results obtained in that manner have been questioned. It is not known whether the uptake of radioactivity results from diffusion from the tissue fluids or from the vascular circulation. Radiochromium-tagged blood cells suggest a method of further study.

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Con, R., M.D.  
Medicine-Metabolic

rgesen, F., M.D.  
Orthop. Surg.

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INVESTIGATOR &  
DEPARTMENT

Havel, R. J., M.D.  
Medicine & CVRI

ISOTOPE & PROJECT

$^{14}\text{C}$  contd. insufficient to account for the energy needs of these subjects as measured by oxygen consumption. It is considered that free fatty acid flux may limit the magnitude of exercise during non-steady state conditions. It is felt to be important to carry out similar studies during steady state exercise and in highly trained subjects who can carry out high work; such subjects are necessarily young. These studies require the use of 25 microcuries of  $^{14}\text{C}$  because of the high turnover rate of free fatty acids.

$^{14}\text{C}$ : The palmitic acid will be converted to the sodium salt by addition of an aqueous solution of sodium bicarbonate and the solution sterilized by heat. The soap solution will be added to a quantity of sterile human serum albumin solution to give a concentration of 1 to 2 moles fatty acid per mol albumin. The resulting complex will be injected intravenously in subjects hospitalized at Moffitt or San Francisco General. The conversion of the fatty acid to other circulating lipids, especially triglycerides, will be studied to derive information regarding pool sizes and turnover rates under varying conditions of diet and in certain hyperlipidemic states. Available evidence indicates that the biologic half-life of palmitic administered in this manner to humans is about 24 hours. For each study, the minimum quantity necessary to provide the required information will be used.

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Hine, C.H., M.D.  
Pharmacology

Titaniumtritide coated on 0.001" thick stainless steel foil: a sealed source--total activity not to exceed 250mc.

Lopper, J. Jr., M.D.  
Medicine & CVRI

$^{51}\text{Cr}$ : We use our own modification of Sterling & Gray's method for measurement of blood volume (Scand J. Clin. & Lab. Invest. 14:355, '62). Ten ml. of the patient's blood is tagged with  $^{51}\text{Cr}$  using sterile precautions. A carefully measured volume of tagged cell suspension is given intravenously and a portion of suspension is reserved for use as a standard. Blood is taken from the patient at suitable intervals for determination of hematocrit and radioactivity. The latter is compared with the radioactivity of suitable dilutions of the tagged cell suspension. Patients are only those selected for special study because of advanced conditions associated with edema or abnormalities of serum protein. Plasma volumes are measured with T 1824. Volunteers will be limited to a few individuals with extreme abnormalities of body build.

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INVESTIGATOR &  
DEPARTMENT

Havel, R.J., M.D.  
CVRI

ISOTOPE & PROJECT

<sup>14</sup>C Palmitic acid: This palmitic acid will be converted to the sodium salt by addition of an aqueous solution of sodium bicarbonate and the solution heat sterilized. The soap solution will be added to a quantity of sterile human serum albumin solution to yield a concentration of 1 to 2 moles fatty acid per mol of albumin. The resulting physiologic fatty acid-albumin complex will be injected intravenously in young labile diabetic subjects hospitalized on the metabolism ward of Moffitt Hospital on three occasions: during adequate chemical diabetic control; at the onset of ketosis after withdrawal of insulin; and during the presence of moderate ketosis prior to reinstitution of insulin therapy. From appropriate analyses of serial blood samples, the turnover rate and miscible pool of unesterified fatty acids will be calculated during these periods. The data obtained will be correlated with quantitative analysis of plasma glucose, ketone, and lipo-protein concentrations during the periods of study. The blood samples will be processed at the Hooper Foundation and the radioactive assays will be performed at the Radioactivity Research Center. On the basis of a 24 hour half-life of the palmitic acid in the body, Dr. Kenneth Scott has calculated that total body radiation for the entire study would be 5-6 mr. per subject.

<sup>90</sup>Sr: The isotope is contained in an ionization detector which forms a part of a gas-liquid chromatograph apparatus to be purchased from Research Specialties, Inc. The source for this detector has been shielded in accordance with AEC requirements. The <sup>90</sup>Sr is alloyed with gold and covered with gold foil and should represent no radiation hazard since it is a β emitter and is shielded by this equipment.

<sup>14</sup>C; <sup>131</sup>I, <sup>3</sup>H, <sup>32</sup>P: (1) Metabolic studies in rabbits, dogs, and possibly other animals. (2) Metabolic studies in tissue slices and homogenates. (3) Membrane transport studies.

<sup>3</sup>H: Isotopically labeled compound to be fed to animals in order to label chylomicrons or lipoproteins which will then be isolated and injected into recipient animals.

<sup>14</sup>C: Preliminary studies in subjects over 40 receiving constant intravenous infusions of palmitic acid-1-<sup>14</sup>C during exercise have shown that both influx and efflux of free fatty acids in the blood plasma are accelerated during exercise. The total

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INVESTIGATOR &  
DEPARTMENT

Hall, J.B., Ph.D.  
Biochemistry

Harper, H.A., Ph.D.  
Experimental Surg.

ISOTOPE & PROJECT

$^{14}\text{C}$ : Yeast is grown in a medium containing the labeled compound. The nucleic acid from this yeast is examined to determine whether a specific nucleotide is formed from orotic acid.

$^{59}\text{Fe}$ : The effect of portacaval shunt on absorption of iron from gastrointestinal tract into blood will be studied on patients with liver disease.

$^{59}\text{Fe}$ : The effect of portacaval shunt on absorption of iron from gastrointestinal tract into blood will be studied on four animals.

$^{198}\text{Au}$ : This isotope will be injected into a peripheral vein and multiple rapid samples will be taken from a peripheral artery to measure its rate of disappearance from the blood. This rate of disappearance will also be compared with the rate of disappearance of radioactivity from the hind limbs as measured by scintillation counter.

To measure the liver's efficiency in removing the isotope, it will be injected along with T-1824 in a known ratio into a mesenteric vein and the ratio of isotope to T-1824 will be measured for the first sixty seconds after injection in the blood of the inferior vena cava above the diaphragm.

This study will be done in normal dogs that have been fed carbon tetrachloride. It will also be done pre and post operatively in animals having various operations for portal vein decompression.

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INVESTIGATOR &  
DEPARTMENT

Grodsky, G., Ph.D. contd.

ISOTOPE & PROJECT

<sup>131</sup>I: The labeled growth hormone will be incorporated into an immunological assay for growth hormone. The insulin <sup>131</sup>I from Abbott Labs. is used in an immunological assay for insulin in biological fluids. All work is in vitro.

<sup>131</sup>I: Current studies on distribution of bilirubin-<sup>3</sup>H in rats require accurate estimation of residual blood in the tissues. Albumin <sup>131</sup>I purchased from Abbott will be used for this estimation while simultaneously counting the tritium labeled bilirubin.

<sup>14</sup>C: In vitro studies involving metabolism of labeled intermediaries by tissue slices and homogenates. Tracer use for chromatographic localization.

<sup>14</sup>C: Incubation of tissue slices with <sup>14</sup>C acetate or mevalonate with subsequent isolation and counting of cholesterol activity.

<sup>131</sup>I: The synthesis of insulin (in vitro) in incubating pancreas slices from the mouse will be studied by measuring the incorporation of <sup>131</sup>I tyrosine into the insulin produced. The insulin will be isolated and assayed using immunological and counting procedures previously described in earlier isotope applications. Insulin levels in human serum will be assayed by this same procedure.

<sup>131</sup>I: An in vitro assay of growth hormone will be developed, utilizing the principle of proportional displacement of iodinated growth hormone (G.H.) from a G.H.-antibody complex by unlabeled G.H.

<sup>14</sup>C: Glycine <sup>14</sup>C and Glutamic Acid <sup>14</sup>C will be perfused through an isolated rat liver in vitro Bromsulfalein (BSP) will be added to perfusate shortly after and the bile collected. The BSP metabolite after isolation and purification will be investigated for glycine <sup>14</sup>C and glutamic <sup>14</sup>C contents.

<sup>3</sup>H: Synthesis of tritiated glutathione (GSH) by the Wiltzbach procedure. Use of the GSH in studies of BSP metabolism in isolated perfused rat liver (a BSP-GSH conjugate is suspected).

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INVESTIGATOR AND DEPARTMENT

Greenspan, F., M.D.  
Medicine

contd.

ISOTOPE AND PROJECT

<sup>125</sup>I: Will be given orally to patients with various types of thyroid disease. Blood will be drawn at 24 and 48 hours and subjected to column and paper chromatography to separate iodinated compounds. This is currently being done with 150µc <sup>131</sup>I. <sup>125</sup>I will provide higher blood counting rates, with a longer (60 day) half life, and at the same time deliver less radiation to the patients because of no beta emission. Chromatography of iodinated compounds in blood will provide valuable information in regard to the nature of the defect in thyroid hormone biosynthesis in nontoxic goiter thyroiditis, thyrotoxicosis and thyroid carcinoma. Patients aged 10-12 inclusive, will be limited to 350µc <sup>125</sup>I which corresponds approximately to the same radiation dose obtained from 25µc <sup>131</sup>I. Other patients may receive up to 1 mc. or weight in Kg x 1 mc. whichever is less.  
70 Kg.

<sup>131</sup>I: Anterior pituitary hormones (growth hormone, ACTH, TSH) will be labeled with <sup>131</sup>I and used for study of in vitro distribution of the labeled hormone in normal and hyperthyroid patient's serum. The labeled hormone will also be used to study its in vivo distribution in rats.

<sup>125</sup>I: Pituitary hormones (TSH, growth hormone, etc) will be labeled with <sup>125</sup>I, 100mc will be used for each labeling. The labeled hormones will be studied for chemical and immunochemical properties and for its ability to bind to its target organ. This is currently being done with <sup>131</sup>I, <sup>125</sup>I provides a better label as it is less destructive to the hormone--no beta emission, and has a longer half-life.

<sup>111</sup>Ag. Anterior pituitary hormones (growth hormone, TSH) will be labeled and then used for an in vitro assay involving binding of the labeled hormones to tissues from hypophysectomized rats.

<sup>203</sup>Hg: Anterior pituitary hormones (growth hormone, TSH) will be labeled and then used for an in vitro assay involving binding of the labeled hormones to tissues from hypophysectomized rats.

<sup>3</sup>H: Tritiated bilirubin will be infused into small animals and used to study clearance, distribution and metabolism of this pigment.

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Grodsky, G.M., Ph.D.  
Metabolic Unit

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INVESTIGATOR AND DEPARTMENT

Greenberg, D.M., Ph.D.  
Biochemistry

Greenberg, L.D., Ph.D.  
Pathology

Spenspan, F., M.D.  
Medicine

ISOTOPE AND PROJECT

$^3\text{H}$ : Nucleosides and Nucleotides to be used to study conversion of ribonucleotides to deoxyribonucleotides in vivo and in vitro.

May also be used in experiments with lipids and amino acids. These are not yet projected. Dosage would be at same level as in the above.

$^{14}\text{C}$ , Riboflavin: Investigation of intermediate metabolism of riboflavin in the monkey.

$^3\text{H}$ : Preparation and investigation of the intermediate metabolism of tritiated pyridoxine in the rat and monkey.

$^{131}\text{I}$ : Anterior pituitary hormones (growth hormone, ACTH, TSH) will be labeled with  $^{131}\text{I}$  and used for study of in vitro distribution of the labeled hormone in normal and hyperthyroid patient's serum. The labeled hormone will also be used to study its in vivo distribution in rats.

$^{131}\text{I}$ : We are attempting to develop a quantitative immunochemical assay for human growth hormone. Gamma globulin, prepared from rabbits immunized with human or bovine growth hormone, will be labeled with  $^{131}\text{I}$ . The labeled gamma globulin which contains growth hormone antibodies will react with purified growth hormone in a precipitin test. If a constant amount of growth hormone antibody is used, the distribution of radioactivity between supernatant and precipitate in the precipitin test should be proportional to the amount of growth hormone antigen present.

$\text{I}_2^{131}$ : Anterior pituitary hormones (growth hormone, ACTH) will be labeled with  $\text{I}_2^{131}$  by Dr. Peng and then used for an in vitro assay involving binding of the labeled hormones to tissue slices obtained from hypophysectomized rats.

$^{51}\text{Cr}$ ,  $^3\text{H}$ ,  $^{111}\text{Ag}$ : Anterior pituitary hormones (growth hormone, TSH) will be labeled and then used for an in vitro assay involving binding of the labeled hormones to tissues from hypophysectomized rats. Dr. Peng will tritiate the pituitary hormones with  $\text{H}_2^3$ .

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Ganong, W.F., M.D.  
Physiology &  
Preven. Med.

Gardner, R.E., M.D.  
Surgery

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Glass, L., Ph.D.  
Anatomy

continued:

measure renal blood flow in dogs during stimulation of the medulla oblongata. It will be infused intravenously at a constant rate and the amount present in sequentially collected universal blood samples determined by counting in a well-type scintillation counter.

<sup>51</sup>Cr: To determine if there is inherent structural damage to the red blood cell and/or the reticulo-endothelial system of the dog while the animal is undergoing extra-corporeal circulation.

<sup>14</sup>C (as cholesterol): It is known that on cardiopulmonary bypass, a certain amount of damage is done to the lungs which is reflexed in the study of surface tensions. Chemical work by Dr. Jno. Clement's laboratory reveals that fatty acids and cholesterol seem to inhibit the surface acting substances of the lung. In the past three years we have developed the method of repeatedly producing injury to the lung by cardiopulmonary bypass and have demonstrated various methods of improving this condition. In order to further elucidate the inhibition possibilities of cholesterol, it is planned to tag these animals with 25 µg of carbon tagged cholesterol, check its distribution through the lungs following which we will use cardiopulmonary bypass and determine if there is significant increase found in the lungs of cholesterol. It is hoped that by this method we will be able to further study the methods of reducing this hazard in the clinical patient. Dogs will be used in this experiment.

<sup>131</sup>I (as NaI). Post operative cancer patients primarily those who have carcinoma of the lung will be given <sup>131</sup>I in order to measure plasma <sup>131</sup>I levels during therapy with histamine and serotonin blocking agents in order to evaluate efficacy of drug action. Unwanted radiation to the thyroid will be avoided by the administration of <sup>127</sup>I prior to test.

<sup>3</sup>H (trit. adenine, trit. uracil); <sup>3</sup>H (trit. thymidine, trit. methionine) <sup>35</sup>S (DL-methionine); <sup>131</sup>I (carrier free NaI): In vivo and in vitro labeling mouse eggs and serum proteins.

<sup>131</sup>I (albumin); Tritium (albumin <sup>3</sup>H): In vivo and in vitro labeling mouse eggs and serum proteins.

<sup>3</sup>H; <sup>35</sup>S: Intravenous injection into mice; in vitro labeling oocytes obtained from oviduct.

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Fineberg, R.A., Ph.D.  
Biochemistry

<sup>59</sup>Fe: To study the uptake of iron by iron-storage proteins incubated with radioactive iron is to be used for the quantitative estimation of the incorporation of micrograms of iron. This assay method will be employed, for example, to guide the isolation of an unknown active principle in liver extracts that mediates the uptake of ferric ion by apoferritin, and which may be a physiological regulator of iron storage. The assay will also be used for kinetic studies of the mechanism of the reaction.

Inkle, A.L., M.D.  
Biochemistry

<sup>85</sup>Krypton: Inert gas diffusion measurement of renal blood flow. Arterial-renal venous <sup>85</sup>Kr differences will be measured in instances where the electromagnetic flowmeter indicates a rate less than 400 ml/min/Kg body weight. One  $\mu$ c of <sup>85</sup>Kr dissolved in saline will be administered intravenously with the PAH infusion solution during a period of 10 minutes. During this time, renal venous and femoral arterial blood will be collected continuously through the indwelling radiopaque polyethylene catheter (of equal length to insure accurate sampling), into siliconized tubes. The radioactivity of the specimens will be determined by means of a multi-channel gamma-ray spectrometer.

Long, W.F., M.D.  
Physiology &  
Preven. Med.

<sup>14</sup>C (hydrocortisone-4-<sup>14</sup>C): The hydrocortisone will be injected into dogs, their urine collected and the specificity of a urinary metabolite of hydrocortisone determined. From this information, the rate at which hydrocortisone is secreted can be calculated.

Tritium (aldosterone 1,2,<sup>3</sup>H) The tritium-labeled aldosterone will be injected into dogs, their urine collected, the specificity of a urinary metabolite of aldosterone determined. From this information, the rate at which aldosterone is secreted can be calculated. This is the same technique used by others in humans for determinations of aldosterone secretion rate.

<sup>131</sup>I; <sup>14</sup>C; <sup>131</sup>I (labeled Diodrast): (1) Renewal for continued study of effect of brain lesions on in vivo thyroid uptake of <sup>131</sup>I, 2 & 3) Renewal, for continued study of adrenal secretion of aldosterone. Plasma extracts are acetylated with tritium-labeled acetic anhydride, purified by two paper chromatographies, and then oxidized before final chromatography. The purified steroid is counted in a liquid scintillation counter and the amount of aldosterone in the original sample calculated from the amount of <sup>14</sup>C indicated lost during purification. The <sup>14</sup>C labeled steroids as indicators to calculate losses. (4) The <sup>131</sup>I Diodrast will be used to

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Eiler, J. J. Ph.D.  
contd.

using  $^{32}\text{P}$   $\text{CO}_2^{14}$ , to study phases of the total reaction. Finally the ATP promoted synthesis of fatty acids in "Wakil" avian liver fractions and in *Tetrahymena* will be studied using acetic- $1-^{14}\text{C}$  acid and the spectrophotometric assay method of Wakil et al.

$^3\text{H}$ ; tritiated phenyl, Doriden, Phenobarbital: Phenobarbital, phenyl ethyl glutarimide (Doriden) and aniline will be tritiated (Radioactivity Center) by the Wilzbach method and the tritiated aniline converted in a one-step synthesis to phenylurethane. Exchangeable tritium will be removed (ethanol) and the compounds purified (Celite columns). The intracellular distribution of the three tritiated narcotics in *Tetrahymena pyriformis* will be followed using autoradiography. Our studies on the biological action of the narcotics in *Tetrahymena* suggest that the endoplasmic reticulum, as well as the mitochondrial membrane may be a locus of distribution.

$^{14}\text{C}$ : The incorporation of palmitic acid, palmital aldehyde and plamityl CoA into phospholipids will be studied using rat brain homogenates. Attention will be directed to the synthesis of esters and vinyl ether linkages from each of the three intermediates.

$^{45}\text{Ca}$ : Will be infused intravenously into dogs, 100mc over a two to four hour interval at a constant rate. Effects of hormones on renal handling of calcium will be evaluated by infusing one kidney simultaneously with the hormone in question and using the other kidney as a control. Renal function will be monitored with insulin and pAH clearances.

$^{14}\text{C}$ : Small animal and isolated tissue studies with  $^{14}\text{C}$  labeled analgetics. Human studies on excretion of  $^{14}\text{C}$  labeled analgetics. These to be done in the office of Prof. H. Rapaport, Old Chemistry Bldg., Berkeley Campus.

$^{14}\text{C}$ : Synthesis of  $\text{N-}^{14}\text{CH}_2$  labeled morphine by means of Wallach reaction. Methylation of normorphine by  $\text{HC}^{14}\text{HO}$  in presence of formic acid and an atmosphere of nitrogen. Reaction mixture to be refluxed about 4 hours and resulting morphine- $\text{N-C}^{14}_2$  to be purified by recrystallization.

$^{14}\text{C}$ : Laboratory studies of calcium oxalate solubility in salt solutions and in urine utilizing isotope dilution techniques. Studies of method for determining oxalic acid in urine. No human use is contemplated. Work being done in Oakland VA Hospital.

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Benberg, E., M.D.  
Medicine

Hott, H.W., M.D.  
Pharmacology

liot, Jas.S., M.D.  
Urology

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FOUND BY	MARY HONES	10/10/84

INVESTIGATOR AND  
DEPARTMENT

Edelman, I.S., M.D.  
Medicine

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Edelman, I.S., M.D.  
CVRI & Gen. Med.

J.J., Ph.D.  
harm. Chem.

ISOTOPE AND PROJECT

$^{24}\text{Na}$ : The study to be undertaken consists of: (a) the measurement of sodium exchange in vitro in rabbit skeletal muscle; and (b) correlations of total exchangeable sodium with changes in blood pressure in patients with essential hypertension before and after therapy.

$^{42}\text{K}$ : The study to be undertaken consists of correlating total body composition ( $K_b$ ) with alterations in serum electrolyte concentrations in patients with congestive heart failure, renal diseases and hepatic diseases.

$^3\text{H}$ : A comparative study of  $^3\text{H}_2\text{O}$  and  $\text{H}_2\text{O}$  will be carried out. The usefulness of these isotopes as tracers for body water metabolism studies will be explored.

$^{35}\text{S}$ : To determine the effect of antidiuretic and other hormones on the permeability of tissues in vitro to  $\text{SO}_4$ . The particular systems to be employed are: frog skin, urinary bladder of the toad, rabbit amnion and rabbit mesentery.

$^{36}\text{Cl}$ ;  $^{28}\text{Mg}$ : Studies on the role of electrolytes in bioelectric phenomena by measurement of isotopic fluxes (frogs, toads, rats, rabbits & dogs).

$^{14}\text{C}$ ;  $^3\text{H}$ ;  $^{22}\text{Na}$ ;  $^{24}\text{Na}$ : Studies in localization of labeled hormones and intermediates in frog skin, toad bladder and other anuran tissues. Studies on the role of electrolytes in bioelectric phenomena by measurement of isotope fluxes.

Tritium: The tritium is to be used to tritiate arginine vasopressin and it will then be used to study the kinetics of the hormone in the toad urinary bladder. In addition, radioautographs will be prepared to localize the site of action of the hormone.

$^{14}\text{C}$ ;  $^{32}\text{P}$ : As a continuation of previous work from this laboratory, it is proposed to study the effect of hypnotic depressants (phenobarbital, Doriden & phenylurethane) on the ATP turn-over and its utilization in *Tetrahymena pyriformis* and in selected liver preparations. The kinetic equations permitting a study of the rate of turn-over, using  $^{32}\text{P}$ , have been formulated. The effect of the drugs on the ATP promoted carboxylation of propionate- $2\text{-}^{14}\text{C}$ -COH will be studied in liver preparations

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INVESTIGATOR AND DEPARTMENT

Crocker, T.T., M.D.  
C.R.I.

Dewey, Marjorie  
Preven. Med.

Garbin, R., Ph.D.  
CVRI

Garle, Chas. M.D.  
Orthop. Surg.

Goldman, I.S., M.D.  
Medicine

ISOTOPE AND PROJECT

$^3\text{H}$  solutions uridine, cytidine, thymidine;  $^{35}\text{S}$  sulfate in solution;  $^{35}\text{S}$ -amino acids, solution amino acids;  $^{14}\text{C}$  solutions acetate, glucose:  
Animal and tissue culture experiments are being done on distribution of labeled compounds in cells and fluids.

$^{14}\text{C}$ : Aminoacids

$^3\text{H}$ ;  $^{32}\text{P}$ ;  $^{14}\text{C}$ ;  $^{35}\text{S}$ : Determine incorporation, synthesis, and turnover of specific labeled compounds into amoebae and tissue culture cells, to be followed by determination of localization and amount of label by means of autoradiography.

$^{35}\text{S}$ : Typical experiments on incorporation of  $^{35}\text{S}$  by mucous glands in rats during 48 hr. after giving label have been completed with radiation-safety advice and clearance after monitoring the experimental area.

$^{14}\text{C}$ : A radioactive tag, 2-nitronaphthalene will be administered to a dog and the urine collected over a 72 hr. period. The urine will be analyzed for metabolic products, using solvent extraction and paper chromatography.

$^{35}\text{S}$  K  $^{35}\text{SCN}$ : Radioautography of frog stomach.

$^{14}\text{C}$ ;  $^3\text{H}$ ;  $^{36}\text{Cl}$ ;  $^{22}\text{Na}$ ;  $^{42}\text{K}$ : Frog gastric mucosa the first 2 isotopes are to be used in labeling parts of the cell associated with secretion (b) Guinea pig smooth muscle. The last three isotopes are to be used in the study of the ionic composition of this muscle.

$^{32}\text{P}$ ;  $^{198}\text{Au}$ : Material is to be injected into the brachial artery of each operative limb. Subsequently, in varying intervals, radioautographs will be obtained in fixed specimens to delineate or demonstrate distribution of the radioactive material.

$^{22}\text{Na}$ ;  $^{36}\text{Cl}$ ;  $^{86}\text{Rb}$ ;  $^{28}\text{Mg}$ : The studies to be undertaken will consist of in vitro measurements of the flux of radioactive substances across the frog gastric mucosa and the toad urinary bladder and the tissue uptake of these substances.

$^{134}\text{Cs}$ ;  $^{137}\text{Cs}$ ;  $^{14}\text{C}$ : The studies to be undertaken will consist of in vitro measurements of the flux and tissue uptake of radioactive substances using frog gastric mucosa and toad urinary bladder. Utilization of metabolic intermediaries by the rabbit diaphragm.

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Coleman, R., D.D.S.  
Dentistry

Antonopoulos, A.N., M.D.  
Anatomy

Corbascio, Aldo, M.D.  
Ped. & Pharm.

Coulson, W., M.D.  
Radiology (SFGH)

Craig, J.C., Ph.D.  
Pharmacy

continued:

On the basis of these findings, the purpose of this investigation is to determine the sites of uptake of  $^{35}\text{S}$  in the palatal shelves of the rat fetus during various stages of normal palatal closure by means of autoradiography. Subsequently, a similar study employing the same dose of  $^{35}\text{S}$  is planned for cleft palate fetuses obtained from mothers given various teratogenic agents for comparison with the normal series.

$^{32}\text{P}$ ;  $^{131}\text{I}$ ;  $^{59}\text{Fe}$ ;  $^{51}\text{Cr}$ ;  $^{131}\text{I}$  will be used for uptake by the thyroids of rats after the injections of different hormones. The turnover and excretion rate of  $^{131}\text{I}$  will be also studied in the same rats. In pregnant rats, the transfer of  $^{131}\text{I}$  through the placenta barrier to the fetus will be examined. The incorporation of  $^{131}\text{I}$  in the different thyroid hormones will be studied and paper chromatography will be used in order to establish the form of circulating and thyroidal  $^{131}\text{I}$ . Increase is due to accumulation of decay because of shipments once a month.  $^{59}\text{Fe}$ : will be used in the determination of Fe turnover in the rats after the administration of different hormones and for the determination of blood volumes in different experimental conditions with the use of radioactive red cells obtained from donors injected previously in the  $^{59}\text{Fe}$ .  $^{51}\text{Cr}$  and  $^{32}\text{P}$  will be used for determination of blood volumes.

$^3\text{H}$  Thymidine:  $^3\text{H}$  Cytidine: Intra-peritoneal injection in mice and rats whose kidneys, intestines, bladder and tongue are removed serially 1, 2, 3 hrs. after the injection.

Tritiated Thymidine: Intra-peritoneal injection of 10  $\mu\text{c}$  in CAF and BALB mice which are sacrificed 1, 3, 6, hrs. later and whose duodenum, bladder, testes and skin are removed and fixed for autoradiography.

$^{60}\text{Co}$ ;  $^{226}\text{Ra}$ : For clinical use in treatment of carcinoma and other diseases requiring radiation therapy.

$^{226}\text{Ra}$ : The Barber Colman instrument contains radioactive foil in the detector chamber. The gold and silver aluminum foil contains 56  $\mu\text{g}$  of  $^{226}\text{Ra}$  heated to  $300^\circ\text{C}$ , safe body burden 0.1  $\mu\text{g}$ . Source will be checked at appropriate intervals for radon leakage and machine visibly labeled as to source amount and that it constitutes a radioactive hazard.

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INVESTIGATOR AND DEPARTMENT

Burbridge, T.N., Ph.D.  
Pharmacology

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uschke, Franz, M.D.  
Radiology

Carbone, J.V., M.D.  
Medicine

Coleman, R., DDS  
Dentistry

ISOTOPE AND PROJECT:

Tritium; <sup>14</sup>C: To be used in studies of the interaction of various chemical agents with the metabolism of the total organism as well as with tissues from various species of laboratory animals. This work is a continuation previously outlined in which the effects of ethanol, tranquilizers and hypnotic sedatives on the incorporation of essential metabolic intermediates in various cellular processes during acute and/or chronic administration of the agents are determined. In addition, the metabolic conversion of ethanol to various cell metabolic constituents is also studied.

Radium; Radon: This application is for the clinical use of radium for treatment of malignancies as indicated by consultation between members of the section of Radiation Therapy, Dept. of Radiology and other departments. Platinum or gold filtered radon seeds to be used in treatment of malignant disorders and occasionally in other tumors as used in standard recognized procedures authorized by the section of Radiation Therapy, Dept. of Radiology.

<sup>60</sup>Cobalt: For clinical use in a teletherapy unit in radiation therapy.

<sup>60</sup>Cobalt: For use in performing standardized therapeutic clinical methods under the supervision of or as directed by the Section of Radiation Therapy. The use is primarily in the treatment of carcinomas of the bladder and nasopharynx.

Tritium: Tritium will be used in an attempt to label bilirubin. If this proves feasible, the labeled bilirubin will be employed to study the bilirubin metabolism in the normal rat and the rat with congenital non-hemolytic icterus.

<sup>35</sup>S: Serial histologic studies on the mechanism of palatal closure in normal fetal rats suggested that the lateral palatine process attained their definitive palatine position by means of an "internal force" rather than by cell proliferation. Several investigators have suspected an accumulation of sulpho-mucopolysaccharides in the lateral palatine processes to be responsible for the turgid force necessary for the elevation of the palatal processes. By contrast, cleft palate animals have indicated a reduction in sulpho-mucopolysaccharides in the lateral palatine processes. There is considerable evidence in the literature that <sup>35</sup>S is incorporated into sulpho-mucopolysaccharides and

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INVESTIGATOR AND  
DEPARTMENT

Biglieri, E.G., M.D.  
Medicine

Postick, W.L., M.D.  
Pathology

Brown, Ellen, M.D.  
Medicine

ISOTOPE & PROJECT

<sup>3</sup>H 1-2 Desoxycorticosterone: (1) There is no information about the secretion of desoxycorticosterone (DOC). We have observed patients with edema and hypokalemia who have increased secretion of DOC and its metabolites. <sup>3</sup>H 1-2 DOC will be chromatographed to purity and sterilized. After an intravenous injection, a 24 to 48 hr. urine will be collected. The adrenal secretory rate of DOC will then be measured by determining the specific activity of a metabolite. (2) A portion of this <sup>3</sup>H 1-2 DOC will be used to quantitate the urinary excretion of DOC by a double labeling method similar to aldosterone.

<sup>198</sup>Au; <sup>32</sup>P; <sup>51</sup>Cr; <sup>90</sup>Y; <sup>3</sup>H; Lanthanum rare earths  
Colloidal solutions injected into mice intravenously are selectively phagocytosed by the cells of the reticuloendothelial system. This property will be utilized to subject the cells of the RES to small doses of radiation in an effort to modify the response of these cells to injection by the "Friend Virus". Mice will be given a single dose of 1 to 50mc, IV and later inoculated with the virus. They will be sacrificed at intervals and the relevant organ analyzed histologically.

Tritium: Tritiated water will be given to dogs and human subjects and blood samples analyzed for determination of total body water. Body water content will be used to estimate the severity of edema in patients with cardiac and renal diseases. Dogs will be used to gain experience with the technique. Each human determination of "tritium space" will be done simultaneously with a determination of circulating red cell volume, using 5mc of <sup>51</sup>Cr per determination. Our purpose is to study relations between blood volume, venomotor activity and edema formation in cardiac and renal patients. Bedside determinations of body water may be done on rare occasions at the San Francisco General Hospital but all laboratory work will be done at the U. C. Medical Center.

<sup>59</sup>Fe: <sup>59</sup>Fe uptake in dog's red cells will be measured in experiments designed to test the acute effects of certain circulatory disturbances (dilutional anemia; experimental arteriovenous fistula; inferior vena caval constriction) on erythropoiesis.

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INVESTIGATOR AND DEPARTMENT

Biglieri, E.G., M.D.  
Medicine

ISOTOPE AND PROJECT

$^{14}\text{C}$ : This material is being used for the determination of plasma and later urinary aldosterone. Ring labeled  $^3\text{H}$  aldosterone is added to sample which is then acetylated with  $^{14}\text{C}$  acetic anhydride and purified by paper chromatography. The steroid is counted in a liquid scintillation counter and aldosterone determined from the  $^{14}\text{C}$  radioactivity and change in specific activity of  $^3\text{H}$  aldosterone.

$^{42}\text{K}$ ;  $^3\text{H}$ : To quantitate total body water and exchangeable K in abnormal adrenal states and correlation with metabolic balance data.

Tritium: Material to be used for determination of urinary aldosterone by double isotope derivative assay. Dried extracts of plasma are acetylated with Tritium labeled acetic anhydride to convert aldosterone quantitatively to aldosterone diacetate. The samples are purified by two paper chromatographies and then oxidized before a final chromatography. The purified steroid is then counted in a liquid scintillation counter. The amount of aldosterone can be determined from the amount of  $^{14}\text{C}$  indicator lost during purification, the yield of Tritium radioactivity, and the specific activity of the Tritium labeled acetic anhydride.

Corticosterone- $4\text{-}^{14}\text{C}$ ; Cortisol- $4\text{-}^{14}\text{C}$ ;  $7\text{-}^3\text{H}$  Aldosterone: These steroids are to be administered intravenously to determine the simultaneous secretion rates of aldosterone corticosterone and cortisol 80-90% of the radioactivity of each steroid appears in its metabolites in 24 hrs. Twenty four hour urines are to be analyzed for specific activity of the steroid metabolites.

$4\text{-}^{14}\text{C}$  Desoxycorticosterone acetate: The acetate will be hydrolyzed off the molecule and the ring labeled  $\text{DOC-}4\text{-}^{14}\text{C}$  will be used to monitor losses in the chromatographic separation of  $1\text{-}2\text{-}^3\text{H}$  which will have been injected intravenously. It will also be used for the double isotope dilution assay of DOC.

$1\text{-}2\text{-}^3\text{H}$  Testosterone in ethanol: Will be chromatographed to purity and sterilized. After intravenous injection, a 24 and 48 hour urine will be collected and the specific activity of testosterone and testosterone glucuronide will be determined in order to calculate the secretion rate. Over 95% of the radioactivity is excreted in 48 hrs. This measurement will be used in conjunction with the secretion rate of dehydroepiandrosterone.

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INVESTIGATOR AND DEPARTMENT

Adams, Gail, Ph.D.  
Radiological Lab.

Adams, J.E., M.D.  
Neurological Surg.

Adler, P.M., M.D.  
Medicine

Anderson, C.E., M.D.  
Orthopedic Surg.

Ad, O., Ph.D.  
Pharmacology

Bennett, L.L., M.D.  
Physiology

ISOTOPE AND PROJECT

$^{137}\text{Cs}$  (200mc) sealed sources for Victoreen chamber calibration

$^{90}\text{Sr} + ^{90}\text{Y}$  (100mc) Portable Radiation Monitor, sealed source in Victoreen Model AFB-20K5-CR

Uranium, Pu-239; Np-237, Threshold detectors for measuring neutron spectra, using photofission to induce activities to be measured.

$^{131}\text{I}$ : The isotope will be used as a tracer to study cerebral circulation times. Equipment is available in the neurosurgical research unit of CVRI on 13th floor. Circulation times will be measured by injection of 50mc of  $^{131}\text{I}$  into the carotid artery and recording the activity over the torcular Herophili by a suitable recording device. The circulation times will then be correlated with the measurement of a total cerebral blood flow by the techniques already in use in our cerebral metabolic laboratory. These studies will first be carried out in normal patients and subsequently in patients with various cerebral vascular and other cerebral diseases. Prior to the study, the uptake of the  $^{131}\text{I}$  by the thyroid gland will be blocked by preliminary medication with Lugol's solution.

$^{131}\text{I}$ : Attempt to put an  $^{131}\text{I}$  label on Dicumerol and Warfarin and trace its metabolic fate in rabbits. Labeling work to be done at Radioactivity Research Center and tagged material then transferred to Children's Hospital for experimental work.

$^{35}\text{S}$ : Tritiated thymidine, tritiated cytidine: Study of uptake in rat cartilage under various conditions

$^{14}\text{C}$ : Study of the mechanism of spermatogenic arrest by nitrofurans.

$^{14}\text{C}$ : 2mc of l-valine will be added to an isolated organ perfusion system (a preparation consisting of rat spleen, pancreas and stomach) and the rates of the incorporation into proteins by the organs being perfused will be investigated.

$^{14}\text{C}$ : Dogs will be kept on a diet of known composition containing known amounts of cholesterol. To this will be added approximately 45mc per day of 4-C $^{14}$ -cholesterol. This ration will be continued approximately 20 days at the end of which time blood and tissues will be removed for isolation of cholesterol and other steroids having specific activity will be determined.

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BIGLIERI, E.G., M.D.  
Medicine

7-<sup>3</sup>H Dehydroepiandrosterone acetate in ethanol: This steroid will be incubated with acetylcholinesterase to form the free compound and then chromatographed to purity and sterilized by filtration. After intravenous injection, a 48 hr. urine will be collected and the specific activity of urinary dehydroepiandrosterone, androsterone, and etrocholanolone will be determined in order to calculate secretion rate of dehydroepiandrosterone. Over 95% of radioactivity is excreted in 48 hours.

Cortisol-4-<sup>14</sup>C; Corticosterone-4-<sup>14</sup>C; 1-2<sup>3</sup>H: These steroids are to be administered intravenously and simultaneously to determine the secretion rates of aldosterone, corticosterone and cortisol. Eighty to ninety percent of the radioactivity of each steroid appears in its metabolites in 24 hours. Twenty four hour urines are to be analyzed for the steroid metabolites by the double isotope labeling technique.

<sup>14</sup>C: To be used for the determination of urinary aldosterone by the double isotope method. Ring labeled <sup>3</sup>H aldosterone is added to sample which is then acetylated with <sup>14</sup>C acetic anhydride and purified by paper chromatography. The steroid is counted in a liquid scintillation counter and aldosterone determined from the <sup>14</sup>C radioactivity and change in specific activity of <sup>3</sup>H aldosterone.

Corticosterone 4-<sup>14</sup>C; Cortisol 4-<sup>14</sup>C; 7 <sup>3</sup>H Aldosterone: These steroids are to be administered intravenously to determine the simultaneous secretion rates of aldosterone, corticosterone, and cortisol. Eighty to ninety per cent of the radioactivity of each steroid appears in its metabolites in 24 hrs; 24 hr. urines are to be analyzed for the specific activity of the steroid metabolites.

Tritium, 2500mc: Material to be used for determination of urinary aldosterone by double isotope derivative assay. Dried extracts of plasma are acetylated with Tritium labeled acetic anhydride to convert aldosterone quantitatively to aldosterone diacetate. The samples are purified by two paper chromatographies and then oxidized before a final chromatography. The purified steroid is then counted in a liquid scintillation counter. The amount of aldosterone can be determined from the amount of <sup>14</sup>C indicator lost during purification, the yield of Tritium radioactivity, and the specific activity of the

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