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RECORDS SERIES TITLE	May 1964 - James C. ...
BANK REPORTS AND FINING	2/7/64
CARTONING	Box 7
FOLDER NAME	Morgan, Sheldon
NOTES	2/3/64
FOUND BY DATE FINING	S. S. ...

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7/22/77

FORM APPROVED: BUDGET BUREAU NO. 68-7249

U. S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE PUBLIC HEALTH SERVICE APPLICATION FOR RESEARCH GRANT (A PRIVILEGED COMMUNICATION)	LEAVE BLANK	
	TYPE	PROGRAM
	REVIEW GROUP	FORMERLY
	COUNCIL	
	NOTICE OF RESEARCH PROJECT	
<input type="checkbox"/> YES <input type="checkbox"/> NO		

A. TO BE COMPLETED BY PRINCIPAL INVESTIGATOR OF PROJECT DIRECTOR

1. TITLE OF RESEARCH PROPOSAL (Limit to 13 letters and spaces)	2. AMOUNT REQUESTED (Same as item 9, page 2)
HUMAN NUTRITION RESEARCH LABORATORY	\$ 246,280
3. TYPE OF APPLICATION (Check one)	4. DATES OF INITIAL PERIOD (Usually 12 months)
<input checked="" type="checkbox"/> NEW PROJECT <input type="checkbox"/> REVISION OF THIS APPLICATION NO. _____ <input type="checkbox"/> RENEWAL OF THIS GRANT NO. _____ <input type="checkbox"/> SUPPLEMENT TO THIS GRANT NO. _____	FROM Sept. 1, 1964 THROUGH Sept. 30, 1965
5. PRINCIPAL INVESTIGATOR (Last name first) OR PROJECT DIRECTOR	DEGREE TITLE OF POSITION
Morgan, Sheldon	M.D. Associate Professor of Human Nutrition
MAILING ADDRESS	TELEPHONE NUMBER AREA CODE EXTENSION
Department of Nutritional Sciences University of California Berkeley 4, California 94720	845-6000 415 4054
ADDRESS WHERE RESEARCH WILL BE CONDUCTED	DEPARTMENT OR SERVICE
Morgan Hall Department of Nutritional Sciences University of California, Berkeley	Department of Nutritional Sciences
	MAJOR SUBDIVISION (PROFESSIONAL SCHOOL COLLEGE, ETC.)
	College of Agriculture
6. CO-PRINCIPAL INVESTIGATOR OR ASSOCIATE PROJECT DIRECTOR	DEGREE TITLE OF POSITION
Calloway, Doris E.	Ph.D. Professor of Nutrition

B. TO BE COMPLETED BY AN APPROPRIATE ADMINISTRATIVE OFFICIAL OF THE INSTITUTION

7. NAME OF INSTITUTION SUBMITTING APPLICATION	8. TYPE OF APPLICANT (Check applicable items)
University of California	<input checked="" type="checkbox"/> PUBLIC INSTITUTION <input type="checkbox"/> FEDERAL <input checked="" type="checkbox"/> STATE <input type="checkbox"/> LOCAL <input type="checkbox"/> OTHER <input type="checkbox"/> PRIVATE INSTITUTION <input type="checkbox"/> NON-PROFIT <input type="checkbox"/> PROFIT <input checked="" type="checkbox"/> INDIVIDUAL
MAILING ADDRESS	9. APPLICANT'S FNS ACCOUNT NO. (Enter if known)
119 Morgan Hall Department of Nutritional Sciences Berkeley 4, California	
10. NAME, TITLE, AND ADDRESS OF OFFICIAL TO WHOM CHECKS SHOULD BE MAILED	11. (Leave blank) TRANSACTION NO.
O. W. Campbell, Vice Chancellor Business and Finance 323 Sprout Hall University of California Berkeley 4, California	

C. TERMS AND CONDITIONS: The undersigned understand and accept the terms and conditions set forth in the statement on the reverse of the original and applicant's retained copy of this page. Sign original copy in ink. Per signatures are not acceptable.

12. PRINCIPAL INVESTIGATOR OR PROJECT DIRECTOR	(Same as item 5 above. Signature only)	DATE
	Sheldon Morgan	1/22/64
13. OFFICIAL AUTHORIZED TO SIGN FOR INSTITUTION	(Type name and title below signature)	DATE

DOCUMENT SOURCE	University of California at Berkeley The Bancroft Library/The University Archives, Berkeley, CA
REPORTS SERIES FILE	1962-1963 Annual Report, Division 7, Fisheries
BANK REPORT NUMBER	44 211 24
CARTON NO.	Box 7
FOLDER NAME	1962-1963, Division 7
NOTES	1/31
FINDING DATE FOUND	1962, Storch

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PART II - PROPOSED RESEARCH PROGRAM

A. Background and Introductory Statement

On July 1, 1962, a new Department of Nutritional Sciences was created on the Berkeley Campus of the University of California. This Department was an outgrowth of the previous Department of Nutrition and Home Economics which, under the direction of Drs. Agnes Fay Morgan and Ruth Okey, pioneered nutritional research on the West Coast. About three years ago Dr. George Briggs was selected to head what was to be the new department. Home Economics was transferred from the Berkeley Campus to the Davis Campus of the University of California and the facilities which had formerly been utilized by the Department of Home Economics were all transformed into research laboratories. The new Department of Nutritional Sciences also incorporated the Department of Food Science and Technology on the Berkeley Campus and the Berkeley Branch of the Institute of Marine Resources.

The orientation of the new Department was redirected towards the study of problems of human nutrition. In order to implement this objective the Department is structured informally into the following divisions: a) Human Nutrition b) Comparative Nutrition c) Nutritional Biochemistry d) Food Science, and e) the Institute of Marine Resources with special interests in both the characterization and utilization of products from the sea.

The main activities of the Department are housed in a modern four-story building with a penthouse, the latter to serve as an excellent central facility for the Human Nutrition Laboratory. In addition, experimental animals are currently located in the Life Sciences Building and some of the offices and laboratories of Food Science and the Institute of Marine Resources are in Hilgard Hall, adjacent to the Nutritional Sciences building.

Since the establishment of the new Department, the informal divisions noted above were augmented and implemented by increasing the number of personnel and the interests represented so as to make a broad program possible.

We believe that this Department, the only one devoted entirely to nutritional sciences on any campus of the University of California or any campus on the West Coast, presents unique opportunities for research and teaching within this discipline. It is our opinion that the research program, personnel, physical plant and geographic setting form an ideal combination that should allow for major contributions within this field.

The serious lack in the present program is the Human Research Laboratory. Without such a facility the principal aim of this Department, namely, studies in human nutrition, cannot be adequately fulfilled.

B. Objectives and Program

The principal objective of this proposed research program-project is to establish a Human Nutrition Laboratory that will allow nutritional studies in humans to be conducted under carefully controlled conditions. The laboratory should be so equipped and organized that "complete" and accurate determinations in many parameters would be possible. Certainly in the case of nutritional investigation this should enable one to do accurate studies of: a) energetics b) body composition c) biochemical determinations, especially utilizing modern instrument technique d) physiological performances, and e) probably psychological evaluation where

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NOTES	Handwritten notes
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indicated.

To date several broad areas of investigation, which it is hoped will finally be encompassed within the program-project research grant, have been undertaken. Several of these are currently under support by the National Institutes of Health. In other cases research grants are pending. Various members of the Department are interested and involved in the following investigations which will become part of the Human Nutrition Laboratory.

1. A study of the influence of amount and source of dietary protein on the dynamics of plasma albumin under the direction of Dr. Sheldon Margen and Dr. Doris Galloway.

RESEARCH PLAN.

A. Introduction and Specific Aims:

One of the important areas of current nutrition research is the attempt at the appraisal of the nutritional status of the organism. Various approaches to this problem have been employed, but the solution must be at the biochemical level. Nutritional appraisal has proven difficult as far as all nutrients are concerned and appears to be particularly difficult in the case of proteins. Although it is clear that severe protein depletion may be recognized clinically, it is certain that in the case of protein, as in other types of deficiencies, the biochemical alterations must of necessity, long precede the obvious biological deficiencies.

To date this problem of the protein nutritional state has been approached mainly by study of the serum proteins, particularly the level of circulating albumin. Balance studies have also been employed. In these later studies when nitrogen has been retained protein synthesis and hence previous depletion has at times been assumed. Both of these techniques are subject to considerable criticism. In the case of the serum albumin level it is clear that the mere measure of a level without any knowledge whatsoever of the "pool size" can give little information regarding albumin or protein content of the organism and even less regarding the status of nutrition. The matter of balance studies is likewise fraught with difficulty of interpretation. Any change in diet leads to a period of altered "balance" and long periods of observation of humans or animals are necessary in order to attempt to answer the questions raised by this technique.

It is generally accepted on the basis of the work of Whipple, *et al.*, that there is a "labile protein pool." Whether this "pool" is merely conceptual and labile protein is potentially present in cells from various tissues or whether there is a more or less clearly defined labile protein pool has not yet been elucidated. Results of some of our investigations would make it appear that the small protein molecule, serum albumin, might well represent or be representative of this labile protein pool. Work to date has shown that serum albumin is in a rapid dynamic state. It is rapidly synthesized by the liver. It can pass rapidly into the intestinal tract where it would be degraded and the available amino acids would again be available for distribution to the organism after being re-absorbed in the small intestine. We know of no evidence that preformed proteins or even peptides are used by the body cells. Therefore, this degradation of albumin as the mechanism of supplying cells with amino acids when dietary protein intakes are inadequate is an intriguing possibility. It would appear, therefore, that a study of plasma albumin distribution, *i.e.*, pool size and of turnover under varying level of protein nutrition should be important and may provide a feasible means of

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REPORT NUMBER	UCRL-10000
PROJECT TITLE	Protein Synthesis Control in Bacteria
REPORT NUMBER	10000
DATE	1968
PROJECT NAME	Protein Synthesis Control
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DATE OF DEPOSIT	10/15/68
DEPOSITED BY	John Drenth

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evaluating the degree of protein nutrition.

B. Methods of Procedure:

Studies will be performed on animals and man.

I. Animals

The animals to be used will be rats and rabbits. "Mature" animals will be used. Protein will be fed at at least 4 levels. One group will be fed an "optimal diet", one a very high but correctly balanced protein diet, the third a minimal protein diet, but adequate to maintain weight, and the last a sub-minimal diet, but one which results in a very slow weight loss. After varying periods of time on this diet, when equilibrium appears to have been reached where possible, labeled albumin will be injected and metabolized, and turnover studies performed by methods as reported in our previous work.

1. The Preparation of Labeled Albumin. Species homologous albumin will be prepared by initial phosphate separation and purification of the albumin on DEAE columns. Albumin prepared by this technique is electrophoretically homogeneous and biologically not denatured. The electrophoretically pure albumin so prepared will then be labeled by one of the various techniques described below.

2. Methods of Labeling. Four methods of labeling will be employed. In some instances the protein will be labeled simultaneously by all three techniques.

1) I-131 Labeling

The albumin will be iodinated either by a method previously described or a method of McFarlane. In our hands either of these methods of labeling yields albumins having similar turnover rates.

2) Labeling by use of the carbaminoanhydride reaction as described in our previous publications. By using this method some labeled amino acids may be used to label the protein at the free amino groups, both terminal and ϵ -lysine. This method gives half lives which are quite similar to those of endogenously synthesized protein. The main objection to this method is the fact that single amino acids are not necessarily attached to protein during the course of reaction, and that polymers of various size may be formed which attach to the protein molecule and may modify its behavior.

3) In the course of the past year considerable work has been done using both C-14 and H-3 labeled amino acids for labeling protein. It has been found that reacting carbamino compounds with oxalyl chloride will produce a compound which will then again react with amines. The compound formed is most likely an "oxamyl" derivative. In addition to this oxamyl compound, a small amount of dimers and trimers, the exact nature of which has not yet been elucidated, are also formed. This oxamyl compound reacts with albumin giving yields of approximately 50%. Hence a very highly labeled serum can easily be prepared from inexpensive and highly radioactive H-3 labeled amino acids. The biological activity of these proteins is currently under study and will be continued under this grant. Preliminary work suggests no significant denaturation of protein with this labeling technique. Furthermore, through this method of labeling it is possible to use unnatural amino acids or amino acid analogs that cannot be reincorporated into protein. Since any

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REPRODUCTION STATE	Handwritten: Jones, D. W. 1968
REPRODUCTION ID NO.	Handwritten: 19/11/68
CARTON NO.	Handwritten: 1000
FOLDER NAME	Handwritten: Jones, D. W.
NOTE	Handwritten: 1000
FOUND OR DATE FOUND	Handwritten: 1000

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carbamino compound can now be used to label albumin, the problem of whether reincorporation of amino acids plays a significant role in altering turnover rate when labeled albumin is used can be answered definitively. The brominated compounds are prepared by H-2 exchange technology and the amino acids purified by high voltage electrophoresis.

4) "Hayesey" method of labeling. A large dose of H-3, C-14 or S-35 labeled amino acid will be given to an animal, blood will be taken after 16 to 24 hours, and the labeled albumin (subsequently labeled) will be prepared as noted above.

3. Turnover Studies

The turnover studies will be conducted in the manner previously described by us. A tracer dose of labeled albumin is injected intravenously. The animals, during the course of these investigations, are allowed to continue to eat (the previous diet) and are kept in metabolic cages, where both feces and urine are separated and collected. After sufficient time for thorough mixing of the albumin in the vascular compartment, usually 5 to 7 minutes, the first sample is drawn. From this can be calculated the plasma volume and the plasma distribution pool of albumin. Both the radioactivity in the blood and radioactivity in urine (and stool) is followed thereafter for a variable period of time, depending upon the species of animal and conditions of the experiment. From the analyses of albumin concentration, albumin specific activity and urine excretion of radioisotope, it is possible to calculate the total albumin pool and determine rates of synthesis and degradation. It should be emphasized that when the urine excretion is used as an index of turnover and degradation, one must have labeled compounds which cannot be reincorporated into protein and/or metabolized. Hence these "complete" studies can only be carried out with I-131 labeled albumin, with albumin labeled with amino acid analogs or other compounds which are not capable of being re-synthesized into proteins or themselves degraded. From these determinations and calculations one will be able to ascertain whether the dietary alterations lead to changes in albumin synthesis and degradation. At the end of the study the animals will be sacrificed, and total carcass analysis for protein will be performed. Whether the pool size and turnover data will correlate with the protein nutritional status of the animal may then be ascertained.

II. Humans

The experiments on each man will require at least several months. The subjects to be studied will be kept as patients within the Human Nutrition Laboratory. They will be fed a constant analyzed diet for varying lengths of time, minimum 3 weeks for each experimental period. The initial control period will consist of "normal" diet, of constant composition, according to NRC requirements. Initially, calories will be adjusted with carbohydrate to keep weight constant. Activity will be regulated and kept constant. Nitrogen and mineral balance, urinary excretion of creatinine, as well as various blood chemical levels, will be followed throughout the study.

Body composition will be determined by both fluid spaces and total body volume measurements (see below). When equilibrium is obtained, an albumin turnover study will be performed by one or more of the techniques described above. When the necessary data has been obtained, the protein content of the diet will be lowered and the procedures outlined above carried out again when a new equilibrium level is reached.

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DOCUMENT SOURCE	University of California at Berkeley, The Bancroft Library, The University of California, Berkeley, CA
REPORTS SERIES TITLE	<i>Protein Turnover Experiment - 1954</i>
BANK REPORT NUMBER	<i>19/1126</i>
CARDINAL NO.	<i>128</i>
FOLDER NAME	<i>Protein Turnover</i>
NOTES	<i>1/31</i>
FOUND BY DATE (MIND)	<i>Sheldon Margen</i>

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Nitrogen equilibrium will be maintained by the subjects until the protein intake becomes quite low, at which time a persistent negative nitrogen balance will be observed. In the face of a persistent protein loss (even though constant) turnover experimentation may not be ideal. However, the estimate of the kinetics should not be too difficult, because the pool size should not be changing too rapidly, so one may be able to assume almost equilibrium conditions.

Suggested Protocol for Turnover Experiment
Period Length - 3 Weeks

Period	Diet (gms/day)			Minerals & Vitamins	Turnover Exp.	Body Composition
	Protein	Carbohydrate	Fat			
I	70	K	K	K		X
II	70	K	K	K	Wk 1	
III	65	K + 50	K	K		X
IV	65	K + 50	K	K	Wk 1	
V	60	K + 50	K	K		X
VI	60	K + 50	K	K	Wk 1	
VII	0	K + 70	K	K		X
VIII	0	K + 70	K	K	Wk 1	
IX	70	K	K	K	X	X

17. Studies in body composition under the direction of Dr. Sheldon Margen.

RESEARCH PLAN

A. Introduction and Specific Aims:

The determination of body composition *in vivo* has presented a challenge to physiological and nutritional investigators for many years. At present the "fluid spaces" can be measured directly by various dilution techniques. The fat and protein content can be derived by indirect methods mainly those involving both fluid space and density measurements of the organism. The problems and assumptions inherent in the *in vivo* measurement of body composition have been reviewed on many occasions. It is clear that any determination aimed at determining body fat by density measurement must of necessity be concerned with body volume.

Two principal techniques have evolved for the volumetric approach to body composition. The first is the technique of underwater weighing, first introduced by Behnke and the second the determination of the body volume by gas dilution as worked out by Siri. The assumptions made when the fat content is calculated from a knowledge of the density or the total body water have been elucidated. The

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Most important variable, that has not yet been measured, has been bone mass. Because of the high specific gravity of bone, errors in the estimation of bone content of the organism lead to the most serious errors in converting density to fat content. It would appear that a rapid and efficient, precise measurement of body volume could be carried out with present day instrumentation. The technique which is proposed is an attempt at determining body volume from changes in air pressure within a closed chamber. In addition, it is proposed to attempt to estimate more exactly the bone mass of the organism by determining the labile calcium pool. Non-radioactive strontium will be used as the indicator of labile calcium. It is hoped that in states where there is not a disturbance of calcium metabolism, the ratio between exchangeable calcium, as measured with strontium, and non-exchangeable calcium (total bone mass) will be constant enough to enable one to determine total bone mass from the measurement of exchangeable calcium.

2. Methods of Procedure

1. Studies of volume alterations by pressure differences.

It is proposed that a small air-tight box be constructed with an easily removable but airtight lid. The box will be of known volume. Connected to this will be an apparatus that can displace a known volume of air. The final type of displacement apparatus is not clear; initial work will be done with the use of a gas-tight syringe. However, it may turn out that rapidly alternating pressures may yield better results, necessitating the construction of a small apparatus that will drive a piston of an air-tight syringe or other cylinder at rapid rates. Blocks of known size will be introduced into this chamber of known volume and attempts will be made to correlate the predicted pressure changes with the observed pressure changes and these measurements corrected to volume. The pressures will be measured by means of sensitive strain gauges with responses such that pressure variation of plus or minus .05 pounds per square inch differential will give an output signal of over 30 millivolts. If the ratio of chamber to subject is kept relatively small, extreme sensitivity, and it is hoped accuracy, should be obtained by means of this technique. Since the pressure measurements are almost instantaneous in time, temperature will cancel out in this system, and hence, the most difficult theoretical objection to a pneumatic method of volume determination, namely, temperature differences, should play no role. After the technique has been standardized with models, rats of varying sizes will be introduced and their volume determined. The animals will then be sacrificed, their volume determined by H₂O displacement, and carcass analysis will be performed. If this system is applicable to small animals, further attempts at adapting this to man would naturally be undertaken. The relationships in this type of volume measurements can be stated by the following formula:

$$V_a = V_c + v \frac{P_1}{P_2 - P_1}$$

- V_a = volume animal
- V_c = volume of empty chamber
- v = volume of gas added to chamber
- P₁ = initial pressure
- P₂ = pressure after displacement of v.

Facilities are currently available within our building for underwater weighing. These facilities have been used by Dr. Albert Behnke during the past summer

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REPORTS AND SERIES TITLE	<i>Handwritten Title</i>
MANUSCRIPT NUMBER	<i>79/112</i>
CARTON NO.	<i>Box 7</i>
FOLDER NAME	<i>Handwritten Folder Name</i>
NUMBER	<i>Handwritten Number</i>
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for studies that he has been conducting in association with the School of Public Health on the body composition of teenagers.

In addition to these research projects on body composition it is proposed that as part of the research activities of the Human Nutrition Laboratory other more standard methods for evaluation of body composition will be standardized and employed. These obviously include measurements such as total body water, extracellular fluid, intracellular fluid, exchangeable sodium and potassium.

B. Determination of calcium mass.

Determination of bone mass by "isotopic dilution". It is proposed to investigate the relationship between the exchangeable strontium and total calcium mass in normal rats. A technique had been developed in humans for determination of calcium turnover studying the labile exchangeable calcium pool expressed in terms of "total plasma unit." In this technique a known dose of non-radioactive strontium was injected intravenously and the plasma, urine and fecal strontium levels were followed. From this it was possible to calculate a calcium turnover value. This calcium turnover value was similar to those published, using Ca^{45} , by other investigators. It is clear that the ability to determine calcium turnover without the use of a radioactive isotope is extremely important in human research. The fact that strontium in small doses behaves metabolically in a similar manner to calcium has long been known.

The technique with strontium will be applied to rats. Both radioactive and non-radioactive strontium will be injected intravenously. The concentration of the radioactive strontium as well as the non-radioactive material in urine and plasma will be followed over the next several days, and from this data it is presumed that a value for exchangeable strontium mass and hence exchangeable calcium mass can be calculated. The animals will then be sacrificed, their viscera removed and the skeleton obtained by enzymatic debridement of the bone. The total bone will then be analyzed for calcium and radio-strontium and the ratio of exchangeable calcium (i.e., strontium) to total calcium determined. It is hoped that this exchangeable mass will bear a constant relationship to the total mass of calcium. If this does turn out to be correct in the rat, the observations will be extended to other species with the hope that this may be applied to man.

III. Studies in carbohydrate metabolism, particularly in patients with diseases associated with alterations in carbohydrate metabolism, under the direction of Dr. Sheldon Margon and Dr. James Richmond.

RESEARCH PLAN

A. Introduction and Specific Aims:

Although considerable work has been done on the metabolic fate of the monosaccharides, fructose, glucose and galactose, much remains to be learned regarding the fate of carbohydrates, particularly that of various oligosaccharides occurring in food. As an example, it is clear that whether glucose, sucrose or purified starch is ingested, the rate of hydrolysis is so rapid that it apparently exceeds the maximal absorption of sugar in the intestine and the shape and slope of glucose appearance and disappearance in the blood is unchanged. However, little work has been done concerning the fate of starches as they occur in natural

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foodstuffs per se or the metabolism of naturally occurring simpler oligosaccharides. These studies become of particular importance in normals and patients with disorders of carbohydrate metabolism such as diabetes or galactosemia. In diabetics, particularly those requiring insulin, where the intake of food must be balanced against the pharmacologic action of insulin, the rates of hydrolysis and absorption of foodstuffs become quite critical. Likewise, in the case of infants with galactosemia the question whether the galactose in certain oligosaccharides is available becomes of paramount importance in dietary regulation of the disease. Little is known regarding the absorption of oligosaccharides.

Because of limitations in methodology little work has been performed to date on galactose metabolism particularly in normals and patients suffering from diabetes. The main methodological limitation has been that of galactose determination which is usually done by reducing glucose through fermentation and determining the residual reducing capacity of the system. It is proposed, therefore, to study the blood levels of glucose, galactose, oligosaccharides and free fatty acids after the ingestion of glucose, galactose, various oligosaccharides in their purified form and the oligosaccharides and starches as they occur in foods. Where possible the degradation products of the compounds listed above will be studied.

B. Methods of Procedure

Initial studies will be carried out in normals, then patients with diabetes and finally probably patients with galactosemia. The individuals, serving as their own controls, will be fed quantities of glucose, galactose, oligosaccharides, starch and foods containing oligosaccharides and starch. The studies will consist of two types:

- a. Short term studies in which the "tolerance" to the various carbohydrates will be tested after an oral or parenteral loading.
- b. Long-term feeding studies in which the effects of various carbohydrates or carbohydrate-containing foods may be studied.

These studies are particularly important in diabetic patients, where the question of amount and type of carbohydrate and carbohydrate-containing food is still unclear. For these latter type studies the controlled environment of the Human Nutrition Laboratory is imperative. The blood and urine, glucose, galactose, oligosaccharides and free fatty acid levels will be determined. The individual will serve as his own control. The methods to be employed in the determinations are as follows:

- 1. Glucose - by use of glucose oxidase. This method is used in our laboratory.
- 2. Galactose - by use of galactose oxidase. This method is being worked on currently. See work done to date below.
- 3. Free fatty acids - by the Glown modification of the Dole procedure.
- 4. Oligosaccharides - determined and characterized by thin layer and gas chromatography.
- 5. Studies of oxidation rates of oligosaccharides and monosaccharides by analyses of O_2 , CO_2 production and O_2 consumption.

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DOCUMENT SOURCE	University of California at Berkeley The Bancroft Library, The University Archives, Berkeley, CA
RECORDS SERIAL TITLE	Medical Diet Correspondence - Papers
BANK NUMBER AND DATE	1971/12/2
CARDINAL NO.	5827
FOLDER NAME	Medical Diet Correspondence
NOTES	pp. 11/31
FOUNDER STATE FILING	Chicago State

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The purified oligosaccharides will be prepared and supplied by Dr. R. S. Shallenbarger, Department of Food Science and Technology, Cornell University, Geneva, New York.

IV. Studies of the physiologic properties of food, under the direction of Dr. David Callaway.

RESEARCH PLAN

A. Introduction and Specific Aims

Coincidental to the provision of essential nutrients, subsistence upon natural and processed foods requires ingestion of an enormous variety of ancillary substances and differing nutrient forms which have profound physiologic effects. Indeed, the form in which nutrients are presented often governs their ultimate utilization. These attributes of foods are of special importance in constructing therapeutic diets for hospital populations and have relevance to all practical feeding situations, as well as theoretical interest.

Known, but essentially unexplained, examples of physiologic effects are the differences in volume, pH and enzyme content of digestive juices produced in response to feeding different foods (such as milk, meat, or bread) and adrenal hypertrophy consequent to continued consumption of chilled fluid food. Ancillary substances that have been identified but not fully evaluated from the standpoint of human nutrition are bovine hormones and transferritins; plant alkaloids in milk; estrogenic compounds, lectins, gums and fiber in plant materials; and anti-enzymes and toxins in many legumes. The influences of phytate, oxalate and lactose on calcium absorption exemplify ways in which utilization of a nutrient may be modified by the food of which it is a part; and the differing cariogenic, cataractogenic, hypercholesterolemic, digestive and metabolic effects of the various sugars show that there are more than interchangeable energy sources.

Typical of problems in this area is that of gas production associated with specific foods. Recently completed studies suggest that former concepts of intestinal fermentation and gaseous exchange require reevaluation. Using laboratory-constructed equipment capable of measuring trace amounts of hydrogen and methane in expired air, as well as the larger concentrations in flatus gases, we have found that gases evolved in the lumen of the intestinal tract are freely exchanged through respiration, provided partial pressure relationships are favorable. In fact, respiratory exchange frequently exceeds flatus egestion. Known to affect both production and exchange are specific dietary components and emotionality; an influence of physical work output is suspected. Incubation of slurries of intestinal contents of fecal dejects indicates that gaseous nitrogen and carbon dioxide are also evolved but present techniques do not permit evaluation of production in vivo. The role of intestinal microflora has not been established.

Only the availability of a metabolic unit would enable us to delineate the various relationships. It is necessary to administer isotopically labeled materials and to carry out more complete measurement of respiratory exchange. The influences of physical work should be quantified by treadmill testing. More adequate sampling of intestinal contents, particularly from the ileum and proximal colon, is needed for bacteriologic evaluation.

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DOCUMENT SOURCE	University of California at Berkeley The Bancroft Library/The University Archives, Berkeley CA
RECORDS SERIES TITLE	Harold Jones Correspondence Papers
BANCROFT ARCH ID NO	79.112
CARTON NO	Box 7
FOLDER NAME	Marion Shelton
NOTES	pg. 12/31
FOUND BY/DATE FOUND	Susan Stetson

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The objective of this research is to determine 1) the manner in which foods affect functional behavior in man, apart from known content of essential nutrients, and 2) the extent to which these physiologic responses aid or interfere with attainment of adequate nutrition.

B. Methods of Procedure:

Initially, unresolved problems of intestinal gas production will be investigated. At least two foods known to have differing effects will be included in the series--a dried legume and milk. The test foods will be substituted, on the basis of proximate composition, into a controlled diet of known composition.

Flatus gases will be collected by rectal tube and expired air will be sampled periodically, the frequency and method of sampling varying with the specific problem under study. Attempts will be made to estimate total body gas content by existing techniques, and to develop improved methods that could be applied to studies of body composition.

Hydrogen and methane can be measured by previously developed techniques, as the origin of these gases is clearly intestinal. Proof of evolution and quantification of nitrogen and carbon dioxide are dependent upon use of labeled materials. N^{15} and C^{14} can be incorporated into beans and milk at the time of production; addition of tritium would be helpful in elucidating stoichiometric relationship. The long-term program in this area will involve detection and quantification of other minor gases of clinical nutritional interest, such as ethanol, acetone, hydrogen sulfide, and ammonia.

An effect of physical work output on the accumulation of flatus gases can be postulated, mediated through variation in splanchnic blood flow or respiratory rate. Data obtained from subjects at bed rest or performing graded amounts of aerobic work, and anaerobic work should clarify these points.

Samples of ileal and colonic contents may be obtained by use of a radio-controlled collection device, administered perorally in conjunction with test and control meals. In this way, enteric organisms may be obtained for enumeration and generic classification and for in vitro fermentation studies. (Cultures obtained in this program will be maintained for other departmental researches such as determination of alpha-galactosidase activity and vitamin synthesis on specific carbohydrate substrates.)

Other categories of behavior and of foods will be added as the program develops. Initial selection of foods will be based upon their relative importance in the human dietary and suspected ancillary effects. Additional criteria for preliminary evaluation might include, but not necessarily be limited to, the following:

- a. Gastrointestinal: transit time; stool frequency, characteristics, bacterial content and polar gases in equilibrium; rate of elevation and maintenance of blood sugar levels; digestibility and absorption; volume, pH and enzyme content of digestive secretions.
- b. Cardiovascular: skin temperature; heart rate; blood pressure; work capability; clotting time; blood lipids.

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- c. Appetite depression or satiety: measured subsequent food intake; onset of subjective feelings of hunger; weight maintenance.
- d. Psychomotor: standard tests of reaction time and psychological testing.

Influences noted in man will be studied in detail by the use of suitably prepared animals in order to delineate causative mechanisms and devise methods for their enhancement or vitiation.

V. Studies in folic acid metabolism under the direction of Dr. E. L. R. Stokstad.

RESEARCH PLAN

A. Introduction and Specific Aims:

Research on folic acid metabolism. A program is in progress for development of new biochemical tests for folic acid. These would consist of tests for metabolic products excreted in the urine during deficiency states. After the development of such tests on the basis of animal experimentation, metabolic tests would be run on normal subjects to study normal metabolic patterns and their influence by diet.

B. Methods of Procedure:

The experimental clinical work on folic acid deficiency will consist essentially of maintaining subjects on a low folic acid diet and studying the various metabolic changes which follow. Biological assays of natural materials for biologically available folic acid will also be made.

1. Composition of basal diet low in folic acid. A diet similar to that used by Victor Herbert (Tr. Assoc. Am. Phys. 75, 307, 1962) consisting of boiled chicken meat as a source of protein and rice as a cereal will be used. This will be supplemented by synthetic vitamin and mineral supplements to give a diet which is adequate in every respect except for folic acid. By this method it is possible to feed a basal diet furnishing 5-10 μg of folic acid per day. Using this basic type of diet Victor Herbert obtained folic acid deficiency in four months as evidenced by a small reduction in hemoglobin and megaloblastic changes in the bone marrow.

2. Biological assay of natural materials for folic acid. Victor Herbert has obtained evidence that 50 μg of folic acid will almost meet the folic acid requirements necessary to maintain normal serum folic acid levels in patients maintained on this experimental low folic acid diet. However, there is evidence of patients in Puerto Rico who have developed nutritional folic acid deficiency on diets which contain between 500-1000 μg of folic acid. Considerable speculation has been made about the availability of folic acid in natural materials because much of that which is present in natural materials is in a conjugated state. Biological assays of this type of material can be made by comparing the changes in blood level and in urine excretion following administration of a given quantity of folic acid in the form of a natural foodstuff (as measured by microbiological assay

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and comparing this with blood and urine changes following administration of comparable quantity of synthetic folic acid.

3. Biochemical changes that would be used to study folic acid deficiency would include: a) formiminoglutamic acid in the presence of a test dose of histidine, and b) excretion of formic acid. An increase in excretion of formic acid has been noted in folic acid deficiency in animals. This is increased following a loading dose of tryptophane in rats. Thus far formic acid excretion has not been measured in patients suffering from folic acid deficiency. Formic acid will be determined either by a chemical method involving reduction of formic acid to formaldehyde with subsequent determination of the formaldehyde chromotropic acid or by an enzymatic method developed by Rabinowitz involving the formylation of tetrahydrofolic acid in the presence of a formate activating enzyme and ATP.

VI. "Metabolic adaptation" to caloric restriction in man under the direction of Drs. Sheldon Margen and Doris Calloway.

RESEARCH PLAN

A. Introduction and Specific Aims:

There is a growing body of evidence which suggests that metabolic patterns may be modified in response to changes in substrate provided from specific foodstuffs, varying both qualitatively and quantitatively. For example, it has been suggested that weight gain is higher with isocaloric feedings of a diet high in fat as compared with a low-fat diet. Energy is stored less effectively, but protein more so, when a given diet is administered in several small meals rather than in one large meal.

Some of these patterns, once established, appear to be retained and recalled rapidly when the original stimulus is presented again. Such biologic memory exists, for instance, for the fasting situation. Both man and animals undergoing a second period of fasting show less metabolic distortion than during the first experience--smaller losses of body nitrogen and diminished acidosis and ketosis.

Prolonged caloric restriction in man is always associated with decreasing oxygen utilization and generally with decreasing nitrogen excretion.

The reasons for these alterations are quite unclear at present. Undoubtedly some of the decrease in oxygen utilization is due to decreased energy needs associated with decreased activity and decreased body mass. However, reports are frequently found of equilibrium concepts existing on as little as 600-800 calorie intake per day, in spite of some activity. If this is true, it would presuppose some major change in efficiency of the metabolic processes or changes in body composition.

B. Methods or Procedure:

Other research areas of the overall program of the Human Nutrition Unit will contribute appreciably to the methodology needed for studies of metabolic adaptation. For example, development of improved techniques for measurement of body composition--fat, lean body mass, total body water--biologically

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defined fluid spaces--will enable us to detect small shifts in body energy storage. Evaluation of potential energy losses through intestinal fermentation will increase the precision of balance studies. Total balance studies will also consider such usually neglected factors as hair and nail growth, skin lipids and nitrogenous compounds.

The facilities will include apparatus for careful standardization of indirect calorimetry over long periods of time. The question of cutaneous exchange of oxygen and carbon dioxide will be re-evaluated to determine if this introduces significant error in studies based on indirect calorimetric methods.

Caloric expenditure and work efficiency for given activities will be established precisely. Activities to be assessed will include not only conventional motor tasks but isometric and static work as well. Attempts will be made to determine the degree to which internal work tasks--as renal clearance, for example--contribute to adaptive performance.

Individuals serving as their own controls will then be assigned to various regimens ranging from total fasting to surfeit feeding. Diets will include a broad range of proportional contributions from fat, protein and carbohydrate. The effects of these alterations on the major parameters noted above will be determined.

After this work is analyzed, effort will be directed toward measuring adaptation in "intermediary metabolism", utilizing labeled substrates. For these studies to have any validity, they should be performed in such a manner as to obtain turnover data--relative if not absolute--by use of constant infusion techniques. Optimum methods would clearly have to be worked out depending on the findings one would obtain from preliminary work.

VII. Biotin requirement of man under the direction of George M. Briggs (in cooperation with Drs. Doris Calloway and Sheldon Margen).

A. Introduction and Specific Aims:

Surprisingly little information is available about biotin, one of the B vitamins, in human nutrition. It is known that a deficiency can be produced in man by eating unheated egg white (avidin source). However, careful studies of clear cut deficiency have never been carried out nor has any significant work been done to establish requirements. It is known that experimental animals develop biotin deficiency readily by means of a dietary source of avidin and classic symptoms appear such as abnormal skin and hair conditions. It is also known that certain animals, such as the chick, turkey, and pig and mouse can develop biotin deficiency without egg white in the diet--merely by its exclusion from a purified diet. Biotin deficiency has been observed in farm animals fed natural foods. Present experiments are being conducted by Briggs with laboratory animals (mouse and guinea pig) on this vitamin. A clear cut biotin deficiency has been produced by us in mice without the use of egg white but by use of antibiotics (submitted for publication).

B. Methods of Procedure

Attempts to produce a deficiency in man would be made with a purified diet, with egg white and with an antibiotic of the neomycin type. Estimates on biotin requirements and balance would be made with measurements of biotin levels of food, feces, urine, and serum in persons fed special diets over extended periods of time--perhaps up to several months. Other parameters of the deficiency would be studied. No one knows at this time if biotin is involved in any observed human diseases--or a metabolic disorder. It is possible that this project might give a clue to this second question.

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The areas described above indicate the current aims of research that will center about the program-project grant. It is clear that as new findings and new staff interests develop, research fields are more likely to be broadened and altered than to remain static.

The facilities will be open to all members of the Department, and it is hoped that in the future joint projects will be undertaken with interested individuals within the University and other closely associated public agencies.

It must be abundantly clear from the outline of experiments above that the Human Nutrition Laboratory is essential for the projects outlined. Unless a facility is available where accurate and careful controls can be maintained, many of the complex problems outlined above are not subject to adequate solution. Since in human research so little can be done to minimize the individual variations between subjects, the least we can do is to carefully control the environment in which the experiment is conducted.

PART III - ESTABLISHMENT, ORGANIZATION AND ADMINISTRATION

A. Physical Resources

Physical resources available are best noted in the attached plans. These plans show the general location of Morgan Hall, which is the principal building of the Department of Nutritional Sciences on the Berkeley Campus, as well as the general outline of the building. All of the third floor of the building, except for one class laboratory, is devoted to research laboratories and offices. The second floor consists of 3 student laboratories, 6 research laboratories and staff offices. The first floor is mainly administration although it does include some research laboratory space, the Department Library and classroom teaching areas. The basement is currently used primarily for research laboratories and offices. There are also 5 research laboratories in adjacent Hilgard Hall and 4 research laboratories in the Life Sciences Building.

The shaded areas indicated in the plan are those areas which will be directly part of the Human Nutrition Laboratory and the proposed use and alterations are noted on Sheets 2 and 3 of the plans. The penthouse portion of the Human Nutrition Laboratory is an almost complete metabolic ward facility. As noted on the plans, it consists of a large central recreation room, dining facility, large kitchen that requires minimal remodeling for conversion to an ideal metabolic kitchen, and bed space. There are currently 7 beds available. However, it is probable that only 5 beds will be used (3 bedrooms) and that one room will be reserved as office-examining room. The bathroom and excreta collection areas are ample, but as noted, will require some remodeling.

The greatest lack in the penthouse area is for a core laboratory. This is being proposed in the application. Space and rough plumbing and electrical connections are available. The construction of the core laboratory will require three additional outside walls. Program-project funds will not be used for this construction. Arrangements for financing have been made from departmental or the University fund.

The third floor space consists of the director's office, secretarial space,

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two large laboratories, and the excreta preparation room, the latter to be within Room 308 (308B).

On the second floor will be located the co-director's office and the human "Metabolic Laboratory" (e.g., facilities for physiological and energetics measurements).

In addition, not noted are facilities shared by the Department--such as cold rooms, deep freeze room, dark room, ultracentrifuge room, etc.

The major equipment currently available within the Department is as follows:

1. 2 liquid scintillation counting systems
2. Gamma spectrometer
3. Well scintillation detector
4. High voltage electrophoresis equipment
5. Two refrigerated centrifuges
6. Spinco analytical ultracentrifuge, Model E
7. Spinco preparative ultracentrifuge, Model L
8. Spectrophotometers
9. Vapor pressure osmometer
10. Recording spectrophotometers (two) - Cary Models 15 and 11
11. Perkin-Elmer freeboundary electrophoresis apparatus
12. On loan - Kathaphorometer
13. On loan - Sanborn 6-channel recorder
14. High-speed, 1 millivolt recorder
15. Dual beam oscilloscope
16. Fraction collectors
17. Gas chromatographs - three within the Department, one in our group
18. Counter current apparatus
19. Recording polarograph
20. Warburg respirometer
21. Beckman Model DK-2 ratio recording spectrophotometer
22. pH stat - two

B. Organization Framework

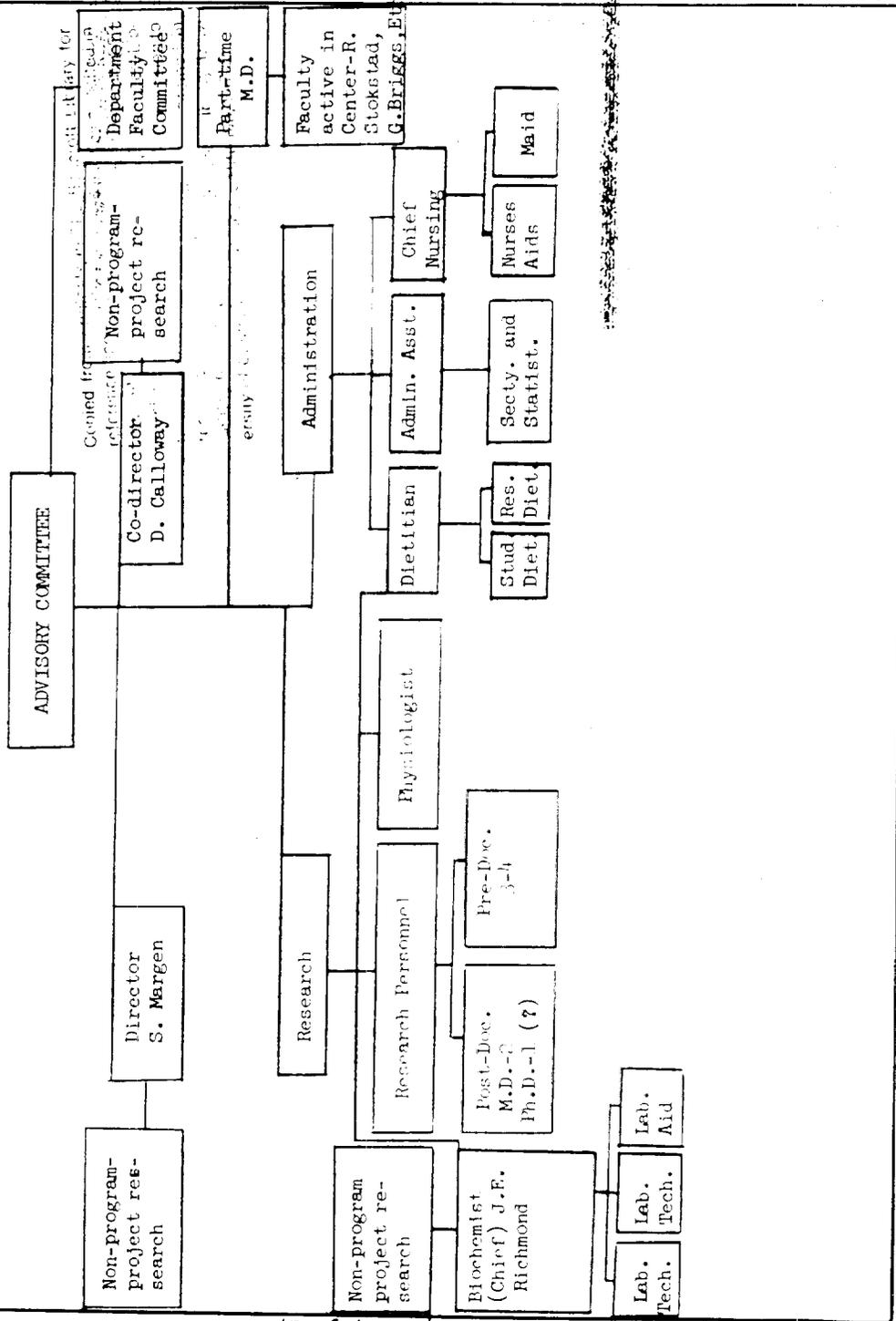
(Diagram attached)

C. Administration

The nature of the administration is quite clearly formulated in the organization framework. The overall Advisory Committee is essentially an interdisciplinary committee from various departments of the University of California, both on the Berkeley and San Francisco Campuses. They will serve mainly in an advisory capacity, and will be called upon for regular meetings during the year and for advice on various programs. Any member of the Department or those of other interested departments will be welcome to submit proposals for research to the project center, as well as to partake within the work of the center. As an example, members of the Department who are interested in lipid chemistry will be allowed and encouraged to participate in the program, either as far as modification of the program for their own research is concerned, or will also be encouraged to institute

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B. Organization Framework



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ADVISORY COMMITTEE

Dr. Lester Breslow	Chief, Division of Preventive Medical Services, California State Dept. of Public Health, Berkeley.
Dr. Isidore S. Edelman	Professor of Medicine and Physiology, and Associate Director of the Cardiovascular Research Institute, Univ. of California Medical Center, San Francisco.
Dr. Harold Harper	Dean of Graduate Division; Professor of Biochem- istry, Univ. of California Medical Center, San Francisco.
Dr. Rita Huenemann	Associate Professor, Public Health Nutrition, School of Public Health, Univ. of Calif., Berkeley
Dr. Hardin Jones	Assistant Director, Donner Laboratory; Professor, Medical Physics and Physiology, Univ. of Calif., Berkeley.
Dr. Nello Pace	Professor of Physiology, Univ. of Calif., Berkeley
Dr. Harold Tarver	Chairman and Professor of Biochemistry, Univ. of California Medical Center, San Francisco.
Dr. Esmond Snell	Professor of Biochemistry, Univ. of Calif., Berkeley.

Ex officio Chairman - Dr. George M. Briggs
Department of Nutritional Sciences
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problems within the project center. There will also be a Departmental Faculty Committee who will review, with the director and co-director, the work of the projects to be instituted within the center. These will meet periodically to review the work of the center and make any recommendations for change. The Departmental Faculty Committee will consist of the Chairman and three other members of the Department selected from among the Academic Senate members of the Department. These will serve for periods of two years and be re-appointed by the Chairman of the Department.

The current staff of the Department of Nutritional Sciences who can be called upon for administrative or professional help is as follows:

Teaching and Research:

- Briggs, George M., Ph.D. (Chairman), Professor of Nutrition, Biochemist in Ag. Exp. Sta.*
- Calloway, Doris H., Ph.D., Professor of Nutrition, Nutritionist in Ag. Exp. Sta
- Joslyn, Maynard A., Ph.D., Professor of Food Technology, Chemist in Ag. Exp. Sta
- Landis, Judson I., Ph.D., Professor of Family Sociology, Research Assoc., Inst Human Devel.
- Mackinney, Gordon, Ph.D., Professor of Food Technology, Biochemist in Ag. Exp. Sta.
- Clcott, Harold S., Ph.D., Marine Food Scientist, Professor of Marine Food Science; In charge of Marine Food Science Laboratory, Inst. of Marine Resources, Berkeley
- Stokstad, E. L. Robert, Ph.D., Professor of Nutrition, Biochemist in Ag. Exp. Sta
- Brown, W. Duane, Ph.D., Assoc. Professor of Marine Food Science, Assoc. Marine Food Scient.
- Lyman, Richard L., Ph.D., Assoc. Professor of Nutrition, Assoc. Biochemist in Ag. Exp. Sta.
- Margen, Sheldon, M.D., Assoc. Professor of Human Nutrition, Assoc. Nutritionist, Ag. Exp. Sta.
- Williams, Mary Ann, Ph.D., Assoc. Professor of Nutrition, Assoc. Biochemist in Ag. Exp. Sta.
- Kennedy, Barbara, M., Ph.D., Asst. Professor of Nutrition, Asst. Biochemist in Ag. Exp. Sta.
- Ostwald, Rosemarie, Ph.D., Asst. Professor of Nutrition, Asst. Biochemist in Ag. Exp. Sta.
- Bennett, Mildred J., Ph.D., Lecturer in Nutrition (Bruce Lyon Memorial Research Lab., Children's Hospital of the East Bay)
- Dougherty, Ellsworth C., Ph.D., M.D., Lecturer in Comparative Nutrition, Specialist in Ag. Exp. Sta.
- McMasters, Virginia, M.S., Lecturer in Dietetics, Assoc. Specialist in Ag. Exp. Sta.

Research and Agricultural Experiment Station Personnel:

- Little, Angela C., M.S., Associate Specialist
- Menzel, Daniel B., Ph.D., Associate in Ag. Exp. Sta. (U.S. Fish & Wildlife Service)
- Richards, E. Glen, Ph.D., Assistant Research Biochemist
- Richmond, Jonas E., Ph.D., Research Associate (Established Investigator-American Heart Association)

* California Agricultural Experiment Station

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Speas, Melinda B., Junior Specialist
 Tinoco, Joan, Ph.D., Research Fellow (National Inst. of Health Post-Doctoral Fellow)
 van der Veen, John, B.S., Assistant Specialist

Lecturers and Research Fellows (primary affiliations elsewhere):

Brody, Burton, M.D., Research Fellow (Permanente Medical Group - partner), Oakland, Calif.
 Entenman, Cecil, Ph.D., Lecturer in Nutritional Sciences (Inst. for Lipid Research, Berkeley)
 Folkers, Karl, Ph.D., Lecturer in Vitamin Chemistry (Stanford Research Inst., Menlo Park, Calif.)
 Henderson, Henrietta, B.S., Cert. Dietitian, Lecturer in Hospital Dietetics (Dietitian, Dietetics Dept., Moffitt Hospital, U.C. Medical Center, San Francisco)
 Huenemann, Ruth L., Ph.D., Lecturer in Public Health Nutrition (Assoc. Prof. of Public Health Nutrition, School of Public Health, Univ. of Calif., Berkeley)
 Lepkovsky, Samuel, Ph.D. (Professor of Poultry Husbandry and Nutritionist in Ag. Exp. Sta., Univ. of Calif., Berkeley)
 Steinkamp, Ruth C., M.D., Lecturer in Human Nutrition (Public Health Medical Officer, State of Calif. Dept. of Public Health, Berkeley)
 Whitlock, Gaylord P., Ph.D., Lecturer in Nutrition Education (Agriculturist, Agricultural Extension, Univ. of Calif., Berkeley)

PART IV - BIOGRAPHICAL SKETCHES

1. George M. Briggs - Professor of Nutrition, Chairman of the Department, Biochemist, Experiment Station, 1960 - Present

Born ; Ph.D., U. of Wisconsin, 1944 (Biochemistry)

Post-doctorate Fellow, Biochem. Dept., U. of Wisconsin, 1944; Assoc. Prof. Poultry Nutr., (1945-46), Prof. Poultry Nutr., (1946-47), U. Maryland; Assoc. Prof. Poultry Nutr., U. Minnesota, 1947-51; Chief, Nutr. Unit, Lab. Nutrition and Endocrinology, Nat'l. Inst. of Arthritis and Metabolic Diseases, NIH, Bethesda, Md., 1951-58; Exec. Sec'y., Biochem. and Pharmacol. Training Committees, Div. Gen. Med. Sciences, NIH, Bethesda, Md., 1958-1960.

Member of Amer. Chemical Soc.; Amer. Inst. of Nutrition (Secretary, 1957-60); Amer. Soc. Biologists; Soc. Exper. Biol. Medicine; Poultry Science Assn.; Animal Nutrition Research Council (Executive Comm. Member, 1954-56); Amer. Public Health Assoc.; Amer. Soc. Animal Sciences; Amer. Assn. Adv. Science (Fellow); Phi Kappa Phi; Sigma Xi; Gamma Alpha; Phi Lambda Upsilon; Phi Eta Sigma; Alpha Zeta.

Borden Award Winner, August 1958.

Editorial Board, Proc. Soc. Exp. Biol. and Med., 1961

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Editorial Board, Journal of Nutrition, 1962 to present.
Journal Board, Journal Amer. Diet Assoc., 1963 to present.

Representative recent publications of a total of 105.

Hegsted, D. M., R. C. Mills, G. M. Briggs, C. A. Elvehjem, and E. B. Hart.
Biotin in chick nutrition. J. Nutrition, 23, 175 (1942).

Reid, M. E. and G. M. Briggs. Development of a semi-synthetic diet for young guinea pigs. J. Nutrition 51, 341 (1953).

Briggs, G. M. Major contributor to tables 2, 3, 4, 5, 6, and 7 and contributor to tables 45 and 80 in "Standard Values in Nutrition and Metabolism" edited by E. C. Albritton, Wright Air Development Center, Technical Report 52-301, pp. 7-17, 72 and 155-163 (1954).

Briggs, G. M., and F. S. Daft. Pantothenic Acid (estimation, occurrence, pathology, and requirements of animals). Part of chapter for "The Vitamins" edited by Sebrell and Harris, Academic Press, pp. 628-630, 633-669, and 682-687 (1954).

Briggs, G. M. Estrogen residues in meat--public health aspects. J. Am. Med. Assoc. 164, 1473 (1957).

Briggs, G. M. Nutrition and Disease. Folic acid deficiency in the mouse. Amer. J. of Clinical Nutrition 7, 390 (1959).

M. Potter and G. M. Briggs. Inhibition of growth of amethopterin-sensitive and amethopterin-resistant pairs of lymphocytic neoplasma by dietary folic acid-deficiency in mice. J. of the National Cancer Institute 28 (2) 341, Feb. (1962).

- 2. Doris H. Calloway - Professor of Nutrition and Nutritionist in Agric. Experiment Station, 1963 - present.

Born ; Ph.D., U. of Chicago, 1947 (Nutrition).

Medical Associates, Chicago, Consultant, Therapeutic Nutrition, 1948-51; QM Food and Container Institute, Chicago, 1951-61 (Chief Nutrition Branch, 1959-61; Head, Metabolism Lab., 1955-59; Nutritionist, 1951-55).

Member of Amer. Board of Nutrition (Diplomate 1951), Amer. Inst. of Nutrition, Amer. Dietetic Assn. and Calif. Dietetic Assn., Inst. of Food Technologists, Research Advisory Council of Inst. of Amer. Poultry Industries, Human Nutrition Div., Sigma Xi.

QM Technical Directors' Honorable Mention, 1955; QMFCI "Man of the Year in Research," 1959; Dept. of Army, Certificate of Achievement, 1959 and 1961; Meritorious Civilian Service Award, 1959.

Representative recent publications of a total of 54

Calloway, D. H. Nutritional properties of refrigerated animal products. Food Technology, 15, 102, 1962.

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Calloway, D. H. and R. B. Potts. Comparison of atherosclerosis in swine fed a human diet or purified diets. Circulation Research, 11, 47, 1962.

Calloway, D. H., R. Hilf, and A. H. Munson. The effects of chronic food restriction in swine. J. Nutrition, 76, 365, 1962.

Thomas, M. H. and D. H. Calloway. Nutritional evaluation of dehydrated food. J. Am. Diet. Assn., 39, 105, 1961.

Calloway, D. H. and A. E. Munson. Response of cereal-fed guinea pigs to dietary broccoli supplementation and X-irradiation. J. Nutrition, 73, 191, 1961.

3. Sheldon Margen - Associate Professor of Human Nutrition and Associate Nutritionist in Agricultural Experiment Station, 1962 - present.

Born _____; M.D., U. of Calif. Medical School, 1941.

Intern, U. of Calif. Hospital, San Francisco, 1943-44; Captain, U.S. Army Medical Corps, 1944-46; Resident, Medicine, U. of Calif. Hosp., San Francisco, 1946-47; Research Assoc., U. of Calif. Medical School, S.F., 1947-49; Clinical Instructor, Medicine, U. C. Medical School, S.F., 1948-56; Endocrinologist, Cowell Memorial Hosp., U. C., Berkeley, 1949-52; Research Assoc., Inst. for Metabolic Research, Highland Hosp., Oakland, 1951-52; Half-time Research Biochemist, Dept. of Biochemistry, U. of Calif., S. F., 1952-62; Coordinator and Director of Medical Education, Herrick Hosp., Berkeley, 1959-62; Chief, Dept. of Medicine, Herrick Hosp., Berkeley, 1962.

Member of Amer. Medical Assn., Amer. Federation for Clinical Research, The Endocrine Soc., New York Academy of Sciences, Western Society for Clinical Research, Alpha Omega Alpha.

Scholar in Medicine, U. C. Medical School, 1941-43; Senior Research Fellow, U. S. PHS, 1947-48; Schering Fellow in Endocrinology, 1948-49; National Research Council, Committee on Growth, Damon Runyon Fellow, 1949-51.

Representative recent publications of a total of 48.

Tarver, H., F. B. Armstrong, J. R. Debro, S. Margen. Catabolism of plasma proteins in the rat, in Symposium on Plasma Protein in Health and Disease, Annals of the New York Academy of Sciences, 94, Article 1, 23, 1961.

Armstrong, F. B., S. Margen and H. Tarver. Plasma Proteins, VII. Site of degradation of serum albumin, Proceedings of the Soc. of Exp. Biol. and Med. 103, 592, 1960.

Margen, S., F. B. Armstrong, and H. Tarver. The site of albumin breakdown, Clinical Research, 8, 142, 1960.

Margen, S. and H. Tarver. The problem of re-utilization of amino acids in turnover on plasma proteins, J. of Clinical Research, 6, 96, 1958.

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Margen, S., and H. Tarver. The deiodination of I¹³¹-labeled albumin, in Symposium on I¹³¹-labeled proteins in biology and medicine, Annals of the New York Academy of Sciences, 1957.

- 4. E. L. R. Stokstad - Professor of Nutrition and Biochemist in Agric. Experiment Station, Sept. 1962 - present.

Born [redacted] (registration as U.S. citizen at birth); Ph.D., U. of California, Berkeley, 1937 (Animal Nutrition).

Western Condensing Co., San Francisco, Chemist, 1937-40; Post-doctorate Fellow-Lalor Fellowship, Calif. Inst. of Technology, 1940-41; Director of Research, Biological Sciences, Agricultural Division, American Cyanamid Co., Pearl River New York, 1941-62.

Member of Amer. Chemical Soc., Amer. Inst. of Nutrition, Poultry Science, Amer. Soc. for Animal Production, Amer. Soc. of Biological Chemists, Soc. for Exper. Biol. and Med., Amer. Assn. for the Advancement of Science, Biochem. Soc. of England.

American Institute of Nutrition - Mead Johnson Award in 1947 for work on folic acid; Tom Newman Memorial Award for Research in Poultry Science, 1951; Border Award - Poultry Science Association - for work in poultry husbandry, 1952.

Representative recent publications of a total of 139.

Stokstad, E. L. R., and T. H. Jukes. Studies of the growth-promoting effect of antibiotics in chicks on a purified diet. Antibiotics Annual 1958-59.

Patterson, E. L., R. Milstrey, and E. L. R. Stokstad. The synthesis of some 2-amino-4-hydroxy-6-polyhydroxyalkyl-pteridines which are active in supporting the growth of the protozoan *Crithida fasciculata*. J. Amer. Chem. Soc., 80, 2018, 1958.

Patterson, E. L., R. Milstrey, and E. L. R. Stokstad. Effect of selenium in preventing exudative diathesis in chicks. Proceedings of the Soc. for Exper. Biol. and Med., 95, 617, 1957.

Bullock, M. W., J. J. Hand, and E. L. R. Stokstad. Reduction of 6-acylamino purines with lithium aluminum hydride. J. of Organic Chem., 22, 568, 1957.

Bullock, M. W., J. J. Hand, and E. L. R. Stokstad. Convenient synthesis of thioctic acid. J. of Amer. Chem. Soc., 79, 1978, 1957.

- 5. Jonas E. Richmond - Research Associate, 1963 to present.

Born [redacted], Miss.; Ph.D., U. of Rochester, 1953 (Biochemistry).

National Research Council Fellow in Radiological Physics, 1948-50; National Cancer Inst., Post-doctoral Fellow, 1953-55; Commonwealth Fund Fellow in Dept of Biochemistry, Oxford Univ., 1955-56; National Foundation Senior Fellow, 1956-57; Established Investigator, Amer. Heart Association, 1957-present.

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Member of Amer. Soc. of Biological Chemists; Radiation Research; Biophysical Soc.; Biochemical Soc. (Great Britain); Sigma Xi; Amer. Chemical Soc.; Amer. Assoc. for the Advancement of Science; N. Y. Academy of Sciences.

Representative recent publications of a total of 23.

Richmond, J. E., W. C. Shoemaker, and D. Elwyn. Rates of Biosynthesis of plasma and liver proteins. *Amer. J. Physiol.*, 205, 848, 1963.

Richmond, J. E. Studies on the metabolism of plasma glycoproteins. *Biochemistry*, 2, 676, 1963.

Elwyn, D., J. E. Richmond, R. H. McMenemy, and W. C. Shoemaker. Flux and turnover rates of glycine in the dog liver perfused in situ. *Amer. J. Physiol.*, 202, 415, 1962.

Richmond, J. E. and A. B. Hastings. In vivo distribution ratios of sulfate between red blood cells and plasma and between cerebrospinal fluid and plasma. *Amer. J. Physiol.*, 199, 814, 1960.

Richmond, J. E., M. G. Ord, and L. A. Stocken. The effect of X-radiation in vivo on protein and nucleoprotein metabolism in the rat. *Biochem. J.*, 66, 123, 1957.

Estimated allocation of time for above personnel and current research support:

Briggs, George M.

20% Research, supported by University and Experiment Station funds
50% Teaching
30% Administration

Calloway, Doris H.

65% Research, supported by University and Experiment Station funds.
(Current research support also through Stanford Research Institute; USPHS, Div. of Radiol. Health, List No. RH-19-63, RH 00257-01, and NASA, 2-1741 through SRI.)
35% Teaching

Margen, Sheldon

50% Research, supported by University and Experiment Station funds, and USPHS grants AM-07723-01 and AM-07765-01.
25% Teaching
25% Clinical activities (including private patients).

Stokstad, E.L.R.

65% Research, supported by University and Experiment Station funds. USPHS grants AM-08632-01 and AM-08171-01 expected to be activated in the immediate future.
35% Teaching

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Richmond, Jonas E.

90% Research, supported currently by American Heart Association and Alameda County and California Heart Associations.
10% Teaching (graduate student training)

PART V - INSTITUTIONAL RESEARCH AND RESEARCH TRAINING SUPPORT

A. Public Health Service Support:

<u>Grant Number</u>	<u>Title</u>	<u>Total Period of Support</u>	<u>Total Amt. for Period Indicated</u>	<u>Current Annual Support</u>
<u>(1) Active Research Grants</u>				
AM 07665-01	Protein Effect on Serum Albumin Turnover.	3 yrs.	\$81,194	\$43,974
AM 07723-01	Studies in Body Composition.	2 yrs.	38,086	23,725
<u>(2) Research Applications Submitted</u>				
AM 08473-01	Metabolism of Starches Oligosaccharides and Hexoses.	3 yrs.	68,250	
AM 08266-02	Glycoproteins, Cellular Environment and Function.	7 yrs.	273,656	
<u>(3) Other Support</u>				
1-K3-AM-4735-01	Metabolism of Conjugated Proteins. Research Development Award-Dr. J. Richmond (Pending)	3 yrs.	17,107 (for 12-month period)	
1-T1-DE-139-01	NIH Div. of Dental Res. Graduate Training Grant. (Approved)	5 yrs.	246,501	42,903
1-T1-GM-1188-01	NIH Div. of General Med. Sciences. Graduate Training Grant. (Pending)	5 yrs.	418,170	86,673

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B. All Other Research Support (including that from applicant institution):

<u>Source</u>	<u>Title</u>	<u>Total Period of Support</u>	<u>Total Amt. for Period Indicated</u>	<u>Current Annual Support</u>
Div. of Nuclear Educ. & Training, U.S.A.E.C. BM-16-1-64	Request for Acquisition of Equipment in Nuclear Tech. as Applied to Life Sciences. (Approved)	1 yr.	\$13,000	
Atomic Energy Commission (No number)	Role of Prosthetic Group of Conjugated Proteins in the Biosynthesis and Metabolism of Proteins. (Awaiting decision)	1 yr.	52,394	

Support from applicant institution includes:

Salaries of below-named key personnel listed under Part IV:

1. George M. Briggs
2. Doris H. Calloway, Co-Principal Investigator
3. Sheldon Margen, Principal Investigator
4. E. L. R. Stokstad

Salaries of an undetermined number of Research Assistants who might become affiliated with the research.

Assistance from a number of "service" personnel paid from department funds.

Facilities, space, utilities, etc.

C. All Support to be Replaced by Funds Applied for in this Application:

(1) <u>Public Health Service</u>	<u>Grant Number</u>	<u>Amount (Current Year)</u>	<u>Duration</u>	<u>Reason for Change</u>
	AM 07665-01	\$43,974	3 yrs.	Research work will be incorporated into work of the Center.
	AM 07723-01	23,725	2 yrs.	(Same as above)
	1-K3-AM-4735-01	17,107	5 yrs.	Salary for Dr. Richmond to be supplied by program-project grant.
(2) Institutional Funds:	None			
(3) All Other Funds:	None			

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PART VI - DETAILED BUDGET FOR INITIAL PERIOD REQUESTED FROM PHS

Projected Salary Scales for 7-Year Period

Personnel	1st Year	2nd Year	3rd Year	4th Year	5th Year	6th Year	7th Year	7-Year Total
Sheldon Margen	--	--	--	--	--	--	--	--
Doris H. Calloway	--	--	--	--	--	--	--	--
Jonas E. Richmond, Chief Biochemist	\$15,100	\$16,600	\$16,600	\$18,400	\$18,400	\$20,200	\$20,200	\$125,500
M.D., Assoc. Prof., (50% time)	6,400	6,800	7,550	7,550	8,300	8,300	9,200	54,100
Melinda Spears, Asst. Specialist	7,368	7,908	7,908	8,520	9,396	10,092	10,860	62,052
Bing Leong, Jr. & Asst. Specialist	6,684	7,368	7,908	7,908	8,520	9,396	10,092	57,876
Lab. Tech./Ph. Technician	7,080	7,428	8,196	8,604	9,780	9,948	10,440	61,476
Lab. Asst./Aid	4,344	4,560	5,028	5,280	5,832	6,120	6,120	37,284
Dietitian	5,832	6,120	6,744	7,080	7,428	7,800	8,196	49,200
Staff Nurse	5,028	5,280	5,832	6,120	6,744	7,080	7,428	43,512
Nursing Aid	3,576	3,756	4,140	4,344	4,788	5,028	5,280	30,912
Nursing Aid	3,576	3,756	4,140	4,344	4,788	5,028	5,280	30,912
Nursing Aid	3,576	3,756	4,140	4,344	4,788	5,028	5,280	30,912
Maid-Housekpg. Aid	3,756	3,948	4,344	4,560	5,028	5,280	5,556	32,472
Admin. Asst.	5,976	6,276	6,912	7,248	7,992	8,400	8,820	51,624
Sec'y.-Steno. (50% time)	2,394	2,514	2,778	2,916	3,216	3,372	3,540	20,730
Totals	\$80,690	\$86,070	\$92,220	\$97,218	\$105,000	\$111,072	\$116,292	\$688,562
Employee Benefits (10%)	8,069	8,607	9,222	9,721	10,500	11,107	11,629	68,855
Grand Totals-Personnel	\$88,759	\$94,677	\$101,442	\$106,939	\$115,500	\$122,179	\$127,921	\$757,417

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2. Movable Equipment

4th Floor:

Refrigerator Freezer (stool and urine storage) 5' x 7' at time of collection	\$ 2,000
Examination Table	500
Autoclave - small	275
Variable small equipment for ward: carts, commodes, serving trays, dishes, stool buckets, balances for patients, examining equipment, nurses station equipment, type- writer.	2,500

Kitchen Equipment:

3 Balances - torsion, shadowgraph, weights, Toledo	700
Mixer - Hobart	250
Blendor - 1 large	275
2 small	100
Cooking equipment	150
Dishwasher (replacement)	300
Garbage disposal	150
Refrigerator and Freezer - kitchen area	1,500

Equipment for Stool and Urine Preparation:

1 Waring Blendor - small	50
1 Waring Blendor - large	275
1 Gifford-Wood Liquid Homogenizer Mill	2,500
1 Muffle Furnace	450
1 Drying Oven	300
1 Freezer - specimens	1,000

Other Equipment:

Respiration patterns analyzer - data in analog and digital form (CO ₂ , O ₂ , C ¹⁴ O ₂)	26,000
Treadmill - 1	2,000
Physiological Recorder - Mechanical (Sanborn)	4,800
1. ECG	
2. Temp. thermistor	
3. Two other D.C. amplifiers	
Spirometer	1,150
Bomb Calorimeter	600
Amino Acid Analyzer	12,500
Microscope	800
2 Kofranyi-Michaelis Meters - \$350 each	700
1 Millivolt Recorder (Leeds-Northrup)	1,200
1 Hydrogen Detector	3,000
1 Methane Detector	500

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3. Consumable Supplies

Food - 6 men/yr. - \$5.00/day (300-day operation/yr.)	\$9,000
Chemicals	2,000
Glassware - dishes, etc.	4,000
Radioisotopes	4,000
Miscellaneous - medication, etc.	1,000
Office supplies	500
Animals	1,000
Laundry allowance	500

4. Travel

Staff (6 persons, 1 national meeting East Coast, each)	3,000/yr.
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5. Other Expenses

Consultative services (e.g., radiological consult, clinical laboratory services, surgical consultations, etc.)	1,000
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PART VII - BUDGET ESTIMATES FOR YEARS OF SUPPORT REQUESTED FROM PHS

	Initial Period	2nd yr.	3rd yr.	4th yr.	5th yr.	6th yr.	7th yr.
1. Personnel	\$88,759	\$94,677	\$101,442	\$106,939	\$115,500	\$122,179	\$127,921
2. Equipment	66,525	5,000	30,000	10,000	10,000	10,000	10,000
3. Consumable Supplies	22,000	23,000	23,000	23,000	23,000	23,000	23,000
4. Travel - Staff	3,000	3,000	3,000	3,000	3,000	3,000	3,000
5. Other Expenses	1,000	1,000	1,000	1,000	1,000	1,000	1,000
6. Indirect Costs	28,996	25,335	27,188	28,787	30,500	31,836	32,983
7. Hospitalization	none						
8. Outpatient/Consultation	none						
9. Alteration and Renovation	36,000	none	none	none	none	none	none
10. Fixed Equipment	none						
TOTALS	\$246,280	\$152,012	\$185,630	\$172,726	\$183,000	\$191,015	\$197,904

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