

ANALYSIS OF PROGRAM ACTIVITIES
NATIONAL INSTITUTES OF HEALTH

1956

NATIONAL INSTITUTE OF
DENTAL RESEARCH - CLINICAL CENTER

NATIONAL INSTITUTES OF HEALTH
PUBLIC HEALTH SERVICE
U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

US

NATIONAL INSTITUTES OF DENTAL RESEARCH

Report of program activities

SUMMARY OF RESEARCH ACTIVITY

January - December 1956

In the area of oral bacteriology, the major program goals are (a) to conduct systematic studies on individual types of oral microorganisms, (b) to study host-parasite relationships of the oral microbial flora in humans and experimental animals, (c) to further explore the relationships of systemic and local oral conditions to dental disease, and (d) to evaluate the effectiveness of various preventive and therapeutic agents and procedures for control of dental disease. Although steady progress has been made in these fields of study, as evidenced by such accomplishments as the determination of growth requirements and enzymatic activities of many heretofore poorly described oral microorganisms, it should be emphasized that the experimental production of dental caries and periodontal disease continues to pose new factors of etiologic significance. Studies planned for the future which should contribute much to our knowledge of these diseases include latent virus infections of the mouth, and observations on "germ-free" animals using nutritionally defined diets and known types of organisms.

In the area of oral and biological chemistry, a number of significant contributions may be cited. For example, the role of dietary protein in experimental caries was further substantiated by evidence that processed wheat cereal diets are highly cariogenic and that L-lysine has anticaries properties in a purified lysine deficient zein-base diet. Another important achievement was the isolation of a new pancreatic enzyme named basic carboxypeptidase, which may be responsible for the rapid availability of lysine and arginine from digested protein. A further observation was the role of lysine in promoting the disposition of calcium in the growing ends of long bones. This is of significance in that it supports the evidence of a relation of protein to calcium metabolism.

Improved analytical technics have also benefited the study of ion-exchange behavior of C^{14} labeled amino acids as well as the effect of C^{14} on a cation-exchange column. By further study of single cell lines grown in tissue culture, it has been shown that tyrosine, phenylalanine and glutamine are all used directly for protein synthesis.

In the category of periodontal disease, oral soft tissues of white rats have been subjected to a newly devised technic for creating a controlled and reproducible inflammation reaction. This procedure has permitted a detailed study of chemical and enzymological changes as well as a more definitive histopathological picture of inflammation.

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Recognizing the role that saliva might play in the etiology of oral diseases, pure parotid secretions have been under analysis for their amino acid and lactic acid content, as well as for electrophoretic patterns.

Continuing to present evidence of the safety of water fluoridation, analysis of skeletal tissues of humans exposed to 8 ppm fluorine for prolonged periods, revealed a maximum content of 0.653% fluoride. Although this is approximately ten times above normal, no deleterious effects were noted. Another study concerned with urinary elimination of fluorine showed that similarly efficient excretion rates exist in artificially and naturally fluoridated communities.

In the field of histology and pathology, long-range objectives include the development of fundamental information concerning the morphological, physical, and histochemical characteristics of the normal oral hard and soft tissues, and the application of this accumulated data in studies of the causative factors and pathological processes involved in oral disease. Morphological studies of the ultra-structure of dental tissues as viewed by the electron microscope are continuing to contribute new knowledge fundamental to our understanding of oral disease. Other work, in which both electron microscopy and electron diffraction are employed, concerns the effects of various chemical agents, such as fluoride compounds, on the structure and properties of the outer enamel surfaces of teeth. Particularly illustrative of the important gains made by the collaborative work with the Section of Molecular Biophysics of the National Institute of Arthritis and Metabolic Diseases is the exploration of applications of the newly developed projection X-ray microscope to the examination of hard and soft tissues.

In the field of histochemistry, studies are being extended in which protein constituents and enzymatic activities in various tissues are characterized chemically and observed with the optical microscope. Emphasis in these studies is placed on determining and comparing the localization of proteolytic activities in normal and diseased tissues including salivary glands, mucous membranes and tongue. In the use of this approach, it is necessary to develop new and advanced chemical procedures for revealing hitherto unexplored cellular components. Other continuing investigations concern the histochemical properties of connective tissue in general, with special attention focused upon normal and diseased supporting tissues of the teeth.

As a part of continuing studies of dental caries at both the microscopic and gross levels, animal experimentation is being pursued in an effort to standardize a regime for the initiation of uniform and reproducible lesions in hamsters. It is believed that this study will facilitate future research on the etiological and pathological factors in dental caries.

In the field of epidemiology and biometry, the broad goals include an amplification of the descriptive and determinative epidemiology of oral disease. It is significant that a study of dental caries by this approach developed the fluoride-caries relationship, as well as established the safety and practicability of fluoridation of domestic water supplies. Further work is in progress to describe more fully the sequence of caries inhibition and, thereby, establish hypotheses on the mechanics of the fluoride effect.

Recognizing that a majority of adults are victims of periodontal disease and that this condition is a most important cause of tooth loss in middle and later life, emphasis is currently being placed on this category of oral disease. Following the development and testing of a field method for mensuration of the periodontal diseases in populations, the broad foundations of a descriptive epidemiology have been laid. Patterns of prevalence related to age, sex, race, and social status have been under study, as well as an analysis of the etiologic role of various chronic systemic illnesses.

In the course of establishing the prevalence of certain hereditary defects of the enamel and dentine, a group of "racial isolate" people in Southern Maryland were selected for study. This group of inter-related people, consisting of some 5,000 persons, has been under study for the past year. Preliminary surveys to date have shown that not only is the prevalence of hereditary dental defects quite high, but also an unusual prevalence of other genetically-determined diseases exists. These include albinism, deaf-mutism, and mental deficiency. It is hoped that information will be gained not only regarding the cellular level in tooth development, where these genetic defects are initiated, but also of the interrelationship of the various types of defects.

During 1958 the program of NIDR will continue to include a wide range of research activities.

Work in electron microscopy will be extended to include more complete examination of tissues involved by caries and periodontal disease (pyorrhoea). Also, new histochemical methods for studies of protein and enzyme components of soft tissues, tooth and bone will be explored and developed, and applications made of these histochemical methods in the field of diagnostic surgical pathology. It is further planned to emphasize the investigations of periodontal disease. In addition to the currently employed pathological approach, using principally diseased human material collected at biopsy or post-mortem, studies on experimentally-induced disease in animals will be emphasized.

Work on experimental caries will also be continued to the end of exploring and evaluating various potential agents for control of this disease. In the area of epidemiology, emphasis will be placed on the

relationship of systemic illness, aging and socio-economic factors to periodontal disease. These studies will be expanded to utilize patient material from other public health service hospitals as well as the Clinical Center, NIH. Another area of increased activity will be the genetic study in a population group of racially isolated individuals for whom exhaustive and accurate pedigrees and histories are being obtained.

Expanding studies in oral biochemistry, namely, the chemical composition of saliva and the metabolism and function of salivary glands as secreting cells, should provide more basic knowledge of those diseases affecting both the calcified and the soft tissues of the mouth. Also to be continued will be studies on the relation of dietary protein to dental diseases, major emphasis being placed on the relation of such proteins to calcification of bones and teeth. Other projected investigations, which may shed additional light on the mechanism of dental decay, will include an evaluation of the chelating agents which possess the property of decalcification in a non-acid medium. Studies on the relation of protein chemistry of the cells involved in the tooth formation process will be continued. In the field of oral bacteriology, the studies to develop more effective means for minimizing the danger of bacteremia and endocarditis, subsequent to oral surgical procedures in rheumatic fever patients, will be emphasized.

CLINICAL INVESTIGATIONS

The Clinical Investigations Branch of NIDR has a major responsibility for encouraging the clinical application of basic laboratory findings as they might relate to cause, diagnosis, treatment and prevention of oral disease. By such coordination of clinical and basic research, an ever-increasing benefit may be contributed to the dental health needs of the nation. With this realization of a broadened scope of responsibility for the future, a variety of major fields of clinical study will be emphasized. For example, studies of periodontal disease (pyorrhoea) will include an evaluation of the efficacy of standard methods of treatment. Coupled with continued studies clarifying the relationship of systemic disease to pyorrhoea, much progress is promised for combating this difficult public health problem. In a similar manner, studies of dental caries will continue to be directed toward a better understanding of the types of microorganisms involved, their enzymatic activities, the biochemical role of saliva in the disease process, and the relationship of caries to the organ system as a whole. Other studies will continue to be related to such fields as the physiologic response of ambulatory patients to general anesthesia; histochemical reactions of oral tissues in health and disease with particular attention to the salivary glands; and prosthetic reconstruction for maxillo-facial defects with formulation of principles of design that might contribute to improved function of speech as well as the teeth and jaws.

In the important area of growth and development, studies of normal and abnormal patterns of cranial and facial growth will continue to be made by special cephalometric and laminographic technics. Particular emphasis in these studies will be placed on young children with congenital and acquired deformities.

Relative to some current problems in practical dentistry, the biologic effects of certain instrumentation procedures (high speed drilling and ultrasonic cutting) are being evaluated on both the dental pulps and surrounding tissues.

EXTRAMURAL PROGRAM

The increased Congressional appropriations (FY-1957) during 1956 allowed for the first time in the history of NIDR the development of a well-rounded and integrated Extramural Program consisting of Research Grants, Fellowships, and Training Grants.

Beginning in May, 1956, steps were taken to develop "Research Training Centers" using a block of funds allocated from research grants. However, in July when specific training grant funds became available, the "Centers" idea was modified into a full-scale graduate training program. Project site visits were made to all dental schools that evoked an interest in having a training program. As a result, applications have been received totalling in their requests far in excess of the funds available. Additional schools have indicated they plan to send in applications early in 1957. In order to develop the overall training program and to initiate training in as many institutions as possible where such programs might well be carried on, the NADRC found it advisable to reduce drastically the budgets requested. It is hoped that future appropriations will allow for supplemental requests so that funds will be adequate in terms of the training program which a given institution is competent to handle. Almost all schools submitting a graduate training program proposal requested a yearly increment for future years of support. The NADRC, faced with the problem of over-commitment for future support, decided at its October meeting to maintain future year moral commitments to training grants at the first year level. This procedure has not been favorably received by grantee institutions, inasmuch as a well-devised training program should be allowed to increase gradually to its maximum potential over a period of years. It is felt that the potentialities in the graduate training area in dental medicine have been barely touched and that additional support for development of this program is imperative. Most grants have been made to institutions where some training has been already underway and personnel, research facilities, and trainees are readily available. On the other hand, efforts also have been made to initiate training programs on a small scale in those institutions where the need is obvious for more research-trained personnel. Op-

portunities for future development along these lines are limited only by the availability of funds.

The availability of funds for fellowships allowed for an increase of the part-time dental students fellowships per institution from 4 to 6. This program has been highly praised by numerous dental schools as one of the most worthwhile programs available in terms of initiating undergraduate students to research. It is hoped to raise the number per institution to 8 in the near future.

A broader usage of the Special Research Fellowship was introduced during the last half of 1956 in order to supply adequate stipends for holders of a dental doctoral degree who desire to obtain specialized research training, and who will use such training because of their association with a dental school. It is already indicated that by this means more individuals are being encouraged toward development of an interest in research than ordinarily would be the case. Finally, all dental schools have been individually informed as to the details of each type of fellowship available, and where appropriate, they have been encouraged to integrate and supplement their training program by means of fellowships.

The response of dental schools to the Senior Research Fellowship program was somewhat disappointing; however, steps have been taken to have dental schools use this special type of fellowship to build up their basic science disciplines. The next deadline date of September 1957 is certain to bring forth more worthwhile applications from dental schools for the Senior Research Fellowships.

The impetus given to dental research by the seven-fold increase in Congressional appropriations for Research Grants is adequately attested to by the influx of applications between July 1 and December 1, 1956, for review by the March 1957 Council. These applications now total over 3 million dollars with only 1.3 million available as of December 31, 1956, to pay these requests. Based on the 40 - 50 percent approval rate expected, the FY 1957 appropriation is expected to fall short of the needs.

Consideration was given late in 1956 to the development of program grants in the field of oral pathology in order to supply the needs in this special area. Several dental schools have evinced an interest in such a program. Applications for these grants should be submitted in time for review by the March 1957 Council under special study section assignment.

Future plans call for program type grants to schools now conducting little or no research. By means of such grants it is hoped that research will be stimulated and developed in those institutions where only a small amount of research is now being done.

At the October meeting of the ADA a program sponsored by the ADA Council on Dental Research effectively presented a panel discussion of the NIDR Extramural Programs.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 1

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. - -
SECTION OR SERVICE

5. - -
LOCATION (IF OTHER THAN BETHESDA)

6. Nutrition and Dental Caries with Emphasis on Protein and Heat
Processed Foods
PROJECT TITLE

7. F. J. McClure
PRINCIPAL INVESTIGATOR

8. J. E. Folk* and L. A. Bavetta (Visiting Scientist)
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

This program is directed toward obtaining information on the relation of experimental caries to protein losses of milk powders and cereal foods caused by excessive heat processing. Results of the past year confirm the role of lysine in preventing caries induced by special heat processed skim milk powder diets. L-lysine given by water, stomach tube and food, significantly reduced caries. It appears, however, that L-lysine given by intraperitoneal injection is probably not effective, which permits some speculation as to how L-lysine acts to reduce caries, in this particular diet. Special

* Research Associate, American Dental Association, at the National Institute of Dental Research.

10. PROJECT DESCRIPTION:

attention has been paid to diets containing a large percentage of wheat cereal protein, i.e. diets containing (a) native raw wheat flour, (b) commercial whole wheat flour, (c) whole wheat flour autoclaved with lactose and (d) shredded wheat biscuit. Severe smooth surface caries results from these inadequate diets. Supplements of calcium, phosphorus and L-lysine have had pronounced inhibitory effects on the cariogenic property of these diets. A role of post-eruptive minerals in the etiology of caries is suggested and bears investigating. Further studies are attempting to relate heat processing of cereal foods to dental caries.

In cooperation with Dr. L. A. Bavetta (Visiting Scientist), it was shown that irradiation of a spray process skim milk powder, did not alter its cariogenic potential. Experiments supervised by Dr. Bavetta demonstrated that synthetic diets which contained 13% casein, particularly after autoclaving the casein with lactose, were highly cariogenic. With 24% casein very little caries was produced, emphasizing the fact that the quantity of protein poses an important consideration in these diets. Addition of 11% casein to a skim milk powder diet also reduced caries, again pointing to the significance of the quantity of protein.

In cooperation with Dr. Bavetta, it was shown that the B-vitamins added in above optimum quantities, did not affect caries produced by Diet 636 which contained autoclaved skim milk powder.

Two significant experiments (completed in cooperation with Dr. Bavetta) gave further evidence of a possible role of L-lysine in caries etiology. Synthetic diets containing zein (lysine free) as a source of protein were distinctly cariogenic. Addition of 1.00 L-lysine, however, had a significant anti-caries effect. These are our first successful studies pertaining to L-lysine as a supplement in "synthetic" lysine-deficient diets.

The accumulated evidence of the past year in retrospect has advanced the possible role of quality of protein (L-lysine), as well as quantity of protein (13% vs. 24% casein), as cariogenic factors. It has injected the possible interrelation of minerals and protein, especially through information concerning the cariogenic effects of inadequate cereal protein diets, particularly in the presence of an inadequacy or an imbalance of calcium and phosphorus.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 1
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
31,205	3,614	34,819	2	2 2/3	4 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
5	2	7			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Dr. Howard Andrews, Radiation Branch, National Cancer Institute.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 1
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

McClure, F. J., Folk, J. E. and Rust, J. D. Smooth Surface
Caries in White Rats. Effect of Fluoride, Iodoacetate,
Penicillin, Crisco, Butterfat and a Salt Mixture. J. Am.
Dental Assoc. 53:1-5, 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 2
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Biochemistry of Oral Soft Tissue
PROJECT TITLE

7. Bernard K. Forscher
PRINCIPAL INVESTIGATOR

8. H. R. Stanley, Jr.
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

The objectives of this project are to elucidate the pattern of biochemical changes which characterize a classic inflammatory response in oral soft tissue and to determine how this pattern is modified by various systemic conditions.

Methods Employed:

An inflammatory reaction is generated in the palate of the white rat by stimulation with a controlled pulse of radio-frequency current. Tissue samples are taken before and at

10. Methods Employed (Continued):

standard intervals after such treatment. These samples are subjected to histopathological study and chemical analysis. This procedure is carried out on normal rats and on rats previously subjected to some specific systemic condition.

Major Findings:

Curves describing the concentration changes of a number of tissue components during an acute inflammatory response have been developed. These components are: total tissue water, glycogen, hexosamine, tyrosine, proline, hydroxyproline, inorganic phosphate, acid-soluble phosphorus, residue phosphorus, total nitrogen, non-protein nitrogen, ribonucleic acid and deoxyribonucleic acid.

The method of inducing inflammatory change has been found to be consistently reproducible.

The effect of prolonged oral administration of Dilantin on the acute inflammatory response was a marked change in the concentration of the acid-soluble phosphorus fraction.

Effects of alloxan diabetes in rats were studied and it was found that acutely inflamed palatal tissue showed a significantly altered glycogen curve.

Significance to Dental Research:

Periodontal diseases involving the supporting structures of the teeth cause almost half the tooth loss in this country. This project represents a fundamental approach to etiology and is based on long standing clinical observations that certain systemic conditions predispose subjects to periodontal disease. Comparisons between the biochemical pattern of inflammatory response in normal tissue and in systemically predisposed tissue may lead to elucidation of the factors that control resistance and susceptibility to inflammation, and, by extension, to periodontal disease. The animal tissue used in these studies is analagous to human gingival tissue in many respects, thus allowing application of these findings to later studies on human material.

Proposed Course of Project:

Studies on the effects of diabetes will continue. Arrangements

10. Proposed Course of Project (Continued):

have been completed for initiation of studies on the effects of age on the inflammatory response. Other systemic factors to be studied in the immediate future include the effects of splenectomy as well as pretreatment with ACTH and with cortisone. Further studies will be made on samples of human tissue from patients on Dilantin therapy in order to verify findings on animal tissues. Studies also will continue in an effort to produce a standard experimental chronic inflammation.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 2
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
18,036	3,613	21,649	1	2 1/4	3 1/4
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	4	5			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 2
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Forscher, B. K. and Stanley, H. R., Jr. A New Experimental
Method to Produce Acute Inflammation. Arch. Pathology,
In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 3

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Proteolytic Enzymes; Organic Chemistry and Kinetics
PROJECT TITLE

7. J. E. Folk *
PRINCIPAL INVESTIGATOR

8. J. A. Gladner, K. Laki (NIAMD Subject A)
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

A. The isolation in pure form and the thorough characterization of a new carboxypeptidase (carboxypeptidase B) first observed in this laboratory.

B. The preparation of synthetic low molecular weight peptide substrates for various proteases and peptidases and determination of enzyme specificity by means of these compounds.

C. The comprehensive study of the effect of the glucose-amino acid reaction on enzymatic digestion.

* Research Associate, American Dental Association, at the National Institute of Dental Research.

Methods Employed:

A. A good deal of time is being devoted to isolation of carboxypeptidase B. Standard methods of protein separation are being employed as well as uncommon procedures such as digestion of contaminating protein and fractional crystallization of certain interfering enzymes. One difficulty encountered during separation is an apparently strong protein-protein interaction between classical carboxypeptidase and the new enzyme, which complicates satisfactory separation. However electrophoretic patterns show that enormous amounts of impurities have been removed during the purification procedures.

Activity and percent-recovery experiments are being conducted employing both arginine and lysine substrates. Low molecular weight peptide derivatives are being prepared and tested to learn (1) if basic amino acids, other than lysine and arginine, are cleaved from the carboxyl terminal position, (2) what effect the adjacent amino acid has on the release of the basic amino acids, (3) if the enzyme has esterase activity and (4) if the enzyme will split carbon-carbon bonds.

Kinetic studies, inhibitor studies and complete electrophoretic and ultracentrifugal pictures are being obtained.

B. Peptide derivatives of proline and hydroxyproline have been prepared by the carbobenzoxy masking method in conjunction with the azide, chloride, mixed anhydride and carbodiimide coupling methods and these are being tested as possible substrates for bacterial collagenase and as a searching tool for a possible mammalian collagenase or gelatinase.

C. Many studies employing paper chromatographic and paper electrophoretic methods for identification of products, have been conducted on peptide substrates for the major pancreatic enzymes. Methods of identifying products of sugar-peptide combinations before and after enzymatic hydrolysis have been devised.

Major Findings:

A. Carboxypeptidase-B has been identified as an individual hitherto unreported major proteolytic enzyme of bovine pancreas. It has been shown to be an enzyme specific for the release of carboxyl terminal basic amino acids. It has been partially purified and preliminary studies have been made on its specificity, kinetics and inhibition.

Major Findings (Continued):

B. A few of the proline and hydroxyproline peptide derivatives which have been prepared are: prolyl- β -naphthylamide, hydroxyprolyl- β -naphthylamide, CBZO-glycylprolylhydroxyprolylglycine ethyl ester and CBZO-glycylprolylhydroxyprolylglycine amide. Testing of these compounds as substrates is underway at present.

C. Data have been accumulated which indicate that the decrease in nutritive value of proteins which have been heated, cooked, or stored with reducing sugars is primarily a result of their incomplete digestion by pancreatic enzyme.

Significance to Dental Research:

A and C. An understanding of the alterations in the release of lysine from protein before and after its reaction with sugar, is important in evaluating factors affecting the production and prevention of experimental smooth surface dental caries. Even more fundamental is an understanding of the mechanism of release of the basic amino acids from ingested protein. The specificity of action of carboxypeptidase B at least partially explains this phenomena. Moreover, a practical tool for the determination of protein structure is foreseen in the isolation of carboxypeptidase B.

B. Thus far practically nothing is known of the specificity of bacterial or mammalian collagenases. Keeping in mind the possible importance of collagenase in dental disease; it is essential to learn as much as possible concerning their mechanism of action.

Proposed Course of Project:

A. During the coming year a good deal of time will be devoted to comprehensive studies of carboxypeptidase B. Studies on its specificity must be extended to protein and high molecular weight polypeptides and its value as a tool for protein structural determination must be demonstrated.

B. Further attempts to classify the mode of action and specificity of collagenases are underway.

C. The original aims of this project have been satisfied, i.e. to demonstrate the fact that pancreatic digestion was significantly influenced by the sugar-lysine reaction. However an additional study of the effect of the sugar reaction of arginine and possibly histidine on pancreatic protein digestion may be made.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 3
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
7,089	3,131	10,220	2/3	1	1 2/3
FY'57					

BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
-	1	1			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

American Dental Association

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- Part C: Honors, Awards & Publications
15. NIDR - 3
SERIAL NUMBER
16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956:
- Folk, J. E. Reactions of Glucose with Lysine. Arch. Biochem. & Biophys. 61:150 (1956).
- Folk, J. E. The Influence of the Lysine-Glucose Reaction on Enzymatic Digestion. Arch. Biochem. & Biophys. 64:6 (1956).
- Folk, J. E. and Burstone, M. S. Enzymatic Hydrolysis of Prolyl- and Hydroxyprolylnaphthylamides. Arch. Biochem. & Biophys. 61:257 (1956).
- Folk, J. E. A New Pancreatic Carboxypeptidase. J. Amer. Chem. Soc. 78:3541 (1956).
- McClure, F. J., Folk, J. E. and Rust, J. D. Smooth Surface Caries in White Rats: Effects of Fluoride, Iodoacetate, Penicillin, Crisco, Butterfat and a Salt Mixture. J. Amer. Dental Assoc. 53:1 (1956).
- Burstone, M. S. and Folk, J. E. Histochemical Demonstration of Aminopeptidase. J. of Histochem. & Cytochem. 4:217 (1956).
17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956:
- None

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 4
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Amino Acid and Protein Biochemistry
PROJECT TITLE

7. K. A. Piez
PRINCIPAL INVESTIGATOR

8. H. Eagle (NIAID, subprojects 2 and 4), F. Irreverre and B. Witkop
(NIAMD, subproject 3), R. C. Likins (NIDR, subproject 7)
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

It is the broad purpose of this project to provide both basic information relating to amino acid and protein chemistry of general interest and specific information of possible application to dental problems. This broad objective may be subdivided as follows:

1. To establish a general theory of pH gradient elution to aid in the selection of conditions for the analysis of amino acids.
2. To examine a C^{14} isotope effect on the ion exchange chromatography of amino acids.

Objectives (Continued):

3. To provide methods for the quantitative analysis of hydroxyproline, aldehydohydroxyproline, and other cyclic imino acids and to use these methods to examine collagens from various sources, normal and pathological, for possible structural variations related to disease or metabolic state.
4. To study the amino acid and protein metabolism of human cells grown in tissue culture.
5. To isolate and analyze the proteins of the teeth and to compare them with similar proteins from other sources.
6. To measure the metabolic turnover of tooth collagen in relation to a possible role in the caries process.

Methods Employed:

The major laboratory tools employed are ion exchange methods of amino acid analysis and radioactive tracer techniques (C^{14}). In addition, paper chromatography, spectrophotometry, and other analytical methods are used. Tissue culture techniques are used by NIAID in cooperative work.

Major Findings:

1. Suitable equations have been derived which allow the prediction of the form of a pH gradient given the experimental conditions. Various types of gradients have been considered and methods for obtaining them described.
2. The ion exchange behaviour of a large number of C^{14} -labeled amino acids has been studied. It has been shown that labeling of an amino acid in the 1 or 2 position results in slower movement, relative to the unlabeled amino acid, on a cation exchange column. Labeling in positions not adjacent to an ionized group has no effect on the behaviour of the amino acid.
3. Methods for the quantitative analysis of cyclic imino acids have been developed and applied to a preliminary analysis of dates.
4. Employing several different cell lines grown in tissue culture, the composition of the free amino acid pool has been examined quantitatively. Using improved techniques, it appears that though the cells concentrate some of the essential

Major Findings (Continued):

amino acids, they are lost when removed from the medium. The utilization of tyrosine, phenylalanine, and glutamine has been extensively studied. All are used directly for protein synthesis; glutamine amide N is not exchanged; phenylalanine and tyrosine are not interconverted except by one variant line which can synthesize a small amount of tyrosine from phenylalanine. A rapid intercellular turnover of protein has been shown to exist.

5. Methods are being devised to obtain enamel protein, and possibly enamel cuticle protein, free from other materials.

6. Preliminary experiments have been planned to measure collagen turnover in dentin and other collagens in the rat, employing C¹⁴-labeled lysine.

Significance to Dental Research:

In general, this basic information concerning proteins and amino acids is of equal importance to dental research as well as various divisions of the medical sciences. The proteins of teeth, saliva, oral soft tissues, and bone have, in some respects, received less attention than proteins from other sources.

1, 2, and 3. The three subprojects related to pH gradient elution, a C¹⁴ isotope effect, and the analysis of cyclic imino acids have contributed to the methods available for the analysis of amino acids and should have wide utility.

4. The tissue culture experiments are providing basic information on metabolism in cells derived from human tissues. The simplified system allows studies to be done which could not be done on a whole animal because of the difficulty of interpretation in a complex system. At the same time the results are more readily transferable to the whole animal than in the case of bacteria. Of considerable importance is the fact that malignant tissues can be grown and studied by these techniques.

5. Similarly, very little is known about enamel protein even though many consider that it plays an important part in the caries process.

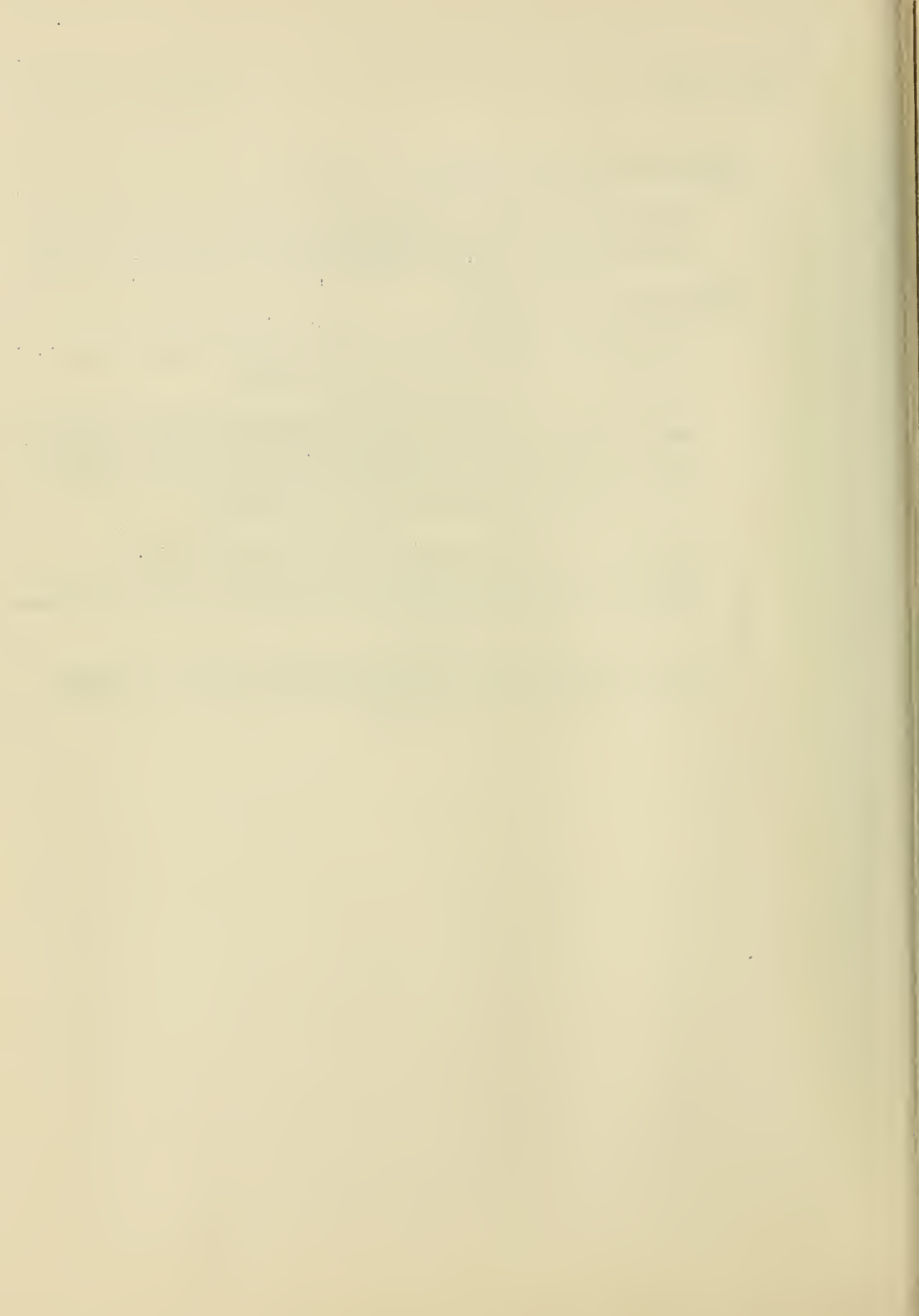
6. The turnover of dentin collagen is being studied in an attempt to evaluate the metabolic activity of dentin and to determine whether the protein can or can not be affected by systemic or dietary conditions. It is of interest to know

Significance to Dental Research (Continued):

whether the collagen, once formed, plays only a passive role in the caries process or whether it can contribute by virtue of systemically induced modifications.

Proposed Course of Project:

- 1, 2 and 3. These problems, concerned with methods, are complete and either published or in press.
4. Studies on the free amino acid pool, glutamine utilization, and tyrosine and phenylalanine utilization in tissue culture are well advanced. It is planned to study the utilization of other amino acids, intercellular protein turnover, and amino acid transfer across the cell membrane.
5. It is planned to isolate pure enamel protein and characterize it chemically, and to initiate animal studies in which dietary protein and amino acid variations may be related to enamel protein chemistry.
6. It is proposed to determine turnover rates of collagen from various tissues of the rat and to examine the effect of age and perhaps other variables.



PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 4
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
20,060	3,613	23,673	1	2 2/3	3 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	3	4			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

NIAMD (see B. Witkop & F. Irreverre)
 NIAID (see H. Eagle)

THE UNIVERSITY OF CHICAGO

PHYSICS DEPARTMENT

PHYSICS 311

LECTURE 1

MECHANICS

1.1 Kinematics

1.2 Dynamics

1.3 Energy

1.4 Momentum

1.5 Angular Momentum

1.6 Oscillations

1.7 Relativity

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 4
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

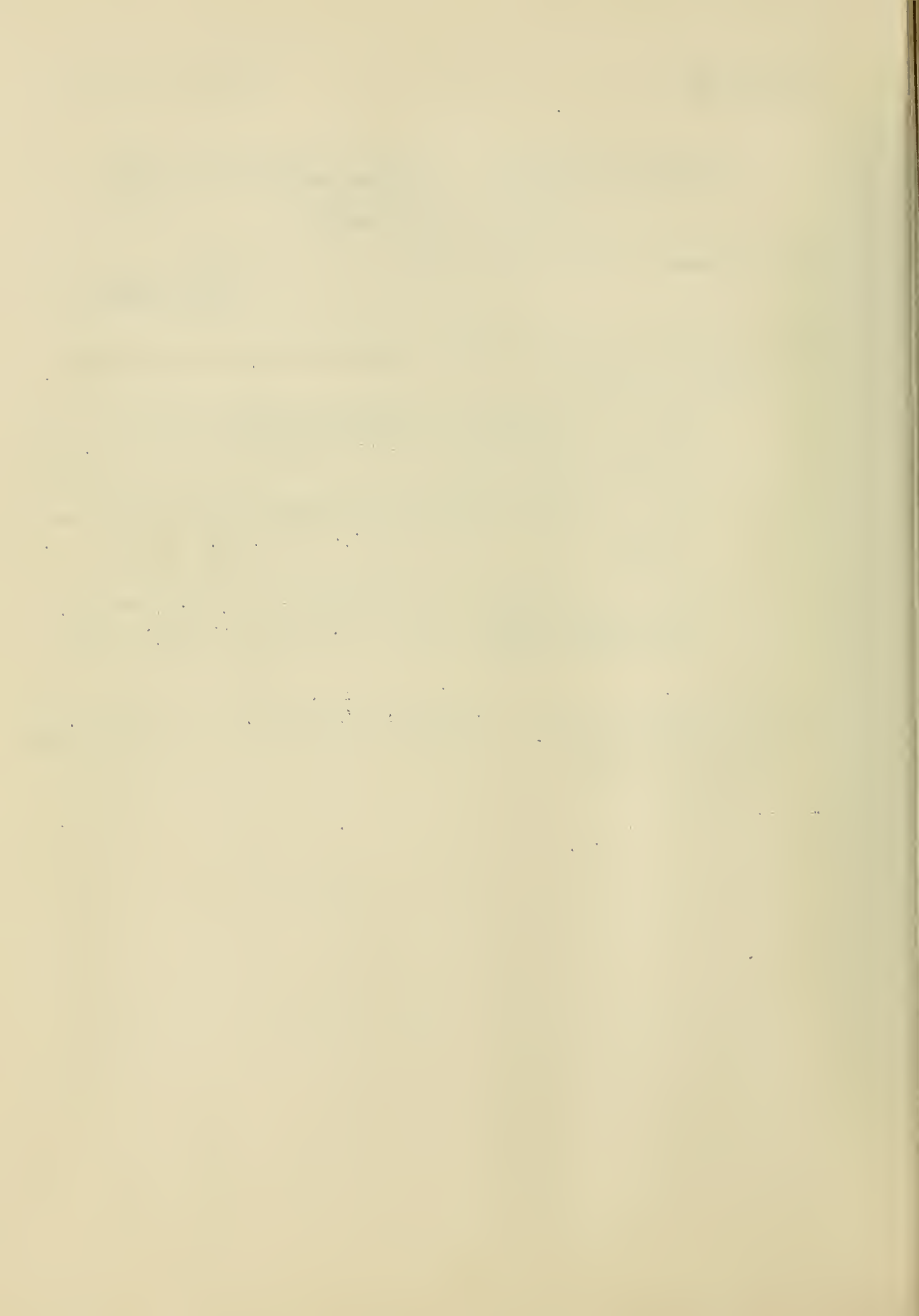
Piez, K. A. and Eagle, H.: C^{14} Isotope Effect on Ion
Exchange Chromatography of Amino Acids. J. Am. Chem. Soc.
78:5284 (1956).

Piez, K. A. Some Theoretical and Experimental Considerations
of pH Gradient Elution Analysis. Anal. Chem. 28:1451
(1956).

Piez, K. A., Irreverre, F. and Wolff, H. L. The Separation
and Determination of Cyclic Imino Acids. J. Biol. Chem.
223:687-697 (1956).

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956.

None



PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 5
SERIAL NUMBER

2. Dental Research 3. Oral and Biological Chemistry
INSTITUTE OR DIVISION LABORATORY, BRANCH, or DEPARTMENT

4. -- 5. --
SECTION OR SERVICE LOCATION (IF OTHER THAN BETHESDA)

6. Study of the Inorganic Chemistry of Mineralized Dental Tissues; the
Relationship of this Chemistry to the Associated Organic Tissues
and to Dental Caries.
PROJECT TITLE

7. H. G. McCann
PRINCIPAL INVESTIGATOR.

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To find (a) what reactions take place between mineralized tissues and certain other substances such as fluoride which offer some protection to the teeth against caries, (b) effect of the inorganic composition of the teeth, as regulated by diet, on caries susceptibility, (c) mechanism of calcification and its relation to the organic tissues, particularly collagen.

Methods Employed:

Reactions of stannous fluoride were studied in vitro by analysis of products formed under various conditions and by determination of comparative solubilities. An in vivo study is being carried out on Clinical Center patients.

The effect of diet on the composition of rat teeth and resultant caries susceptibility is being determined by analyses of the teeth and bones of rats receiving diets having variable calcium-phosphorus ratios.

The effect of various calcifying solutions on the amount of calcification of decalcified rat bone and of Achilles tendon collagen, is being determined.

Major Findings:

Approximately 3-4 gamma of tin can be detected in 100 mg. of enamel by the spectrophotometric procedure. SnF_2 treatment reduces the acid solubility of powdered enamel considerably more than NaF at a similar fluoride concentration. The amount of reaction of SnF_2 and enamel is dependent on the surface area.

Significance to Dental Research:

The more that can be learned about the reactions and composition of mineralized tissues that influence dental caries, the sooner the use of less empirical methods may be employed in the prevention of this disease.

Proposed Course of Project:

As soon as at least 12 patients have completed brushing their teeth for a 30 day period with a stannous fluoride containing dentifrice, the surfaces of their extracted teeth will be ground off and analyzed for Sn and F along with the control teeth extracted prior to the brushing.

Analyses of the teeth and bones of rats fed on high calcium, normal phosphorus and high phosphorus normal calcium diets vs. controls are being analyzed for Ca , P , CO_2 , and ash. The relation of the calcium and phosphorus content of the diet, and the chemistry of the teeth will be studied in relation to the caries experience in these rats.

Proposed Course of Project (Continued):

It is proposed to find the difference in calcification conditions for a tissue with all the necessary enzymes and factors present as in rachitic or decalcified rat bone versus Achilles tendon collagen and other collagens, in an attempt to find what relationship exists between the inorganic and organic components of the teeth and bones.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 5
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
16,084	3,613	19,697	1	1	2
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	1	2			
FY'57					

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|-------------------------------------|-------------------------------------|--------------------------|
| RESEARCH | <input checked="" type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 5
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

McCann, H. G. and Bullock, F. A. The Effect of Fluoride
Ingestion on the Composition and Solubility of
Mineralized Tissues of the Rat. J. Dent. Res. In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 6
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Biochemistry and Physiology of the Salivary Secretions
PROJECT TITLE

7. I. Zipkin
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To study the basic chemistry of the secretions of the parotid and submaxillary glands and of whole saliva, and its relation to oral diseases.

A. The lactic and pyruvic acid content of parotid and whole saliva.

Methods Employed:

Lactic acid was determined by a modification of the

Methods Employed. (Continued):

Barker-Summerson procedure. Pyruvic acid was determined by the Friedemann-Haugen procedure.

Major Findings:

The mean and range of the lactic acid concentration of parotid saliva was 2.0 mg. % (0.7 - 3.5 mg. %). The mean rate of secretion was 1.5 ml/min (0.4 - 3.0 ml/min). The rate of lactic acid secretion in mg/hr was 1.8 with a range of 0.3 - 5.1. The concentration of lactic acid in parotid saliva showed a significantly positive correlation with the rate of secretion. Approximately 60% of the whole saliva is contributed by the parotid glands. The concentration of pyruvic acid in both whole (0.09 - 0.46 mg. %) and parotid saliva (0.01 - 0.37 mg. %) is very low and comprises the greatest part of all the keto acids.

B. Ultraviolet Absorption Spectrum of Parotid Saliva.

Objectives:

To develop a quick and simple procedure for determining the tyrosine, tryptophane and protein content of parotid saliva.

Methods Employed:

The absorption spectrum of 5-fold dilutions of parotid saliva with 0.1 N HCl, H₂O, and 0.1 N NaOH was determined using the DK-2 Beckman ratio recording Spectrophotometer. Total N is being determined by Kjeldahl; tyrosine by the Udenfriend and Cooper procedure; tryptophane by the Shaw and McFarlane procedure, protein by the Hiller et al procedure, and tryptophane and tyrosine combined, by the Folin procedure.

Major Findings:

Parotid saliva shows a characteristic absorption peak in 0.1 N HCl at 280 m μ and in 0.1 N NaOH at 290 m μ . Considerable variation is seen from individual to individual in the peak density. The chemical procedures are being adapted to saliva and the tyrosine, tryptophane and protein content of parotid saliva by chemical procedures will be correlated with their spectrophotometric determination,

C. Objectives:

To determine the free amino acids in whole saliva and in pure salivary secretions and to study their relation to serum amino acids and oral contamination from food and bacteria.

Major Findings:

The free amino acids in parotid saliva have been examined quantitatively. A typical analysis of the basic amino acids shows: lysine 0.03, histidine 0.03, and arginine 0.07 mg. %. This compared with a typical whole saliva with 0.58, 0.25 and 0.35 mg. % respectively. A number of unidentified ninhydrin reacting substances have been found in both parotid and whole saliva.

D. Electrophoresis of Parotid Saliva.

Objectives:

To separate various components in saliva by electrophoresis and to characterize them.

Methods Employed:

Six samples of parotid saliva from 5 individuals were concentrated 5-fold, dialyzed against veronal buffer at pH 8.6 and 0.1 ionic strength and submitted to Dr. H. Saroff (NIAMD) for electrophoresis using the Aminco Apparatus.

Major Findings:

Five distinct components were identified with average mobilities as follows: + 1.8, 0.0, -2.3, -3.1, -4.3, all $\times 10^{-5}$ cm²/sec volt. The percentage composition in percent was 10.0, 52.3, 23.7, 8.0 and 6.0 respectively. It will be observed that the component in the highest concentration has an isoelectric point at pH 8.6.

Significance to Dental Research:

Since saliva is in intimate contact with the teeth and other oral structures, it is important to study its chemistry in both normal and pathological states. By studying the composition of both the parotid and the whole saliva, it is possible to study the role of bacterial activity in the saliva. Thus, as an example, it has been shown that the lactic acid content of whole saliva may be 3 to 4 times that in the

Significance (Continued):

parotid saliva and in addition its content is highly variable. Lactic acid, in a sense, is the end product of anaerobic glycolysis and hence may afford some measure of glycolysis within the oral cavity.

A study of the ultraviolet spectrum of saliva may furnish an easy procedure for determining the tyrosine, tryptophane and protein content.

The source of salivary amino acids has never been adequately evaluated. The picture is complicated by the presence of bacteria and debris in expectorated saliva. The composition of saliva and its relation to serum components is fundamental to the study of oral disease.

A study of the electrophoretic pattern is an important index of the number of proteins present in parotid saliva. Attempts will be made to separate some of these proteins on a preparatory scale and to identify them.

Proposed Course:

Factors affecting the chemistry of pure salivary secretions such as the parotid, will be thoroughly investigated in the normal individual. These criteria will be extended to the study of parotid saliva from individuals with rampant caries and with no caries experience, to determine if there are differences from the normal. The relation of the chemistry of saliva to other oral diseases will be investigated.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 6
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
16,797	2,652	19,449	1/3	2 2/3	3

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	--
1	3	4	

FY'57

13. BUDGET ACTIVITY:

RESEARCH

ADMINISTRATION

REVIEW & APPROVAL

PROFESSIONAL &
 TECHNICAL ASSIST-

BIOLOGIC STANDARDS

ANCE

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Project D above done in cooperation with H. A. Saroff and E. Adamik of NIAMD.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. MIDR - 6
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Zipkin, I., Bullock, F. A. and Mantel, N. The Relation of
Salivary Sodium Potassium, Solids and Ash Concentration
to Dental Caries Experience in 5-6 and 12-14 Year Old
Children. J. Dent. Res. In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 7

SERIAL NUMBER

2. Dental Research

INSTITUTE OR DIVISION

3. Oral and Biological Chemistry

LABORATORY, BRANCH, OR DEPARTMENT

4. ---

SECTION OR SERVICE

5. ---

LOCATION (IF OTHER THAN BETHESDA)

6. Non-dental Physiological Effects of Fluoride

PROJECT TITLE

7. I. Zipkin and F. J. McClure

PRINCIPAL INVESTIGATORS

8. N. C. Leone, H. C. McCann and P. Geiser

OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS; OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To study the deposition and effect of fluoride in the body skeletal tissues.

Sub-project A.

The content of fluoride in human bones as related to fluoride ingested via the drinking water.

Methods Employed:

Specimens of rib, vertebra, iliac crest, sternum and intervertebral disc were obtained on post-mortem from individuals with authenticated histories of water fluoride exposure, and who had died sudden deaths. These were analyzed for ash and fluoride by routine procedures. Some analyses included calcium, phosphorus, magnesium and carbon dioxide.

Major Findings:

Individuals residing in areas where the drinking water contained 0.2 - 0.5 ppm F, retained 0.023 - 0.115% fluoride in various, dry, fat-free bone specimens, and little variation was found between different bones. The intervertebral discs (cartilage) contained 0.001 - 0.006% F. Individuals receiving 2.5 ppm F in drinking water showed 0.104 - 0.548% fluoride in the various bones. The intervertebral discs contained 0.001 - 0.007% F. Individuals receiving 3.5 - 4.0 ppm F in the drinking water retained 0.095 - 0.564% F in the various bones. The intervertebral discs contained 0.001 - 0.013% F. One individual drinking water containing 8 ppm F had a concentration of 0.488 - 0.620% in the various bones analyzed. The intervertebral cartilage contained 0.006% F.

Sub-project B:

The fluoride content of renal and biliary calculi.

Objectives:

To determine the relation of the fluoride content of renal and biliary calculi to the water fluoride exposure.

Methods Employed:

Renal calculi were qualitatively analyzed for carbonate, ammonium, calcium, phosphate and oxalate ions, and for uric acid and cysteine. Biliary calculi were qualitatively analyzed for carbonate, calcium, phosphate iron and copper ions, and for cholesterol, bilirubin and biliverdin. Both types of calculi were analyzed quantitatively for calcium, phosphate and fluoride using standard procedures in all cases.

Major Findings:

The calcium, phosphorus and fluoride concentrations calculated on a dry basis, showed the following ranges respectively, for

Major Findings (Continued):

renal calculi: 1.9 - 29.8%, 0.3 - 19.6%, and 0.039 - 1.30%. There appeared to be no consistent Ca/P, Ca/F or P/F ratio, and no relation of the fluoride concentration of the calculi to the fluoride exposure of the individual, was observed. The biliary calculi were essentially free of fluoride.

Sub-project C:

Chromatographic Separation of Fluoride and Phosphate.

Objectives:

To quantitatively separate small quantities of fluoride from large amounts of phosphate, without following the customary distillation procedures.

Methods:

Dowex 1-10, 100-200 mesh, chloride form anion exchange resin was prepared in the hydroxyl form. Fluoride and phosphate were placed on the column. P^{32} was used as tracer indicator for phosphate. Phosphate was determined by measuring the activity of successive eluates using a fraction collector. Fluoride was determined spectrophotometrically without distillation. Fluoride was also separated semi-quantitatively using paper partition chromatography.

Major Findings:

Twenty-five μg of fluoride were quantitatively separated from 12.5 mg. P ($F/P = 1/500$). Fluoride was easily separated semi-quantitatively by paper partition chromatography on Whatman #3 MM strips using an ammoniacal methanol solvent.

Significance of Studies:

The data accumulated thus far indicate that the deposition of fluoride in the skeleton is directly related to the fluoride intake. The data are not sufficient to establish this correlation too accurately at this time. A maximum concentration of .653% fluoride in skeletal tissue was associated with a prolonged exposure to 8.0 ppm of fluoride in the drinking water.

The studies on the deposition of fluoride in calculi corroborate previous evidence that calcified structures

Significance of Studies (Continued):

incorporate fluoride readily whereas soft tissue, body fluids and cartilage do not. Apparently renal calculi will retain fluoride, whereas biliary calculi inasmuch as they are essentially uncalcified, do not incorporate significant amounts of fluoride.

It has been demonstrated that small quantities of fluoride may be effectively separated from large quantities of phosphate by ion-exchange technics. It seems possible that this procedure may be adapted to separate fluoride from phosphate in certain biological fluids, and thus circumvent the tedious process of distillation.

Proposed Course of Project:

The investigations on the deposition of fluoride in the human skeleton will be extended to include additional individuals drinking essentially fluoride-free water and to individuals drinking fluoridated water.

The study on the fluoride content of renal and biliary calculi is completed.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 7
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
14,714	3,131	17,845	2/3	1 1/3	2
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
2	1	3			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(s):

Study "C" of this project was carried out at the Univ. of Minnesota Medical School in collaboration with Drs. W. D. Armstrong and L. Singer.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 7
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Zipkin, I. and Scow, R. O. Fluoride Deposition in Different
Segments of the Tibia of the Young Growing Rat. Amer.
J. Physiol. 185:81 (1956).

Zipkin, I., Likins, R. C., McClure, F. J. and Steere, A. C.
Urinary Fluoride Levels Associated with Use of Fluori-
dated Waters. Pub. Hlth. Rep. 71:767 (1956).

Zipkin, I. and Leone, N. C. The Rate of Urinary Fluoride
Output in Normal Adults. Amer. J. Pub. Health. In Press.

Zipkin, I., Armstrong, W. D., and Singer, L. The Chromato-
graphic Separation of Fluoride and Phosphate. Anal.
Chem. In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 8
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Enzymological Studies in Relation to Oral Tissue and Periodontal Disease.
PROJECT TITLE

7. S. A. Narrod*
PRINCIPAL INVESTIGATOR

8. J. E. Folk*, R. R. Omata, and B. K. Forscher
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To study enzyme systems in relation to the structural integrity of dental supportive tissue. This includes (a) elaboration of collagenase degradation and (b) a study of enzyme processes during inflammation of the oral soft tissue.

* Research Associates, American Dental Association, at the National Institute of Dental Research

Methods Employed:

(a) Standard protein fractionation procedures are being employed to free collagenase preparations of peptidases, in an effort to demonstrate the primary action of this enzyme. The crude collagenase has been obtained by growing a pure culture of Clostridium perfringens in a liquid medium and then precipitating the extra-cellular enzymes by addition of solid ammonium sulfate. The activity of the enzyme has been measured in terms of hydroxyproline liberation. Paper chromatography has been used to identify amino acids and peptides resulting from the collagen hydrolysis.

Major Findings:

In addition to native collagen, the following peptides were found to be hydrolyzed by crude collagenase: prolyl-glycine, glycyl-proline, hydroxyprolylglycine, glycyl-asparagine, and glycyl-tryptophan. Alcohol fractionation completely destroyed the ability of the collagenase preparation to hydrolyze collagen; however, the peptidase activity was unaltered. Treatment of the preparation with Darco G-60 was found to remove a material which appeared to interfere with collagenase activity and thus gave an apparent ten-fold increase in specific activity.

Methods Employed:

(b) Following a standardized insult to the palate of female rats of the Sprague-Dawley strain, the animals were sacrificed at varying time intervals; the palates were excised and homogenized in cold distilled water. The homogenates were assayed for phosphatase, peptidase, and glycolytic activities. Reactions have been followed by colorimetry, manometry and paper chromatography. Protein has been determined with the phenol reagent of Folin and Ciocalteu and the specific activity (unit enzyme reaction per gm. of protein) determined.

Major Findings:

The specific activities of alkaline and acid phosphatases were found to increase with time following tissue insult; rising to a maximum value on the fourth day and subsequently returning to a normal value. Aminopeptidase similarly rose to a maximum value in four days; however, it remained at this elevated level throughout the periods tested. Although the enzymes studied were also found in the leukocytes of these rats, their presence in the inflamed tissue wholly from

Major Findings (Continued):

leukocytic infiltration is dubious since the rate of reaction of one enzyme as compared to the rate of another differs with time after insult; appearing not to be brought in on equal units from the cells. Since the glycolytic enzymes were only slightly demonstrable, more sensitive methods are being examined.

Significance to Dental Research:

The structure of collagen, its formation and its breakdown are important to Dental Research inasmuch as the protein matrix of bone and dentin is largely collagen. A change in metabolic patterns, as has been demonstrated in oral soft tissues, can possibly have an influence on the dynamic state of surrounding soft and hard tissues and thus lead to the bone resorption and periodontal involvement found in periodontal diseases.

Proposed Course of Project:

(a) Although the collagenase preparations have been purified several fold, no significant amounts of intermediary peptides have accumulated. Therefore, additional fractionation procedures will be carried out.

(b) The clinical use of proteolytic enzymes to reduce inflammation has been used for some time; however, the mechanisms involved are unknown. An effort is being made to localize this reaction with standardized tissue insult and trypsin injection.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 8
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
12,533	3,613	16,146	1	2 1/2	3 1/2
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
-	3	3			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

American Dental Association

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 8
SERIAL NUMBER

16 - 17. None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 9

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Chemical Agents Which Inhibit or Potentiate Experimental Rat Caries
PROJECT TITLE

7. R. Larson and I. Zipkin
PRINCIPAL INVESTIGATORS

8. F. J. McClure
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To elucidate the etiology of caries by studying the effect of various chemical compounds on experimental rat caries.

A. The caries potentiating effect of dehydroacetic acid (DHA) when administered to the rat by various routes.

Methods Employed:

Dehydroacetic acid was incorporated in cariogenic diet 636 at

Methods Employed (Continued):

levels of 0.05% and 0.01%. This compound was also given in the drinking water, by stomach tube and by intraperitoneal injection in equal amounts. Suitable controls were employed. At the end of sixty days, the rats were sacrificed and the extent of dental caries diagnosed.

Major Findings:

It has been shown that DHA is significantly and similarly effective in potentiating caries by administration in the diet, in drinking water, by intubation, and by intraperitoneal injection.

B. The effect of intubation of ethylenediamine tetraacetic acid (EDTA) on experimental caries.

Methods Employed:

Rats receiving two different cariogenic diets were administered EDTA as the sodium salt by intubation for 56 days, and the caries experience compared to those of rats receiving EDTA in the diet.

Major Findings:

Both the extent and severity of caries were highly comparable in the groups receiving EDTA in the diet and by intubation. The caries was significantly potentiated by EDTA.

Significance to Dental Research:

The increased caries resulting particularly from the intraperitoneal injection of DHA and EDTA indicate that systemic factors may be involved in this potentiation of caries.

Proposed Course of Project:

Attempts will be made to determine what physiological factors may be involved in this effect of EDTA and DHA on caries. EDTA is a well characterized chelating agent and DHA may also possess chelating properties in this instance. Efforts to elucidate the role of metal chelation in caries potentiation may be explored by use of specific metal chelates of EDTA. Also the effect of other routes of administration of EDTA will be investigated. The systemic effects particularly of DHA and their relation to caries will be investigated.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 9
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
17,699	4,093	21,792	1 1/3	2	3 1/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
2	4	6			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications	15.	<u>NIDR - 9</u> SERIAL NUMBER
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16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Zipkin, I. and McClure, F. J. The Effect of Sodium Lauroyl
Sarcosinate, and Dehydroacetic Acid on Sulcal and Smooth
Surface Caries in the White Rat. J. Am. Dent. Assoc.
In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 10
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral and Biological Chemistry
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Biochemical and Biophysical Studies of Calcification and its
Relation to Dental Caries
PROJECT TITLE

7. R. C. Likins
PRINCIPAL INVESTIGATOR

8. See item 14
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Sub-project A

Objectives:

To investigate the properties of the mineral phase of dental enamel as they relate to caries susceptibility.

Methods Employed:

Radioactive calcium has been used as a tracer to study mineral exchange in the enamel of caries-susceptible and caries-resistant rats, and to compare the properties of enamel mineral with closely related synthetic apatites.

Major Findings:

The results indicate that a decreased susceptibility to dental caries is associated with a reduction in the rate and extent of uptake of labelled calcium by the dental enamel. This correlation has been observed in rats which differ in their caries susceptibility as a result of (1) heredity, (2) the ingestion of fluoride and (3) differences in age.

In investigating this relationship major emphasis has been placed on the effect of fluoride on calcium exchange. The results of these studies indicate that fluoride (1) affects the post-eruptive deposition of calcium, (2) does not affect the calcium content of the saliva (3) does not alter the deposition of calcium in mineralizing enamel.

The possibility that the degree of enamel crystal-perfection is responsible for differences in radiocalcium uptake is now under consideration. The rationale for this is based on evidence which indicates that (1) the apatite portion of enamel mineral is a low-calcium, non-stoichiometric hydroxyapatite and (2) synthetic non-stoichiometric apatites can take up calcium from solution and approach the ideal stoichiometry of hydroxyapatite. Results to date support the belief that enamel apatite can undergo perfection. Thus rat molar teeth treated with calcium solutions in vitro show a reduced affinity for radiocalcium and a decreased solubility in acids.

Significance to Dental Research:

It is conceivable that the little understood process of tooth maturation may involve perfection of enamel crystals through acquisition of calcium (from the saliva) post eruptively. If correct, this mechanism may serve to explain the increased resistance to caries which accompanies advancing age.

Proposed Course of Project:

Emphasis will be placed on studies of the defect structure of enamel mineral.

Sub-project B

Objectives:

To investigate the role of lysine in the metabolism of bone mineral.

Methods Employed:

The deposition of orally administered radiocalcium was compared in the tibial ends and shafts of normal and lysine-deficient rats.

Major Findings:

The addition of lysine to a diet deficient in this amino acid promoted the deposition of radiocalcium in the tibial ends without appreciably affecting its uptake by the shaft. X-ray diffraction and chemical studies of bone from normal and lysine deficient rats revealed no differences in (1) crystal texture or (2) percent of calcium, phosphorus and carbonate in the ash. In vitro isotopic exchange studies showed that radiocalcium present in the tibial ends of lysine deficient rats was more labile than that deposited in the tibial ends of lysine supplemented animals. These findings are consistent with the belief that a more rapid rate of loss of skeletally deposited calcium is responsible for the diminished uptake of isotope in lysine deficiency.

Significance to Dental Research:

Investigations conducted at this Institute have shown that lysine can inhibit experimentally induced rat caries. Data relative to the role of lysine in mineral exchange may serve to clarify the nature of the relationship.

Proposed Course of Project:

The role of lysine in the calcification and mineral metabolism of the dental tissues will be investigated.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 10
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL	
23,654	3,613	27,267	1	2	3

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	--
1	2	3	

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

A. S. Posner, American Dental Association Research Associate
at the Bureau of Standards

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 10
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Likins, R. C., McClure, F. J. and Steere, A. C. The Urinary
Excretion of Fluoride Following Defluoridation of a
Municipal Water Supply. Pub. Hlth. Rep. 71:217 (1956).

Zipkin, I., Likins, R. C., McClure, F. J. and Steere, A. C.
The Urinary Fluoride Associated with Use of Fluoridated
Waters. Pub. Hlth. Rep. 71:767 (Aug. 1956).

Likins, R. C., Bavetta, L. A., and Posner, A. S. Calcifica-
tion in Lysine Deficiency. Arch. of Biochem. & Bio-
physics. In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 11
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
15,014	3,613	18,627	1	1	2
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	1	2			
FY'57					

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|-------------------------------------|-------------------------------------|--------------------------|
| RESEARCH | <input checked="" type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 11
SERIAL NUMBER

16.- 17. None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

- Part A. Project Description Sheet 1. NIDR-12 (C)
SERIAL NUMBER
2. Dental Research 3. Oral Bacteriology
INSTITUTE OR DIVISION LABORATORY, BRANCH OR DEPARTMENT
4. _____ 5. _____
SECTION OR SERVICE LOCATION (IF OTHER THAN BETHESDA)
6. Direct Studies of Microorganisms in the Oral Cavity in Relation
to Dental and Systemic Conditions in Clinical Center Patients.
PROJECT TITLE
7. Dr. Robert M. Stephan
PRINCIPAL INVESTIGATOR
8. --
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE
ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF
PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None
10. PROJECT DESCRIPTION:

Objectives:

(1) To study macroscopically and microscopically the occurrence and morphology of visible growths of parasitic microorganisms on the teeth, gingivae, and oral mucus membranes in relation to dental diseases and systemic conditions.

(2) To investigate differences in bacterial plaque formation, food retention, salivary flow rates, and pH levels found associated with caries and periodontal disease in comparison with normal dental conditions.

(3) To secure quantitative samples of surface microbial material from normal areas and pathological lesions of teeth and oral mucus membranes for related cultural studies on specific types of microorganisms.

Methods Employed:

Direct stereomicroscopic examinations of the teeth and oral cavity are made at 6 X to 40 X magnifications with the Zeiss "Otoscope", in order to determine the appearance and localization of visible microbial growths. Patient material is made available by the Dental Clinic of the Clinical Center. Phase contrast microscopical examinations at 1000 X magnifications are made on material removed from tooth surfaces, carious lesions, gingival crevices, periodontal pockets, and lesions of the oral mucus membranes in order to determine the nature and morphological types of microorganisms present. Direct pH measurements are made on this material in the oral cavity using micro-antimony electrodes and, where applicable, micro-glass electrodes. Measurements of parotid salivary flow rates are made using the Lashley cup apparatus in individuals receiving radiation treatment around the oral regions and in other individuals where interference with normal salivary flow produces a special problem in oral hygiene and health.

Samples of the oral microbial flora from specific areas of the mouth are taken using specially designed nichrome micro-scrapers. Samples are weighed under sterile conditions in a micro-balance, and distributed to other investigators in the Laboratory of Oral Bacteriology for quantitative cultural studies on specific types of microorganisms.

Major Findings:

This project is still in the early stages of development, and consequently only a preliminary statement of findings can be made. Dental caries and periodontal disease appear associated with visible overgrowths of innumerable microorganisms, the so-called "dental plaque." Different individuals have different distributions and types of microorganisms and the microorganisms differ both qualitatively and quantitatively in different areas of the same mouth.

There are different types of motile organisms commonly present on the teeth and gingivae, and in certain cases, yeast-like fungi which can be easily recognized with the phase microscope. Also several types of microorganisms have

been seen which have not as yet been isolated or studied in culture media. Various types of leukocytes are seen in material from around the teeth and oral mucus membranes which may be related to either local or systemic diseases.

Significance to Dental Research:

Although oral microorganisms have been studied for a long time in relation to dental diseases, thus far no single type of organisms have been shown to be responsible for the etiology of these diseases. This study will furnish a more exact and comprehensive foundation for finding whether specific microorganisms are qualitatively or quantitatively associated with dental diseases, or whether the etiology of dental diseases is necessarily multifactorial in nature. Since not only localized growths of oral bacteria, but also salivary flow, localized pH levels, food retention, abnormal oral functions, and systemic conditions will be studied in this project, any essential interrelationships between these various factors in the etiology of dental disease may be determined.

Proposed Course of Project:

At the present time this project is exploring the possible range of observations and findings which can be made with the methods and materials described. As more observations and data become available, and as related cultural studies are developed, plans and procedures will be worked out for concentrating efforts to define more precisely the etiology of dental diseases.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIDR-12 (C)

SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
9,385	2,662	12,047	2/3	1/3	1
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
2	1	3	--		
FY'57					

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|-------------------------------------|-------------------------------------|--------------------------|
| RESEARCH | <input checked="" type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Dr. Ralph Lloyd, of the Dental Department of the Clinical Center, is furnishing the clinical subjects employed in this study.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C. Honors, Awards & Publications 15. NIDR-12 (C)
SERIAL NUMBER

16 & 17 - None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-13
SERIAL NUMBER
2. Dental Research
INSTITUTE OR DIVISION
3. Oral Bacteriology
LABORATORY, BRANCH, OR DEPARTMENT
4. --
SECTION OR SERVICE
5. --
LOCATION (IF OTHER THAN BETHESDA)
6. The Relationship of Pathogenic Fungi to Diseases of the Oral Cavity.
PROJECT TITLE
7. Dr. Arden Howell, Jr.
PRINCIPAL INVESTIGATOR
8. --
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None
10. PROJECT DESCRIPTION:

Objectives:

To study the incidence and identity of pathogenic or potentially pathogenic fungi in the normal mouth and to study the possible relationship of these organisms to dental caries and to other diseases of the oral cavity or related areas.

Methods Employed:

The initial objective of this study concerns primarily the

incidence and identity of filamentous and yeast-like organisms in selected samples from the oral cavity. The nutrition of one group of the filamentous fungi which have been reported to occur in the oral cavity (Actinomyces Spp.) has been studied by growing them on various types of artificial culture media under both aerobic and anaerobic conditions; using standard methods, experiments have been undertaken to attempt to develop satisfactory methods for the isolation of these organisms from the oral cavity. In addition, using standard procedures, the incidence of yeasts and yeast-like organisms in the oral cavity has been studied in selected groups of individuals.

Major Findings:

A. Actinomyces: - 1. Intensive studies on the oxygen tolerance of five known strains of Actinomyces isolated from various human sources, indicates that this group of organisms are essentially anaerobes or micro-aerophiles but some strains have the ability to grow in the presence of atmospheric oxygen, or aerobically under increased carbon dioxide tension. Their ability to grow under the latter conditions has been found to be dependent on - 1) the size of the original inoculum, and - 2) the composition of the medium.

2. Since the successful cultivation of these organisms on a synthetic medium with starch (Howell, A. Jr. and Pine, L.: J. Bact. 71(1);47-53, 1956) considerable progress has been made in determining the nutritional requirements of these organisms and in growing them on a simplified synthetic medium.

3. Some progress has been made in the development of techniques for the isolation of these organisms from the oral cavity.

B. Yeast-like organisms: As indicated above, the incidence of yeasts and yeast-like organisms in the saliva of selected groups of individuals, begun in 1954, has been continued in 1956. In a study of normal school children it was found in one group, that from 30 to 40% harbored Candida albicans in their saliva, whereas, in a second group, the percentage was slightly higher, averaging 40 to 50%. The children in each group were sampled on four different occasions over an 8-month period. In the first group, 22 to 26% of the children sampled four times had this organism in their saliva on all four occasions; in the second group, this percentage ranged from 31 to 37%. Use of a bacitracin mouth wash once or twice daily did not appear to influence the percentage of individuals

harboring this organism. Further analyses of these data are in progress.

A similar study of the incidence of C. albicans in approximately 1500 patients seen at the Dental Clinic of the Clinical Center has been carried out but the data has not as yet been completely analyzed.

Significance to Dental Research:

As pointed out previously, numerous reports may be found in the literature concerning the presence of filamentous organisms in the oral cavity or adjacent areas. However, in the majority of instances complete descriptions of the organisms isolated or specific designations have not been given so that the true incidence and importance of such organisms in the oral flora is still open to question. The successful cultivation of these organisms on a medium of known composition has permitted the initiation of critical studies on the growth requirements of these forms. Conclusive evidence that strains of Actinomyces differ markedly in their oxygen tolerance and the development of methods for the critical evaluation of such differences will lend substantial assistance to species differentiation and hence permit a more accurate estimate of the incidence of the various forms in the oral cavity and related regions and of the possible role (s) they may play in the ecology or diseases of these areas.

Proposed Course of Project:

During the coming year it is anticipated that (1) further studies will be carried out on the nutritional requirements of species of Actinomyces and (2) intensive studies on the incidence and identity of these forms in the oral cavity will be initiated. As such information becomes available the possible relationship of these organisms to dental caries or to other diseases of the oral cavity will be investigated. Further analysis of the Candida studies will be undertaken.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR-13

SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
24,464	5,055	29,519	2	1 1/3	3 1/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
2	2	4	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST* ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Laboratory of Infectious Diseases, NLAID, provided space and materials for some of these studies from April 1, 1956 to June 15, 1956.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C. Honors, Awards & Publications 15. NIDR-13
SERIAL NUMBER

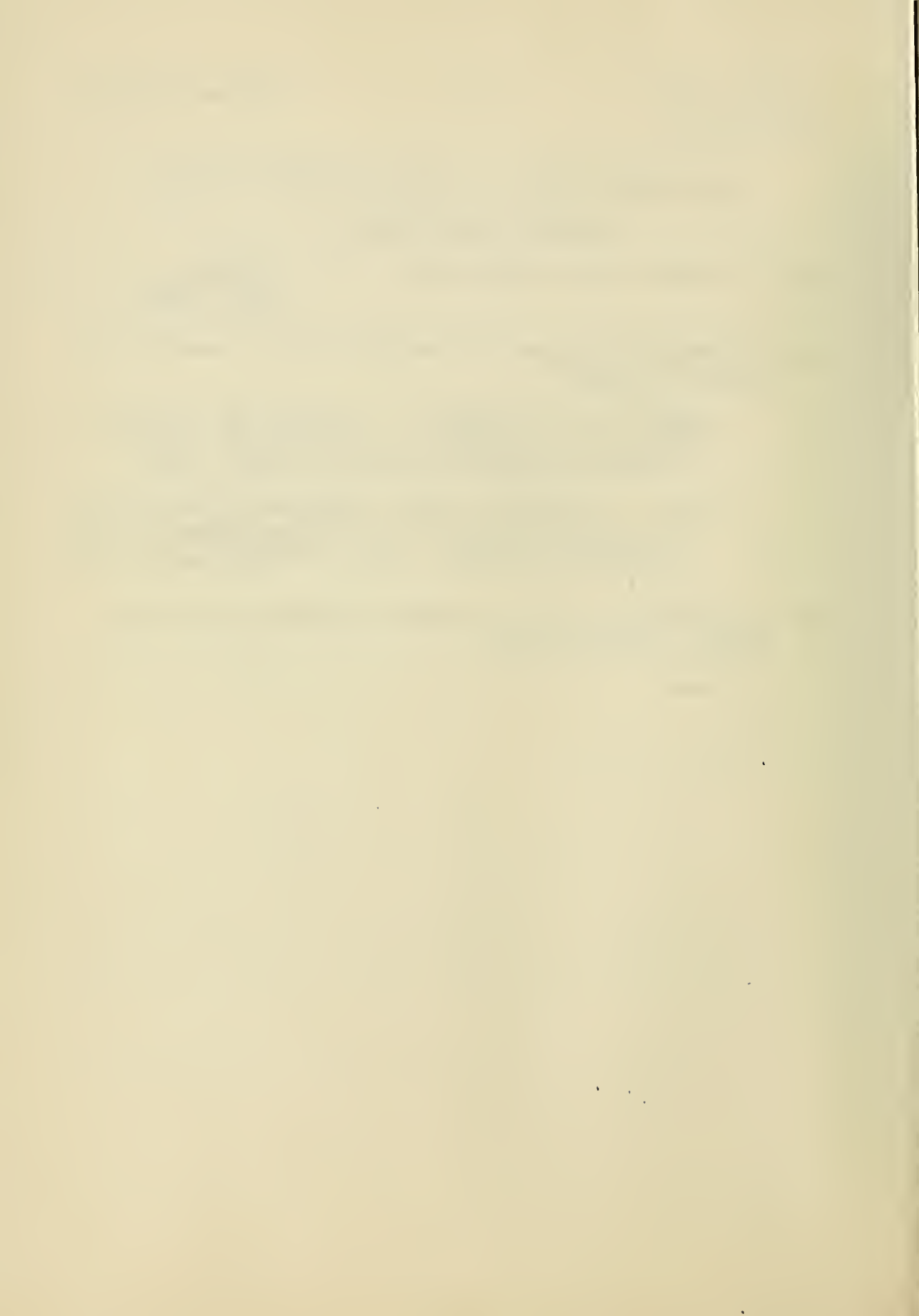
16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Howell, A. Jr., and Pine, L.: Studies on the Growth of
Species of Actinomyces. I. Cultivation in a Synthetic
Medium with Starch. J. Bact. 71(1): 47-53, 1956.

Pine, L., and Howell, A. Jr.: Comparison of Physiological
and Biochemical Characteristics of Actinomyces Spp. with
Lactobacillus bifidus. J. Gen. Microbiol. 15:428 (Dec)
1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None



PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-14
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH, OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Studies on Latent Virus Infections
PROJECT TITLE

7. Dr. William D. McBride
PRINCIPAL INVESTIGATOR

8. --
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To study variations in the virulence of viruses with special reference to "virulent-temperate" conversions of human viruses.

Methods Employed:

A. Continuing attempts are being made to establish a "lysogenic type" infection of human virus in an established line of cells in culture. This is being done by 1. establishing conditions selecting for cell variants capable of propagating provirus, 2. changing conditions to select for temperate viruses, and 3. treating virus-cell complexes with mutagenic agents in an attempt to destroy the virulent component leaving a temperate component.

B. Animals are inoculated with viruses which produce clinical latent infections in man e.g. Herpes simplex. Survivors of such inoculations are studied to determine their capacity to maintain a latent infection of the lysogenic type, i.e. contain provirus.

C. The kinetics of serological neutralization of viruses are being studied in order to develop means for differentiating serologically related viruses, e.g. strains of type I Poliovirus. (Poliovirus I is being used as the prototype for these experiments pending greater availability of assay materials for Herpes simplex). Attempts will be made to correlate virulence with antigenicity as determined by inactivation constants with different sera.

D. In cooperation with Dr. C. P. Li, Division of Biologic Standards, studies are being conducted on host-induced modifications of animal viruses. Variations in virulence for different cell types are being studied by propagation of the virus in single cells in microdrops.

Major Findings:

1. HeLa cells previously infected with poliovirus (which were carried in this laboratory on two different occasions) have been shown to be carrier strains and not latently infected. This virus-cell system has been deleted from our work.
2. Strains of HeLa and human skin #1769, carrying Herpes simplex have been established. Attempts are being made now to determine the nature of the virus in this system.
3. The neutralization indices of a large number of type I poliovirus strains have been established. Although the work is not complete, it seems most probable that the various strains of Poliovirus I, e.g. Mahoney, Parker, Brunhilde, etc. can be differentiated from one another by this test.

Significance to Dental Research:

There are numerous lesions which occur on the mucous membranes of the oral cavity for which the etiology is unknown. The clinical course of many of these parallels those caused by Herpes simplex. Numerous attempts to find the cause of the lesions by conventional procedures have failed. It is felt that elucidation of the basic host cell-virus relationship necessary for the maintenance of latent herpetic lesions will accomplish 1. the establishment of that information

necessary to allow a rational study of chemotherapy of herpetic infections, 2. the development of technics which can be used to study the etiology of the aforementioned lesions, and 3. further elucidation on the overall mechanisms involved in latent infections which are currently of great interest to cancer research.

There is at present no adequate means of classifying strains of Herpes simplex. It is anticipated that the serological technics under investigation will accomplish this end. As mentioned above, Poliovirus I is being used as the prototype for these studies due to the greater availability of assay technics. Positive results in this study would have important consequences: 1. One could identify a virus isolated from an individual as being identical or different from that used to vaccinate the individuals and, thus, either incriminate or absolve the vaccine of responsibility for the infection. 2. It is probable that the procedure will offer a rapid and inexpensive way to screen viruses for degree of antigenicity and hence for vaccine production.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 14

SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
22,091	3,613	25,704	1	3	4
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	3	4	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

Form No. ORP-1
October 1956

- 5 -

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PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR - 14
SERIAL NUMBER

16. & 17. - None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORTS

Part A. Project Description Sheet

1. NIDR-15

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Studies on the Ecology of the Oral Microflora
PROJECT TITLE

7. Mr. Morrison Rogosa
PRINCIPAL INVESTIGATOR

8. Dr. T. Shiota*
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

(1) To determine the biological distribution of the total oral flora in health and disease, particularly the strongly acidogenic and acid-consuming microorganisms, and (2) to assess the role of the oral microflora in relation to such oral diseases as dental caries and periodontal lesions. This assessment depends largely on a proper understanding of the physiology of these bacteria under various conditions. The following major problems are under study:

* Research Associate, American Dental Association, at the National Institute of Dental Research.

- (a) Taxonomic studies which include quantitative biochemical studies on the formation of end-products during the biochemical attack on available substrates.
- (b) Study of the changes in the oral flora of the hamster and rat which occur with the development of caries.
- (c) Study on the utilization of lactic and the organic acids in the oral environment.

Methods Employed:

Animal experimentation using cariogenic and non-cariogenic diets; sampling and culturing of oral samples on selective media developed for this project; pure culture studies using biochemical and other analytical methods; use of nutritional test media to determine nutritional requirements of microorganisms; use of Warburg technique, etc.

Major Findings:

- (1) The diphtheroid-like organisms were discovered to be a numerous group in the oral cavity of the rat and also man. Early methods for their selective cultivation have been improved and work is continuing to develop more highly specific media. Extensive cultural and biochemical studies of the diphtheroids from the rat revealed that there are 8 major groups. Studies have been initiated to characterize the human strains including some strains isolated from blood in bacteremia.
- (2) The Veillonella medium is now employed successfully routinely. See below for publication.
- (3) Further and confirmatory cultural and biochemical studies of 500 oral strains from the rat comprising chiefly streptococci, diphtheroids, Veillonella, bacteroides, and micrococci were completed. Their general ecological distribution and relation to dental caries was determined. These data are being prepared for publication.
- (4) A study of the Bacteroides was undertaken. Nutritional, cultural and biochemical data have been accumulated showing the diverse nature and biochemical activities of the group. Studies are continuing to assess their importance in hamsters and rats.

Significance to Dental Research:

It is now generally agreed that microorganisms are involved in the development of dental caries. How they are concerned is the problem. The formation of acid seems necessary for the initiation of dental decay. However, information on the dissipation of acids is almost completely lacking. Since it is highly likely that there is an active competition between the production and consumption of organic acids by different groups of organisms, it is obvious that a beginning must be made in the study of the utilization of organic acids by the oral flora.

Proposed Course of Project:

During the coming year work is to be continued to gain a knowledge of the nutrition and biochemistry of the Veillonella. A study of the bacteroides has been initiated, a study of the nutrition and general physiology of the diphtheroids has been initiated also.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIDR-15
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
26,696	4,573	31,269	1 2/3	3	4 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
2	5	7	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

American Dental Association

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR-15
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Rogosa, Morrison. A Selective medium for the isolation
and enumeration of the Veillonella from the oral
cavity. J. Bact., 72:533-536, 1956.

Rogosa, Morrison, Johansen, E. J., and Disraeli, M.
The relation of streptococci, lactobacilli and the
general oral and fecal flora to the progression of
dental caries in the hamster. J. Dental Res. - in press

Johansen, E. J., and Rogosa, Morrison. The pH of saliva,
soft tissues, and sound and carious tooth surfaces in
the hamster. J. Dental Res., - in press

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

Elected Counsellor to the Society of American Bacteriologists
for the year 1956-1957.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- Part A. Project Description Sheet
1. NIDR-16
SERIAL NUMBER
2. Dental Research
INSTITUTE OR DIVISION
3. Oral Bacteriology
LABORATORY, BRANCH, OR DEPARTMENT
4. --
SECTION OR SERVICE
5. --
LOCATION (IF OTHER THAN BETHESDA)
6. Microbial enzymes as factors in periodontal disease
PROJECT TITLE
7. Dr. Robert R. Cmata
PRINCIPAL INVESTIGATOR
8. --
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:
- None
10. PROJECT DESCRIPTION:

Objectives:

To investigate the role of microbial products, specifically enzymes of a proteolytic nature, as factors in periodontal disease.

Methods Employed:

In its current phase this project is concerned with the isolation of various types of microorganisms from periodontal disease pockets and gingival crevices and testing for their ability to produce enzymes capable of degrading certain protein substrates. Special attention is directed to the study of organisms which can produce collagenase, since this enzyme could presumably break down the collagen-containing

tissues which support the teeth in the jaw. Studies are also being conducted on the isolation and purification of collagenase of microbial origin in an effort to determine how this enzyme attacks the collagen molecule.

Major Findings:

Findings to date indicate that there are no readily available pure substrates which can satisfactorily replace collagen in culture media designed for the isolation of collagenase-producing microorganisms. In addition, collagens prepared from various natural sources such as the rat tail or calf Achilles tendon show variations in response to attack by microbial enzymes.

Significance to Dental Research:

In the past it has been impossible to implicate any single type of microorganism as a specific etiological factor in periodontal disease. The present study is based on the concept that possibly a number of different types of bacteria may play a contributing role due to the production of a common enzyme such as collagenase. Should this approach be fruitful, it will provide a major advance in the understanding and treatment of periodontal diseases.

Proposed Course of Project:

In addition to continuation of the basic studies outlined above, it is planned to conduct some epidemiological studies using a selected group of local school children in which the incidence of periodontal disease is unusually high in an effort to see if they also harbor in their oral cavity a correspondingly increased proportion of collagenase-producing microorganisms. Studies are continuing on the problem of obtaining suitable substrates.

In addition, studies on the role of the fusiform bacteria in the oral cavity will be continued. This project was reported on last year and certain aspects of the distribution and physiology of this group of oral microorganisms will be the subjects of further study.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR-16
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
12,594	3,613	16,207	1	1	2
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	1	2	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR-16
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Omata, Robert R., and Disraely, Murray. A selective
medium for oral fusobacteria. J. of Bact. 72:677-680,
Nov. 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- Part A. Project Description Sheet
1. NIDR-17
SERIAL NUMBER
2. Dental Research 3. Oral Bacteriology
INSTITUTE OR DIVISION LABORATORY, BRANCH, OR DEPARTMENT
4. -- 5. --
SECTION OR SERVICE LOCATION (IF OTHER THAN BETHESDA)
6. Studies on the bacterial and chemical changes in incubated salivas.
PROJECT TITLE
7. Dr. T. Shiota*
PRINCIPAL INVESTIGATOR
8. --
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:
- None
10. PROJECT DESCRIPTION:

Objectives:

The objectives of this project are: (1) to study the bacterial and chemical changes in incubated salivas (whole and pure salivary secretions), and (2) to study the effects of changing the incubating conditions on the above.

Methods Employed:

To follow the bacterial changes, a variety of selective bacterial and culture media were used. They were the SL Agar for lactobactilli, CVI for streptococci, and FM agar for

* Research Associate, American Dental Association, at the National Institute of Dental Research.

fusiforms. Other media - to be used in subsequent experiments are: V₁₂ for Veillonella and a medium for diphtheroids. The development of the latter medium is now in progress and is described in a similar report by H. Rogosa. To follow the chemical changes, the analytical procedures developed for carbohydrate, protein, nitrogen, ammonia, indole and hyaluronic acid determinations were used.

Major Findings:

Test on native salivas incubated for 30 hours in screw-cap bottles at 37 degrees C, showed that the lactobacillus population decreased, the fusiform counts increased. In some samples, the streptococcal population generally decreased. During this period, ammonia and indole were formed with a rise in pH. Hyaluronic acid showed a decrease.

Significance to Dental Research:

The growth of certain fastidious microorganisms in saliva is indicative of the presence of unidentified growth promoting substances in saliva. Thus far, fusiforms were shown to increase about 10 fold in their number under the conditions described above. The chemical changes which occurred may have been brought about by the fusiforms, or by other microorganisms which are metabolic active, or both.

Proposed Course of Project:

Similar studies as outlined above, using pure salivary secretions, are to be carried out in the near future. Furthermore the effects of pH, aerobic and anaerobic conditions and altering the carbon nitrogen ratio of saliva on the bacterial and chemical changes in saliva, are to be studied. The biochemical changes brought about by enzymes in saliva and/or bacteria, are of great interest and such investigations at the chemical level are contemplated. One such reaction, is the study on the degradation of mucoprotein.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget data

11. NIDR-17
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
5,066	3,131	8,197	2/3	1	1 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
--	1	1	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S).

American Dental Association

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PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR-17
SERIAL NUMBER

16. & 17. - None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- Part A. Project Description Sheet
1. NIDR-18
SERIAL NUMBER
2. Dental Research
INSTITUTE OR DIVISION
3. Oral Bacteriology
LABORATORY, BRANCH OR DEPARTMENT
4. --
SECTION OR SERVICE
5. --
LOCATION (IF OTHER THAN BETHESDA)
6. Antibiotics and Dental Caries
PROJECT TITLE
7. Dr. Robert J. Fitzgerald
PRINCIPAL INVESTIGATOR
8. --
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

Part of work in conjunction with Dr. Frank Law, Dental Director, Region III, U. S. Public Health Service.

10. PROJECT DESCRIPTION:

Objectives:

This is a continuation study, the broad objectives of which are to study the actual and potential uses of antibiotic and chemotherapeutic agents in the control and treatment of oral diseases and conditions.

Methods Employed:

At the present stage the project is mainly concerned with the problem of dental caries although in the course of the studies on caries several observations have been made suggesting applications to studies on periodontal disease and calculus

deposition. The caries problem has been approached by the following methods:

1. In vivo studies testing the effects of antibiotics on the development of caries in rats.
2. In vitro studies on the effects of antibiotics on representative strains of oral microorganisms.
3. Testing of antibiotic-containing mouthwashes and troches in humans for potential usefulness as agents for caries prevention on a large scale.

Major Findings:

Most of the antibiotics in common use will inhibit caries development in the rat when mixed in the diet at concentrations between 10 and 100 micrograms per gram. A comparison of the in vivo anti-caries effects of these agents with their in vitro antibacterial spectrums suggests that the anti-caries effects may be primarily due to suppression of the gram-positive oral microflora of the rat which includes organisms in the lactobacillus, streptococcus and diphtheroid groups.

In collaboration with Dr. Frank Law, of P.H.S. Region III, a bacitracin-containing mouthwash was tested in school children. Under the conditions employed, no significant effect on caries or the oral microflora were noted. The results indicated that there was insufficient contact between the drug and the oral microflora, when it is used in the form of a mouthwash. On the other hand, carefully supervised studies with some selected rampant caries cases in the Clinical Center Dental Clinic, have shown reductions in the acidogenic oral bacteria and decreased caries activity on clinical examination with the use of a bacitracin-containing mouthwash.

Significance to Dental Research:

The antibiotic studies described have revealed several drugs which might be of potential usefulness for the control of caries in humans if means can be devised to assure adequate contact of effective concentrations with the bacteria on tooth surfaces. The combination of in vivo and in vitro tests on the oral microbial population of the rat, has made it possible to select certain promising groups of microorganisms for future testing in Germ-free animals where single strains of bacteria will be tested for the ability to

produce caries.

Proposed Course of Project:

It is expected that the present studies will be continued along established lines and will be expanded to include more complete coverage of individual types of oral micro-organisms as better methods for their study become available. Promising new antibiotics will be tested as they become available with special emphasis on agents which may not be expected to have widespread clinical use in other fields of medicine since the use of these drugs as anti-caries agents will by-pass some of the problems of developing drug-resistance or sensitivity reactions to antibiotics used in treating other diseases. Since bacitracin is one of the most effective anti-caries agents in animals, attempts will be continued to develop suitable methods to exploit its potential anti-caries effects in humans.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR-18

SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF.	OTHER	TOTAL
16,050	3,613	19,663	1	1 2/3	2 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
2	4	6	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-19
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Investigation of spirochetel organisms present in non-exposed, non-vital pulps of human teeth.
PROJECT TITLE

7. Dr. Edward G. Hampp*
PRINCIPAL INVESTIGATOR

8. --
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

(1) To determine the mode of entrance of the oral treponemes into the non-vital pulp of teeth and ascertain their role in the initiation and progress of such infections.

(2) To study these organisms both biochemically and serologically and compare them with stock cultures of other oral

* Senior Research Associate, American Dental Association, at the National Institute of Dental Research.

treponemes.

(3) To study the spread of spirochetes, dental granulomas and periapical tissues obtained from non-exposed infected teeth.

Methods Employed:

Material employed for cultivation of the oral spirochetes is obtained aseptically from non-exposed, non-vital pulps. Isolating the tooth by rubber dams and using sterile procedures, the pulp is exposed and samples are removed for cultural study employing the well-plate method developed in this laboratory for the isolation and cultivation of the oral spirochetes. Thus far, 67 patients have been used in the culture studies with a total of 69 teeth being examined. In addition, 7 granulomas have been obtained from 7 patients for histologic studies.

Major Findings:

Of the 69 samples obtained from 67 patients, spirochetes have been successfully isolated in 9 instances. In 4 samples spirochetes were present in the cultures but were not isolated and cultivated and these cultures are being retained for further study. In 8 cases, spirochetes were found in small numbers in the inocula by microscopic examination, but failed to grow. In 5 cases, cultures were negative for any types of organisms. The remaining cases were found to be devoid of spirochetes both by microscopic and cultural studies. The organisms thus far obtained in this study are morphologically similar to our pure strains of small oral treponemes. They vary to some degree in certain cultural characteristics, and two of the strains are active gas producers which heretofore has not been encountered in spirochetes obtained from the oral cavity. Attempts have been unsuccessful in developing a sugar free medium to further study these organisms. Preliminary study of the growth of these organisms in a "synthetic" medium seems promising.

Attempts have been made to obtain granulomas and/or periapical tissues from patients with non-exposed, non-vital teeth, however, patients with such conditions have not been available for study. However, in granulomas obtained from 7 patients with carious teeth no spirochetes have been observed thus far. This work is still under investigation.

Significance to Dental Research:

These investigations may contribute to our fundamental

knowledge concerning the classification, metabolism, pathogenicity and ecology of spirochetel organisms present in non-exposed, non-vital pulps of human teeth.

Proposed Course of Project:

To determine the mode of entrance of these microorganisms into non-exposed dental pulps and determine whether or not they are pathogenic. It is further proposed to study their metabolism and to classify and compare these organisms with other pure strains of oral spirochetes. In addition, attempts will be made to procure additional granulomas as well as periapical tissues from both exposed and non-exposed, non-vital teeth for further study for the presence of spirochetes.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIDR-19
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MEN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
2,818	2,651	5,469	1/3	2/3	1
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
-	2	2	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

The American Dental Association in cooperation with the National Institute of Dental Research, is sponsoring this project. Salary and travel are paid by the A.D.A. for the Senior Research Associate. In addition, this study is being done in cooperation with the Naval Dental School, National Naval Medical Center, Bethesda, Maryland.

The material for histologic study is being obtained from Dr. Driscoll of the NIDR Branch, Clinical Investigations.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C. Honors, Awards & Publications

15. NIDR-19
SERIAL NUMBER

16 & 17 - None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-20
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH, OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Ulcerative Gingivo-Stomatitis: The significance of the oral
spirochetal flora in the etiology of certain ulcerative lesions
of the oral cavity.
PROJECT TITLE

7. Dr. Edward G. Hampp*
PRINCIPAL INVESTIGATOR

8. --
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

(1) To develop routine methods for the isolation and pure cultivation of oral spirochetes.

(2) To develop methods for sound classification and identification of this little understood group of oral bacteria.

(3) To determine whether or not they are responsible for certain ulcerative lesions of the oral cavity.

* Senior Research Associate, American Dental Association, at the National Institute of Dental Research

It is further expected that these findings may be of use in our attempts to cultivate the virulent Treponema pallidum.

Methods Employed:

Although all the known morphologic types of oral spirochetes have been isolated and grown in pure cultures, further study of the biochemical and serologic methods for classification have been hampered by the lack of a chemically defined medium for investigating their metabolic requirements. This is further complicated by the definite requirement of these organisms for ascitic fluid which is a complex material of uncertain composition. Many of the experiments contemplated for determining the etiology of these organisms to oral lesions are dependent on obtaining an ascitic fluid-free medium.

Major Findings:

During this period a moderate amount of success has been made toward the solution of the problem of obtaining a chemically defined medium. Many attempts have been made to grow our pure cultures in known chemically defined media without success. More recently, the "synthetic" medium described by Eagle and co-workers for the growth of the Reiter treponeme was employed in these studies. It consists of a mixture of amino acids, vitamins, purines, pyrimidines, salt mixture and crystalline bovine serum albumin. It was found that this medium as constituted would not support the growth of oral treponemes or borrelias either under anaerobic conditions or in rubber stoppered 15 x 125 mm test tubes filled within 1.5 ml of capacity. However, it was found that the oral treponemes would grow very well under either condition in the basic medium modified by deleting ascorbic acid and serum albumin and the addition of 0.1% glutathione and 10% ascitic fluid. Borrelia vincentii and Borrelia buccale did not survive beyond 48 hours and did not exhibit visible growth. Since the above medium containing ascitic fluid is not a chemically defined medium as constituted, investigations are in progress on the fractionation of ascitic fluid to identify the factor (s) required by the treponemes. Studies are in progress to determine what additional factors are needed in the medium for the growth of the borrelias.

Although a large amount of time has been devoted to the development of a routine method for the isolation of the B. buccale, this work has not been completely successful. However, the stock strains isolated thus far can be carried

successfully in pure culture. It will be essential to work out their metabolic requirements before routine isolation procedures can be developed. Some success has been encountered during this period in preserving viability of these organisms by freeze-drying methods. This problem is of extreme importance since stock strains of B. buccale will not survive in our basic medium for more than four days.

Significance to Dental Research:

These investigations will contribute to our knowledge concerning the spirochetes peculiar to man and animals. Further, any information gained from these studies may be applicable to the isolation and pure cultivation of known pathogenic strains of spirochetes such as T. pallidum. Investigations are in progress on this problem. From the dental research aspect, these investigations will contribute toward the fundamental knowledge of the oral flora of man and its relationship to oral disease.

Proposed Course of Project:

A considerable portion of the time during the next year will be devoted to the elucidation of the factor (s) present in ascitic fluid essential for the growth of the oral spirochetes. As soon as the fractionation of ascitic fluid has been accomplished, studies will be conducted on the "synthetic" medium to determine what substances in the medium are essential for the growth of these organisms and thereby work out their metabolic requirements. Further, when the foregoing phase of the problem is accomplished, investigations will be turned to the classification, pathogenicity and ecology of the oral spirochetes. In addition, any findings of significance on the metabolism of these organisms will be used in an attempt to isolate and cultivate T. pallidum.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIDR-20
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			M.N. YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
3,842	2,411	6,253	2/3	2/3	1 1/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
--	1	1	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

The American Dental Association in cooperation with the National Institute of Dental Research is sponsoring this project. The Association provides salary and travel for the Senior Research Associate.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C. Honors, Awards & Publications

15. NIDR-20
SERIAL NUMBER

16 & 17 - None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-21

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Nutritional Studies on Selected Lactobacilli from the White Rat.
PROJECT TITLE

7. Dr. Harold V. Jordan
PRINCIPAL INVESTIGATOR

8. --
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

The objective of these studies is to gain a better understanding of the nutrition of certain types of lactobacilli which are found in the white rat. Of particular interest are the types which do not grow well on ordinary culture media. There is evidence to believe that these types may constitute an appreciable segment of the lactic acid flora. The immediate aim of nutritional studies is to devise better methods of sampling and culture of these apparently unique organisms.

Methods Employed:

It has been demonstrated that certain unknown types of rat

lactobacilli can be isolated on Orange Serum Agar. These strains will not grow on Rogosa's SL medium, which is the medium of choice for lactobacillus sampling from the oral cavity. In addition, numerous pin point colonies observed on this latter medium cannot be subcultured. Conventional assay methods have been employed to investigate some of the nutritional peculiarities of these lactobacilli. Emphasis has been on the use of chemically defined media whenever possible. A rat strain of Lactobacillus acidophilus was considered to be representative of many of the fastidious lactobacilli. This strain was isolated from the oral cavity of a white rat and identified as to species in this laboratory.

Major Findings:

A selected strain of the lactobacilli isolated from Orange Serum Agar was found to be greatly stimulated by putrescine. In addition, ascorbic acid appears to stimulate the growth of this organism. These compounds are not normally added to media used in the routine isolation of lactobacilli.

Studies have continued on the amino-acid metabolism of the fastidious lactobacilli from rats mentioned in last year's report (NIDR 19). High concentrations of the dicarboxylic amino acids, glutamic and aspartic acids, and of the basic amino acid, arginine, have been shown to exert a beneficial effect on the growth of these organisms. Attention is now centered on peptides of these amino acids. Results of testing a very limited number of peptides showed that alpha glutamyl-peptides may be more stimulating than gamma glutamyl-peptides. Both types were more stimulating than the constituent free amino acids. Testing of a single aspartic acid peptide showed it to be more active than the free constituent amino acids.

Partial hydrolysates of protamine which are assumed to contain high concentrations of arginine peptides were shown to be more stimulating than free arginine for the growth of a fastidious lactobacillus.

Significance to Dental Research:

Immediate significance lies in the development of better methods of cultures for those lactobacilli which grow very poorly on available laboratory media and about which very little is known. Ultimately there may be a greater significance in the correlation of nutritional and metabolic data of the oral flora, with various steps in the chain of events which culminate in dental caries or other oral conditions.

Proposed Course of Project:

Research will continue on the nutrition and metabolism of the fastidious lactobacilli with emphasis on the dicarboxylic amino acids and arginine and their peptides.

Demonstration of the putrescine-stimulated lactobacilli raises the possibility of even more groups of lactobacilli in the oral cavity of man and animal which are as yet undiscovered because of inadequate sampling methods.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIDR-21
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
13,409	3,613	17,022	1	1	2
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	1	2	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C. Honors, Awards & Publications

15. NIDR-21

SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Jordan, Harold V., Fitzgerald, R. J., and Faber, J. E., Jr.
Studies on the Aciduric Oral Micrococci. J. Dent. Res.
35:404-412, (June, 1956).

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-22

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. Interrelationships between local and systemic factors in the etiology of dental diseases in rats.

PROJECT TITLE

7. Dr. Robert M. Stephan
PRINCIPAL INVESTIGATOR

8. ---
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

(1) To determine more adequately the essential experimental conditions responsible for the development of dental caries and periodontal disease in laboratory rats:

(2) To study the formation of bacterial plaques, localized food retention, and pH on tooth surfaces in relation to the formation of carious lesions: and

(3) To study the relationship of factors which affect tooth formation to caries susceptibility in the incisor teeth, using vital stains to indicate periods of tooth formation and direct microscopic examinations to observe subsequent

caries development.

Methods Employed:

On the basis of previous multifactorial experiments on this project, strains of rats and diets have been employed which produce unusually extensive caries in both the molar and incisor teeth, and which also induce considerable periodontal disease within experimental periods of 42 to 56 days. These diets are of the nutritionally defined type with casein, salts, sucrose, and known vitamins, and therefore the relation of dental conditions to the nutritional adequacy of the diet and the effect of nutritional supplements can be readily determined.

Nutritional supplements have been given to determine systemic effects and relationship of growth to caries and periodontal disease. Bacterial plaque development has been studied microscopically on the incisor teeth, and direct pH measurements have been made with the antimony and micro-glass electrode and with pH indicators. Glucose, sucrose, fluorides and other chemical substances have been added to the drinking water in order to determine the effects on caries. Vital stains have been added to the drinking water to serve as an indicator of the early stages of caries. Vital stains have also been injected intraperitoneally to mark tooth substance formation in incisors so that any changes in caries susceptibility and resistance resulting from the simultaneous administration of other substances which may invisibly affect tooth formation, can be determined after eruption of the teeth.

Major Findings:

The addition of sucrose and glucose to the drinking water markedly increased the development of caries. The increase was greater in the incisor teeth than in molars, and was in proportion to the level of sugar added. Bacterial plaque formation on the incisor teeth also increased greatly with the addition of glucose and sucrose to the drinking water. The reduction of the protein (casein) content of the diet from 12% to 8% increased the development of caries. The increase of the protein content to 16% decreased the development of caries. In general, the most severe caries and periodontal disease developed in animals which gained the least weight.

The vital stains alizarin Red S and sodium carminate were

found to be superior to alizarin for vital staining of teeth and as indicators for the early detection of carious lesions.

Incisor caries can be induced in both the Hunt "caries resistant" and "caries susceptible" strains of rats.

Significance to Dental Research:

The development of improved methods for inducing extensive caries in the molar and incisor teeth of rats using nutritionally defined type of diets, furnishes a promising experimental basis for demonstrating the interrelationship of systemic and local factors in the etiology of caries. The use of vital stains has furnished means for the early detection of caries and also for the marking of tooth substance during formation so that its relative susceptibility to carious attack can be later determined. The development of periodontal disease within an experimental period of 56 days in rats fed these diets has furnished a useful experimental basis for the study of this disease in rats.

Proposed Course of Project:

Experiments on this and other projects have indicated that many dietary and nutritional factors which affect growth and the general systemic condition may also affect the development of caries and periodontal disease in rats. It is planned to direct experiments toward finding out how some of these systemic factors affect the localized conditions on tooth surfaces where lesions develop. Special attention will be directed to the continuously forming incisor teeth because of the possibility of demonstrating the effect of tooth formative factors in them, and also because of their greater accessibility for in vivo tests than the molar teeth. These tests will include direct microscopic observations of tooth surfaces for the development of carious lesions, direct pH measurements on tooth surfaces and the use of indicators and vital stains, and the selective removal of plaque material for bacteriological studies.

It is also planned to study factors of aging as well as certain other nutritional differences as they might relate to dental disease.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIH-22
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
14,799	3,131	17,930	2/3	1	1 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	1	2	--		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR-23

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Oral Bacteriology
LABORATORY, BRANCH OR DEPARTMENT

4. --
SECTION OR SERVICE

5. --
LOCATION (IF OTHER THAN BETHESDA)

6. The use of Germ-free animals in the study of problems relating to oral diseases and conditions.
PROJECT TITLE

7. Dr. Robert J. Fitzgerald
PRINCIPAL INVESTIGATOR

8. --
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

It is proposed by the use of germ-free rats to attempt to identify the etiological agents of oral conditions such as caries, periodontal disease and calculus depositions by introducing suspected microorganisms into the oral cavity of rats maintained in the complete absence of all other microbes.

Methods Employed:

The present stages of the work are all preliminary to the actual studies on the germ-free animals with the main effort

directed toward testing the effects of sterilization on the diet customarily used in our rat caries experiments (Coarse particle diet #585).

Major Findings:

It was found that when non-germ free rats are fed diet #585 which has been sterilized by autoclaving for 30 minutes at 120 degrees C. they fail to gain weight at the rate shown by rats provided the unautoclaved diet. Although the rats are much smaller in size, they seem to be healthy and normal in other respects. Caries development is at least as extensive and usually more extensive than that found in animals fed the unautoclaved diet. Addition of vitamins to the autoclaved diet in the form of yeast extract, 1%, results in only slightly better growth. Supplementation of the diet with 1% L-lysine has no effect on growth.

Significance to Dental Research:

It would be premature to assess the significance of these results at this stage of the work because it is impossible to say whether the same findings would result when the autoclaved diet is fed to germ-free rats. However, since it appears most likely that diets for the germ-free animals will be sterilized by autoclaving, the results have provided a basis for planning diets suitable for use under germ free conditions.

Future Course of Project:

Since the only possible way to continue these studies adequately is to do so in germ-free animals, the conduct of future studies will depend on the availability of germ-free animals and the equipment to house them.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B. Budget Data

11. NIDR-23
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			M/N YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
4,971	2,651	7,622	1/3	1/3	2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	1	2	--		

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Facilities of NIH Germ-free unit to be employed when available. Proposed future collaboration with Dr. Bengt Gustafsson, Professor of Germ-free research, University of Lund, Sweden.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C. Honors, Awards & Publications

15. NIDR-23

SERIAL NUMBER

16 & 17 - None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 24
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Diagnostic Surgical Pathology Utilizing Histochemical Techniques.
PROJECT TITLE

7. Marvin S. Burstone
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

The object of this project is to apply existing and newly developed histochemical techniques to the study of freshly removed human surgical specimens, with an emphasis upon cancers. This type of study reveals tissue changes which are not visible with routine stains and may contribute to the elucidation of the pathogenesis of neoplasia.

Methods Employed:

For the last two years a systematic histochemical study has been made in this laboratory of practically every human neoplasm removed in the Clinical Center. To date specimens from over 180 surgical cases have been processed for study. This includes patients scheduled for general and dental surgery and also selected cases to be admitted to the Clinical Center specifically for this study. Normal tissues such as salivary glands have also been studied.

Major Findings:

1. The histochemical finding of proteolytic activity in the connective-tissue stroma adjacent to human neoplasms. The precise localization of the enzyme adjacent to rapidly growing tumors represents one of the first histochemical staining methods to characterize human neoplasms. It has also been found, in vitro, that low concentrations of certain metallic ions will inhibit this proteolytic activity. This finding suggests a new approach to the chemotherapy of tumors; namely, the use of agents which may retard the breakdown of connective tissue adjacent to a growing tumor.
2. The development of a freeze-dry system for the simultaneous processing of a large number of surgical specimens.
3. New findings relating to the enzyme characteristics of normal human salivary glands. These include esterase activity of ducts and demilune cells.

Significance to Dental Research:

The application of histochemical techniques to investigations of neoplastic tissues will provide considerable new information about the pathological alterations and processes involved, which until recently were only studied on a morphologic basis.

Proposed Course of Project:

It would be desirable to expand this program at the professional level so as to increase the scope of the histochemical approach, and to utilize more fully special procedures for diagnosis.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 24
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
12,235	3,131	15,366	2/3	2/3	1 1/3
FY '57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	1	2			
FY '57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 24
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

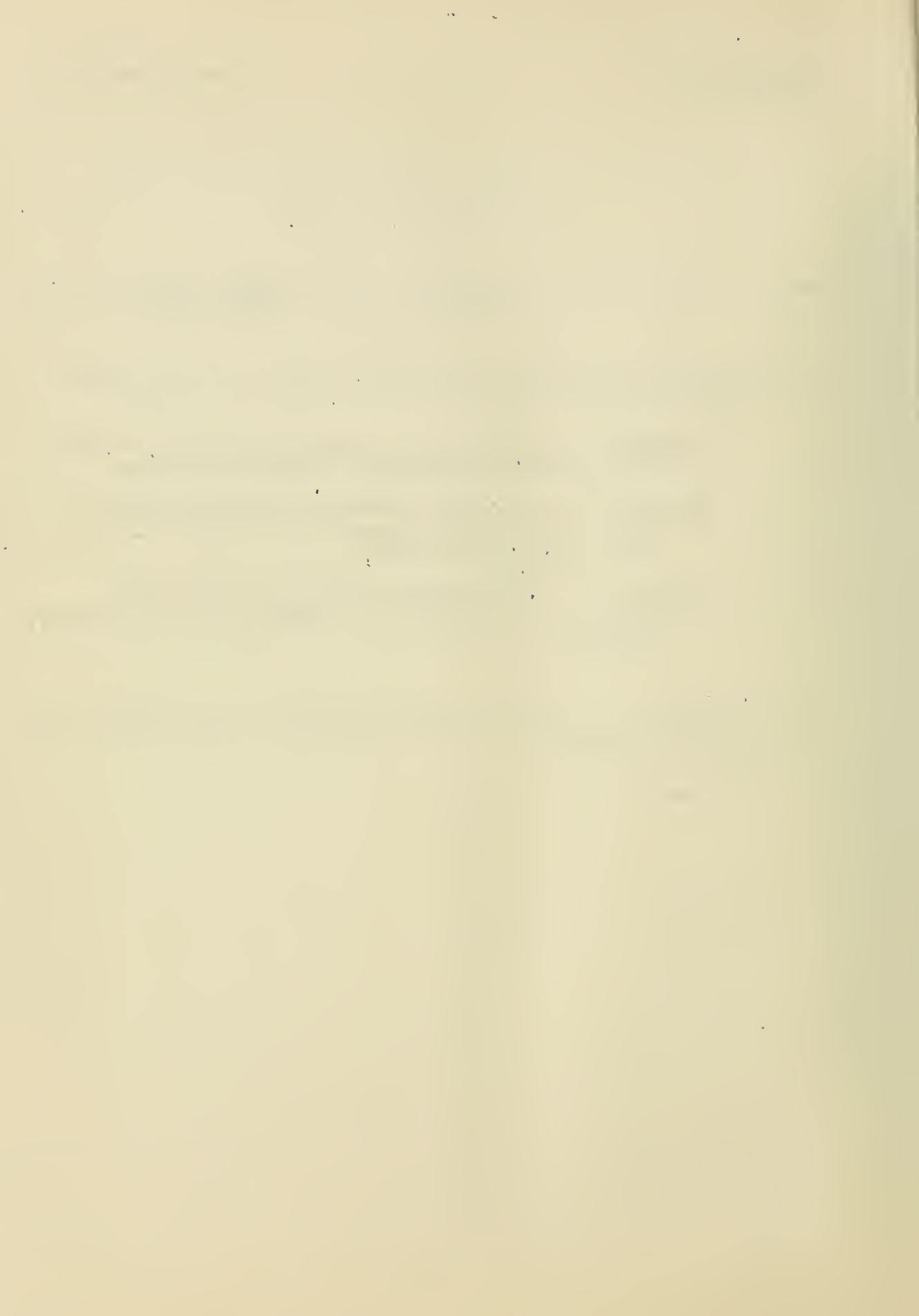
Burstone, M. S. Histochemical Demonstration of Proteolytic
Activity in Human Neoplasms. 16:1149-1154, 1956.

Burstone, M. S. A Method of Freezing and Drying and Its
Application to Histochemistry and Pathology. J. Nat.
Cancer Inst., 17:49-56, 1956.

Burstone, M. S. Application of Histochemistry to Oral
Pathology, Oral Surgery, Oral Medicine and Oral Pathology,
In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None



PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 25
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Studies of the Structural, Physical, and Chemical Properties of
Calcified Tissues by Electron Microscopy, Electron Diffraction and
X-ray Microscopy.
PROJECT TITLE

7. David B. Scott
PRINCIPAL INVESTIGATOR

8. Marie U. Nylén
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

- a. Determination of the crystal structure of calcified tissues by electron microscopy and electron diffraction;
- b. investigation of the reaction of various chemical agents, such as fluoride compounds, on tooth surfaces, with emphasis on effects on acid-solubility of enamel;
- c. development of techniques for the application of contact and projection X-ray microscopes in studies of hard and soft tissues.

Methods Employed:

For electron microscopy shadowed positive carbon replicas and pseudoreplicas are made of the surfaces of samples of fully calcified enamel and dentin. In studies of normal crystal structure the specimens are ground sections of mature teeth; in trials of the effects of chemical agents the specimens are outer enamel surfaces of teeth, some of which are treated with the test compound and subjected to an experimental etching, and some of which are etched only, serving as controls. For electron diffraction, carbon pseudoreplicas of enamel, which contain actual layers of superficial crystallites, are examined by transmission, and specially prepared enamel surfaces are themselves examined by reflection. For X-ray microscopy, gross specimens and sections are photographed both by contact and by projection methods.

Major Findings:

Evidence has been accumulated by electron microscopy and diffraction which indicates clearly the general sizes, shapes and orientation of the crystallites within and between the prisms in normal mature enamel. These investigations are now being extended to the examination of various morphological types of prisms and to various geometrical configurations of prisms in different parts of the enamel.

Studies of the effects of fluorides on the acid-solubility of the enamel surface have indicated that a much greater protection is afforded by the stannous than by the sodium compound. Numerous experiments, aimed at ascertaining the mechanism of the protective reaction, have been carried out, the most interesting being those in which it was found that stannous compounds not containing fluoride also reduce enamel solubility very effectively. These results have led to the recent initiation of investigations of the reaction of tin itself with enamel.

Several new techniques for specimen preparation have been developed for use in X-ray microscopy, which is a new field of instrumentation. These procedures are making it possible to begin investigations of the distribution and character of the mineral component in mature teeth and bones, and as it is progressively laid down during development. Explorations to date have indicated that X-ray microscopy will prove a most useful complementary method in basic studies of the calcified tissues.

Significance to Dental Research:

The present type of studies is essential to a complete understanding and definition of the fundamental structure of the mineralized tissues. All of the crystallites which constitute the major portion of these tissues are submicroscopic in dimension and can only be studied visually by electron microscopy. Direct crystallographic evidence can also be best provided by X-ray or electron diffraction.

The work with fluoride compounds provides both basic data on the properties of the enamel, and information which bears on the mechanism and possible effectiveness of compounds proposed or in actual clinical use as caries-inhibiting agents.

The recently developed X-ray microscopes are of considerable potential in studies of hard tissues, and it is important to explore their applicability in the problems under investigation. The techniques being developed will also be of general use to other workers in the field.

Proposed Course of Project:

Continuation of all aspects of these studies, and further extension into investigations of dentin and bone about which even less is known than enamel.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 25
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
22,746	3,613	26,359	1	1 1/3	2 1/3
FY 1957					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	3	4			
FY 1957					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 26
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Studies of the Ultra Structure of Mature and Developing Calcified
Dental Tissues by Electron Microscopy of Thin Sections.
PROJECT TITLE

7. Marie U. Nylen
PRINCIPAL INVESTIGATOR

8. David B. Scott
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

- a. Development of a new technique for thin sectioning of soft tissues for electron microscopy; b. study of the cytological morphology of the enamel- and the dentin-forming cells before, during and after development of the hard tissues; c. investigations into the origin and ultra-fine structure of the organic components of developing and mature dentin and enamel.

Methods Employed:

Specimens are fixed, dehydrated and embedded by special methods. Thin sections are cut on a modified Spencer microtome and studied in the electron microscope.

Major Findings:

- a. Technical developments: Several commercially available microtomes for thin sectioning have been tested. Since the results obtained with these instruments, both qualitatively and quantitatively, have not been satisfactory, a new method has been developed. A standard Spencer microtome No. 820 has been modified in such a way that continuous ribbons of ultra-thin sections (Ca 250A⁰) may be cut routinely. This modified Spencer microtome has proven itself superior in all respects to any other microtome designed for thin sectioning which has been tested in this laboratory. In addition, special new techniques or modifications in procedure have been developed for fixation of tissue, preparation of embedding plastics, cutting and inspection of glass knives, and preparation of mounting substrates.
- b. Intracellular structure: Observations to date of the odontoblasts and the ameloblasts have shown that these cells possess a cytological organization fundamentally identical to the one observed in other cell types. It has been demonstrated that the organelles exhibit changes in differentiation, orientation, and distribution with different stages of enamel and dentin formation.
- c. Extracellular structure: The elaboration of the enamel and dentin matrices occur extracellularly and constitute a problem separate from that of cytological organization. So far the fibrillar component of the dentin has been investigated from a point where the first single collagen fibrils appear at the distal end of the odontoblasts up to the beginning of mineralization.

Significance to Dental Research:

The information obtained about the morphology and organization of the ameloblasts and odontoblasts at various stages of enamel and dentin formation is important as a basis for the study of cellular changes which may result from pathologic conditions, such as nutritional deficiencies and metabolic and hormonal disturbances. In themselves, the cells, due to their special short-lived function, represent a unique

Significance to Dental Research (Continued):

possibility for a study of their cytological organization as related to the various stages of enamel and dentin formation which may be of value for the understanding of the function of the various organelles. In addition the embryologic studies have a direct bearing on the investigation of mature tissues which is also being carried on.

Proposed Course of Project:

Continuation of all aspects of technical development and of studies of sectioned normal, developing and mature dental tissues. In addition an investigation will be started into possible changes in the ameloblasts and odontoblasts as a result of experimentally induced pathologic conditions.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIH - 26
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS			
DIRECT REIMBURSEMENT TOTAL	PROF	OTHER	TOTAL	PROF	OTHER	TOTAL
20,719	3,613	24,332	1	2	3	

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	---
1	3	4	

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 26
SERIAL NUMBER

16 - 17. None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 27
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Development and Application of Histochemical Methods in the Study
of Hard and Soft Tissues.
PROJECT TITLE

7. Marvin S. Burstone
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

The object of this project is to develop new histochemical procedures and modify existing ones for the microscopic characterization of hard and soft tissues.

Methods Employed:

A. Histochemical methods for the visualization of protein groups. This consists of evaluating existing procedures and devising new methods and modifications. It should be pointed out that some of the older protein methods (Millon, Ninhydrine, Xanthoproteic) are essentially unsatisfactory for microscopic histochemistry.

B. Histochemical methods for demonstration of enzymes. The latter include esterases, peptidases, phosphatases, sulfatases, and glucuronidases. The use of frozen dried tissue makes it possible to utilize many poorly hydrolyzed substrates which would be unsatisfactory with conventionally fixed tissues. The following new esterase substrates have been synthesized and an attempt will be made to use them histochemically. These substrates include naphthylmethacrylate, naphthyl cinnamate, naphthyl hydroxy cinnamate and naphthyl crotonate. Several amino acid naphthylamides are also being used.

Major Findings:

A. Four histochemical procedures: the dinitrofluorobenzene, the ninhydrin-Schiff, the alloxan-Schiff, and the chloramine-Schiff methods have been found to be of use for the microscopic demonstration of certain protein groups on tissues. Good chromogenic results were observed in a variety of tissues of several species (rat, mouse, rabbit, man). Also studied were tooth and bone structure.

B. A study of acetone fixed mouse and rat salivary glands fails to reveal activity in serous and mucous cells (except for serous cells of the eugland glands, with a number of esterase substrates (naphthol AS acetate, alpha-naphthyl, alpha-naphthyl butyrate, alpha-naphthyl propionate). However, with frozen-dried tissues, discrete areas of activity are noted. Generally speaking, the active areas are associated with the more terminal portions of ducts and "special serous cells" of the submaxillary gland. Of interest is the observation that serous cells of the tongue are highly active (alpha-naphthyl acetate) while serous cells of the submaxillary gland are completely negative - even though they appear morphologically identical. (Esterase of salivary glands. J. Histochem. & Cytochem. 4:130-139, 1956)

C. Development of a new histochemical method for a proteolytic enzyme, and aminopeptidase. This involved the use of

Major Findings (Continued):

two chromogenic substrates, DL-alanyl-beta-naphthylamide and L-leucyl-beta-naphthylamide. The successful demonstration of aminopeptidase with this procedure is dependent upon the use of frozen-dried material. Distribution of aminopeptidase in a variety of tissues including salivary glands was studied.

D. Enzyme (esterase) activity has been found in developing bone and tooth matrices using several new substrates.

Significance to Dental Research:

Since normal and abnormal characteristics of hard and soft tissues are probably characterized by basic protein and enzyme differences, newer methods and modifications for demonstrating these differences are of use in definite morphology of various tissues in different species.

Proposed Course of Project:

Present investigations will be continued and extended. Included are studies on the effect of various elements upon the protein and enzyme characteristics of developing bone.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 27
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
6,120	2,651	8,771	1/3	1/3	2/3
FY 1957					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	1	2			
FY 1957					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR -27
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Burstone, M. S. Esterase of the Salivary Glands. J. Histo-
chem. & Cytochem. 4:130-139, 1956.

Burstone, M. S., and Folk, J. E. Histochemical Demonstration
of Aminopeptidase. J. Histochem. & Cytochem. 4:217-226,
1956.

Burstone, M. S. The Cytochemical Demonstration of Esterase.
J. Nat. Cancer Inst. In Press.

Burstone, M. S. Esterase Activity of Developing Bones and
Teeth. Arch. Path. In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 28
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Dental Disease in Syrian Hamsters.
PROJECT TITLE

7. Paul H. Keyes
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH.

None

10. PROJECT DESCRIPTION:

Objectives:

Long Range Objectives: To develop ways and means of using hamsters for bio-assaying factors associated with dental caries and periodontal disease. Hamsters have certain advantages over rats for this purpose in that the teeth and gingival tissues can be observed in detail in the living animal during the course of a study.

Emphasis will be placed on the isolation of a strain of both golden and albino hamsters which will develop a relatively consistent pattern of dental caries in a short period of time (35-42 days).

Objectives (Continued):

Long Range Objectives (Continued): Because these animals are more delicate than rats, it is necessary to standardize various factors associated with the consistent induction of rampant caries. After the establishment of a basic regimen-dietary, housing, etc., -experimental deviations can be made with confidence.

Short Term Objectives: To test the effect of various dietary supplements and alterations in the caries picture. This includes the use of possible cariostatic agents such as fluc-rides, antibiotics, etc.

Methods Employed:

Under reasonably well standardized laboratory conditions, hamsters are raised and tested for susceptibility to dental caries. Animals are selected for propagation on the basis of susceptibility and reproductive potential in order to standardize as well as maintain the colony.

When specific factors are tested, e.g. the effectiveness of cariostatic agents, selected animals are litter paired into control and test groups and tested in usual manner.

Major Findings:

During the past year approximately 1000 animals have been tested and assayed for susceptibility to caries. An improved method for recording and scoring dental caries in live hamsters enables one to assess an animal in 1-2 minutes and gives a permanent record which can be added to at various intervals of time.

Preliminary observations indicate that caries is less readily induced in animals kept in isolation than in those maintained in groups of approximately four. Reasons for this are not known.

There is evidence that the carious process can be arrested following a change in diet and that there is difficulty in starting the process again by a return to the cariogenic ration.

The effect of sodium lauryl sarcosinate and tri-sodium para periodate has been treated for possible cariostatic effects. No particular benefit was observed. Animals on 0.5% SLS in

Major Findings (Continued):

the drinking water developed hyperkeratotic changes on the dorsal surface of their tongues.

Golden hamsters have been tested for 42 days on cariogenic diets. This period may be further reduced as more susceptible strains are selected. There have been problems of reproduction in the golden lines.

Albino hamsters are now being assessed and selected for susceptibility to caries. Under current conditions albino animals develop rampant decay in 35 days. These animals continue to be susceptible and to reproduce on a commercial diet.

Further progress has also been made on methods of evaluating the caries pattern induced in rats on high-carbohydrate low-fat diets. The effect of fluoride and sodium lauroyl sarcocinate has been tested in rats fed one such high-carbohydrate low-fat diet; data awaits processing.

Significance to Dental Research:

Hamsters seem to have certain advantages over rats for caries and periodontal assays. Not only can caries be induced in 35-42 days in better than 99% of animals and 95% of teeth, but also the process can be followed at daily intervals if one so desires. Precise cultures and topical treatments can be made in precisely localized areas of the molar dentition.

The induction of rampant decay within 35 days is often associated with visible evidence of cavitation in 10 to 15 days, and occasionally there may be almost complete destruction of maxillary 2nd molars in 21 days. This is in marked contrast to former experimental periods of 100 days.

The consistency of present observation suggests that certain bio-assays can be made quickly and with relatively small groups of animals. Observations can be repeated and double checked in less time than formerly used for a single assay.

Animals can be assessed with good accuracy at the end of an experimental period without being killed. This process saves especially susceptible animals for propagation and maintenance of the colony.

Proposed Course of Project:

The golden line of hamsters will be further selected and re-fined. These animals will be retested from time to time against animals produced in the N.I.H. breeding station.

The second generation albino lines now in the process of assessment will be reduced to two and if possible one. This will be an initial step toward development of an inbred strain.

Purified diets, cariostatic agents, and other factors will be tested as time permits.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 28
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
20,669	3,613	24,282	1	2 1/3	3 1/3
FY '57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	3	4			
FY '57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROACH	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 28
SERIAL NUMBER

16 - 17. None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 29
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Histochemical Studies of Connective Tissues
PROJECT TITLE

7. Harold M. Fullmer
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To determine the chemical composition and the reactive groups of normal and diseased connective tissues through use of existing histochemical methods. In addition, some time will be devoted to the development of new methods.

Methods Employed:

Human and animal tissues are obtained from autopsy and surgical material. Specimens to be sectioned are embedded either directly after freezing and drying or after chemical fixation

Methods Employed (Continued):

and dehydration. Under controlled conditions, the sections are exposed to various reagents designed to determine the site and quantity of a reactive group or substance.

Major Findings:

The mechanism of reaction of a number of stains used in studies of connective tissues had to be determined in order to understand the significance of their reactivity with particular tissue components. Several elastic tissue stains (orccin, orcinol new-fuchsin, Verhoeffs, and paraldehyde fuchsin) have been investigated in detail. They were found to react with some acid groups present in elastic tissue. Some degenerative collagenous tissues react with several of the elastic tissue stains. It was found that collagen can be artificially altered by chemical means (acetylation or benzoylation) so that it reacts with elastic tissue stains. This approach provides additional information about the differences in structure of elastic tissues and collagen. The collagen in lysine-deficient rats was found to be profoundly altered, both morphologically with respect to fiber size and quantity and histochemically with respect to its free amino acid content. Some time has been devoted to a study of the mechanism of hematoxylin reaction. Although the mechanism has not yet been completely elucidated, it has been established that the reactivity is not that of a simple basic dye. The common practice of designating substances "basophilic" solely on their staining behavior with hematoxylin therefore appears hazardous.

Some time has been devoted to working out the normal protein and polysaccharide histochemical reactions in developing human teeth and jaws.

Significance to Dental Research:

Periodontitis and periodontosis are diseases of connective tissues. It is believed that information gained about the nature of normal connective tissues and their alteration in diseased states will contribute to a better basic understanding of the pathological processes involved in periodontal disease.

Proposed Course of Project:

Next year most of the time will be devoted to continued histochemical study of normal, aged, and diseased connective tissues.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 29
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
20,111	3,613	23,724	1	2	3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	2	3			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROACH	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 29
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Fullmer, H. M., and Lillie, R. D. The Staining of Collagen
with Elastic Tissue Stains. J. Histochem. & Cytochem.
In Press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 30

SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Histology and Pathology
LABORATORY, BRANCH OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Physical Properties and Mineral Metabolism of Bone.
PROJECT TITLE

7. William B. Savchuck
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To study the relation of longitudinal, transverse, and overall, or peripheral growth of bone to its physical and chemical properties.

The implications of a study of bone growth in its several aspects are first, - that a base-line is established, serving as a reference for a variety of influences on normal bone development, e.g., - radiation, paralysis, aging, circulatory disturbances of bone, the action of various drugs and minerals during the period of bone plasticity, etc. Second, the newer

or more sensitive techniques evolved incidental to a study of the component factors of bone growth (replaced or supplementing the standard roentgenographic and histological methods) can serve to define more specifically the developmental effects of the various agents or factors enumerated above.

Methods Employed:

Measurement of length, total volume, and breaking strength of the femora, tibiae, and humeri of rats receiving various control and mineral-supplemented diets.

Analysis of bones for ash and strontium contents to determine the long-range deposition of strontium and its effect on the mineral content of different long bones at different ages.

Two of the techniques employed for procuring physical measurements were developed in this laboratory and afford very sensitive measurements on the small bones of very young animals, viz., - the measurement of a bone whose total volume is only 0.100 ml. can be determined to ± 0.001 ml., while the strength of such a bone can be measured to within a fraction of an ounce. The chemical method detects 0.1 microgram of strontium by neutron activation analysis.

Major Findings:

Preliminary results show neither a retarding nor an accelerating effect of strontium on the growth of femora of normal rats at different ages. Other physical and chemical findings are being analyzed statistically in order to determine whether there are interrelations between the type of bone (and its function), the sequence of epiphyseal union, the age of the animal, the dietary alteration, and the three types of growth (longitudinal, transverse, and peripheral). There seems to be only a slight correlation of the strength of a tubular bone with the animal's body weight, but a good correlation of strength with the mineral content of the bone.

Significance to Dental Research:

The study contributes to a better knowledge of basic factors controlling the development of bone in length, in cross-sections, and in mass. These component factors can be useful as criteria for defining objectively the histophysiological and physical effects of various agents on the development of bone.

Proposed Course of Project:

Growth and repair of bone to be studied from the beginnings of ossification to maturity and senescence by radiomicrography.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 30
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
17,979	3,613	21,592	1	1 1/3	2 1/3
FY '57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	--		
1	2	3			
FY '57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR - 30
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Savchuck, W. B. Effects of Strontium and Fluoride on the
Repair of Unreduced Humeral Fractures in Adult Rats.
J. Bone and Joint Surg., Jan. 1957. In Press.

Pugh, M. H. Water Repellency of Silicone on Microburet Tips.
Anal. Chem., 28:557, April, 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 31
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Epidemiology and Biometry Branch
LABORATORY, BRANCH, OR DEPARTMENT

4. _____
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Epidemiology of the periodontal diseases
PROJECT TITLE

7. Dr. Albert L. Russell
PRINCIPAL INVESTIGATOR

8. Dr. Richard L. Hayes, Dr. Norman W. Littleton,
Dr. Charles J. Donnelly, Mr. Carl L. White
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

None

10. PROJECT DESCRIPTION:

Objectives:

To compile a descriptive epidemiology of the group of disease entities commonly called "pyorrhea".

Methods Employed:

Direct examination of population groups, particularly adults and older children, followed by statistical analysis of examination data to determine relative risk under varying conditions.

Major Findings:

Prevalence and severity of disease in white Baltimore adults was generally similar to findings for groups previously examined in Colorado Springs, Colorado, and in Bartlett and Cameron, Texas; were lower than previous findings for adults of Boulder, Colorado, and for a group of white uranium miners. They were similar to findings for normal controls and for persons with uncomplicated eye conditions examined in the Clinical Center, but lower than findings for most Clinical Center patients with chronic disease. Incidence patterns seem to differ for white males and females. Disease was more prevalent and more severe in Baltimore negroes than in Baltimore whites. Social factors which condition severity of disease, once initiated, do not explain differences in prevalence; the true etiological factors in periodontal disease may be independent of those factors which influence its course once it is initiated.

Use of a fluoride domestic water has no relation with the severity or prevalence of periodontal disease.

Significance to Dental Research:

After dental caries, the periodontal diseases are the second most important cause of tooth loss, and affect about 70 per cent of all persons 50 years of age or older. Epidemiological study of dental caries led to fluoridation of domestic water supplies, which will reduce treatment needs for caries by about two-thirds. Ultimate aim of this study is mass preventive measures for the periodontal diseases.

Proposed Course of Project:

Field examinations of older children will be continued and extended in an effort to determine the characteristics of those children who show signs of the disease at the earlier age, and hence are presumably the more susceptible. A field study of a minimum of 4,000 white and negro male and female employed persons in Birmingham, Alabama, is being planned for the next calendar year.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 31
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
18,163	4,093	22,256	1 1/3	1	2 1/3
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
3	3	6	-----		
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 31
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Russell, A.L. A system of classification and scoring
for prevalence surveys of periodontal disease. J. Dent. Res.,
35:350-9, June 1956

Russell, A.L. Longitudinal technics in the study of oral
disease. Am. J. Pub. Health, 46:728-35, June 1956

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 32
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Epidemiology & Biometry Branch
LABORATORY, BRANCH, OR DEPARTMENT

4. _____
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. The relationships between periodontal disease and general systemic condition, systemic disease, and aging
PROJECT TITLE

7. Dr. Albert L. Russell
PRINCIPAL INVESTIGATOR

8. Dr. Norman W. Littleton, Dr. Charles J. Donnelly, Mr. Carl L. White
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

None

10. PROJECT DESCRIPTION:

Objectives:

To determine whether periodontal disease is a manifestation of general systemic condition, or due primarily to aging.

Methods Employed:

Each patient examined in the dental clinic of the Clinical Center is scored for periodontal disease. This score is then related to data obtained from the patient's medical record. The scoring method permits direct comparison with findings obtained from examination of persons not hospitalized and free of known illness. Initial analysis is proceeding on the basis of within-group comparisons.

Major Findings:

This activity has been hampered by personnel shortages. It now appears that there may be a general association between chronic disease and periodontal disease. With the exception of normal controls and persons with uncomplicated eye conditions, most of the broad groups under study in the Clinical Center show a higher prevalence and a greater severity of periodontal disease than do non-hospitalized persons studied in other communities.

Significance to Dental Research:

Periodontal disease is generally considered to be the resultant of local irritating factors combined with systemic factors which interfere with tissue response and repair. Evidence as to these systemic factors is conflicting.

Proposed Course of Project:

Continuation along the present lines until enough records have been processed for valid findings and logical hypothesis. Processing must wait until the individual patient has been dismissed and his medical record has been assembled in final form. Some broad findings may be possible when about twice as many data as have been processed at this time have been tabulated. Investigations of some smaller subgroups (for example, patients with scleroderma) must be continued past that point until sufficient numbers of persons have been studied.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 32
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
14,181	3,613	17,794	1	2/3	1 2/3
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
3	2	5	-----		
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Dental Clinic Examining Staff, Clinical Center Medical
 Records Section, Clinical Center

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 32
SERIAL NUMBER

16 - 17 None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 33
SERIAL NUMBER
2. Dental Research
INSTITUTE OR DIVISION
3. Epidemiology and Biometry Branch
LABORATORY, BRANCH, OR DEPARTMENT
4. _____
SECTION OR SERVICE
5. _____
LOCATION (IF OTHER THAN BETHESDA)
6. The effects of sodium fluoride tablets on dental caries
PROJECT TITLE
7. Mr. Carl L. White
PRINCIPAL INVESTIGATOR
8. Dr. F. A. Arnold, Jr., Dr. F. J. McClure
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To determine if dental caries is inhibited in children who have ingested sodium fluoride, provided in the form of tablets.

Methods Employed:

During the past 12-14 years, tablets containing one milligram of fluoride (F) as sodium fluoride were issued to professional personnel for administration to their children, or to children of others for whom they would assume responsibility. Depending upon the fluoride concentration of the family water supply, directions were given so that the child's fluoride ingestion (exclusive of food-borne fluoride) was adjusted to an intake equivalent to the fluoride furnished by a domestic water containing one part per million of fluoride (F). This regimen was to be continued throughout the calcification period of the permanent teeth. Caries

experience in these children (as reported by individual private examiners) is compared with the caries experience of similar children using fluoride-bearing and fluoride-free waters.

Major Findings:

In the study groups, the mean numbers of DMF teeth by age groups are about the same as those observed in Aurora, Illinois, a natural fluoride community. Caries experience of the study children is generally as favorable as that of children using fluoridated water in Grand Rapids, Michigan, Newburgh, New York, and Brantford, Ontario. The mean numbers of decayed extraction indicated, and filled deciduous teeth are somewhat lower than those observed in these areas. Chemical analyses indicated that there was very little more fluoride in deciduous teeth of these children than in deciduous teeth from areas with fluoride-deficient water supplies.

Significance to Dental Research:

The study indicates that dental caries may be inhibited by ingestion of fluoride in tablet form. This inhibitory effect seems to compare favorably with ingestion of a fluoridated domestic water. The method offers a means of caries control for individuals who are not provided with a water supply containing an optimum quantity of fluoride.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 33
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
2,658	2,651	5,309	1/3	--	1/3

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
1	---	1	----

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

Form No. ORP-1
October 1956

- 4 -

Calendar Year 1956

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 33
SERIAL NUMBER

16 - 17 None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 34
SERIAL NUMBER
2. Dental Research
INSTITUTE OR DIVISION
3. Epidemiology and Biometry Branch
LABORATORY, BRANCH, OR DEPARTMENT
4. _____
SECTION OR SERVICE
5. _____
LOCATION (IF OTHER THAN BETHESDA)
6. Biometric methods in dental epidemiology.
PROJECT TITLE
7. Dr. Richard L. Hayes
PRINCIPAL INVESTIGATOR
8. _____
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

Complements: NIDR-29, 31, 32 (1955)

10. PROJECT DESCRIPTION:

Objectives:

To develop and apply biometric methods in dental epidemiology. At present these methods are being applied to the description of the eruption of teeth as a group phenomenon.

Methods Employed:

The principal methods employed are analytical in nature, but if adequate data are not available, examinations are performed to secure the data needed. During the past year, the principal statistical methods used were the iterative procedures of Finney and Cornfield and Mantel.

Major Findings:

The results indicate that the eruption of the canine teeth, as a group phenomenon, follows the normal probability curve. Adequate data were not available for other tooth types.

Significance to Dental Research:

A description of the eruption of teeth will aid in the definition of the risk factor in dental caries and periodontal disease. Further investigation may determine whether dental age should be described on an arithmetic or logarithmic scale. This concept might be of importance in studies of caries or periodontal disease. The information on average eruption time will allow categorization of persons as having early or late dental development. This might have some relation to other growth processes and, indirectly, to the speed of the aging process. Information on various eruption patterns might also be useful to practicing dentists.

Proposed Course of the Project:

To secure more adequate data, it is planned that examinations will be performed on 20,000 to 25,000 school children ranging from Kindergarden to Seniors in High School, with the majority of the examinations being made at the lower age levels. From these data on eruption status, the eruption curves for each tooth type will be computed, along with error terms. These curves will be related to each other to find a general pattern, if one occurs. The data will also serve as the basis for computation of tables for time at risk of each tooth type.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 34
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
4,347	2,651	6,998	1/3	---	1/3
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	---	1	-----		
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. .NIDR - 34
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Hayes, R.L., McCauley, H.B., and Arnold, F.A., Jr., Clinical
and roentgenographic examinations for dental caries in
Grand Rapids, Michigan. Public Health Rep., in press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 35
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Epidemiology & Biometry Branch
LABORATORY, BRANCH, OR DEPARTMENT

4. _____
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. The Epidemiology of Dental Caries, including the Fluorine-Caries
Relationship
PROJECT TITLE

7. Dr. Richard L. Hayes
PRINCIPAL INVESTIGATOR

8. Dr. Albert L. Russell, Dr. Norman W. Littleton,
Dr. Charles J. Donnelly, Mr. Carl White
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

Complements Grand Rapids-Muskegon study

10. PROJECT DESCRIPTION

Objectives:

Further to define the epidemiological characteristics of dental caries; to elicit evidence as to the basic nature of this disease and the tissues it attacks so that present methods of control may be perfected and, possibly, new methods of control can be evolved.

Methods Employed:

Direct examination of population groups, including adults as well as children, followed by statistical analysis of examination data to determine relative risk under varying conditions.

Major Findings:

Sodium fluosilicate, which is cheaper, is as effective as sodium fluoride for fluoridation of public water supplies. After four years of fluoridation in Montgomery and Prince Georges Counties, Maryland, there has been a significant reduction in caries in first molars which were newly-erupted at the time fluoridation began.

Significance to Dental Research:

Data from direct observations of human populations provide a bridge whereby findings from animal studies may be applied to human disease. Present attention is concentrated upon several areas where basic information is scanty or equivocal; for example, analysis of the selective action of a fluoridated water used while teeth are calcifying, while young calcified enamel is maturing, and after adult enamel is present, is expected to add information as to the basic mechanics and sequences in calcification and maturation of enamel.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 35
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
22,545	4,093	26,638	1 1/3	2	3 1/3
FY '57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
3	4	7			
FY '57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 36
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Epidemiology and Biometry Branch
LABORATORY, BRANCH, OR DEPARTMENT

4. _____
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Grand Rapids-Muskegon Fluoridation Study
PROJECT TITLE

7. Dr. Norman W. Littleton
PRINCIPAL INVESTIGATOR

8. Dr. David B. Scott, Dr. Robert C. Likins, Mr. Carl L. White
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

The epidemiology of dental caries, including the fluorine-caries relationship (NIDR Serial No. _____)

10. PROJECT DESCRIPTION

Objectives:

This project was initially designed to determine whether or not the fluoridation of a community water supply was an effective measure for dental caries control. Certain aspects of the dental economics and dental manpower needs of a community are under study. Factors relating to caries etiology and the physiology of fluorides are being appraised. Periodontal status is under continuing observation.

Methods Employed:

This study has been in progress since 1944. During the ten years following fluoridation annual examinations were made of approximately 5,000 school children in Grand Rapids, (the study

city) and about 3,000 in Muskegon (the control). Changes in dental caries prevalence were noted from year to year, and studied from the standpoint of the cause of the disease and the problems involved in treatment. Epidemiological and statistical methods were used to evaluate these factors.

In addition to this basic study of dental caries, special studies, such as the elimination of fluorides via urine, have been added from time to time. Since 1952 a longitudinal study of periodontal disease has been carried out with a subgroup of the Grand Rapids population and with a small sample of elementary school children in Muskegon.

The study plan was altered beginning with the eleventh year of fluoridation. At that time the ultimate result had been observed in children aged 11 years and younger. The study is now limited to children in junior high schools in Grand Rapids; these children will be followed until the full caries-inhibitory effect has appeared, and until the full prevalence of fluorosis can be estimated. The periodontal study is being continued in Muskegon.

Major Findings:

There has been a consistent decrease in the incidence of dental caries in Grand Rapids school children since the inauguration of the study. The change is most significant in persons born since fluoridation, but a significant effect could be inferred from the findings for children whose teeth had already been formed prior to starting the study. This finding was amplified in a special study, utilizing detailed clinical and roentgenographic examination, of all school children still resident in the towns who, in the initial examination in 1944, exhibited at least two permanent first molars in eruption. After 11 years of fluoridation, these first molars showed fewer and less extensive lesions in Grand Rapids children than in Muskegon children, indicating that fluorides have some caries-inhibitory effect upon teeth formed and erupted prior to fluoridation. The progressive diminution of caries previously observed continued during the 11th year in the whole population studied.

Results of bacteriological examination of salivas from these children suggest that there has been a change in the oral flora, though its significance is not clear. Studies related to the non-dental effects of fluoridation support the belief that this level of fluoride in a water has no known non-dental effect. Periodontal disease is somewhat less prevalent in native white children of Grand Rapids than in migrant children, who have used the water for a shorter period of time.

Significance to Dental Research:

This study not only proves the effectiveness and safety of water fluoridation as a caries control procedure, but also furnishes important leads to further research into the etiology of caries and of periodontal diseases. In particular, significant findings of clinical importance are resulting from the data obtained on changes in individual and specific tooth susceptibility.

Proposed Course of Project:

The study will be continued, on the limited scale described, for about three more years, or until the full inhibitory effect has been attained in all school-age children and the prevalence of fluorosis has reached its maximum point. Grand Rapids examinations are limited to junior and senior high school students, in the age range of 10 through 17 years. The small Muskegon sample will be observed yearly, primarily in a study of periodontal disease by longitudinal technics.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 36
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
9,721	2,651	12,372	2/3	1/3	1
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	1	2	-----		
FY'57					

13. BUDGET ACTIVITY

- | | | | |
|--------------------|-------------------------------------|-------------------------------------|--------------------------|
| RESEARCH | <input checked="" type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL &
TECHNICAL ASSIST- | |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | ANCE | <input type="checkbox"/> |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 36
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Arnold, F.A., Jr., Dean, H.T., Jay, Philip, and
Knutson, J.W. Effect of fluoridated public water
supplies on dental caries prevalence. Pub. Health
Rep., 71:65208, July 1956

17. LIST HONORS AND AWARDS TO PERSONNEL RELIATING TO THIS PROJECT
DURING CALENDAR YEAR 1956.

None

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 37 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Maxillofacial Prosthetics
PROJECT TITLE

7. Ralph S. Lloyd
PRINCIPAL INVESTIGATOR

8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

10. PROJECT DESCRIPTION:

Objectives:

To evaluate methods of treatment, designs of appliance and to observe the response of the patients.

Methods Employed:

Different types of appliances are being constructed for individuals who have had destruction of tissues of the head and neck with surgery and patients afflicted with cleft palate. Improvement in esthetics, ability to ingest food (both solid and liquid), function of appliance and improvement in speech are observed. Speech therapy is given where

advisable. The cephalometric measurements are utilized to help design these appliances, to determine the amount of freeway space, as well as to properly place the bulb in cleft palate devices.

Major Findings:

The well being of the patients in cancer therapy and patients with cleft palate is greatly influenced by a properly made prosthetic device. The design of such a device is the basis of their success.

During this past year a paper was submitted for publication describing a case, and the method by which the cephalometric x-ray was used to properly place the bulb in cleft palate device.

A paper was also given on this subject at the National Meeting of the American Society Cleft Palate Rehabilitation.

Significance to Dental Research:

This is an area where very little work has been done, and any contribution will be of great assistance in the treatment of these unfortunate patients.

Proposed course of Project:

To further investigate methods of construction, design of appliances and patient response to maxillofacial prosthetic devices.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 37 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO (S):

Dr. Ralph S. Lloyd is on the Staff of the Clinical Center.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR - 37 (C)
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Lloyd, Ralph S., D.D.S. "Prosthetic Rehabilitation of A
Cleft Palate Patient Subsequent To Multiple
Surgical and Prosthetic Failures," was published in
The Journal of Prosthetic Dentistry.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 38 (C)
SERIAL NUMBER
2. Dental Research
INSTITUTE OR DIVISION
3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT
4. ---
SECTION OR SERVICE
5. ---
LOCATION (IF OTHER THAN BETHESDA)
6. Pulpal Response to High Speed Cutting and Grinding of Teeth
PROJECT TITLE
7. H. Swerdlow and H. R. Stanley, Jr.
PRINCIPAL INVESTIGATORS
8. None
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

10. PROJECT DESCRIPTION:

Objectives:

This study is designed to evaluate the effects on the dental pulp following standard operative procedures performed at high r.p.m. with and without a coolant and with various types of rotary instruments.

Methods Employed:

Patients of either sex and any age over six (6) years are used. They must have vital non-infected, caries free teeth to be extracted for reason such as:

- (1) Orthodontic therapy
- (2) Hopeless periodontal prognosis.
- (3) Unusable malpositioned teeth, i.e. prosthesis.

A histologic valuation was made of the effect of a coolant on the pulpal response of 60 sound human teeth in which cervical cavity preparations were cut with an inverted cone diamond stone at 20,000 r.p.m. 33 preparations were cut with a water spray, and 27 without. The cavities were then filled with zinc oxide and eugenol, and the teeth were extracted at intervals ranging from one hour to 36 days. Multiple sections were cut and studied.

22 patients with 153 teeth were employed for histologic study. This investigation is now ready for publication.

Major Findings:

All the specimens extracted after the first 24 hours, demonstrated definite injury to the pulp. Extensive cellular damage, and abscess formation were present only in "non-spray" specimens. Evidence suggesting repair was found only in "with spray" teeth.

An explanation was sought for the prominent finding of "aspirated" odontoblasts in the dentinal tubules. The fact that this phenomenon was not seen in specimens taken shortly after cavity preparation but appeared at the same time as the inflammatory response suggested that the odontoblasts were forced into the tubules by increased intrapulpal pressure rather than drawn into the tubules by suction. Thus, the term "displaced" odontoblasts may be more appropriate.

Significance to Dental Research:

The tendency today in operative procedures is for higher rotary speeds with little regard to pulp damage. Clinical information concerning these pulpal reactions is greatly needed in order to determine the safest and most efficient methods for cavity preparation.

Proposed Course of Project:

To expand clinical investigations of the pulpal responses to higher rotary speeds, varying rotary instruments and other standard operative procedures.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 3G (C)
 SERIAL NUMBER

12. BUDGET DATA:

<u>ESTIMATED OBLIGATIONS</u>			<u>MAN YEARS</u>		
<u>DIRECT REIMBURSEMENT TOTAL</u>			<u>PROF</u>	<u>OTHER</u>	<u>TOTAL</u>
FY'57					
<u>BUDGETED POSITIONS</u>			<u>PATIENT DAYS</u>		
<u>PROF</u>	<u>OTHER</u>	<u>TOTAL</u>			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO (S):

Dr. H. Swerdlow is on the Staff of the Clinical Center.

Form No. ORP-1
October 1956

- 4 -

Calendar Year 1956

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 38 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 39 (C)
SERIAL NUMBER

2. Dental Research

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Malocclusion as Related to Traumatic Occlusion.
PROJECT TITLE

7. H. Swerdlow and A. W. Mann. (NIDR Consultant)
PRINCIPAL INVESTIGATORS

8. ---
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

10. PROJECT DESCRIPTION:

Objectives:

To evaluate the influence of corrected occlusal balance of natural dentitions on the periodontal tissues, facial muscle tone and the temporo-mandibular joint.

Methods Employed:

Selective grinding is the method or procedure. Adult patients with approximately 28 teeth in occlusion are selected. A demonstrable though slight malocclusion and some gross evidence of periodontal disease must be present.

The existing occlusion will be recorded on an anatomical articulator and all necessary pretreatment records taken, i.e., mandibular movements, photographs, roentgenographs, etc. After functional analysis, the occlusion will be corrected by selective grinding and the clinical course of the disease charted.

To date, 35 outpatients have been under study. Their total visits for treatment and observation have totaled 215.

Major Findings:

The preliminary work done thus far has helped to delineate the methods of approach. Special tools developed in the course of this study are:

1. A clinical camera designed to accurately measure change in gingival color and contour. At present this camera is in the Instrument Shop for modifications before clinical testing can be performed.
2. A method for recording the sounds of occluding teeth on tape. This provides a technic for demonstrating premature occlusal contacts versus balanced occlusion. The method, using a bell type stethoscope tip connected to a tape recorder seems to offer the best possibility thus far, for recording occluding tooth sounds.

Nine cases with temporo-mandibular joint dysfunction have demonstrated improvement.

All patients in the study have had relief of pain and improved chewing function.

Significance to Dental Research:

It is generally accepted that malocclusions and malfunctions of the teeth are important local causative factors in periodontal disease. It is usually noted, also, that in periodontal disease, the occlusal pattern is unbalanced and not in harmony with the temporo-mandibular joint. This affects not only the tissues adjacent to the teeth but also the facial muscles, ligaments, and other allied structures.

Proposed Course of Project:

It is hoped that tools being developed will aid in the measurement of the changes that occur in the teeth and surrounding structures. Accurate findings in this study will help to determine the value of selective grinding in order to balance occlusions in the therapy of periodontal disease.

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PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 39 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 40 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. The Effect of Relaxin on the Salivary Glands, Gingival and Peri-
dontal Tissues of the Rat. Part I
PROJECT TITLE

7. Paul N. Baer
PRINCIPAL INVESTIGATOR

8. Harold R. Stanley, Bernard K. Forscher
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES, OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To study the roentgenologic and histologic effects of the hormone relaxin on the gingivae, periodontium, and salivary glands.

Methods Employed:

Seventy-two female rats, 3 months of age, will be arranged in 4 groups:

Methods Employed (Continued):

Group I - will receive estradiol benzoate in sesame oil, 4 mgm. subcutaneously, on first and third day. The animals will be sacrificed on the eleventh day and at weekly intervals thereafter for the next six weeks.

Group II - Same as Group I, except on fourth day, 5 μ g. of relaxin is injected subcutaneously.

Group III - Same as Group II, except 50 μ g. of relaxin is injected.

Group IV - Same as Group II, except 500 μ g. of relaxin is injected.

The following structures will be studied in a routine manner histologically and special stains used only where indicated: 1) gingiva; 2) periodontium; 3) salivary glands, 4) pubic symphysis; 5) ovaries and uteri.

Biochemical analysis will be made of the palatal tissues.

Part II

Title: The Effect of Experimentally Produced Occlusal Trauma and Gingival Inflammation on the Periodontal Tissues of the Monkey Pretested with Relaxin.

Principal Investigator: Paul N. Baer

Other Investigator: James J. Kennedy

PROJECT DESCRIPTION:

Objectives:

To study the roentgenographic and histologic effects of the hormone relaxin on periodontal tissues which have been subjected to experimentally produced trauma and inflammation.

Methods Employed:

Four female adult monkeys, age 4-6 years, will receive subcutaneous injections of 4 mgm. of estradiol benzoate in sesame oil on first and third day, and a subcutaneous injection of 500 mgm. of relaxin on the 4th day. Also on the 4th day a "high" amalgam filling will be placed in the mandibular right second premolar and a wire ligature placed as far gingivally as possible around the mandibular left premolar.

Four female adult monkeys will serve as controls. They will be treated the same as the experimental group except that they will receive no injections.

The animals will be sacrificed at the following intervals: 3 days, 1 week, 2 weeks, 4 weeks.

The following structures will be studied in a routine manner histologically and special stains used only where indicated: 1) gingiva; 2) periodontium; 3) salivary glands; 4) pubic symphysis; 5) ovaries and uteri.

Part III

Title: The Effect of Relaxin on Producing Congenital Defects in the Offspring of Pregnant Mice and Rats

Principal Investigator: Paul N. Baer

PROJECT DESCRIPTION:

Objectives:

To study grossly and histologically the effects of the hormone relaxin on the offspring of pregnant mice and rats, with particular emphasis placed on the mouth and dentition.

Methods Employed:

Twelve pregnant rats, Sprague-Dawley strain, 12 pregnant mice, C57/BR strain, and 12 pregnant mice, STR/1N strain will be used. Animals should be not more than 10 days pregnant.

Methods Employed (Continued):

Ten animals in each group will receive subcutaneously injections of 100 μ g. of relaxin every Monday, Wednesday and Friday until term. Two animals in each group will serve as controls and will receive no treatment.

All offspring will be sacrificed as soon as possible, examined grossly for anomalies and their jaws and teeth studied in a routine manner histologically. Special stains will be used only where indicated.

Significance to Dental Research:

To see whether the hormone relaxin is responsible for the periodontal changes observed clinically during human pregnancies, and whether it may also play a role in the production of congenital defects in the offspring.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 40 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF.	OTHER	TOTAL
17,266	14,685	31,951	1	1 1/3	2 1/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
2	2	4			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

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PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIIDR - 40 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 41 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. Medical Investigations
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Medico-dental Studies - Associating Systemic Conditions with Specific Dental Problems
PROJECT TITLE

7. Nicholas C. Leone, M.D.
PRINCIPAL INVESTIGATOR

8. Edgar Benjamin, Edward Driscoll, Paul Baer, Peter Cocco, Patricia Geiser
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Four separate studies in which calcium metabolism (ionizable and bound calcium), dysmenorrhea, periodontal disease and stomatitis are studied through the combined efforts of one or more clinical or laboratory groups, coordinated in the evaluation and treatment of oral and systemic effects in man. Both hospitalized and out-patients are being utilized.

1. A study of the measurement and clinical significance of protein bound and unbound (ionizable) blood calcium.
2. Treatment of dysmenorrhea by the use of Chlorprophenpyridamine Maleate, 12 mgm. (antihistaminic) sustained release capsules and the simultaneous evaluation of attendant gingival change.
3. Clinical study of the etiology of periodontal disease.
4. Clinical study of the etiology and treatment of chronic stomatitis, including Lichen Planus.

Objectives:

Respectively:

1. To develop simplified and reliable methods of measuring bound and unbound calcium in blood serum and to apply the findings in terms of various clinical circumstances and the relationship to tooth and bone effects.
2. To evaluate the effect of special medication on the discomfort associated with menses and tissue response of the mucous membranes of the body to this medication, with particular reference to the gingiva and oral mucosa as a whole. To determine whether or not oral changes occur in dysmenorrhea.
3. To obtain information on general systemic conditions which may be factors in the etiology of periodontal disease.
4. To obtain information on the systemic relationship, etiology, underlying causes and treatment of chronic oral lesions.

Methods Employed:

1. As a means of evaluating the blood of patients and large animals under normal and abnormal circumstances including fluoride exposure at toxic levels, a new type of apparatus has been devised for the separation of bound and (ionizable) physiologic calcium. Patients with osteoporosis have been put on daily sodium fluoride (5 mgm.) to aid in the retention of calcium and increase bone density. These patients are also being studied in a similar manner.

	<u>Visits</u>	<u>Number</u>	<u>Total Days of Hospitalization</u>	<u>Average Days in Hospital</u>
In-Patient Admissions		4	93.2	23.3
Out-Patient Visits	9			

2. Adult females with long history of severe dysmenorrhea. Medical history, physical examination including pelvic examinations. Also, vaginal smear for cancer and culture for trichomonas and monilia (oral and vaginal) made. Gingival examination and evaluation with dental prophylaxis at start of study and subsequent examinations made at intervals during patients' menstrual cycle. Daily patient records of symptoms, medications, etc. throughout the study. Each patient under study for an initial period of six months, three months of which they are given medication and three months placebos. A system of randomization, set up by the study statistician with arrangements for the distribution of the medication through the Clinical Center Pharmacy. Members of the study team have no knowledge as to when the respective participant is receiving placebos or antihistaminic.

Female employees of the National Institutes of Health

Number of patients (1956) 35

Number of visits 94

3. Complete physical and dental evaluation of patients including extensive family history, past and current medical history, review of systems, laboratory studies of blood, urine and other body fluids and X-ray bone and dental studies. All patients to be hospitalized and studied on identical basis.

A statistically satisfactory number of male and female adults with primary and maximal periodontal disease as compared with control patients are to be utilized.

4. Similar procedures to those outlined in (3) above, in the study of chronic stomatitis and oral lesions.

Patients with oral lesions and chronic stomatitis.

	<u>Visits</u>	<u>Number</u>	<u>Total Days of Hospitalization</u>	<u>Average Days in Hospital</u>
In-Patient Admissions		16	372.8	23.3
Out-Patient Visits	31			

Major Findings:

All four studies are still in preliminary stages and no conclusions can be drawn at this time.

Significance to Dental Research:

These studies are of importance in the evaluation of bone and tooth formation, growth and development, aging process, exposure to fluorides, and other substances, infections, with particular reference to periodontal disease.

This approach affords opportunity to correlate systemic and dental conditions as a means of establishing etiologic factors of periodontal disease and other unknown or unidentified chronic oral conditions preliminary to treatment.

Proposed Course of Projects:

Continuation and expansion of all activities.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 41 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
27,678	34,265	61,943	2 1/3	1/3	2 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
4	1	5	465		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Jacob Lieberman, Office of the Director; John Lynch, M.D., Mrs. Frances Wolford, Employee Health Service

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PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 41 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- Part A. Project Description Sheet
1. NIDR - 42 (C)
SERIAL NUMBER
 2. Dental Research
INSTITUTE OR DIVISION
 3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT
 4. ---
SECTION OR SERVICE
 5. ---
LOCATION (IF OTHER THAN BETHESDA)
 6. Fluoride Investigations - Studies of the physiologic and toxicologic effects of fluorides on man and animals.
PROJECT TITLE
 7. Nicholas C. Leone, M.D.
PRINCIPAL INVESTIGATOR
 8. Erving F. Geever, Frank J. McClure, Isadore Zipkin, Patricia B. Geiser
OTHER INVESTIGATORS
 9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None
 10. PROJECT DESCRIPTION:

Objectives:

 1. To determine the long range effects of fluorides on man.
 2. To establish human control material to afford comparisons with fluoride effects.

Objectives (Continued):

3. The development of special roentgenographic materials and techniques to permit standardized radiologic field studies.
4. To determine the immediate and long range effects of fluorides by various methods of administration on animals.

Methods Employed:

Five separate studies:

1. Human necropsy studies (epidemiologic, with chemical and histologic evaluation of bone and soft tissues).

From fluoride areas	43
From non-fluoride areas	40
2. Pharmacologic studies of the intravenous and oral effects of fluoride on dogs and mice.

Dogs	22
Mice	300
3. Roentgenologic epidemiological study of a population group at Framingham, Mass. (non-fluoride). Part of 30-year heart study of over 5,000 persons.

Adult males and females (to-date)	700
-----------------------------------	-----
4. Colorado Springs (2.5 ppm F) necropsy study. An evaluation of the clinical history, autopsy protocols and histologic sections of 980 cases.
5. Large animal (bovine) fluoride studies
 - a. Autopsy (histologic) 4 animals
 - b. Serial peripheral blood and bone marrow studies

fluoride	8 animals
normal	3 animals

Methods Employed (Continued):

c. Serial bone (rib)
biopsy studies

fluoride	10 animals
normal	6 animals

Major Findings:

1. Chemical and histologic analyses of human autopsy material so far has shown no detrimental effects ascribable to ingestion of fluoride in water supplies, though age and exposure may be a factor in the fluoride content of bone.
2. Small animal studies show a wide margin of safety in the use of intravenous and oral fluoride. When interpreted in terms of human effects, there appears to be a wide margin of safety in the experimental use of fluorides intravenously or orally.
3. Establishment of multiple radiologic field studies has proven the value of the standardization procedures and has permitted close inter-study integration and interpretation of results. Findings similar to those in high fluoride areas are being found in the non-fluoride exposed.

Significance to Dental Research:

In response to widespread inquiries and the need for sound information on the safety, value and effects of fluoridation of water supplies, data are being assembled on the physiologic effects of fluorides on humans. Animal studies provide the necessary data which lend direction as well as comparative material for definitive human studies. They supply much needed information on the pharmacology and toxicology of fluorides.

Proposed Course of Project:

Continuation of studies in progress.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIHR - 42 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
17,767	14,685	32,452	1	2/3	1 2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
2	1	3			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

- Framingham Heart Study (serial number)
- Air Pollution Medical Program, Division of Special Health Services, Bureau of State Services

14. (Continued):

4. Utah Valley Hospital, Provo, Utah
5. Utah State Agricultural College, Logan, Utah
6. New York State Health Department
7. Eastman Kodak Company, Rochester, New York
8. Laboratory of Chemical Pharmacology, National Heart
Institute (serial number)
9. Laboratory of Pathology and Histochemistry, NIMH

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 42 (C)
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Leone, Nicholas C., Moran, Neil, Geevor, Erving F., with
the technical assistance of Butler, William M., Jr.,
Geiser, Patricia B., Watts, James S.: Acute Toxicity
Studies of Sodium Fluoride in Animals
Public Health Reports, 71:5, 459-467, May 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- Part A. Project Description Sheet
1. NIDR - 43 (C)
SERIAL NUMBER
 2. Dental Research
INSTITUTE OR DIVISION
 3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT
 4. ---
SECTION OR SERVICE
 5. ---
LOCATION (IF OTHER THAN BETHESDA)
 6. Biological Effects of Ultrasonic Drilling
PROJECT TITLE
 7. James J. Kennedy
PRINCIPAL INVESTIGATOR
 8. OTHER INVESTIGATORS
 9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None
 10. PROJECT DESCRIPTION:

Objectives:

Both human and animal tissues are being used to determine the possible harmful effects of ultrasonic radiation not only on dental tissues but other tissues and organs as well in areas distant to the point of application during drilling.

Methods Employed:

- A. Human Phase: Seventy-two mature, fully developed teeth previously condemned for orthodontic, periodontic or prosthodontic reasons were utilized. Cavities were prepared with both rotary high speed and ultrasonic instruments and the teeth extracted at varying intervals. A post operative histopathological examination was made to determine the comparative effects of these two instruments on the pulp.

- B. Animal Phase: In order to observe the comparative effects of ultrasonic and rotary instrumentation over a longer period and to study the effects on developing tissue, it was necessary to utilize animal material. The incisor teeth of the guinea pig were chosen principally because of their continuously erupting properties. Fifty-eight animals were used. Seventy-two incisors were exposed to rotary cutting, 92 incisors were exposed to ultrasonic cutting, and 68 teeth were maintained as controls. Prior to operative procedure the animals were anesthetized and individual teeth isolated with the rubber dam. Periodic examinations were made at 7-day post operative intervals and the teeth examined clinically over a period of 72 days.

Major Findings:

Experiments utilizing mature human teeth indicated that ultrasonic cutting was no more traumatic than conventional rotary methods although the observation time was necessarily quite short. Animal experiments demonstrated decisively that some factor connected with the ultrasonic cutting device initiated changes of a more severe nature than those associated with the rotary instruments. Without exception, the incisors of the rotary group erupted to normal occlusion approximately 14 days after exposure to cutting. Five incisors did exhibit minor enamel defects which have since disappeared. All teeth are now in function and normal in all other respects. The ultrasonic group of teeth exhibited the following post operative manifestations: 1) enamel defects, 2) discoloration, 3) mobility, 4) fractures, 5) aberrant tooth structures, 6) missing teeth, 7) retardation of eruption, 8) eruption completely arrested, 9) soft tissue inflammation.

Significance to Dental Research:

Ultrasonic vibrational cutting was introduced to the dental profession on a commercial basis without the benefit of a single experiment designed to evaluate the safety during dental procedures. Only after several hundred of the instruments had been placed in dental offices did the first publication appear. These papers have offered conflicting results with regard to safety as have those experiments conducted at high frequencies for medical, therapeutic, and diagnostic use. It seems imperative that these applications on living tissue should require a thorough investigative phase in order that the variations that apparently exist may be recognized and understood.

Proposed Course of Project:

We propose in the future to continue to study the effects of ultrasonics on a basic level and to: 1) Follow up gross clinical observations on animals with complete histopathological study of oral lesions, 2) In cooperation with neurologists to examine, histopathologically, the brain and spinal cord of a selected number of animals in each group, 3) To study the effect on tissue culture of ultrasonic and rotary vibration, 4) To study the mechanism of transmission of ultrasonic vibration in living tissues.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 43 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
28,227	24,475	52,702	1 2/3	2 2/3	4 1/3
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
2	3	5			
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Capt. Arne G. Nielsen, U.S. Naval Dental School, Bethesda, Md.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR - 43 (C)
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Nielsen, A. G. and Kennedy, J. J. Gross Manifestations of
Tissue Response to Rotary and Ultrasonic Dental Cutting
Procedures. In press.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A: Project Description Sheet

1. NIDR - 44 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Clinical Studies of the Effect of Specific Intravenous Therapy on Wound Healing in the Oral Cavity and on Cases of Intractable Gingivo-Stomatitis.
PROJECT TITLE

7. N. C. Leone, and E. J. Driscoll
PRINCIPAL INVESTIGATORS

8. ---
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None.

10. PROJECT DESCRIPTION:

Objectives:

There is reason to believe, based on previous research, that certain vitamin preparations (notably B complex and C), when given intravenously, may favorably alter the body tissue response to injury, infection and other extraneous insults.

The purpose of the present project is to test objectively the hypothesis of beneficial effect of these intravenous medications, using the tissues of the oral cavity as a yardstick in the measurements.

Methods Employed:

All patients are given a thorough physical examination, in order to properly disclose and evaluate underlying physical disorders which might confuse or alter the final results. A two-phase approach is being made to the problem of evaluation:

1. Bilateral oral surgical conditions of a similar nature are being operated upon. Such procedures as multiple extractions, impactions of the same type and alveolectomies are being performed. The surgery is performed on one side without the co-administration of the intravenous medication and serves as a control. The opposite side is the experimental side and the surgery is performed at a later date along with the intravenous medication regimen.

The degree of swelling, pain, bleeding and trismus serve as objective criteria in the evaluation of the effect of the therapy. This phase is intended to measure the tissue healing potential of the drugs.

2. The second phase is designed to measure the healing as well as the anti-infection and anti-inflammatory properties of the agents. For this project, patients with gingivo-stomatitis have been chosen. Desquamative and desquamative-like cases of gingivo-stomatitis are being utilized as the yardstick of the efficiency of the remedy in this phase. All of the patients are given oral prophylaxis and the mouth is put in as good order as possible. Then half of the patients are treated with the intravenous preparations and the other half are given placebos and are used as controls. Again suitable objective criteria have been set up for the measurement of the results.

Patient Material:

Bilateral Oral Surgical Procedures:

Controls	30
Experimental	20

Major Findings:

In the case of multiple extractions and alveolectomies there is far less ecchymosis and edema in the experimental side than on the control. The pain, trismus and other clinical criteria do not seem to be materially affected by the intravenous vitamins (B complex and C).

In the case of impactions, the experimental and controls were the same. For some unknown reason there does not seem to be any favorable response to intravenous vitamins in the case of impacted teeth. Whereas, in multiple extractions there is less ecchymosis and swelling but no apparent effect as far as pain is concerned.

The effect of intravenous vitamin B complex and C in the case of stomatitis is not specific but is supportive to other local and systemic treatment.

Significance to Dental Research:

The rate at which tissue heals, as well as the conditions which surround healing are of paramount importance in oral surgery and oral medicine.

The possibility exists that certain routine post-operative sequelae such as pain, edema, hemorrhage and trismus may be favorably altered by therapy.

If tissue healing can be assisted and resistance can be increased, then many of the intractable cases of stomatitis may be improved by this approach.

Proposed Course of Project:

1. The oral surgery series is complete.
2. The stomatitis phase will be continued to include more cases.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 44 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
10,948	4,895	15,843	1/3	1/3	2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	1	2			
FY'57					

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|-------------------------------------|----------------------|--------------------------|
| RESEARCH | <input checked="" type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & | |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | TECHNICAL ASSISTANCE | <input type="checkbox"/> |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR 44 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 45 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. General Anesthesia (Dental) Baseline Data
PROJECT TITLE

7. Edward J. Driscoll
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

Dental general anesthesia is different from ordinary hospital anesthetics in several important respects:

1. The patients are generally ambulatory and not usually sedated.
2. The operations are performed in as light a plane as possible.
3. The operations are performed in or about the airway.

Objectives (Continued):

Because of these major differences, the background of knowledge in general dental anesthesia is not for the most part complete, accurate or comparable.

There is a great need in dental anesthesia for a background of fundamental data concerning the alterations in the physiological mechanisms. The body functions may be altered within certain limits. However, beyond these limits exist great hazards. One of the purposes of the study is to define these limits.

The accumulated data will also be used as a baseline of comparison for the many new anesthetic drugs which are being proposed for use in oral surgery.

Methods Employed:

All routine oral surgical procedures are being performed under general anesthesia.

In the first phase of this project, the intravenous agent sodium pentothal is being thoroughly investigated. After a sufficient amount of data has been recorded concerning sodium pentothal administered alone, the various supplements which are commonly used with pentothal will be studied. These include nitrous oxide, demerol, scopolamine, anectine, etc.

Physiologic status and alterations being studied and recorded are:

1. The effects of the drugs on blood pressure and pulse.
2. Cyanosis, syncope and other circulatory changes.
3. The response of the heart, arrhythmias, etc.
4. Apnea, hypernea, tidal volume and other respiratory phenomena.
5. Cortical (brain) activity is being recorded and studied.
6. The possible general physiological effects which might be produced by painful stimulation under light anesthesia with no pre-medication are being studied.

Methods Employed (Continued):

The ordinary instruments employed in physical diagnosis such as sphygmomanometer, stethoscope, etc. are at present being employed.

In addition, information is being gathered by continuous recordings of E.K.G.; E.E.G.; and a sphygmotonomograph (continuous blood pressure).

Important technical data such as amount of drug used in units of time, length of operation and duration of sleep will be recorded.

Pertinent patient data such as age, race, sex, and emotional status in relation to the conduct of anesthesia are being recorded, as well as post anesthetic sequelae, like headache, nausea and vomiting, depression and hiccoughs.

Patient Material:

The project was started on October 1, 1956 and we now have complete records on 30 anesthetics. The anesthetics were performed on 15 adult male and female out-patients.

Major Findings:

1. The electro-encephalogram is indicating that our anesthesia is so light, that the term "anesthesia" may not be descriptive. The stage for the most part is stage I of the Kernsey-Faulcover classification.
2. The E.K.G. is indicating some arrhythmias which may be from the drug, from stimulation or from other sources.
3. Blood pressure instead of dropping as the medical literature indicates, almost consistently rises significantly.

Significance to Dental Research:

The search is constantly being made in dentistry for safer general anesthetics and without such baseline material the search has no foundation. The possibility also exists for improvement and refinement of present methods as well as laying a sound foundation for further anesthesiology research.

Proposed Course of Project:

For the most part the initial study will be concerned with gathering the data on various types of good risk patients, particularly out-patients. Later, after sufficient material has been accumulated, the newer drugs will be evaluated.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 45 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
10,946	4,895	15,841	1/3	1/3	2/3

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	---
1	1	2	

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 45 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 46 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Study of Cysts and Radioluscent Areas
PROJECT TITLE

7. Edward J. Driscoll
PRINCIPAL INVESTIGATOR

8. M. S. Burstone and Harold R. Stanley
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

The project is designed: (a) To study previously untried or little tried diagnostic methods such as aspiration and punch biopsies, (b) To see if there are any histochemical similarities or consistent differences between granulomas and cysts, and (c) To study the surgical treatment of these areas by comparative methods, i.e., enucleation, marsupialization, etc.

Methods Employed:

- (a) Patients are given a thorough physical examination to disclose any underlying or complicating disease.
- (b) The lesions are treated surgically and the material which is removed, whether granulomatous or cystic, is sent to the laboratory for histopathological analysis.
- (c) The lesions are treated by various surgical means, such as open and closed method, gelfoam penicillin space filling, etc., and the data is accurately compiled for later comparative study.

Patient Material:

Out-patient:	Number of patients	4
	Number of visits	60
	Large cysts:	
	radicular	2
	follicular	1
	ameloblastomas	1

Major Findings:

Gelfoam penicillin has been described as an excellent space filler for the large cystic areas. This has been corroborated in that postoperative periods are measured in weeks rather than months. There have been no consistent histochemical similarities or differences and on advice of the histochemists (NIDR) this phase has been eliminated from the study.

Significance to Dental Research:

In the near future some of the recently discovered bone space fillers like anorganic bone and despreciated bone will be ready for clinical trial. This present cyst series will serve as a good comparison since it is typical of the best surgical treatment of cysts during the past ten years.

Proposed Course of Project:

Continuation to include as many cysts as possible.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 46 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
10,946	4,895	15,841	1/3	1/3	2/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	1	2	---		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 46 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 47 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Facial Growth and Development During Orthodontic Therapy
PROJECT TITLE

7. Donald R. Poulton
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To investigate the mechanisms responsible for changes in facial and dental morphology as a result of orthodontic therapy.

Methods Employed:

Application of force from an occipital headcap to the maxillary dentition of children between the ages of 8 and 12 referred by the local orthodontic and general dental groups is contemplated. Therapy results will be evaluated with the aid of

Methods Employed (Continued):

cephalometric headfilms, facial photographs, and articulated casts of the dentition. Untreated children of the same ages will be used as a control group. Treatment will be evaluated as to permanence of result and time required for correction.

Patient Material:

Approximately 30 children will be included in this study.

Major Findings:

The recent initiation of this study precludes any statement of findings.

Significance to Dental Research:

An understanding of the growth and developmental mechanisms responsible for the changes obtained with the upper headgear would greatly increase the possibility of rational and consistent orthodontic therapy by the dental profession. Explanations for the success of this type of treatment vary greatly and a study adequately reported and with satisfactory controls might serve to resolve the question.

Proposed Course of Project:

The active headgear therapy in the cases under study should be completed within 12 to 18 months. Follow-up observations should be continued as long as personnel are available.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 47 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
16,709	14,685	31,394	1	2 1/3	3 1/3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	3	4			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

J. D. Subtelny, Eastman Dental Dispensary, Rochester, N.Y.
 W. L. Wylie, University of California, San Francisco, Calif.

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October 1956

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Calendar Year 1956

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 47 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 48 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Histopathologic Study of Periodontal Disease in BALB/cann Mice
PROJECT TITLE

7. Harold R. Stanley, Jr.
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To determine whether apical migration of periodontal tissues occurs with age if animals are kept under optimal laboratory conditions.

To assess the constancy of specific distances within the anatomic components of the periodontal tissues in step-serial sections and how these distances fluctuate in relation to local pathologic factors.

Objectives (Continued):

To determine how many sections per millimeter of tissue need to be studied in order to observe all obvious structural variations that might occur.

Methods Employed:

Step-serial sectioning of the jaws of BALB mice, ranging in age from 1 to 22 months, has been carried out. Specific distances are measured at a magnification of x100. A stage micrometer is employed. Differences in these distances reflect changes in the anatomic components as successive sections are studied and these differences will be statistically analyzed in relation to local pathologic factors when present.

Major Findings:

Human data indicates that essentially the same results are obtained by the study of every 20th section (6 microns thick) as every 5th section. However, the procedure requires that the number of sections examined be sufficiently large to guarantee a valid estimate of the distribution; that is, provides a representative sampling. In human material, distribution appears adequately described by 8 to 10 sections per millimeter of tissue.

Significance to Dental Research:

To correctly evaluate the degree of periodontal damage, multiple sections are essential in histologic studies.

Proposed Course of Project:

A similar key for studying step-serial sections will be worked out for the periodontal tissues of BALB mice. This data will be essential to the possible establishment of a cyclic phenomenon in animals.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 48 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			FISCAL YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
8,834	4,895	13,729	1/3	1	1 1/3

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
1	3	4	---

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Form No. ORP-1
October 1956

- 4 -

Calendar Year 1956

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. MIDR - 48 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 49 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. The Effect of Sodium Dilantin on BALB Mice
PROJECT TITLE

7. Harold R. Stanley, Jr.
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To determine whether or not the odontogenic tissues of BALB/C mice are sensitive to sodium dilantin in dosages low enough not to interfere with normal reproduction.

Methods Employed:

Daily intraperitoneal injections of sodium dilantin. Records are kept of weight variations, clinical lesions, and animal behavior. Offsprings are studied for odontogenic or other variations.

Major Findings:

In previous phases of this study, a wide range of dosages of sodium dilantin was given to Swiss mice and many lesions related to an intoxicated state, but not specific for sodium dilantin, were produced. No odontogenic variations were observed clinically or microscopically. Resistance to large doses by some animals was apparent.

Significance to Dental Research:

Thousands of epileptics undergo a gingivectomy, often repeatedly, due to sodium dilantin therapy. A controversy exists as to whether the gingival hypertrophy is due to a preceding gingivitis or to the dilantin itself. A controlled disturbance without gingivitis, if found, would indicate that the odontogenic tissues were specifically sensitive to this drug. If similar lesions could be manifested in animals, perhaps an adjustment could be made in therapy, either by adding or eliminating some factor that would not hinder the efficiency of controlled epilepsy but inhibit gingival hypertrophy.

Proposed Course of Project:

Having found no odontogenic disturbances in Swiss mice it is hoped that the inbred BALB/C strain which are generally more responsive to various stimuli might reveal some odontogenic manifestation with the administration of sodium dilantin.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. MIDR - 49 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
7,632	4,895	12,527	1/3	2/3	1
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	2	3			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL &	
BIOLOGIC STANDARDS	<input type="checkbox"/>	TECHNICAL ASSISTANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

None

Form No. ORP-1
October 1956

- 4 -

Calendar Year 1956

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 49 (C)
SERIAL NUMBER

16 - 17 None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 50 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. ---
LOCATION (IF OTHER THAN BETHESDA)

6. Autolytic Changes in Pulp of Human Teeth
PROJECT TITLE

7. Harold R. Stanley, Jr.
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

To determine whether or not certain morphologic characteristics of pulps are pathologic or the result of inadequate fixation.

Methods Employed:

Following extraction, virgin human teeth are allowed to dry specific periods of time before being placed in fixatives. Also mated teeth from the same patient are treated in various manners, such as cutting off the root ends, splitting the crowns, and using different fixatives.

Major Findings:

Apparently certain characteristics of pulps are not due to pathology but autolysis. Accepted methods of fixation are evidently not sufficiently efficient to permit preservation of the pulp before autolysis begins. One is actually studying a combined picture of autolysis and fixation.

Significance to Dental Research:

Confusion in pulp studies is universally acknowledged. Any contribution that would permit recognition of artifactual characteristics or their elimination will be of great value.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 50 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
7,632	4,895	12,527	1/3	2/3	1
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	2	3			
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL &	
BIOLOGIC STANDARDS	<input type="checkbox"/>	TECHNICAL ASSISTANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957, IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR-50 (C)
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Swerdlow, H. and Stanley, H. R., Jr.: Reaction of the Human
Pulp to Cavity Preparation. 1. At 20,000 R.P.M. With and
Without Water Spray. In manuscript form.

Stanley, H. R., Jr.: The Value of Step-Serial Sectioning in
the Morphologic Study of Human Periodontal Disease.
Accepted for publication in the Journal of Periodontology.

Forscher, B. and Stanley, H. R., Jr.: A New Experimental Method
to Produce Acute Inflammation. Accepted for publication in
the A.M.A. Archives of Pathology.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

None.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 51 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. Brandywine, Maryland
LOCATION (IF OTHER THAN BETHESDA)

6. Hereditary Defects in Enamel and Dentin
PROJECT TITLE

7. Carl J. Witkop, Jr.
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

1. To determine the prevalence of inherited defects in the formation of enamel and dentine.
2. To describe their clinical and histological appearance.
3. To determine their mode of transmission and the cellular level where the genes have their effect.

Objectives (Continued):

4. To determine the best method of treatment.

Methods Employed:

A survey conducted with the State of Michigan Department of Dental Health to determine the prevalence of these traits in children seen during the years 1954, 1955, and 1956 in the Topical Fluoride Program and in children seen in Grand Rapids and Muskegon during the NIDR Water Fluoridation Program. Cases found are visited and diagnosed. A pedigree of each family is made and all relatives living in Michigan are visited and examined. Blood, saliva, and taste tests for PTC are made for linkage studies. Patients are brought to the Clinical Center for detailed study and to find methods of repair of the defects.

Patient Material:

Cases found during the survey are utilized for the clinical phases of the study.

Major Findings:

About 95,000 children have been surveyed to date. Five distinct genetic defects of enamel have been identified and their modes of inheritance determined. Two have been previously undescribed. All enamel defects classified as hereditary amelogenesis imperfecta occur about once in 14,000 to 20,000 children in the State of Michigan. They have been classified by their clinical and histological appearance as follows:

1. Hypoplasia of enamel - Sex-linked or sex-modified dominant.
2. Hypocalcification of enamel - Autosomal dominant.
3. Hypomaturation of enamel - Sex-linked recessive.
4. Hypomaturation with pigmentation - Unknown probably autosomal dominant.
5. Local hypoplasia - Autosomal dominant with incomplete penetrance.

Major Findings (Continued):

Two distinct genetic defects of dentin have been described: dentinogenesis imperfecta and dysplasia of dentine.

1. Dentinogenesis imperfecta occurs once in 7,000 to 9,000 children in the State of Michigan. Dentinogenesis imperfecta gene is linked with the gene for PTC taste and is transmitted as an autosomal dominant with complete penetrance. There is no indication of partial sex-linkage.
2. Dentin dysplasia occurs about once in 64,000 children or more in the State of Michigan. It is transmitted as an autosomal dominant.

Various methods of repair of these defects were tried at the Clinical Center. Certain methods appear to be better than others. Certain relationships of these diseases to lactobacillus counts and carious lesions were investigated.

Significance to Dental Research:

This program has contributed to our general knowledge of dental diseases. It has described two new hereditary dental diseases. It has collected basic epidemiological, histological and clinical material in a field that has been somewhat neglected. The material has been used to aid in the determination of the load of genetic mutations in man. It has clarified a somewhat confused area of dental pathology. It has led to a new technic in the epidemiological approach to genetic disease.

Proposed Course of Project:

This project is in the final stages of completion. The field investigations are completed. The clinical phases are to be completed in the near future. Analysis of data and writing of reports and papers is in progress. Two phases of the family data are still to be investigated before the material is ready for publication.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11 NIDR - 51 (C)
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
8,589	4,895	13,484	1/3	1	1 1/3
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	---		
1	2	3			

FY'57

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL &	
BIOLOGIC STANDARDS	<input type="checkbox"/>	TECHNICAL ASSISTANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Department of Dental Health, Michigan Department of Health supplies 45 dental hygenists who spend a small part of their time looking for initial cases; Biologic Standards - Blood Bank(s). Typings.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORTS

Part C: Honors, Awards & Publications

15. NIDR-51 (C)
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Witkop, C. J., Jr.: Hereditary Defects in Enamen and Dentin.
Proceedings of the First International Congress of Human
Genetics. Aug. 1-8, Copenhagen, Denmark (In press).

Kifer, P. E., Hunt, H. R., Hoppert, C. A., and Witkop, C. J.:
A comparison between the widths of the fissures of the
lower molars of caries-resistant and caries-susceptible
albino rats (*Rattos Norvegicus*), *J. Dent. Res.*, 35:620-9,
Aug. 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

Paper selected as one of eight by the American Society Human
Genetics to receive travel grant to attend First International
Congress of Human Genetics, Copenhagen, Denmark.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 52 (C)
SERIAL NUMBER

2. Dental Research
INSTITUTE OR DIVISION

3. Clinical Investigations
LABORATORY, BRANCH, OR DEPARTMENT

4. ---
SECTION OR SERVICE

5. Brandywine, Maryland
LOCATION (IF OTHER THAN BETHESDA)

6. Genetic Study in Southern Maryland
PROJECT TITLE

7. Carl J. Witkop, Jr.
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH:

None

10. PROJECT DESCRIPTION:

Objectives:

1. To find all of the genetically determined disease occurring in a racial isolate comprising 5,000 living individuals of Caucasian, Negro and American Indian ancestry, who have in-married for over 350 years.
2. To determine the relationships these various diseases have with each other and environmental factors.

Objectives (Continued):

3. To supply various clinical investigators at NIH with patient and biological material for various projects and investigations.
4. To determine the mode of inheritance and the linkage of various hereditary defects with other inheritable factors.
5. To investigate the sociological causes for the distribution of various intrinsic diseases in populations in the U. S.

Methods Employed:

The study is divided into three phases:

1. A census, pedigree, and medical questionnaire survey is made of the entire population by trained public health nurses. Hospitalization history of each individual is verified from hospital records. From church records all relationships back to 1741 are verified (Grant, Father Thomas Harte).
2. Field, dental, medical, ophthalmological and radiological bone examinations of each individual, as well as a complete blood typing, hemoglobin survey, urinalyses, and saliva studies are in progress.
3. Patients with diseases of interest to various investigators at NIH are referred into the Clinical Center by their physicians for detailed studies.
4. Analysis of data by aid of IBM.

Patient Material:

Selected patients are referred to the Clinical Center for study on other projects. Some of these include: a study of mental deficiency - NINDB, a study of glaucoma - NINDB, a study of sickle-eye disease - NINDB, a study of bone metabolism - NCI & NIAMD, a study of dentin defects - NIDR, a study of diabetics - NIAMD, a study of fibrocystic disease - NIAMD, a urine survey - NHI.

Major Findings:

1. A tri-racial isolate which has in-married for over 250 years resides in southern Maryland.
2. The prevalence of many genetic diseases is much greater in this group than in the general population.
 - a. Three per cent of this population (152 cases) has dentinogenesis imperfecta. This contrasts with a prevalence of one case per 7,000 to 9,000 individuals in the general population.
 - b. One per cent of the population (47 cases) are albinos. This is the highest rate of albinism reported in humans.
3. The dentin defect has been thought to be as many as six different defects. A study of this population suggests that all the forms reported are only different manifestations of the same defect.
4. The reproductiveness of the average female is very high even in the face of this large defective genetic load. The average female has 5.6 offspring.
5. Some 22 pathological hereditary traits, or traits which we strongly suspect have a genetic factor, have been identified in this population.
6. Some unusual forms of disease or combinations of diseases have occurred. Five cases of a hitherto undescribed bone disease tentatively called "generalized hyperostosis, integrated with leontiasis" have been found. The deaf-mutism is due to agenesis of both the cochlear and vestibular apparatus.
7. Some 26 like groups of people have been identified residing in the eastern United States. A preliminary survey of these groups indicates that they also have a large deficit of manifest genetic disease. These populations comprise some 100,000 individuals. The size, location and surnames of the families comprising these groups have been identified.

Major Findings (Continued):

8. A preliminary analysis of the data from 780 dental examinations tends to indicate that there is a high percentage of the population with low caries scores and low lactobacillus counts. The analysis of the water supplies indicates that there are only minute trace amounts of fluorides (.02 ppm).
9. The preliminary blood typings indicate that there is an unusual distribution of blood type. Of the first 150 typed, none are Rh negative (expected Rh negative - White U.S. 15%, Negro U.S. 8%). Sickling tests indicate that there is an unusual prevalence of the sickle gene.

Significance to Dental Research:

1. Through this study we hope to better define the role of genetic factors in dental disease and disease in general.
2. This program helps in bringing workers in various widespread fields of interest into a common meeting ground in the study of not only human ills, but also the sociological factors involved in the appearance, manifestation and distribution of intrinsic disease.
3. We hope to develop new techniques applicable to epidemiology

Proposed Course of Project:

1. We feel that this one year's work is indicative of a field that should be investigated thoroughly by as many means as possible.
2. The study is planned for a period of five years. It will continue with emphasis on the biochemical aspects for the next four years.
3. A more thorough investigation of other population isolates should be made. We plan to investigate the distribution and prevalence of intrinsic disease in other groups.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 52 (C)
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT TOTAL			PROF	OTHER	TOTAL
17,508	9,790	27,298	2/3	2 1/3	3
FY'57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	3	4	---		
FY'57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

14. (Continued):

NIHID, NCI, NHI, NIMH, NIAMD, Biologics Control, Grants Branch
Howard University, School of Dentistry
Catholic University, Department of Sociology
University of Michigan
Dr. Melvin Alper, Civilian
Library of Congress, Legislative Reference Department
Department of Agriculture - Population Section

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 51 (C)
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956:

Hursey, R. J., Witkop, C. J., Jr., Miklasheck, Doris, and Sackett, L. M.: Dentinogenesis Imperfecta in a Racial Isolate with Multiple Hereditary Defects. Oral Surg., Oral Med., and Oral Path. 9:641-58, June 1956.

Witkop, C. J. Jr., Dyson, Hazel R., and Sackett, L. M.: A Study of Hereditary Defects Occurring in a Racial Isolate Residing in Southern Maryland. Clin. Proc. of the Children's Hospital, Washington, D. C. 12:29-33, Feb. 1956.

Witkop, C. J., Jr.: A Study of Tri-Racial Isolates in Eastern United States. Proc. of the First International Congress of Human Genetics, Copenhagen, Denmark, Aug. 1-8, 1956 (In press)?

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956:

Travel grant of \$380.00 awarded as one of eight contributors sent to attend the First International Congress of Human Genetics by the American Society of Human Genetics.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 53
SERIAL NUMBER

2. _____ 3. Office of the Associate Director
INSTITUTE OR DIVISION LABORATORY, BRANCH, OR DEPARTMENT

4. _____ 5. _____
SECTION OR SERVICE LOCATION

6. Office of the Associate Director (In Charge of Research)
PROJECT TITLE

7. Seymour J. Kreshover
PRINCIPAL INVESTIGATOR

8. Supporting Staff
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

10. PROJECT DESCRIPTION

The Office of the Associate Director (In Charge of Research) has the responsibility for outlining the scope of direct research activities as dictated by the overall dental health needs of the nation. By establishing such programs, providing direction, and reviewing and evaluating their progress, more meaningful application of basic research to clinical problems may be realized. Recognizing the essential of a qualified professional staff to meet these obligations, it is a further responsibility of this office, in cooperation with the laboratory chiefs, to provide selection, organization, and leadership in the various laboratory and branch areas of investigation and a general guidance of the overall intramural program in dental research. Also provided by this office is a general supervision of the Information Officer's activities which develop policies and procedures for a nationwide informational program necessary to the accomplishment of the program objectives, and coordinate information and public relations between the Institute and other segments of PHS and HEW.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11.

SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
29,587	3,460	33,047	1	4	5
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
1	4	5			
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input checked="" type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 53
SERIAL NUMBER

16 - 17 None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 54
SERIAL NUMBER

2. _____
INSTITUTE OR DIVISION

3. Extramural Programs Branch
LABORATORY, BRANCH, OR DEPARTMENT

4. _____
SECTION OR SERVICE

5. _____
LOCATION

6. Extramural Programs Summary Data
PROJECT TITLE

7. F. Earle Lyman
PRINCIPAL INVESTIGATOR

8. Supporting Staff
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

10. PROJECT DESCRIPTION

Calendar year 1956 proved to be the most eventful thus far in the history of the dental research program. A seven-fold increase in total funds available for the extramural program was almost immediately reflected in the increased volume of applications received. With training grants appropriated for the first time, it became possible to assist the various academic institutions toward producing an even higher calibre of dental research investigators.

Research Grants: The 93 research grant applications approved during the year were increased by an additional 21, previously approved but unpaid during the first part of the year because of insufficient funds. This total of 114 applications was paid in the amount of \$859,181. Approximately 200 new and continuation applications, totalling approximately \$2.5 million now await study section and council recommendation for payment from the \$2.7 million appropriated.

Training Grants: Twelve training grant applications were reviewed at the October meeting of the National Advisory Dental Research Council, totalling \$73,501 in excess of the \$475,000 available. (\$25,000 of the total appropriated was set in reserve for projects in Epidemiology and Biometry). Of these 12 applications, 9 were recommended for approval at a total of \$269,809, thus establishing a foundation for support of this essential area of dental research training.

Fellowships: With 212 fellowships already awarded since the beginning of fiscal 1957 in the amount of \$162,388, it is evident that the five fold increase of funds to \$500,000 was in keeping with the needs. Categorically, the applications approved include 20 regular, 1 special and 188 part-time dental student fellowships.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 54
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
60,000	19,000	79,000	2	5	7
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
2	5	7	-----		
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST-	
BIOLOGIC STANDARDS	<input type="checkbox"/>	ANCE	<input type="checkbox"/>

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Form No. ORP-1
October 1956

Calendar Year 1956

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. NIDR - 54
SERIAL NUMBER

16 - 17 None

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. NIDR - 55
SERIAL NUMBER

2. Dental Research 3. _____
INSTITUTE OR DIVISION . LABORATORY, BRANCH, OR DEPARTMENT

4. _____ 5. _____
SECTION OR SERVICE LOCATION

6. Administration of the National Institute of Dental Research
PROJECT TITLE

7. Dr. Francis A. Arnold, Jr.
PRINCIPAL INVESTIGATOR

8. Supporting Staff
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

10. PROJECT DESCRIPTION

Objectives:

The Institute Director establishes with his staff the overall administrative policies under which the institute functions. This area of operation is responsible for seeing that the program objectives are effectively carried out. The staff maintains an effective liaison with other institutes, public and private organizations whose programs closely relate to our research operations.

Significance to Dental Research:

The expansion in our Grants Program from \$521,000 to \$3,600,000 in Fiscal Year 1957 imposed a fairly heavy work load on the Administrative staff during the last six months of the calendar

year. Part of these funds were used to inaugurate a Training Grant Program which required a considerable amount of planning to get the program under way. Due to the increase in the Review and Approval activity for fiscal year 1957, the administrative staff had to expedite the recruitment of staff, the purchase of equipment and acquire suitable space in order that this function be immediately prepared to assume the increased work load incurred by the expansion in the grants area.

Increased effort was directed toward coordinating the research activities, improving our lines of communication, fixing responsibility for certain areas of work, and establishing a more comprehensive internal promotion policy.

The preparation of documents for travel, personnel and supplies more than doubled over the previous years due to the overall program expansion.

During the year our staff worked with the personnel in the Division of Research Service in formulating renovation plans for building 2. During the months of May, June and July we moved the major segment of our staff into the renovated area.

These moves required a considerable amount of planning with the personnel in the Arthritis Institute, due to the exchange of space between building four and two. The move schedules had to be worked out to coincide with the contractors schedule for completing various areas in order to prevent major loss of research time.

Staff time was also allocated to the preparation of plans and specifications for the new dental building. The staff work was performed on this project jointly with the personnel in the Division of Research Services.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. NIDR - 55
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
62,800	37,200	100,000	1	10	11
FY' 57					
BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL	-----		
1	10	11			
FY' 57					

13. BUDGET ACTIVITY:

RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input checked="" type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSIST- ANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. NIDR - 55
SERIAL NUMBER

16 - 17 None

C L I N I C A L

C E N T E R

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13432-33

SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION3. Admissions and Followup Department
LABORATORY, BRANCH, OR DEPARTMENT4. _____
SECTION OR SERVICE5. _____
LOCATION (IF OTHER THAN BETHESDA)6. Organization and administration of Admissions and Followup Department
PROJECT TITLE7. Miss Beatrice N. Marino
PRINCIPAL INVESTIGATOR8. None
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS) IDENTIFY SUCH RESEARCH: (BY SERIAL NO.(S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION:

Objectives: (For 1957)

To correlate the functions of the nursing and clerical staff so that the department can provide the best possible service to the patients and physicians.

To improve the lines of communication within the department.

To broaden and carry out a staff education program.

To study methods of evaluation of personnel performance.

To compile a manual of administrative routines and directions for the department.

Methods employed:

New inpatients, readmissions and first visit of followup patients are all processed in an admitting area of the department. The followup patients are scheduled by receptionists in three different wings of the department which have been assigned to specific institutes on designated days of the week. The transportation unit schedules and provides transportation for patients.

In September, 1956, the initial steps to combine the clerical functions of the department with the nursing services were instituted and the Normal Control Program was separated from the Department.

Progress and Improvement Achieved During the Year:

An increase in staff, providing for better coverage of clinic and Clerical areas.

As a result of definite doctor assignments and of adjusted clinic schedules, patients are seen more quickly, with a minimum of waiting.

ADMISSIONS AND FOLLOWUP DEPARTMENT
STATISTICAL REPORT

JANUARY 1956 --- NOVEMBER 1956

	JAN	FEB	MAR	APR	MAY	JUNE	JULY	AUG	SEPT	OCT	NOV	TOTAL
<u>Admissions</u>	228	185	177	198	184	209	213	197	193	234	322	2340
Inpatients	72	105	79	92	91	94	93	87	83	92	94	982
New Patients	156	80	98	106	93	115	120	110	110	142	115	1245
Readmissions	105	82	103	112	172	87	94	98	104	134	103	1194
Followup (1st Visit)	6	5	10	14	10	14	12	10	10	12	10	113
Walkins	0	1	0	0	1	0	5	0	6	1	0	14
Emergency												

<u>Followup</u>	604	598	593	640	676	643	604	611	594	692	40	203
** Patients	1604	1711	1654	1700	1834	1679	1673	2003	1508	1991	322	2340
** Visits												

Preadmission letters to physician
MAY 1956 --NOVEMBER 1956

<u>Admission letters to referring physicians</u>	12	33	12	33	35	30	25	28	25	28	40	203
	228	185	177	198	184	209	213	197	193	234	322	2340

<u>Patients transported</u>	51	85	142	59	91	66	71	44	41	83	73	806
Car	50	19	26	37	27	19	32	58	39	24	34	365
Ambulance	266	239	343	334	247	298	206	256	234	537	230	3190
Taxi												

<u>Photofluorograms</u>	177	187	182	204	263	181	187	185	187	226	197	2176
All New Patients	125	105	112	115	124	104	88	96	96	114	95	1174
Taken	.70	.56	.61	.56	.47	.57	.47	.52	.52	.50	.48	.54
Percentage taken												

<u>Patients property storage room</u>	37	49	64	71	64	62	62	112	64	73	111	707
Patients serviced	4	8	0	4	4	0	0	5	3	8	5	41
Regular hours												
Weekend & Holidays	53	70	78	107	75	96	96	152	76	86	116	909
Items transferred	4	10	0	6	6	0	0	6	8	11	6	57
Regular Hours												
Weekend & Holidays												

** FIGURES NOT AVAILABLE

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-33
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL	
78,600	78,600	1	12	13	

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
1	12	13	

FY'57

13. BUDGET ACTIVITY:

X RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Not Applicable.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13432-34
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION

3. Anesthesiology Department
LABORATORY, BRANCH, OR DEPARTMENT

4. Anesthesiology Department
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Anesthesiology Department
PROJECT TITLE

7. C. L. Hebert, M.D., Chief
PRINCIPAL INVESTIGATOR

8. J. W. Severinghaus, M.D., (In charge of Anesthesia Research Laboratory),
John E. Merzig, M.D., and M. G. Bransome (Inhalation Therapy)
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OR PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Resembles no other project.

10. PROJECT DESCRIPTION:

Description of objectives and activities of Anesthesiology Department, Clinical Center

Objectives:

The primary objective of the Anesthesiology Department has been to provide safe anesthesiological care and supportive therapy for patients undergoing therapeutic and diagnostic surgical procedures carried out by the surgical services of the several Institutes. Secondly, we have provided all types of inhalation therapy as part of the medical treatment of Clinical Center patients.

Form No. ORP-1 (Cont'd)
Serial No. 13432-31.

Calendar Year 1956

3. The cardiac monitoring device, the Telecor, was devised and constructed.
4. A new type of demountable plastic tub for cooling or warming patients on the operating table was devised and constructed.
5. A new project was begun in measuring blood oxygen tensions by polarographic means. Work was done in collaboration with the surgical clinic of NHI in devising an extra corporal circulation apparatus.

ANESTHESIOLOGY DEPARTMENT
STATISTICAL REPORT

PART I - ANESTHESIOLOGY

12 MONTHS OF DECEMBER 1955 - NOVEMBER 1956 INCLUSIVE

Administration of Anesthesia and Supportive Therapy for Surgical Procedures.

	A n e s t h e s i a T i m e - - - H o u r s												Total No. of Operations	Standbys			
	-1/2	-1	-1 1/2	-2	-3	-4	-5	-6	-7	-8	-9	9+		Pts.	Time		
INSTITUTES																	
CANCER	9	29	29	19	43	37	45	17	11	14	6	5	264	8	4 hr 56 min		
MENTAL	1	3	2	2				1					9	1	1 hr 15 min		
HEART	13	24	18	20	50	33	21	16	15	6	5	1	222	10	22 hr 40 min		
DENTAL	17	6	2	3	2	2							32				
ARTHRITIS	1	5	4	7	4	3	4	1	1				30	1	50 min		
NIAID	2	7	11	6	2	1							29	1	15 min		
NEURO.	3	29	52	35	32	21	8	19	14	11	7	5	236	2	3 hr 40 min		
TOTAL	46	103	118	92	133	97	78	54	41	31	18	11	822	23	33 hr 36 min		

ANESTHESIOLOGY DEPARTMENT
 STATISTICAL REPORT
 PART II - INHALATION THERAPY
 12 MONTHS OF DECEMBER 1955 - NOVEMBER 1956 INCLUSIVE

INST	Oxygen Tent Therapy		Humidity Tent Therapy		Oxygen by nasal catheter or mask		Aerosol Therapy		I.P.P.B. combined with aerosols		Respirators		Rocking Beds		Misc. Special Treatments		Gas Mixtures	
	Pt.	Hrs.	Pt.	Hrs.	Pt.	Hrs.	Pt.	Tr.	Pt.	Tr.	Pt.	Days	Pt.	Days	Pt.	Hrs.	Pt.	Hrs.
NCI	49	4205	12	907	45	1621	65	5279	23	848			9	512	3	12		
NIMH	1	17	1	1	1	23												
NHI	35	2624	69	4738	19	555	7	188	23	2422			2	99	5	165		
NIDR																		
NIAMD	2	96	2	97	3	101	3	162										
NIAID	9	1434	34	9809	3	105	8	832	1	4	3	38			6	335	1	9
NINDB	11	272	6	172	8	85	2	132			1	1			6	46		
TOTAL	107	8648	124	15724	79	2490	85	6593	47	3274	4	39			23	992	9	186

Regular teaching and demonstration sessions (1½ hours each) in use of Inhalation Therapy equipment were held for 152 Professional Nurses, 42 Practical Nurses, and 89 clerks and attendants.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-34
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS		MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
102,900	102,900	6	4	10

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
7	5	12	

FY'57

13. BUDGET ACTIVITY:

X RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

During the first six months of the year Dr. John W. Severinghaus conducted the Anesthesia Research Laboratory under the auspices of NHI. Research activities of this laboratory were as follows:

1. Studies of respiratory physiology in man with particular reference to the dead space were carried out.
2. Studies were made of the temperature gradients during hypothermia in dogs and man. These studies indicated that the esophageal temperature gave a truer index of the core temperature of the body.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. 13432-34
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956.

Severinghaus, J. W., "The Telecor: An esophageal probe monitoring device for body temperature, stethoscopic sounds and an audible EKG." Submitted to the Review of Scientific Instruments.

Stupfel, M., and J. W. Severinghaus, "Internal body temperature gradients during anesthesia and hypothermia and the effect of vagotomy". J. Applied Physiology. In press.

Severinghaus, J. W., and M. Stupfel, "Effects of hypothermia on pulmonary function". Presented at Federation Meeting, Atlantic City, N. J.

The above papers originated from the work done by Dr. Severinghaus and his group.

Ebert, C. L., L. R. Radigan, Jr., and J. W. Severinghaus, "Management of Patients during Hypothermia". Presented at Congress of Anesthetists, Miami, April 14, 1956. To be published in Current Researches Analgesia and Anesthesia, Jan. 1957.

The above paper originated from our clinical experiences utilizing hypothermia.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956:

Mr. M. G. Bransome, Inhalation Therapist, was given a cash award for continuous sustained performance of duties during a nine month period ending April 1956.

Methods and Laboratory Controls:

Standard laboratory test procedures were modified to increase precision and reproducibility and controls were instituted to avoid errors. In cooperation with the Chiefs of the Hematology and Clinical Chemistry, the Control Laboratory instituted surveys of blood chemistry and counting operations utilizing standardized pooled serums and patient sample results for daily control charts. Control charts were maintained for sodium, potassium, cholesterol, phosphorus, white blood counts, red blood counts, hemoglobin determinations and mean corpuscular hemoglobin determinations. These charts indicated excellent control of the general accuracy and reproducibility of test procedures during the test periods. Occasional discrepancies were detected and analyzed to determine and correct the causes. (Ref. appended chart).

In addition, the Control Laboratory Service completed the evaluation of calcium determination in blood and urine by flame photometry and established this as a routine procedure in the Clinical Chemistry Service. They continued studies on the dye binding properties of blood albumin because there are occasional patients whose dye binding capacity is considerably out of the normal range and unexplained. The study must be continued to determine the cause for this phenomenon because the dye binding capacity is the basis for determining blood albumin. Paper electrophoretic technique for serum proteins and hemoglobins was set up, evaluated by comparison with the Tiselius method and instituted as a routine measure for study of patients' samples. A project to examine and evaluate the more sensitive methods for determination of serum magnesium has been started and will be continued in order to select the most sensitive and yet most reliable method for routine use. Methods have been set up for determination of urinary 17 keto steroids and corticoids and early in 1957 we hope to establish these as routine procedures. During the last six weeks we have started to evaluate an autoanalyzer from the Technicon Company of New York. This instrument was developed by Dr. Skeggs of Western Reserve University Medical School for automatic accurate analysis of blood sugar and urea nitrogen. It utilizes well established chemical procedures on the basis of comparative concentrations and continuous flow spectrophotometry and records the results at the rate of 40 per hour. If found practical, reliable, and accurate, it will contribute very much to efficiency in our department.

Services:

During the calendar year of 1956, 244,509 laboratory test procedures were performed and reported on an average patient census of 302 in the 6 Institutes for a total of 93,879 patient-work-days. The

accompanying chart and table depict the rate of increase as well as the absolute levels of test procedures performed and relates them to the average patient census for each month of the calendar year and the number of patient-work-day - follow-up visits.

Problems:

Personnel and workload:

The major problems during the present year were due to disproportionate workload in relation to the available technical staff and difficulties of obtaining specimens early enough each morning to start the day's work at 8:30. The attrition rate of personnel in our department for this year was 23%. Only recruiting of technologists is still difficult because of the short supply of well-qualified persons in this field and the marked disparity in salary scale for technologists in medical laboratories in comparison to positions with higher grades and salaries they can obtain in clinical and basic research laboratories.

Recruitment has been slow and discouraging for new positions and replacements due largely to the lack of qualified candidates and the delays in the Civil Service Commission of grading examinations. An attempt was made to correct this situation by requesting authority from Civil Service to establish a training school for medical technologists in our department. Authority was refused by Civil Service Commission on the grounds that the GS-3 registry is ample to fulfill our needs. In reply to an invitation from Civil Service Commission, we submitted recommendations for reclassification and addition of a new professional series of medical technology called "Clinical Pathology Technologists" patterned on standards of Bacteriologists, Biologists and Chemists, starting with college graduation at grade 5.

During the year an exhibit of Medical Technology in the Clinical Center was constructed by the Medical Illustration Department. It will be loaned to the colleges in nearby states.

Progress:

During the calendar year, further improvements, stream-lining and shortening test procedures were accomplished. The organization of the individual laboratories was improved to increase efficiency in time and effort expended by technologists. Examinations are accomplished by grouping specimens into large batches for each analytical procedure.

As mentioned in the annual report for 1955 under "Plans", the management analysis group of NIH were invited to assist the staff of Clinical Pathology Department in a survey study for more efficient operation.

In the area of mechanization and improved instrumentation, the Coulter Electronic Counter is now an integral part of our hematology operation. It saves time of one to two technologists and has increased the capacity of our laboratory. Similar evaluations of the Arithmometer and Chemical Blood Autoanalyzer are under way. Devices for automatic high-speed pipetting and automatic chloride analyses are under study.

Significance of the Activities of the Clinical Pathology Department to The Clinical Research Program:

The diagnostic laboratory procedures and follow-up evaluation of patients by chemical, hematological, and microbiological procedures are basic to all clinical research. As expected, proper care of research patients requires much more than customary laboratory examinations. The division of so-called "patient care procedures" and "research procedures" is impossible in daily practice in a research hospital. Furthermore, when a patient is under treatment by a new procedure, it is to the best interests of the patient and mandatory for his proper care that repeated and pertinent laboratory tests be done to avoid unexpected or hazardous situations. The laboratory data are also of much importance in proper evaluation of the clinical research observation. The amount of clinical pathology required depends considerably on the type of clinical research; as indicated in the following table. Very ill patients in NCI and NIAID require two or three times the patient laboratory care demanded by metabolic and surgical problems.

Average Monthly Test-Procedure Volume by Patient Categories

	<u>1956</u>
Cancer	128
Metabolic	49
Heart	63
Microbiological	125
Neurological	24
Mental	7
Dental	69

Examples of Progress and Significance of Special Procedures and Services Required by the Research Nature of the Patients in the Clinical Center

Diagnostic Virology

For the past two and a half years there have been frequent requests for diagnostic virology service. A Virology Diagnostic Laboratory was included in the original plans for Clinical Pathology, but the need had

not been sufficient to justify diversion of our main efforts into this area until now. A survey of the actual needs and available services in diagnostic virology were completed in November. This survey and conferences with the Clinical Directors involved indicate that provision of diagnostic virology in the Clinical Center constitutes an actual need which will increase considerably in the future, and must be solved soon by either contracting this work to an outside agency or by developing our own screening facility in Clinical Pathology.

Clinical Chemistry

The following procedures were established for examination of patient specimens, in addition to the procedures which had been offered the previous year.

Choline Esterase

Ascorbic Acid

Blood pH

Serum protein paper electrophoresis

Paper chromatographic identification of urine sugars

Blood protein-bound iodine

Fecal fat

Fecal Urobilinogen

Hematology

A new fibrinogen method has been developed which utilizes a method of direct reading on the DU spectrophotometer without the necessity of micro Kjeldahl digestion. A new Arithmometer was designed with modifications and improvements suggested by our evaluation last year. We are now retesting its usefulness for white cell counting. This should save considerable technologist time if it is proven reliable and accurate.

Microbiology

Phage typing of enteric organisms has been instituted and a study of the chromogenic acid fast organisms from Clinical Center patients is under way to distinguish them from pathogenic tuberculosis organisms.

Adaptation of Research Technics. The ultraviolet television microscope has been utilized further for examination of fresh bone marrow preparations for correlation with diagnostic information from phase microscopy and stained smears.

Proposed Activities for the next calendar year

The objectives of this Department in patient service are such that clinical pathology procedures with new applications from the research fields of medical physics, medical chemistry, and medical biology, will be required as long as the Clinical Center operates for clinical research. In addition, specific objectives include further emphasis on evaluation and development of instrumental and mechanical methods for improving the speed and accuracy of diagnostic procedures. We are in the process of establishing methods for determination of urinary keto steroids and corticoids and plan to thoroughly study our glucose method for standardization of the autoanalyzer and to evaluate the accuracy of the current technics. It has been found recently that it will be necessary to check the methods now utilized for determination of urine urea.

Control Charts on standard pooled frozen sera will be continued in all areas where applicable in order to closely watch the accuracy and reproducibility of our methods. Continued studies will be done to establish the accuracy and to improve the reproducibility of methods for serum magnesium and other similar analytical procedures as problems develop.

As indicated above, the need for diagnostic virology is becoming more important and several alternative plans for solving this problem will be submitted for consideration.

1956

	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total	Av.	Increase No. %
Av. Pt. Census	285,34	304,5	301.1	299.72	298.64	308.28	307.71	296.73	283	313.7	331	302.7	3632.42	302.7	36 13
Pt. Workday	5993	6090	6624	6294	6570	6474	6462	6825	5378	7214	6620	6413	76957		8265 12
Test Procedures	18,362	18,981	19,846	19,870	20,931	18,353	20,860	22,876	18,020	23,935	22,099	20,376	244,509		68,199 39
Test / Pt. Wkd.+FU	2,54	2,60	2,05	2,65	2,66	2,39	2,69	2,6	2,8	2,7	2,46	2,56	30,7	2,56	.36 16
Test / Patient	63	61	64	65	69	58	66	75	62	74	65	66	788	66	12 22
Technical Staff	37.7	37.7	38.8	39.1	40.6	38.8	37.6	38.1	38.4	39.5	41.2	38.9	466.4	38.9	9 30
Test / Tech / Day	23.2	25.2	23.3	24.0	23.4	22.5	26.4	26.1	24.7	26.3	26.8	24.7	296.6	24.7	.3 1.2
						Average	Tests Per Patient								
NCI	111	112	126	135	138	120	123	141	129	150	118	128	1531	128	
NIAID	130	126	137	128	135	108	119	138	98	125	130	125	1499	125	
NHI	54	49	51	60	60	46	107	73	59	71	61	63	754	63	
NIAMD	53	51	44	37	50	42	36	66	48	59	51	49	586	49	
NIINDB	29	23	24	20	23	19	23	25	23	25	25	24	283	24	
NIMH	4	5	7	9	10	7	5	8	4	8	8	7	82	7	
NIDR	135	108	67	61	67	52	39	35	67	79	49	69	828	69	

ORGANIZATION CHART

CLINICAL PATHOLOGY DEPARTMENT

Chief, G. Z. Williams, M. D.
Mrs. Arnold, Secretary

Laboratory Services

<u>Clinical Chemistry Service</u>	<u>Hematology Service</u>	<u>Microbiology Service</u>	Laboratory Control Service
Chief, Dr. Elizabeth Frame Asst. Clin. Chemist-Mr. Nishi Residents-Dr. Herrold Dr. Hicklin	Chief, Dr. George Brecher Asst. Hematologist-Dr. Peden Residents - Dr. Dutcher Dr. Bellomy	Chief, Dr. Ernest Singer Virologist-Dr. Lee Resident-Dr. Kirschstein	Chief, Dr. Ness Asst. Chemist - Mr. Dickerson
Nitrogen Laboratory Medical Tech. Supvr. GS-7	Blood Coagulation Laboratory Medical Tech. Supvr. GS-7	Screening Culture Lab. Medical Tech. Supvr. GS-7	
Electrolyte Laboratory Medical Tech. Supvr. GS-7	Blood Counting Laboratory Medical Tech. Supvr. GS-7	Special Bacteriology Lab. Medical Tech. Supvr. GS-7	
Steroid-Lipid Laboratory Medical Tech. Supvr. GS-7	Blood Cytology Laboratory Medical Tech. Supvr. GS-7	Mycology & Parasitology Lab. Medical Tech. Supvr. GS-7	
Enzyme Laboratory Medical Tech. Supvr. GS-7	Hemoglobin Laboratory Medical Tech. Supvr. GS-7	Virology Laboratory Medical Tech. Supvr. GS-7	Special Procedures Chief, Dr. Peacock
Metabolic Function Laboratory Medical Tech. Supvr. GS-7		Serology Laboratory Medical Tech. Supvr. GS-7	

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-37
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATION		MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
488,100	488,100	14.5	59.5	74

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
15	61	76	

FY'57

13. BUDGET ACTIVITY:

RESEARCH (SERVICE) <input checked="" type="checkbox"/>	ADMINISTRATION <input type="checkbox"/>
REVIEW & APPROVAL <input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE <input type="checkbox"/>
BIOLOGIC STANDARDS <input type="checkbox"/>	

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

NCI (research project of Chief-George Z. Williams, Serial No. 201
 NCI-Field Investigation Branch (test evaluation-Dr. Peacock,
 Serial No. 112)
 NIAMD-Hematology Section (research project of Dr. Brecher
 Serial No. 86)

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. 13432-37
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956:

Evaluation of Electronic Red Blood Cell Counter by George Brecher, M. D., Marvin Schneiderman, M. A., and George Z. Williams, M. D,

Direct Observation of Cellular Absorption by Ultraviolet Television Microscopy by George Z. Williams, M. D.

A Study of the Penn-Hall Seroflocculation Reaction for Cancer, by Andrew C. Peacock, Ph.D. and George Z. Williams, M. D.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956.

Cash Awards made to following personnel:

Kathryn Hilliard, Jullia Pastewka, Dorothy Egan, Martha Schoonover, Jeanne Brown, Anne Jennings, Anne Stampe, Dorothy Moore, Sarah Tupy, Roena Bayes, Minna Feld, Anastasia Stanley, Henry Dickerson.

Letter of Commendation awarded to following personnel:

Janet Brooks, Joan Dorman, William C. Bowie, Jr., Mary Johnston, Thomas Rayford, Caroline A. Rowan, Vivian Thierry, Ada Murphy, Alice Wayerski, Rema J. Gillette.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13432-36
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION

3. Professional Services Dept.
LABORATORY, BRANCH, OR DEPARTMENT

4. Dental Department
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Dental Department
PROJECT TITLE

7. Dr. Ralph S. Lloyd
PRINCIPAL INVESTIGATOR

8. Dr. Herbert Swerdlow, Dr. John H. Duffy, Dr. Jerry D. Niswander,
Dr. Norman Buckman
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS) IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable

10. PROJECT DESCRIPTION:

Project: Dental Department, Clinical Center

OBJECTIVES:

The objective of this Department is to provide a complete diagnostic and dental treatment service for the various institutes of the National Institutes of Health.

Methods employed:

It is the aim of the dental department to perform a complete dental examination on every patient when requested. Recommendations for treatment were made and where requested, dental treatment was rendered to those examined. Full mouth dental radiographs were included in every dental examination.

Number and Kinds of Major Services Rendered:

The Dental Department is prepared to and did render every type of dental treatment which was found necessary to perform on the patients examined. The number of dental treatments are still progressively increasing from month to month, just as they were last year. It is not our aim to render complete dental treatment for all of the patients who are admitted to the Clinical Center. We do, however, attempt to perform dental treatment on those patients which would aid research. There are many patients who could not, because of their physical condition obtain dental treatment from any other source. A great percentage of the patients of the Clinical Center are in need of dental services, and it is our impression that many of them could not afford the same, and that many of them have dental conditions which directly affect their health, and their utilization in research projects in other Institutes. We attempt to determine if the patients have a private dentist, and if they can afford the services of a private dentist. If at all possible, we recommend that they return to him to have their work completed.

Major Problems Encountered:

The dental staff has reached the point where it is complete, according to our organization plans laid out previously. There are no further plans for additions to the staff, unless it is determined that a change in conditions regarding the treatment of patients or demand for services shows such a need. We are, so far, meeting all the requirements demanded of us, and anticipate that we will be able to satisfactorily do the same in the future with our present organization.

We have obtained the services of a young orthodontist, assigned to the Growth and Development Section of the Nation Institute of Dental Research. He is handling our obligations encountered in the Clinical Research in this area by previous investigators. He is, also planning some clinical research projects.

Arrangements have been made with the Chief of our Pharmacy Department, for them to take over the responsibility for handling our supplies. The supplies have created a problem in our area, because we have had no one on our staff who could accept this responsibility according to their job description and job rating.

Important Progress Achieved:

Arrangements have been made for a meeting of the D. C. Dental Society to be held in the Clinical Center this year. Perhaps, this would be a significant contribution by us, if it were continued from year to year. Without question, it would serve as a means of advertising our needs for patient referral in research projects of all Institutes. The assigning of patients' beds to the National Institute of Dental Research, was accomplished sometime previously. The patient responsibility, and these inpatients, were assumed in part by the staff of the dental department.

The Committee of Hospital Accreditation of the American Dental Association inspected the hospital during the past year, and we were assured that we would be approved in due time, after the meeting of the National Committee. Plans are being instituted for a dental residency training program in the field of oral pathology. So far, it is agreed that the responsibility for this program should rest in the Chief Dental Officer of the Clinical Center.

Significance to Clinical Research Program:

Many clinical projects of other institutes were facilitated by dental treatment. Rehabilitation of masticatory apparatus in debilitated patients was of help. Emergency dental procedures are constantly arising wherever a large number of patients are assembled, and were successfully treated in every case. Many special dental consultations related to patient care were handled. The dental department furnished facilities, and in some cases some personnel time for clinical dental research.

Several clinical research projects are being participated in by the staff of the Dental Department. A study of the effects of premature contacts on the health of the periodontium is still under way. Dr. Swerdlow, a member of the staff of the Dental Department, has completed a significant study on the effect of high speed drilling techniques on the health of the dental pulp. This has been reported at several meetings, and plans are under way for other such reports and publications. Dr. Lloyd gave a paper at the Society for Cleft Palate Rehabilitation at their annual meeting on the utilization of the cephalometer in the position of the bulb obturator. This is being published in "The Journal of Prosthetic Dentistry." A number of other clinical studies by the staff of the National Institute of Dental Research, required the facilities of the Dental Department, and the assistance of our staff.

In the field of maxillo-facial prostheses, a number of patients of the National Cancer Institute, The National Institute of Neurological Diseases and Blindness, and The National Institute of Arthritis and Metabolic Diseases were benefited by special prosthetic devices. Clinical research in methods of treatment of cleft palate patients utilizing prosthetic devices is under study.

Proposed Course of Project:

A member of the staff of the Dental Department, Dr. Peter J. Coccaro, was detailed to post-graduate School of Orthodontia and Growth and Development at the Eastman School of Medicine and Dentistry, Rochester, New York. He will be in training for two years. So far, the first portion of his training has been paid for by the Clinical Center.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-36
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL	
123,000	123,000	6	12	18	

FY '57

BUDGETED POSITIONS			PATIENT DAYS	
PROF	OTHER	TOTAL		
6	14	20		

FY '57

13. BUDGET ACTIVITY:

RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

The Dental Department has instituted several cooperative research studies in conjunction with the National Institute of Dental Research. They are:

1. The effects of premature contacts and trauma on health of the periodontoclasia.
2. Tissue resistance.
3. Stomatitis and gingivitis.
4. Affects of drilling techniques on the dental pulp.
5. Cleft palate prosthetics.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. 13432-36
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956:

"Prosthetic Rehabilitation of A Cleft Palate Patient Subsequent To Multiple Surgical and Prosthetic Failures."
Ralph S. Lloyd, D.D.S.
Published in "The Journal of Prosthetic Dentistry."

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956:

Not applicable.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13432-35
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION

3. _____
LABORATORY, BRANCH, OR DEPARTMENT

4. Diagnostic X-ray Department
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Diagnostic X-ray Department
PROJECT TITLE

7. Dr. Theodore F. Hilbish
PRINCIPAL INVESTIGATOR

8. Dr. Eugene L. Bronstein, Dr. Byron E. Besse, Jr., Dr. Lee B. Lusted
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable

10. PROJECT DESCRIPTION:

Project:

Diagnostic X-ray Department, Clinical Center.

Objectives:

The objective of this Department is to provide a complete diagnostic radiological service for the various Institutes of the National Institutes of Health.

Methods Employed:

In order to accomplish the above objectives, trained personnel and suitable X-ray equipment were procured. All types of radiographic examinations were performed during calendar year 1956.

Number and Kinds of Major Services Rendered:

A total of 29,964 X-ray examinations, exclusive of animal radiography and photofluorograms, were performed during the 12-month period from December 1, 1955 through November 30, 1956*.

Table I reflects the workload by Institute on a monthly basis for both inpatients and outpatients. Table II portrays the same data by Institute on an annual basis. The special radiographic studies consummated during the 12-month period specified are depicted in Table III.

As in preceding years, numerous radiographic procedures were completed upon request on animals. It is anticipated that animal radiography will be materially expanded in 1957 when full-time animal radiographic equipment is available in the Clinical Center.

A total of 3420 photofluorograms were procured, processed and interpreted by the Diagnostic X-ray Department. Approximately one-half of this number represents films on outpatients and hospital admissions. The other half were photofluorograms obtained on employees during the annual chest X-ray screening program at the National Institutes of Health.

In addition to extensive radiological services provided, a series of lectures were initiated for staff members of the Clinical Center. These lectures were undertaken on the request of numerous physicians. These involve didactic instruction on the various phases of diagnostic radiology.

Major Problems Encountered:

The one outstanding problem that plagued the Department throughout the year was the difficulty of employing X-ray technicians. As

*This period was adopted since data were available for these months. If December 1956 were utilized instead of December 1955, approximately 400 additional studies would have been reflected in the total number of X-ray examinations.

the workload steadily increased throughout the year, the need for additional technicians became more acute. Several suitable candidates were located but technician register requirements, clerical shortages, and Civil Service delays, frustrated all attempts at employing technicians. Not a single, full-time, permanent X-ray technician was secured during the 12-month period specified above. As of this writing, it appears that two full-time technicians will be employed during December 1956. This will meet, in part, the immediate needs of the Department but real effort will be required and expended in an attempt to alleviate this same problem during the ensuing year.

Important Progress Achieved:

A Seimen's Universal Planigraph was installed providing special facilities for horizontal and vertical laminography. This unit will also be used for intravenous pyelography when the requested self-centering tray and the special multi-film holding cassette are delivered.' This equipment permits as many as six laminographic films on a single X-ray exposure, thus appreciably reducing the X-radiation to patients and greatly decreasing the time of examination.

Plastic tubes for transportation of exposed but undeveloped films from radiographic rooms to the darkroom were perfected and put into active use. These tubes have proved to be very valuable and are free of repair and replacement problems.

Double banks of X-ray film view boxes were installed in staff viewing rooms. These view boxes have greatly facilitated the interpretation of multi-film serialographic X-ray examinations. A "gravity-grip" type of film holder was designed by the Department. This has proved to be more efficient than commercial devices and the cost is but a fraction of similar products on the market.

A complete diagnostic radiological service was provided for all Institutes at the Clinical Center. All requests for radiological studies were fulfilled and many special radiographic procedures were accomplished.

Significance to Clinical Research Program:

As in preceding years, the majority of the clinical research programs in progress at the Clinical Center were dependent on X-ray control. The evaluation of the efficacy of many drugs, viruses, and antibiotics, as well as radiographic therapy was dependent on periodic X-ray examinations. Many of the research studies could not have been undertaken without the service provided by the Diagnostic X-ray Department.

Proposed Course of the Project:

The activities of the Diagnostic X-ray Department will be governed to a large extent by the needs of the Institutes. Any type of diagnostic procedures requested will be accomplished by the Department, if at all possible. Toward this end, special radiographic techniques have been and will continue to be developed within the Department. Likewise, special equipment will be procured or designed to meet the requirements. Every effort will be expended to provide films of excellent diagnostic quality in order to facilitate and guide research activities by the various Institutes.

TABLE I

NUMBER OF X-RAY EXAMINATIONS
(December 1955 through November 1956)

MONTH	INSTITUTE (By Type of Patient)																TOTAL
	NCI		SMT		M1AD		M1AD		M1H		M1DB		M1DA		M1S		
	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	In- Pt.	Out- Pt.	
DEC.	532	191	123	27	138	67	117	55	5	--	204	90	10	5	--	532	2096
JAN.	739	204	219	39	111	77	159	47	29	1	244	78	20	5	--	443	2415
FEB.	566	200	183	59	224	101	223	37	16	--	220	70	36	3	--	515	2453
MAR.	649	177	219	76	176	92	139	62	25	--	227	91	7	16	--	578	2534
APR.	663	254	217	36	211	85	134	37	27	2	242	86	11	4	--	557	2566
MAY	766	258	205	56	174	98	116	47	29	3	289	72	17	2	--	582	2714
JUNE	761	233	234	76	145	66	130	36	35	--	226	60	13	5	--	719	2739
JULY	719	190	198	68	159	60	145	65	10	--	292	62	22	3	--	399	2392
AUG.	692	234	199	72	169	63	115	71	15	3	267	26	12	4	--	596	2538
SEPT.	549	195	205	35	163	53	122	52	12	--	238	67	10	9	--	487	2197
OCT.	673	286	241	42	219	69	234	62	23	4	263	42	10	2	--	683	2853
NOV.	610	217	245	51	189	79	172	73	25	--	213	75	13	5	--	500	2467
TOTAL	7919	2639	2488	637	2078	910	1806	644	251	13	2925	819	181	63	--	6591	29964

TABLE II
NUMBER OF X-RAY EXAMINATIONS
 (December 1955 through November 1956)

INSTITUTE	INPATIENTS	OUTPATIENTS	TOTALS
NCI	7919	2639	10558
NHI	2488	637	3125
NIAID	2078	910	2988
NIAMD	1806	644	2450
NIMH	251	13	264
NINDB	2925	819	3744
NIDR	181	63	244
INSTITUTE TOTALS		5725	23373
EHS		6591	6591
TOTALS	17648	12316	29964

TABLE III
SURGICAL PROCEDURES PERFORMED IN DIAGNOSTIC X-RAY DEPARTMENT
(December 1955 through November 1956)

MONTH	T Y P E O F S P E C I A L P R O C E D U R E									
	ANGIOCARDIO-GRAMS	AORTO-GRAMS	INTRACARDIAC OR AORTIC CATHETERIZATIONS	CEREBRO-ARTERIO-GRAMS	BRONCHO-GRAMS	CYSTOSCOPY AND CYSTO-GRAMS	MYELO-GRAMS	PNEUMOENCEPHALOGRAMS & VENTRICULO-GRAMS	SIALOGRAMS	MISCELLANEOUS SURGICAL *PROCEDURES
DECEMBER	9	3	2	5	1	1		18	3	
JANUARY	13	2	4	2	5		1	23	8	2
FEBRUARY	8	1	1	4	1	1	3	15	12	
MARCH	11	4	7	3		1	1	26	3	3
APRIL	9	2	2	3		3	1	12	1	
MAY	9	1	1	6		3	1	11	3	
JUNE	8	4	1	9		4		14		
JULY	2	4	4	6		3	1	11	2	
AUGUST	13	6	3	5		3		19		
SEPTEMBER	4	1	1	7	3	3	1	11		
OCTOBER	9	2	1	6		5	2	14		1
NOVEMBER	9	6	2	5	2	2		2		1
TOTAL	104	36	29	61	12	29	11	176	33	7

*Miscellaneous Surgical Procedures includes: Duodenal Drainage; Splenograms; Femoral Venograms; Urogenital Sinus Injections; Fistula Injection.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-35
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
	171,200	171,200	5	22	27

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
5	23	28	

FY'57

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|-------------------------------------|-------------------------------------|--------------------------|
| X RESEARCH | <input checked="" type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Funds for operation of the Diagnostic X-ray Department are provided by the Institutes on a pro-rata basis. The major function of the Department is that of research service. However, certain research studies, of a more or less independent nature, are undertaken by the Department in cooperation with pharmaceutical companies. Likewise, equipment improvements and diagnostic techniques are developed through experience. Several such activities undertaken during the past year are listed as follows:

The efficacy of teridax and telepaque was evaluated as contrast agents in cholecystography. These products were provided to the Department without charge by the respective pharmaceutical companies. This investigation lead to the conclusion that telepaque was more effective and better tolerated than teridax.

A similar investigation was conducted on a cooperative basis utilizing the products of miokon, renografin, and hypaque. This study revealed that hypaque was the most suitable product for intravenous pyelography.

A "gravity-grip" X-ray film holder was designed within the Department and fabricated by the Metal Shop in the Clinical Center. This type of holder was installed throughout the Department at a very low cost and proved to be very efficacious, facilitating the rapid interpretation of films.

As indicated previously, a plastic cylinder for film transportation was designed and produced within the Clinical Center. This film container has expedited the handling of films and has circumvented the necessity of frequent repairs such as were encountered with the use of our previous metal cylinders.

PUBLIC HEALTH SERVICE -- NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications 15. 13432-35
SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

McAfee, John G.; Hilbish, Theodore F.; and Stewart, K. Royal, "Angio-
cardiography in the Preoperative Diagnosis of Mitral Stenosis and
Insufficiency." RADIOLOGY, Vol. 67, No. 6, 321-332, September 1956.

Hilbish, T. F. "Roentgen Manifestations of Malignant Melanoma."
Accepted for publication by the AMERICAN JOURNAL OF ROENTGENOLOGY,
RADIUM THERAPY AND NUCLEAR MEDICINE.

Hilbish, Theodore F., and Cooley, Robert N. :Congenital Mitral
Stenosis; Roentgen Study of Its Manifestations." AMERICAN JOURNAL
OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE, Vol. 76,
No. 4, 743-757, October 1956.

Rubin, Philip, and Besse, Byron E., Jr. :The Sialographic Differentia-
tion of Miklicz's Disease and Mikulicz's Syndrome." Accepted for
publication by RADIOLOGY.

Besse, Byron E., Jr.; Dahlin D.; Pugh, E.; and Ghormley, R.
"Aneurysmal Bone Cysts - Additional Considerations." CLINICAL
ORTHOPEDICS, April 1956.

Bronstein, Eugene, "Angiocardiography Today" CATHODE PRESS, Vol. 13,
No. 1, February 1956.

Lusted, Lee B. "Medical Electronics, a Rapidly Expanding Field."
RADIOLOGY October 1956.

Lusted, Lee B., and Miller Earl R. "Progress in Indirect
Cineroentgenography." THE AMERICAN JOURNAL OF ROENTGENOLOGY, RADIUM
THERAPY AND NUCLEAR MEDICINE. Vol. 75, No. 1, January 1956.

Lusted, Lee B., and Pickering, Donald E. "The Hypothyroid Infant and
Child." RADIOLOGY, Vol. 66, No. 5, 708-18, May 1956.

Lusted, Lee B.; Mortimore, Glenn E., and Hopper, James Jr. "Needle
Renal Biopsy Under Image Amplifier Control." THE AMERICAN JOURNAL
OF ROENTGENOLOGY, RADIUM THERAPY AND NUCLEAR MEDICINE. Vol. 75,
No. 5, 953-55, May 1956.

Lusted, Lee B.; Miller, Earl R. "An Electronic Position Timer for the Fluoroscope." RADIOLOGY, Vol. 67, No. 2, 259-262, August 1956.

Morel, Joseph M. "Technicians' Vacation Periods." X-RAY TECHNICIAN, Vol. 27, No. 2, September 1955.

Pickering, D. E.; Lusted, Lee B.; Foran, R. F.; and Crane, J. T. "Chemical Growth Dynamics of the Skeleton in the Immature Rat." A.M.A. JOURNAL OF DISEASES OF CHILDREN, Vol. 92, pp. 292-296, September 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956:

Mr. Joseph M. Morel, Chief X-ray Technician, received an award of \$100 plus an award certificate for the development of a balsa wood head holder for use in conjunction with cerebroarteriography. The award was presented to Mr. Morel by the Chairman of the Incentive Awards Committee during a department staff meeting in March 1956.

Mr. William H. Plante received first prize for his exhibit on laminography which was presented at the Mid-Eastern Conference of X-ray Technicians in November 1956.

Mr. Joseph M. Morel was appointed as General Chairman of the forthcoming Second International Convention of X-ray Technicians to be held in Washington, D. C. in June 1957.

Dr. Lee B. Lusted was reappointed National Vice-Chairman of the Professional Group on Medical Electronics of the Institute of Radio Engineers.

The Chief of the Department presented a paper at the Eighth International Congress of Radiology in Mexico on the subject "Selective Intracardiac Angiocardiography." He was also delegated as a representative of the American College of Radiology at the 50th Anniversary Celebration of the Pure Food and Drug Law.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13432-45
SERIAL NUMBER2. Clinical Center
INSTITUTE OR DIVISION3. Medical Record Department
LABORATORY, BRANCH, OR DEPARTMENT4. Professional Services Department
SECTION OR SERVICE5. _____
LOCATION (IF OTHER THAN BETHESDA)6. Medical Record Department - Annual Report
PROJECT TITLE7. Gloria S. Burich, R.R.L., Chief, Medical Record Department
PRINCIPAL INVESTIGATOR8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION:

To insure the accuracy and completeness of all medical records of patients registered at the Clinical Center; to constantly examine their contents and maintain the standard of the Clinical Center and the Joint Commission on Accreditation of Hospitals.

To maintain permanent indexes on diseases and manifestations and operations according to the Standard Nomenclature of Diseases and Operations for the purpose of providing basic data to physicians conducting medical research.

To maintain a permanent index on clinical research projects, a compilation of which is distributed at regular intervals to authorized administrative, clinical and research directors.

To routinely compile and distribute statistical data regarding patient care which is utilized by administrative and research personnel.

Comparative statistics on bed activation and patient movement

	<u>1954</u>	<u>1955</u>	<u>1956</u>
Bed Complement	332	396	469
Bed Activation	171	64	73
Total Admissions	1452	1889	2452 ^{1/}
Total Discharges (incl. Deaths)	1326	1875	3342 ^{1/}
Total Visits to Followup Dept.	9371	14,606	20,623 ^{2/}

Major Problems:

Recruitment of qualified personnel, particularly in the Medical Record Transcribing Unit, which is partially due to the inadequate grade structure which impels the employment of untrained persons who require 4 to 6 months of intensive on-the-job training.

Significant Progress:

Establishment of standard operating procedures for the entire department.

Initiated and implemented orientation program for physicians participating in patient care and nursing department personnel.

Reviewed and revised related policies and procedures of Admissions and Followup Department and of Social Service Department which resulted in defining of duties and profitable working relationship.

Established and supervise a permanent pathological disease index file for the Pathological Anatomy Department and instructions given in the maintenance of same.

Accepted the appointment and responsibility for the control, initiation and revision of patient care reports.

^{1/} Includes estimated figures for December 1956.

^{2/} Includes estimated figures for October, November and December 1956.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-45
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
	174,300	174,300	3	41	44

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
3	41	44	

FY'57

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|--------------------------|-------------------------------------|--------------------------|
| X RESEARCH | <input type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Not Applicable.

PART C - NOT APPLICABLE.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13442-51-59
SERIAL NUMBER2. Clinical Center
INSTITUTE OR OTHER NIH UNIT3. Nursing Department
LABORATORY, BRANCH OR DEPARTMENT

4. _____

5. _____
LOCATION6. Nursing Activities
PROJECT OR ACTIVITY TITLE7. Ruth L. Johnson, Chief, Nursing Department
PRINCIPAL INVESTIGATOR OR OTHER RESPONSIBLE HEAD OF ACTIVITY

Louise C. Anderson, Ass't, Chief, Nursing Department
 Josephine I. O'Connor, Ass't. to Chief, Nursing Department
 Agnes B. Middleton, Chief, Psychiatric Nursing Service
 Mary Louise Burgess, Chief, Cancer Nursing Service
 Nina A. Ramacciotti, Act. Chief, Heart Nursing Service
 Margaret Hulburt, Chief, Neurology and Blindness Nursing Service
 Margaret E. Benson, Chief, Infectious & Tropical Diseases Nursing Service
 Marie M. Ceglarek, Chief, Arthritis and Metabolic Diseases Nursing Service
 Janet Fitzwater, Chief, Surgical Nursing Service
 Beatrice Marino, Act. Chief, Admissions & Followup Nursing Service

8. Odile M. Morneault, Education Officer
OTHER SENIOR INVESTIGATORS OR PRINCIPAL ASSISTANTS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH; (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable

10. PROJECT DESCRIPTION:

Objectives:

To cooperate in planning for and in rendering service for the admission, clinical care, research activities and followup of patients admitted to the Clinical Center.

To provide a high standard of nursing care for patients and assistance to the clinical research staffs in the categorical Institutes.

To foster the research point of view among members of the nursing staff through better understanding of the goals of the clinical research projects.

To carry out a staff education program which will enable nursing personnel to function most effectively in the patient care program and help them to derive satisfaction from their work.

To cooperate with all departments and services in working toward the goals of the Clinical Center.

Major Problems Encountered:

The major problem has been concerned with a lack of sufficient number of applicants to enable us to fill all positions at the GS-5, GS-6, GS-7 and GS-9 levels. Although there has been an active recruitment program, we do not believe that we are yet seeing the results of this program to any great degree. There has been an increase in our accessions in relation to separations and it appears that the turnover rate is down somewhat.

Another problem is related to the lack of office space for the Chiefs of several of the Nursing Services. More space is also needed for recreational activities for children patients and for the care of psychotic patients. Insufficient parking space for personnel reporting on duty at 4:00 p.m. has been a perennial problem and has not improved during this past year. The demands for escort and messenger services have increased until it is impossible to meet the needs.

There have been many unsolved problems in various special program areas of one Nursing Department which are described in the reports of the Chiefs of the individual Nursing Services.

Progress or Improvement:

The new qualifications standards and job specifications for the Professional Nurse Series have been published by the Civil Service Commission. An experienced staff nurse can now be employed at the GS-6 level - this in itself should assist in recruitment. The core training program for nursing assistants GS-2 is now 100 hours in conformance with the new standards. A review and evaluation of the practical nurse GS-3 position is almost completed. Additional training of 50 hours will be provided for all practical nurses who have been employed at least one year.

Assistant Chiefs have been appointed on all Nursing Services and Supervision on all Services during the evening and night tours of duty has now been provided.

This has made it possible to give more direct supervision to nursing personnel during all tours of duty and has resulted in the provision of more expert nursing care to patients and in better utilization of personnel.

The relationships between nursing and medical personnel have improved immeasurably. This has been due to better communication as well as better understanding of each other's problems.

Significance of Activities to the Clinical Research Program

Details of many significant activities contributed to the Clinical Research Programs by the Nursing Services are given in the reports by those services which are on file in the Director's office.

Nursing Research

Two major research projects have been initiated and are being carried out.

In the Operating Rooms

Investigator: Janet Fitzwater

Title: A Determination of the Bases for Selection of Instruments for Major Operations

Purpose: To establish criteria for the selection of instruments for major operations in the areas of cardiac surgery, gynecological surgery, head and neck surgery, abdominal surgery, vascular surgery and genito-urinary surgery.

Scope: Study will include an analysis of 300 major operations. To date data has been collected on 150 operations and is being used as a basis for the collection of data on the remainder of the cases.

On the Psychiatric Nursing Service

Investigators: Gwen T. Will and Agnes B. Middleton

Title and

Project No.: A study of a particular administrative process in terms of patient and nursing staff participation (PN-1)

This study has been in progress for almost three years and data collected will soon be ready for analysis and evaluation.

For projects being conducted jointly with other groups, see reports of Chief, Psychiatric Nursing Service and Chief, Cancer Nursing Service on file in the Director's Office.

Objectives for 1957:

The Departmental objectives for 1957 are the same as for 1956 with the following additions:

- A. To focus on the areas of management which appear to need reinforcement and review.
- B. To continue with plans for field experience programs for graduate nurses.

Addendum: (All statistics are for period January 1 - November 30, 1956)

A. Number of Personnel on Duty

	<u>Jan. 1, 1956</u>	<u>Nov. 30, 1956</u>
Professional Nurses	257	309
Practical Nurses and Nursing Assistants	150	184
Clerical Staff	<u>32</u>	<u>36</u>
Total	439	529

- B. Overall average number of Nursing hours available per patient per day for 1956 was 6.45.

Average number of Nursing hours available per patient per day for each Nursing Service during 1956 was:

Arthritis and Metabolic Diseases	5.89
Cancer	7.34
Heart	5.10
Infectious & Parasitic Diseases	7.50
Neurology & Blindness	6.14
Psychiatry	7.26

C. Number of hours of continuous Nursing care (special nursing to individual patients) during 1956 was: 41754

Arthritis and Metabolic Diseases	1892
Cancer	9066
Heart	6337
Infectious and Parasitic Diseases	4252
Neurology and Blindness	19726
Psychiatry	481 1/2

D. Number of hours of paid overtime work during 1956: 5895

Admissions and Followup	159
Surgery	581-1/4
Arthritis and Metabolic Diseases	279-1/2
Cancer	2041
Heart	742-1/4
Infectious and Parasitic Diseases	439-1/2
Neurology and Blindness	620-1/4
Psychiatry	1032-3/4

E. Number of hours of WAE Nursing during 1956: 29842-1/4

Arthritis and Metabolic Diseases	544
Cancer	13546-1/4
Heart	164
Infectious and Parasitic Diseases	144
Neurology and Blindness	11931-1/2
Psychiatric Nursing Service	2628
Admissions and Followup	884

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13442 - 51 thru 59
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL	
2,495,300	2,495,300	67	505	572	

FY'57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
74	587	661	

FY'57

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|--------------------------|--|--------------------------|
| X RESEARCH | <input type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL &
TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S).

Not applicable

N

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. 13442-51 thru 59
SERIAL NUMBER16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

Margaret A. Benson "A guide for Handwashing in Practice of Medical Asepsis", prepared for publication early in 1957 by the American Journal of Nursing.

Agnes Middleton and Louise C. Anderson, "The Supervisory Process in Administration", Military Medicine, November 1956.

Agnes Middleton, "A Method of Staffing for a Psychiatric Nursing Service", for publication early in 1957 by Nursing Outlook.

Marjorie Kvarnes, "The Role Played by Nurses in Psychiatric Research on Families in which One Member is Schizophrenic", for publication early in 1957 by Nursing Outlook.

Jane Wilcox, Virginia Silvis and Isabelle Ambrose, "Studies of Anti-Hypertensive Drugs", prepared for publication in the American Journal of Nursing.

Janet Fitzwater, "New Ideas for Efficient Operating Rooms", The Modern Hospital, August 1956.

Marie M. Ceglarek, Bertha E. Bryant, G. Donald Whedon, M.D., "A Manual for Metabolic Balance Studies", ready for publication early in 1957.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT
DURING CALENDAR YEAR 1956:

Not applicable.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13451-61-66
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION

3. Nutrition Department
LABORATORY, BRANCH, OR DEPARTMENT

Patient Dietetic Services Food

4. Production and Cafeteria Services
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Nutrition Department
PROJECT TITLE

7. Edith A. Jones, Dietitian Director, Chief, Nutrition Department
PRINCIPAL INVESTIGATOR

Ann Reimer, Sr. Dietitian (R), Chief, Patient Dietetic Services

8. Margaret Vance, Sr. Dietitian (R), Chief, Food Production and Cafeteria Services

Eileen Kenny, Sr. Asst. Dietitian (R), Assistant-to-Chief

OTHER SENIOR INVESTIGATORS OR PRINCIPAL ASSISTANTS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OR PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Plant Safety Branch, DBO
Sanitary Engineering Branch, DRS

10. PROJECT DESCRIPTION:

OBJECTIVES AND METHODS EMPLOYED

The overall objectives of the Nutrition Department of the Clinical Center, National Institutes of Health, was to provide within a budgetary framework nutritional research services to the patients, and as an adjunct to provide food service for personnel on a nonprofit yet self-supporting basis.

Since the Nutrition Department acts in a supporting role to all research programs, the services were developed so as to comply with the needs of the investigator and at the same time meet the emotional and physical needs of the individual. In addition, at the request of the investigators, diet histories are taken and dietary instruction are provided as an in or follow-up patient service.

To fulfill the responsibility of the Clinical Center's role, consultative services were provided--to the Hospital Division, Indian Health Service, and other Federal Agencies (Naval Medical Center, Veterans Administration, U. S. Army and Air Force), other divisions of the Public Health Service, Maryland State Department of Health, as well as some non-Federal groups. The Department served as a source of information for associations of medical personnel concerned with patient care and also for a number of foreign visitors interested in hospital care.

NUMBERS AND KINDS OF MAJOR SERVICES RENDERED

From January 1, 1956 to present; the Main Kitchen provided cooked food for and distributed food to 12 Floor Kitchen Units and provided raw food to 2 Metabolic Research Kitchen Units for 294,099 patient meals. Also, food was provided for sale in the Clinical Center Cafeteria and Coffee Shop for 730,411 customers within the year. (See Tables I and II attached.)

From January 1, 1956 to present, 322,294 meals were served to patients. The following indicates the percent to each Institute:

NCI	21%
NHI	20%
NIAID	8%
NIAMD	14%
NIMH	17%
NINDB	20%
NIDR	Less than one-half of one percent

Of the 282,070 meals served in the Floor Kitchens, 57% were directly or indirectly related to research, defined as those involving weighing, measuring and calculating of daily intake of one or more nutrients or total intake.

Approximately 4% of the meals (12,029) served in the Clinical Center during this year were serviced by two Metabolic Kitchens, all of these are directly related to research and are constant research diets.

In order to meet research needs it is necessary to operate a full-time formula room which provides services to all Institutes. These services include baby formulas, constant liquid formulas, constant tube feedings, etc.

MAJOR PROBLEMS ENCOUNTERED

A. Inadequate staff

1. To meet program needs in patient area.

Staff coverage has been limited by budget available, and has been inadequate to provide coverage adequate enough to meet program needs in the patient area, in the main kitchen area, and also to provide coverage in the Department for annual leave, sick leave, leave without pay as warranted and for absence without leave which occurs unexpectedly.

2. Staff turnover has been considered at the first of the year because of the very low wage rate of the 1st Wage Board Scale. Within the year, 47 have resigned or been released for other positions.

IMPORTANT PROGRESS OR IMPROVEMENT ACHIEVED

Several diet booklets were completed to be used in conjunction with discharge instructions to patients.

1. Low Fat Diet
2. Low Calorie Diet
3. Low Purine Diet
4. Supplement of Low Sodium Recipes

Several work simplifications have been established in various areas. Ex. Bulk loadings of food carts in the Main Kitchen; new method used for tray set up.

Formal training was initiated for employees

1. A two-week orientation class for all employees
2. A course commenced for special training for our food service supervisors.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13452-61-68
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF.	OTHER	TOTAL
	938,300	938,300	28	166	194

FY'57

BUDGETED POSITIONS			PATIENT DAYS		
PROF	OTHER	TOTAL			
30	182	212			

FY'57

13. BUDGET ACTIVITY:

- | | | | |
|--------------------|--------------------------|-------------------------------------|--------------------------|
| X RESEARCH | <input type="checkbox"/> | ADMINISTRATION | <input type="checkbox"/> |
| REVIEW & APPROVAL | <input type="checkbox"/> | PROFESSIONAL & TECHNICAL ASSISTANCE | <input type="checkbox"/> |
| BIOLOGIC STANDARDS | <input type="checkbox"/> | | |

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S).

Not applicable

PUBLIC HEALTH SERVICE - -NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15. 13451-61-66
SERIAL NUMBER16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING
CALENDAR YEAR 1956:

1. Food Services and Dietetics-review of 1955 literature and trends. August 1, 1956. Part II Guide Issue of HOSPITALS. Edith A. Jones, Chief, Nutrition Department.
2. Efficient Food Service Requires Step-By-Step Planning. March 1956.
3. A Book-Shelf on Low Sodium Recipe Manuals and Meal Planning Booklets- For Journal of the American Dietetic Association. Ann Reimer, Chief, Patient Dietetic Service.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING
CALENDAR YEAR 1956:

1. Eight awards were given to Nutrition Department employees under the Employee Incentive Award Program (1) for work performance, (7) for suggestions for a more efficient food service.
2. Chief, Nutrition Department received a Distinguished Service Award from the University of Alabama for having made outstanding contributions to the profession and to human welfare.
3. This year the Chief, Nutrition Department was elected to the Executive Council of the American Dietetic Association for a three-year term.

Table I

Meals Served in Clinical Center-By Food Service Area
1957

<u>Month</u>	<u>Floor Kitchens Total Meals Served</u>	<u>Metabolic Kitchens Total Meals Served</u>	<u>Total</u>
January	24,133	1,266	25,399
February	24,628	1,285	25,913
March	25,940	1,435	27,375
April	24,723	1,071	25,794
May	25,759	1,283	27,042
June	25,783	1,144	26,927
July	26,249	1,417	27,666
August	26,209	561	26,770
September	24,384	153	24,537
October	27,274	1,038	28,312
November	26,988	1,376	28,364
<u>December</u>			
<u>Totals</u>	282,070	12,029	294,099

TABLE II
1956

Percentage Rations Served Related Directly or Indirectly to Research

	<u>NCI</u>	<u>MHI</u>	<u>NIAD</u>	<u>NIAMD</u>	<u>NIINDB</u>	<u>NIIMH</u>	<u>NIIDR</u>
January	68% (1736)	65% (1305)	63% (360)	41% (771)	16% (429)	9% (92)	
February	65% (1736)	60% (1305)	58% (360)	49% (771)	14% (429)	8% (92)	
March	68% (1350)	68% (1043)	45% (341)	52% (705)	14% (333)	5% (96)	
April	75% (1606)	70% (1131)	47% (597)	63% (611)	19% (571)	6% (84)	
May	81% (1764)	74% (1083)	76% (567)	75% (465)	33% (465)	7% (157)	51% (19)
June	84% (1043)	71% (484)	79% (611)	57% (716)	39% (146)	10% (146)	27% (33)
July	70% (1738)	66% (1038)	66% (472)	39% (684)	9% (710)	9% (207)	36% (14)
August	82% (1491)	69% (995)	65% (539)	72% (672)	41% (655)	12% (127)	12% (19)
September	82% (3470)	72% (997)	71% (693)	67% (519)	37% (545)	8% (166)	22% (32)
October	77% (1581)	70% (1175)	71% (873)	55% (461)	30% (596)	10% (63)	46% (46)
November	79%	68%	62%	67%	35%	4%	71%
December							

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Description Sheet

1. SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Pathologic Anatomy Department
LABORATORY, BRANCH, OR DEPARTMENT
4. Cytodiagnosis Service
SECTION OR SERVICE
5. LOCATION (IF OTHER THAN BETHESDA)
6. Exfoliative Cytology applied to Human Diagnostic Problems and Research Problems.
PROJECT TITLE
7. Dr. Albert W. Hilberg
PRINCIPAL INVESTIGATOR
8. Dr. Roger O'Gara and Dr. Richard Malmgren
OTHER INVESTIGATORS
9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable

1C..PROJECT DESCRIPTION

The first and most important objective of the Cytodiagnosis Section is to provide to the clinical staff of the Clinical Center a complete and satisfactory exfoliative cytology service. The second objective is to provide a research tool to be used in various clinical research projects for evaluation of therapy, refinement of diagnosis and assessment of various physiological and anatomical changes in the human body. A third objective is the development and refinement of the techniques and morphological criteria as used in exfoliative cytology so as to further the value and efficiency of the first two stated objectives of the Cytodiagnosis Section.

Methods employed:

The methods involved in this project are primarily those of routine Papanicolaou staining of preparations of human specimens and careful screening and evaluation of morphological changes in cellular material. Of importance to the proper evaluation of these morphological changes are additional methods of special preparation of human materials and special staining techniques applied to the preparations. For example: preparations of some fluid specimens may involve the use of refrigerated

centrifugation, differential separation of the strata of sediment obtained by centrifugation, fixation of the material so obtained in various special fixatives (i.e. modified Carnoy, sodium chloride solution, etc.), and then staining the preparations by special staining techniques. Examples of the staining techniques are: Periodic acid Schiff reaction, Kurnick's method for DNA and RNA, Gomori's acid and alkaline phosphatase method, Laidlaw's Method for Dopa oxidase and numerous others.

Patient Material:

The figures compiled below are for only the first ten (10) months of the present calendar year - 1956.

<u>Type of material examined</u>	<u>Accessions</u>	<u>#slides examined</u>	<u>#slides prepared</u>
Vaginal and cervical	1265	2781	2781
Miscellaneous fluids	269	2312	3657
Sputums and Bronchial Washings	144	501	501
Gastric Washings	8	94	94
Prostatic	7	35	35
Total	<u>1693</u>	<u>5723</u>	<u>7068</u>

<u>Institute</u>	<u>Accessions*</u>	<u>Slides*</u>
NCI	1326	4915
NHI	75	308
NIMH	13	49
NIAMD	69	228
NIAID	107	400
NINDB	11	66
NIDR	52	54
No Institute identification	20	70

*Figures for first ten months of 1956 only.

Major Findings:

In respect to diagnostic service to the clinical staff the major findings would concern useful information leading to a diagnosis or to a greater ability to handle therapeutic measures. This is difficult to assess and evaluate in an exact manner. The Cytodiagnosis Service lead to the detection of early diagnosis of several early carcinomas of the cervix, some early tumors of the lung and several sites of metastatic tumor which had been previously undiagnosed. In addition exfoliative cytology provided the first, and in some instances, the only tissue confirmation of neoplastic disease before death of the patient.

In the wound washing project carried on with the Surgical Branch many operative sites were found to have fragments of tumor tissue in them as determined from the washing of these sites.

The evaluation of the sensitivity response of tissues in the oral cavity to irradiation will, it is hoped, provide a more accurate method of treating patients with oral carcinomas. This work is yet too incomplete to properly evaluate the findings.

Evaluation of estrogenic activity as assessed by morphological changes in cells from the vaginal tract and by special staining of vaginal and oral mucus has provided information to clinicians in cases of amenorrhea, precocious puberty, endocrine therapy, postmenopausal patients, and unusual problems dealing with cyclic changes in endocrine studies.

In regard to the problems of refinement of techniques as used in exfoliative cytology the development of the modified Carnoy fixation technique for the removal of blood and cellular debris from fluid specimens has been a definite step forward in the accurate evaluation of human exudates and washing from various sites. The adaptation of special staining techniques for melanin and for nucleic acids has also provided a useful tool for the advancement of morphological studies of cells.

Significance of the program:

The significance of the diagnostic value of exfoliative cytology to the clinical evaluation of cancer and the early detection of cancer is clearly obvious not only from our own activities in the Clinical Center but from the numerous activities throughout the country.

The significance of the wound washing studies now under way is at least twofold. These studies may provide a prognostic device for the surgeon, but more important they have directed attention to an important area for therapeutic investigation.

The studies involving the sensitivity response to radiation therapy though still in the formative stages could provide an accurate method of determination of the efficacy of this means of therapy in cases of oral cancer. The further evaluation of radiation response after therapy is instituted may also provide information regarding the effectiveness of the therapy. These studies are still too early to make positive statements.

The endocrine evaluation studies involving not only non-malignant cases but also the cases of malignancy treated with hormones provide valuable information to clinicians in the determination of diagnostic problems and for the sequential studies of effectiveness of therapy. The further addition of the study of sex chromosomes, which is now under way on a small scale, enhances the value of the endocrine studies to the clinical staff.

The development of new techniques of preparation and staining of cytologic specimens provides valuable new methods for use in all the studies under way and provides information to other investigators in this field to increase the efficiency and value of exfoliative cytology.

Proposed course of project:

Continuation of complete and adequate service to all the clinical staff of all the categorical institutes in the Clinical Center, National Institutes of Health is our first function. Continued collaboration with the clinical staff in various research projects and the continued search for and development of new preparation and staining techniques is a second and most valuable function for the coming years.

A more intensive investigation of the adaptation of evaluation of sensitivity response of radiation in cases of oral cancer is planned along with evaluation of the radiation response after therapy is given. This project is being carried out with the cooperation of the Radiation Therapy Section.

A continued investigation of the problems involved in wound washings following cancer surgery, with the cooperation of the Surgery Branch, and an amplification of this project to include studies of the vascular drainage of the wound site is also planned.

The evaluation of estrogen activity will continue in all types of endocrine problems and for those cases of endocrine therapy for cancer in which the clinical staff desires such studies. In addition the determination of sex chromosome content of cellular material will also continue.

A very important phase of the work of this laboratory is the continued refinement of techniques of preparation and staining of cytologic specimens and the development of new techniques in order to further clarify and identify the important morphologic changes in cells as a result of neoplastic change or in the instances of modification by hormonal influences.

Evaluation of cellular alterations in gastric mucosa in dystrophic diseases of the nervous system, in cooperation with NINDB, has been started this year and will continue. Reports have indicated the possible significance of these gastric changes in some disease processes.

Service & Type of Activity	NCI		NFI		NIAMD		NIAID		NIMH		NINDE		NIDR		TOTAL		REF		
	IN	FU	IN	FU	IN	FU	IN	FU	IN	FU	IN	FU	IN	FU	IN	FU	IN	FU	
Postmortem-Pathologic Anatomy Service																			
# of autopsies performed	133		29		8		8					10		1		192		3	
Blocks of tissue	8015		1551		471		503					527		37		11227		23	
Slides	18645		4225		1256		1344					1441		109		27097		77	
Slides actually stained	10941		2231		711		960					900		94		15867		30	
Surgical Pathology																			
Tissue Specimens	973		139		112		180					47		94		1789		235	
Slides H-E staining	4566		544		633		490					159		205		9743		1303	
Frozen Sections	122		13		9		6					4				154		92	
Special Procedures	817		205		255		321					72		20		1786			

223 cell blocks, 1416 slides; 52 OPC biopsies, 52 H & E's prepared for Cytodiagnosis Section.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A, Projection Sheet

1.

SERIAL NUMBER2. Clinical CenterINSTITUTE OR DIVISION

Surgical Pathology &

4. Postmortem ServiceSECTION OR SERVICE3. Pathologic Anatomy DepartmentLABORATORY, BRANCH, OR DEPARTMENT

5.

LOCATION (IF OTHER THAN BETHESDA)

No specific research projects in this Department. However, the diagnostic service is designed to aid the investigative efforts of the NIH staff

6. responsible for patient care. In many instances investigative study of

PROJECT TITLE pathological tissues is of great importance to clinical research.

7. Dr. Harold L. StewartPRINCIPAL INVESTIGATOR8. See page 3OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

None

10. PROJECT DESCRIPTION (SEE INSTRUCTIONS):

No specific research projects. The services and diagnostic functions of the department during 1956 have included:

a. 192 autopsy examinations (from January 1, 1956 through November 30, 1956)

Since July 1, 1956 when the first resident class was started in the Department of Pathologic Anatomy, the three residents have performed approximately three-fourths of the autopsy examinations. The rest of the staff have performed a variable number of autopsy examinations. The supervision of the autopsy service is divided between Doctors Thomas and Edgcomb.

b. 1789 surgical pathology accessions (January 1 through November 30, 1956)

Most of these specimens are now initially described by the resident staff and then their reports are checked by Doctors Thomas and Edgcomb. Doctors Sokoloff, Swarm, Rabson and Stanley also participate in this service.

The objectives of the Surgical Pathology and Post-Mortem Service in the Clinical Center are twofold: first, to furnish a diagnostic service in autopsy and surgically removed tissues, and second, to aid from a morphological standpoint the various clinical research problems which are under study in the Clinical Center.

The methods used are those standard methods which are used in the description of organs and tissues, the fixing and sectioning of this material and the preparation of histological slides. A wide variety of special staining procedures are used in the histopathology laboratory of the Department. The appended chart shows the cumulative total of work performed in the Surgical Pathology and Post-Mortem Services of the Department for 11 months of 1956.

In addition to the diagnostic services, there are several other functions of the Department which have continued and expanded during the past year. At present there are thirty-five scientists in the various laboratories at National Institutes of Health who have requested particular types of tissue from surgical and post-mortem specimens examined in this Department. On many occasions it is possible to furnish these investigators with fresh human material.

The staff of the Department continues to take active part at numerous Clinical Center staff meetings, and in addition, routinely conducts four Departmental meetings weekly. These are the Brain Cutting Conference on Monday, the Autopsy Conference on Tuesday, the Joint Pathology Staff Conference on Wednesday and the Surgical Pathology Conference on Wednesday and the Surgical Pathology Conference on Friday.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15.

SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956:

1. Progestational Effectiveness of 19 nor-Ethinyl Testosterone by Oral Route in Women, Hertz, Roy; Waite, John H. and Thomas, Louis B., Proc. Soc. Exp. Biol. Med. 91 418: 1956.
2. Clinico-Pathologic Conference; A case of Bacterial Aortitis Following Resection of Coarctation of Aorta, Terry, Luther; Haverback, B.J. and Thomas, L.B., to be published in Heart Bulletin.
3. Mycotic Endocarditis, A Review and Report of A Case Due to Cryptococcus Neoformans, Lombardo, T.A.; Rabson, Alan S. and Dodge, Harold T., Am. J. Medicine (In press).
4. Studies on the Use of Viruses in the Treatment of Carcinoma of the Cervix, Smith, Robert R., Huebner, Robert J., Rowe, Wallace P., Schatten, William E. and Thomas, Louis B., Cancer, November-December, 1956.
5. Some Aspects of the Pathology of Collagen Diseases, Sokoloff, Leon, Bull. N.Y. Acad. Med. 32: 760-767, 1956.
6. Biopsy as a Diagnostic Procedure in Rheumatic Diseases, Sokoloff, Leon, Bull. Rheum, Dis 7, Supplement to Oct. 1956.
7. The Pathology of Gout, Sokoloff, Leon, Metabolism (In press).
8. Vascular Lesions in Rheumatoid Arthritis, Sokoloff, Leon and Bunim, Joseph J., J. of Chr. Dis. (In press).
9. Systemic Lupus Erythematosus, Bunim, Joseph J., Harvey, A. McGhee, Bollet, Alfred J., Hilbish, T.F., Van Scott, Eugene, Sckoloff, Leon and Brecher, George, Circulation 14, 125-134, 1956.
10. The Value of Step Serial Sectioning in the Morphologic Study of Human Periodontal Disease, Stanley, Harold R., Jr., J of Periodontology (In press).

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956:

1. Lecture entitled, Aspiration Biopsy, as a part of the Course in Surgical Pathology sponsored by the International Academy of Pathology, Cincinnati, Ohio, April 1956 by Louis B. Thomas.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13432-42-44
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION

3. Pharmacy Department
LABORATORY, BRANCH, OR DEPARTMENT

4. Pharmacy Service, Pharmaceutical Development Service, Sterile Supply Service
SECTION OR SERVICE

5. Does not apply
LOCATION (IF OTHER THAN BETHESDA)

6. Does not apply
PROJECT TITLE

7. Milton W. Skolaut, Chief, Pharmacy Department
PRINCIPAL INVESTIGATOR

8. Boris J. Osheroff, Chief, Pharmacy Service
OTHER INVESTIGATORS
John A. Scigliano, Ph.D., Chief, Pharmaceutical Development Service
Joseph N. Salvino, Chief, Sterile Supply Service

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable

10. PROJECT DESCRIPTION:

OBJECTIVES:

To provide for the clinical research teams all pharmaceuticals, routine and new, develop new products into usable pharmaceuticals, and supply routine and special sterile and clean supplies. To stay abreast of the ever changing needs of the patient care areas by consultations and provide to them the services best suited to their needs.

Methods Employed:

A closer coordination of many patient care needs under one responsibility by providing pharmaceuticals, developing new pharmaceuticals, supplying clean and sterile supplies, providing other items such as braces, orthopedic shoes, eye glasses and related needs. Continued to strive for faster, more efficient, means of procuring supplies and final receipt.

Services Rendered

Total Number of Department Item and Unit Issues 2,024,793
(Includes estimates for December, 1956)

Total Number of Individual Requisitions
Processed by the Department 29,297

Pharmacy Service Item Issues
Prescriptions 11,493
Other Items 172,687
Total 184,180

Number of Individual Requisitions
Processed for Other Items 10,818

Pharmaceutical Development
Service Unit Issues 3,948
(from August through November,
1956, including estimates for
December, 1956)

Number of Individual Requests
Completed 315

Sterile Supply Service Item Issues
Sterile 1,374,133
Clean 462,532
Total 1,836,665

Items processed in cooperation
with Laboratory of Infectious
Diseases of the National Institute
of Allergy and Infectious Diseases 17,517

Number of Individual Requisitions
Processed 18,164

The Pharmacy Department received approval for and accomplished a reorganization which initiated a new service. The position of Assistant Chief, Pharmacy Department was abolished and the following two services were established: Pharmacy Service and Pharmaceutical Development Service. The Sterile Service completes the Department. The Chief of each of the three services may be designated as Acting Chief during the absence of the Chief of the Pharmacy Department.

A new catalog was compiled and submitted for printing in a revised form which will have a much larger distribution.

The addition of the Pharmaceutical Development Service had added materially to offer a more complete and rounded service. The developmental type services have been separated from the Pharmacy Service allowing a better utilization of pharmacists for the work to be accomplished. Personnel are now assigned to that duty on a full time basis which gives us better and more efficient service, better trained personnel in this speciality, which results in improved end products to the clinical research staff.

Often satisfactory products are developed by personnel in this activity from raw chemicals or drugs before industry has even exhibited an interest in such a product.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13432-42-44
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
	607,600	607,600	11.5	40.5	52

FY'57

BUDGETED POSITIONS			PATIENT DAYS=
PROF	OTHER	TOTAL	
12	42	54	

FY'57

13. BUDGET ACTIVITY:

X RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Not Applicable.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part C: Honors, Awards & Publications

15.

13432-42-44

SERIAL NUMBER

16. LIST PUBLICATIONS OTHER THAN ABSTRACTS FROM THIS PROJECT DURING CALENDAR YEAR 1956:

"Preparation of Small Volume Injections," by John A. Scigliano, Bulletin, American Society of Hospital Pharmacists, Mar-Apr, 1956.

"Trends Indicate Current Direction of Services in Hospital Pharmacies" by Milton W. Skolaut, Hospital Progress, March, 1956.

"How Do You Measure Needle Length?" by Milton W. Skolaut and Joseph N. Salvino, Hospitals, Vol. 30, July 1, 1956.

17. LIST HONORS AND AWARDS TO PERSONNEL RELATING TO THIS PROJECT DURING CALENDAR YEAR 1956.

Milton W. Skolaut: For the American Society of Hospital Pharmacists: Vice President; Chairman, Research and Development Committee; Chairman, Committee on Pharmacists in Government Service; Member of Committee on Pharmacy Operated Central Sterile Supply Service; delivered several addresses representing the Society as Vice President.

For the American Pharmaceutical Association: Represent the group on the Committee on Status of Pharmacists in Government Service; and a member of the Steering Committee of a group representing five national pharmaceutical groups.

For the Federal Civil Defense Administration: Consultant on functional packaging and testing several items, such as sterilizers and gas burners.

Member of a panel discussion at the Maryland, District of Columbia, Delaware Hospital Association Annual Meeting.

John A. Scigliano: President of the Maryland Association of Hospital Pharmacists for approximately eight months of the calendar year.

Joseph N. Salvino: For the American Society of Hospital Pharmacists; Chairman, Committee on Pharmacy Operated Central Sterile Supply Service.

ORP-1 (concl'd)

Calendar Year 1956

Serial No. 13432-42-44

William H. Briner: President, Maryland Association of Hospital Pharmacists for approximately four months and Vice President for the eight previous months.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A: Project Description Sheet

1. 13432-38-40

SERIAL NUMBER

2. Clinical Center

INSTITUTE OR DIVISION

3. Rehabilitation Department

LABORATORY, BRANCH, OR DEPARTMENT

4. Office of Chief

SECTION OR SERVICE

5. _____

LOCATION (IF OTHER THAN BETHESDA)

6. _____

PROJECT TITLE

7. David M. Fried, M. D., Chief

PRINCIPAL INVESTIGATOR

8. V. J. Niebuhr, Chief, Physical Therapy Service

OTHER INVESTIGATORS

M. B. Beach, Chief, Occupational Therapy Service

Heidi Nadel, Speech Therapist

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION:

The Rehabilitation Department has two primary functions:

- (1) To participate in a total care program
- (2) To provide services assisting in research studies

All patients are referred by Institute physicians, and treated compatibly with the research program. Physical Therapy, Occupational Therapy and Speech Therapy are the services available, furnishing recognized modalities, devices and special techniques. Thus in addition

to the application of thermo, electro, hydro, mechano and light therapy, training is given in Activities of Daily Living, including self-care, kitchen and home-making activities; braces and other devices are prescribed. Vocational counseling is obtained through the Maryland Department of Vocational Rehabilitation.

Details of the activities of the Physical Therapy, Occupational Therapy and Speech Therapy Services are attached.

In addition to the staffs of the aforesaid Services there is currently one physician in the Department, the Chief, who came on duty September 17, 1956, the former Acting Chief having left the Department on June 30, 1956. The Department continues to have two consultants.

Activity: Physical Therapy Service, Rehabilitation Department.

Numbers and kinds of services rendered:

The attached Exhibit indicates the activity work-load in respect to number of patients treated, number of patient visits, and number of treatments given. Because of the wide variety of individual treatment or test measures utilized as prescribed, no attempt has been made to itemize them by type.

Major problems encountered: None.

Activity: Occupational Therapy Service, Rehabilitation Department.

Numbers and Kinds of Major Services Rendered:

The programs in occupational therapy for patients from all Institutes fall into the following areas: physical disabilities clinic, pediatric program, ward program for those patients confined to bed, workshop for general medical patients, industrial therapy, and, until November, sports and other recreational activities.

The attached charts set forth the numbers and kinds of services rendered:

I. Patients Seen Individually in Occupational Therapy 1956

<u>1956</u>	<u>Number of Patients</u>	<u>Number of Visits</u>	<u>Hours of Treatment</u>
January	224	1829	1973
February	257	1835	2406
March	289	1971	2196
April	292	2041	2500
May	292	2174	2211
June	310	2072	2198
July	299	1700	1899
August	305	2091	2387
September	252	1709	1772
October	277	1995	2056
November	280	1847	1446
December	259	1695	1867
Total	3,336 ^{1/}	22,959	24,911

II. Group Activities for Patients 1956

<u>Month</u>	<u>Number of Sessions</u>	<u>Number of Patients</u>
January	53	953
February	57	1188
March	63	1231
April	57	945
May	63	1151
June	60	1227
July	52	1234
August	91	991
September	88	931
October	80	1260
Total	664	11,111

1/ Patients are counted each month they are in occupational therapy.

Activity: Speech Therapy Service.

Speech Therapy was initiated as a service of the Rehabilitation Department in November, 1955, with one therapist assigned.

Activity Description:

The Service functioned in the following way for the first year: procedures were formulated, record forms devised, and materials obtained. Evaluation and therapy were instituted for a wide variety of speech disorders, including delayed speech, articulation disorders, voice disorders, aphasia, cleft palate, as well as speech disorders found in cerebral palsy.

Treatment Summary, statistical:

	Number of Patients Treated	Number of Patient Visits
January	12	60
February	14	109
March	16	153
April	9	122
May	9	124
June	10	102
July	7	79
August	8	100
September	9	82
October	5	90
November	9	95
December	10	107
Total	118	1223

Physical Therapy Service

Exhibit V: Calendar years 1954, 1955, 1956: Comparative statistical report, by Institutes

Institute	No. of Patients Treated			No. of Patient Visits			No. of Treatments Given		
	1954	1955	1956	1954	1955	1956	1954	1955	1956
NHI	123	200	298	1074	2054	2876	1789	4214	5317
NIAMD	253	279	275	3563	2185	2871	7627	4838	5949
NCI	39	153	220	402	1201	1606	669	1857	2778
NIAID	35	69	67	438	877	591	898	1872	941
NINDB	147	294	309	1563	3264	2801	3677	7556	5340
NIMH	8	9	1	108	47	1	231	59	2
NIDR	-	2	9	-	8	20	-	33	24
Total	605	1006	1179	7148	9636	10,766	14,891	20,429	20,351

Physical Therapy Service

Exhibit I: Calendar year 1956: Statistical report, by month						
	No. of patients treated		No. of patient visits		No. of treatments given	
	IP	OP	IP	OP	IP	OP
January	81	13	674	52	1359	133
February	82	20	843	87	1658	217
March	90	19	1001	99	2152	234
April	77	17	720	124	1485	317
May	74	16	696	119	1344	289
June	64	16	722	84	1256	181
July	79	13	676	63	1180	139
August	87	17	833	126	1539	241
September	72	12	753	86	1293	166
October	92	15	889	143	1514	219
November	106	13	970	91	1676	138
December	92	12	849	66	1498	123
Total	996	183	9626	1140	17,954	2397
Total	1,179		10,766		20,351	

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13132-38-39-40
SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT REIMBURSEMENT	TOTAL		PROF	OTHER	TOTAL
177,200	177,200		7.5	21.5	29

FY '57

BUDGETED POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
8	23	31	

FY '57

13. BUDGET ACTIVITY:

- RESEARCH
- ADMINISTRATION
- REVIEW & APPROVAL
- PROFESSIONAL & TECHNICAL ASSISTANCE
- BIOLOGIC STANDARDS

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S):

Funds for operation of the Diagnostic X-ray Department are provided by the Institutes on a pro-rate basis. The major function of the Department is that of research service. However, certain research studies, of a more or less independent nature, are undertaken by the Department in cooperation with pharmaceutical companies. Likewise, equipment improvements and diagnostic techniques are developed through experience. Several such activities undertaken during the past year are listed as follows:

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13421
SERIAL NUMBER2. Clinical Center
INSTITUTE OR DIVISION3. Social Service Department
LABORATORY, BRANCH, OR DEPARTMENT4. _____
SECTION OR SERVICE5. _____
LOCATION (IF OTHER THAN BETHESDA)6. Social Service Department
PROJECT TITLE7. Dr. Daniel E. O'Keefe
PRINCIPAL INVESTIGATOR8. See attachments
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS) IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION

Objectives:

The Clinical Center's commitment to the advance of medical knowledge in chronic illness determines the following objectives for the Social Service Department.

1. To provide casework service to patients and their families so that they may be able to participate fully in the research effort and be comfortable enough financially and emotionally to achieve maximum benefit from treatment;

2. To offer appropriate consultation about the social and emotional factors related to illness in order to improve the planning for the individual patient and to participate in policy formulation with respect to the total care and welfare of patients;
3. To participate in research undertaken in the Clinical Center from the standpoint of social, economic, cultural and emotional aspects of illness; to engage in research in social work practice in order to improve the quality of social work at the Clinical Center and, in the process, to advance social work knowledge generally;
4. To utilize the social worker's knowledge of the community for the social treatment of our patients as well as a potential source of patient material and to engage in community activities geared toward better social planning;
5. To participate in interdisciplinary training programs in order to work toward optimum communication and utilization of professional knowledge among the disciplines for the advancement of the research treatment goals.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

Part B: Budget Data

11. 13422-21
 SERIAL NUMBER

12. BUDGET DATA:

ESTIMATED OBLIGATIONS			MAN YEARS		
DIRECT	REIMBURSEMENT	TOTAL	PROF	OTHER	TOTAL
FY '57	188,700	188,700	22.5	8.5	31

BUDGET POSITIONS			PATIENT DAYS
PROF	OTHER	TOTAL	
FY '57			

13. BUDGET ACTIVITY:

RESEARCH	<input type="checkbox"/>	ADMINISTRATION	<input type="checkbox"/>
REVIEW & APPROVAL	<input type="checkbox"/>	PROFESSIONAL & TECHNICAL ASSISTANCE	<input type="checkbox"/>
BIOLOGIC STANDARDS	<input type="checkbox"/>		

14. IDENTIFY ANY COOPERATING UNITS OF THE PUBLIC HEALTH SERVICE, OR OTHER ORGANIZATIONS, PROVIDING FUNDS, FACILITIES, OR PERSONNEL FOR THIS PROJECT IN FY 1957. IF COOPERATING UNIT IS WITHIN NIH INDICATE SERIAL NO(S).

Not applicable

TABLE II

PREADMISSION SURVEYS
CALENDAR YEAR, 1956

MONTH	NIMH		NINDB		NIAMD		NCI		NHI		NIAID	
	No. Pts.	Contacts Required	No. Pts.	Contacts Required	No. Pts.	Contacts Required	No. Pts.	Contacts Required	No. Pts.	Contacts Required	No. Pts.	Contacts Required
January	5	6	3	21	1	5	0	0	1	8	0	0
February	13	18	3	11	0	0	0	0	1	0	0	0
March	12	43	3	3	3	8	1	5	1	7	0	0
April	10	18	2	7	2	0	2	4	0	0	0	0
May	12	5	6	12	1	3	1	17	1	3	0	0
June	10	33	6	16	0	0	2	9	0	0	0	0
July	13	38	6	7	0	0	1	3	0	0	0	0
August	10	8	2	4	1	5	1	3	0	0	0	0
September	13	24	4	10	0	0	2	5	0	0	1	3
October	7	2	3	3	0	0	2	4	0	0	0	0
November	1	0	2	7	0	0	2	6	0	0	0	0
December	1	1	1	2	0	0	3	13	0	0	0	0
TOTAL	107	196	41	103	8	21	17	69	4	18	1	3

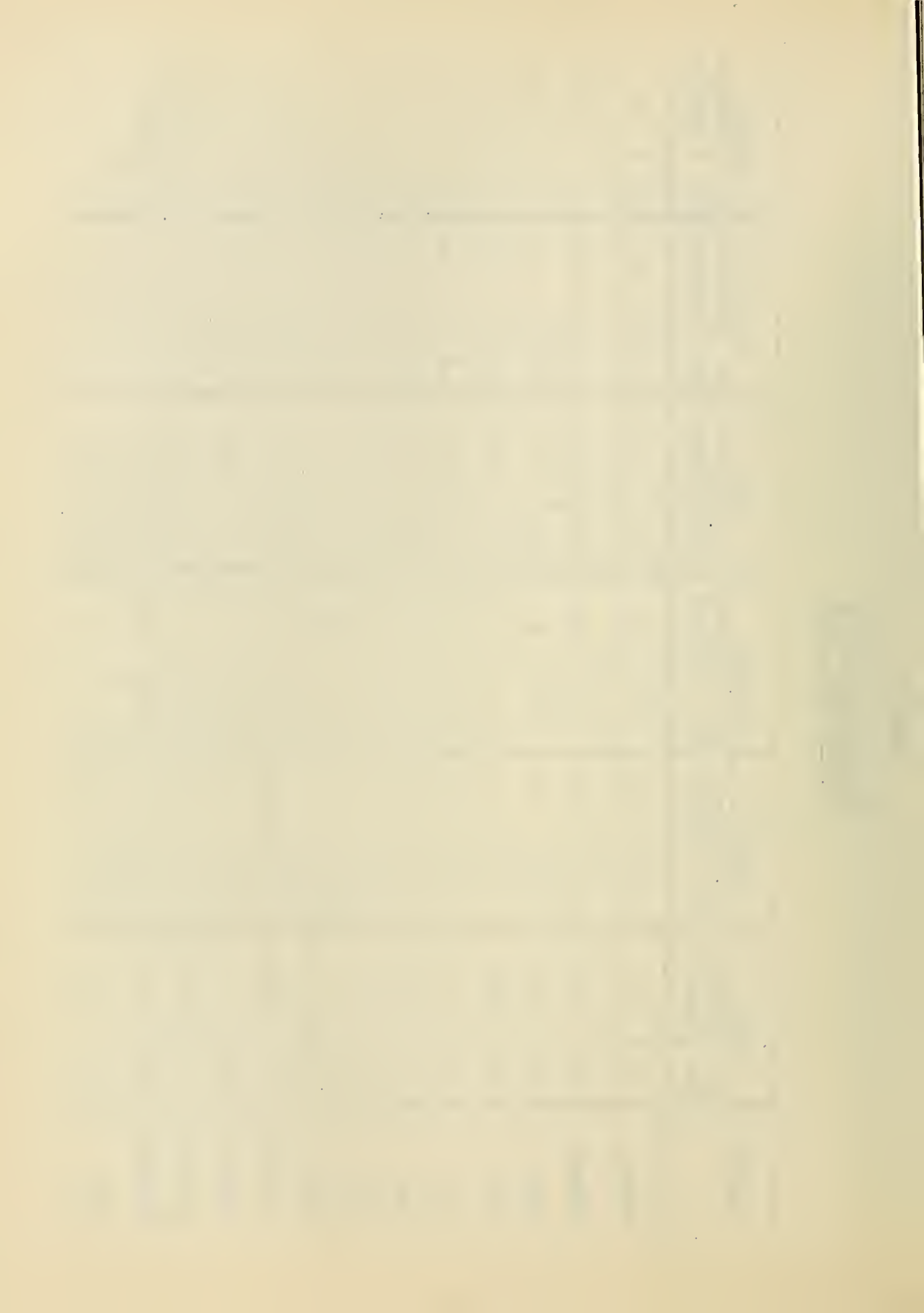


TABLE 1
SOCIAL SERVICES FOR INPATIENTS
Calendar Year 1956

Month	NCI	NHI	NIAMD	NIDR	NIMH	NINDB	NIAID	TOTAL
JAN	477	437	371	0	1,186	311	280	3,095
FEB	531	404	363	0	780	306	253	2,637
MAR	594	473	297	0	768	346	219	2,697
APR	564	334	207	0	860	297	237	2,499
MAY	755	303	187	48	821	376	258	2,748
JUNE	813	470	172	48	656	383	122	2,664
JULY	601	332	205	58	598	342	21	2,157
AUG	694	382	214	59	524	385	21	2,279
SEPT	604	419	150	53	691	274	138	2,329
OCT	599	434	245	1	802	277	199	2,557
NOV	593	393	274	0	666	339	169	2,434
DEC	664	336	330	0	622	326	117	2,395
TOTAL	7,489	4,717	3,015	267	8,974	3,995	2,034	30,491

The number of social services rendered is the total number of interviews which have been held with the patient, a family member, physician, social agency or other concerned person or institution.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13422-21

SERIAL NUMBER

2. Clinical Center

INSTITUTE OR DIVISION

3. NINDB

LABORATORY, BRANCH, OR DEPARTMENT

4. Social Service Department

SECTION OR SERVICE

5. _____

LOCATION (IF OTHER THAN BETHESDA) :

6. A Study of Interpersonal Communication and Cerebral Seizures.

PROJECT TITLE

7. Robert J. Savard, M.A.

PRINCIPAL INVESTIGATOR

8. Dr. Laurence L. Frost, Dr. Maitland Baldwin

OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION:

Objectives:

To determine if there are differences in the social functioning of patients with focal cerebral seizures stemming from the dominant temporal lobe as contrasted to the non-dominant temporal lobe. To describe the nature of the differences, if such are found.

Methods Employed:

The methods employed are a survey of the case records of the patients who have undergone cortical surgery, to analyze their interpersonal

communication in the casework relationship. On a selected number of 18 patients a group interview involving two patients, one of which is a poor communicator and the other a good communicator.

Study Material:

81 patients were studied who have been admitted to the neurosurgery service for cortical seizures where a definite diagnosis of temporal lobe epilepsy is established. The exact number, age and sex distribution will depend on patients available on the neurosurgery service.

On the basis of some preliminary findings, it seems as if patients with lesions in the left temporal lobe display certain basic patterns in their social functioning which differs from patients whose lesions are outside this area. They seem to have difficulty in relating adequately to their environment--especially human. They have a stereotyped method of relating to others which lacks in depth of feeling. They also seem to have difficulty in integrating their desire to reach a goal with activities necessary to reach it. Also, their goals are quite nebulous. To put it another way--wishes are not translated into will except when a relatively simple concrete goal must be reached.

Preliminary Findings:

27 patients were found to be poor communicators in the sense that during the interviews, while they talked, they did not describe their social functioning in a way which allowed the interviewer to formulate a judgment as to their individual situation and feelings regarding their situation. They seldom mentioned people and were prone to be overly abstract or overly concrete. These patients were found to have a significant lesion in the temporal lobe of the dominant hemisphere.

Meaning to the Clinical Center:

This study will integrate well with the overall goal of the neurosurgery research which is concerned with brain function as it reflects itself in brain abnormalities. It will also give much needed data to the Social Service Department in that hopefully by determining whether or not the social dysfunction noted is primarily organically or socially determined so that better methods of casework help can be formulated.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13421-22
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR OTHER NIH UNIT

3. Professional Services Department
LABORATORY, BRANCH OR DEPARTMENT

4. Social Service Department
SECTION

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Distressful States Experienced by Patients in the Clinical Center
PROJECT OR ACTIVITY TITLE

7. Betty Basamania, M.S.W., Paul Blank, M.S.W., Geraldine Connor, M.S.W.,
Ruth Ann Fundis, M.S.W., Mary Ann Fugitt, M.S.W., Shirley Helmich, M.S.W.,
Stanley I. Hirsch, M.S.W., Roberta Peay, M.S.W.
PRINCIPAL INVESTIGATOR (S) OR OTHER RESPONSIBLE HEAD OF ACTIVITY

8. _____
OTHER SENIOR INVESTIGATORS OR PRINCIPAL ASSISTANTS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OR PERSONNEL FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH; (BY SERIAL NO.(S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION

Objectives:

To determine the frequency of patients experiencing instances of stress.

The extent of stressful states.

The patterns of precipitation.

What is being done to alleviate the stressful situations and what further can be done?

Methods Employed:

Data Collection. Data is collected by each investigator interviewing five patients representing a cross section of the patients hospitalized at the National Institutes of Health. The focus of the study is the specific instances of stress patients can recall and the events surrounding them to get to precipitating factors. Objectivity will chiefly depend on facilitating patients to recall with as little distortion as possible. The patient is the primary observer and the investigator functions as an enabling person.

Analysis of the Data. Examination of the interviews to determine existence of instances of stress as measured by criteria established.

To further analyze the relationship between these and precipitating factors associated with hospitalization.

Major Findings:

The initial interviews conducted do not show any definite pattern of causes for the stressful instances. This would seem to indicate that they are individualized and data about the causes are being analyzed further.

Significance to Clinical Center Research:

One of the major interests in patients at the Clinical Center is research, and their comfort and cooperation is essential for carrying out the research goals.

If there are patterns of stress experienced by patients, associated with hospital policy and procedure, this might be of interest to hospital administration in terms of recommending changes. If on the other hand there are no patterns, but sufficient frequency of stressful situations can be demonstrated, this might warrant closer scrutiny in terms of the role other services oriented towards alleviation of individual problems, might play.

Proposed Course of Project:

The methodology used in this study might have significance for other social service research.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13421-22

SERIAL NUMBER

2. Clinical Center

INSTITUTE OR DIVISION

3. Social Service Department

LABORATORY, BRANCH, OR DEPARTMENT

4. NHI

SECTION OR SERVICE

5. _____

LOCATION (IF OTHER THAN BETHESDA)

6. Study of verbalized expressions of patients related to their own death.
PROJECT TITLE7. Ruth T. Hartman M.S.S.W. and Barbara A. Murphy, M.S.

PRINCIPAL INVESTIGATOR

8. _____

OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OR PERSONNEL FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH)

Not applicable.

10. PROJECT DESCRIPTION:

To study the verbalized expression of patients related to their own death.

To examine the social worker's responses to the above material.

To observe patient's reaction to the social worker's handling of death related material in the interview.

Calendar Year 1956

Methods Employed:

Information related to the above objectives will be obtained from microscopically studying this area of case work practice through the medium of the interview. Patient's expressions that are death related, the worker's response and reactions, both overt and covert, of patient to the handling of these will be systematically observed and recorded.

These data will be analyzed relative to what patients say and what their adaptive behavior is toward their eminent death.

Study Material:

NHI patients selected for the study will be chronically ill persons whose disease process has been characterized by a gradual progression of symptoms with increasing incapacitation, whose life expectancy is limited, and who verbalize during the course of case work treatment anxieties and fears concerning their own death.

Preliminary Findings:

There are no preliminary findings available at this time. Work thus far has been focused around the formulation of a manageable question and designing an accurate method of data collection.

Significance to the Clinical Center and Social Service Research:

With the increase of chronic illness and the many cultural changes related to the care of the sick and dying, the hospital social worker is increasingly called upon to give case work service to the chronically ill and terminally ill patient and his family. There is no integrated body of knowledge in the social work field pertaining specifically to that area of case work practice in which the individual's anxieties and fears stem from the threat of death. Therefore, it is hoped that the material derived from this preliminary study may contribute to this area of practice and will stimulate interest in other related areas of research.

PUBLIC HEALTH SERVICE - - NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13422-21

2. Clinical Center
INSTITUTE OR DIVISION

3. NINDB
LABORATORY, BRANCH, OR DEPARTMENT

4. Social Service Department
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. Study of Factors Associated with Sustained Family Interest in Institutionalized Children.
PROJECT TITLE

7. Shirley Helmich, M. A.
PRINCIPAL INVESTIGATORS

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION:

Objectives:

To evaluate whether variances of child's disability, family background, reason for institutionalization bear any correlation with evidence of sustained family interest in child.

Methods Employed:

1. Obtain information on above factors from records of District Training School and from parents and/or other family members whenever available.

2. Evaluation of family's continuing interest in child from District Training School records showing relative visits and contacts and from attitudes determined in interview situation.

3. Analysis of above material.

Study Material:

The 40 cases to be reviewed form a group of patients transferred from the District Training School to NINDB for periods of two weeks in patient studies under Dr. Anatole Dekaban's study of mental deficient. All of patients are mental deficient of varying degrees of deficiency and physical involvement. Ages range at least from 5 years to 46 years. Length of institutionalization will range at least from 1 year to 30 years.

Preliminary Findings:

To date, forty case studies have been completed and are now being reviewed with reference to project objective: evaluation of whether variances in family background, child's disability, and reason for institutionalization bear any correlation with evidence of sustained family interest in an institutionalized child.

Case material is being further reviewed to determine feasibility of increasing number of case studies with additional data obtained regarding parents' adjustment to mentally defective child.

Significance to the Clinical Center and Social Service Research:

The material derived from this study will possibly contribute to the general knowledge of parent reactions to institutionalizing a child. Each such expansion to this knowledge seemingly has meaning to all professional personnel working with parents in planning institutionalization and to personnel within institutions. Specifically, I hope that this study will give clues warranting further study so that more valid evaluations can be made of the existence or lack of parents' sustained interest.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13402-02
SERIAL NUMBER

2. Clinical Center
INSTITUTE OR DIVISION

3. Professional Services Department
LABORATORY, BRANCH, OR DEPARTMENT

4. Clinical & Professional Education
SECTION OR SERVICE

5. _____
LOCATION (IF OTHER THAN BETHESDA)

6. _____
PROJECT TITLE

7. Chief, Dr. Murray C. Brown
PRINCIPAL INVESTIGATOR

8. _____
OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OF PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Not applicable.

10. PROJECT DESCRIPTION:

The Clinical and Professional Education Branch of the Clinical Center is concerned with formal educational activities for professional people, the conduct of staff meetings and other professional activities relating to the growth of professional competence and the maintenance of standards of clinical care. As an interim responsibility this office has also been responsible for Volunteer Services in the Clinical Center and the planning of communication services having potential educational implications. Its Chief also maintains a relationship to the Director of NIH and organizes and conducts educational programs of overall importance to the National Institutes of Health.

CLINICAL CENTER ACTIVITIES

Clinical Fellowships

There are six programs for the training of clinical fellows which have received approval for one or more years of Residency training from the appropriate American Specialty Board. In 1956 Radiology and Neurology extended their clinical training programs. They are now applying for three year approval of their residency programs. All programs for the training of Clinical Fellows with the exception of that in Clinical Pathology, were inspected by the AMA in November. Later in 1956 a new residency program in Oral Pathology was developed. The Medical Board has approved this program and it is now under review by the American Dental Association. This proposal required the prior development of a basis for ADA approval of the Clinical Center as an approved hospital.

There were eight Clinical Fellows appointed in 1956. Clinical Associates whose work closely parallels that of the Clinical Fellows, but who are not involved in formal training programs totaled 78.

Staff Meetings

There have been a total of 17 meetings of the combined clinical staffs of the National Institutes of Health during 1956. Ten of these meetings were Combined Clinical Staff Meetings. Four were Quarterly Staff Meetings and the remaining three were Clinicopathologic Conferences.

Education Committee of the Medical Board

This committee has been meeting on a monthly basis under the chairmanship of the Chief of this Branch. All Clinical Center Residency Programs were reviewed by the committee prior to the AMA inspection. Recommendations that the Neurology and Radiology Residency programs be extended to three years were sent to the Medical Board. Residency Program in Oral Pathology was approved and sent to the Medical Board for approval. Arrangements for the publication of four selected staff meetings in the ANNALS OF INTERNAL MEDICINE was made and approved by the committee. Medical Board approval was secured.

Volunteer Services

Regularly scheduled Volunteer Services have been limited to those provided by a cooperative arrangement between the American Red Cross and the Clinical Center, whereby the Gray Lady Corps of the Montgomery County Chapter created a Clinical Center Unit for this purpose. By January 1, 1957, five classes had been graduated and the group had grown from less than 30 to 73 Gray Ladies, despite the normal attrition to be expected in a volunteer group. During 1956 this group rendered more than 13,000 hours of volunteer service. In October the Gray Ladies were transferred from this Office to the newly created Patient Activities Section.

Television

During 1956 the radio and television distribution system for the Clinical Center was installed. Negotiations for the purchase of equipment to complete the control room are underway.

The 25 television experiments performed in 1955 were analyzed to determine probable values of importance to NIH in this new medium. Three scientific papers and a variety of lectures were presented before scientific bodies on the basis of this experience. A final film report on the experiments was completed. This has been reviewed by the Institute Directors and formed the basis for a projected two year study of the usefulness of television and associates electronic devices at NIH, now expected to begin in January 1957.

The Chief of this office attended RCA's technical school in television to familiarize himself with latest technical developments in this field. Negotiations with ONR, NNMC, USASC and industrial concerns (RCA, DuMont and CBS) have been directed at planning and securing equipment for 1957 studies. A variety of instruments and services will be available without cost for the contemplated studies which are designed to determine the desirability and the extent of usefulness of television in NIH undertakings.

ACTIVITIES CONDUCTED FOR NIH

Orientation of New Employees

The National Institutes of Health has had an organized program for the general orientation of new employees since July 1953. During 1956 eight series of orientation programs were conducted. A total of 2,834 people have attended the Compass Course since its beginning. A special orientation program was held for the medical and dental students on summer training duty.

The Chief of this Branch has also participated in an orientation program for new employees given by the PHS.

Graduate School

In 1954, a program of formal "out of working hours" courses was organized in cooperation with the Graduate School of the Department of Agriculture. Special committees of NIH scientists and other groups with special talents and interests were created to select the content and guide the conduct of these courses. The courses are offered at the employee's expense at the current rates charged by the Graduate School.

In the spring semester of 1956, there were 187 people enrolled in 16 courses. In the fall semester of 1956, there were 375 people registered for 22 courses.

Out of 35 one-course scholarships warded by the USDA to employees in the Washington area, three went to NIH employees. The candidates were nominated for scholarships through their Institutes, and final selection was made by the USDA Graduate School Scholarship Committee.

Scientific Advisory Committee

During 1956 this committee has been meeting on a monthly basis. Most of the committee's time has been spent on the planning of a program for "research associates". This is a combined preceptor and formal integrated basic science program for the development of research competence in young M.D.'s. A definite proposal was drawn up and submitted to the scientific directors for approval. Definite course outlines were also planned. This program has now been approved and appointments of a limited number of M.D. candidates will be made effective July 1, 1957.

PHS Committee on Residency and Internships

Activities of this committee have made increasing demands on this office. All applications for residency training from NIH people have been channeled through this office to the Committee. Also the applications for deferment of men under the Berry plan.

Summer Student Training Program

The NIH employed 50 medical students and 4 dental students for summer training duty in the summer of 1956. The educational aspects of this program and much of the NIH portion of its administration were handled by this office. A special orientation program was held for the students. Regular weekly seminar type scientific meetings were also held for the students. Plans are now going forward for the summer of 1957. The program will involve approximately 100 students in 1957. The Chief of this Branch has been made Chairman of the PHS Committee responsible for this program.

Committee on Training Outside the Service

Counseling of younger staff members regarding their professional development has been increasing. The Chief of this Branch was made a member of this Committee in October 1956. An increasing number of NIH applications for such training are reviewed by this office and staff work incidental to them is increasing.

In-Service Training

In November of 1955 this office secured the services of a training officer and a Public Health Educator, whose duties are to stimulate and coordinate instructional programs designed to improve the work performances at NIH. An orientation program for the Housekeeping Section, a program for Animal Caretakers, orientation program for the Guard Force and a Junior Management Intern Program were all undertaken in 1956.

In-Service Training at Sub-Professional Levels

Histology Course - At the request of the Technicians Study Group of the NCI, Laboratory of Pathology, a class in Histology was organized as a voluntary undertaking without academic credit and initiated in the research laboratories of the NCI for the technical staff of the LP. It was begun in April, 1956, discontinued for the summer months, and resumed in September to continue through December 1956. The course is given chiefly on the students' own time and does not involve Government working hours, except the lecture hour from 4 to 5 p.m. There are 33 students enrolled in the class. A total of approximately 110 hours of medical school level instruction was offered.

Patient Orientation Program - A proposal for this activity has been under study by a Clinical Center Committee chaired by Mr. Staton of this office.

Miscellaneous

The Chief of this Branch has been active on the Interagency Committee on Medical Education for National Defense throughout the year and has assisted in the planning of presentations for Deans and Coordinators of the Medical Schools participating in the MEND Program. He has attended national meetings of those organizations dealing with medical education.

There has been an increasing demand for programs for medical students in local medical schools regarding the PHS and NIH functions. A number of two hour programs have been set up for these students and for occasional groups visiting from a distance. In this connection a formal program of instruction for visiting medical students in preventive medicine is under consideration.

Ad Hoc Committee re Policy on Visitors - Recommendations re the NIH policy on the management of visitors has been given by this committee.

High School Science Teachers - The 1957 program has been placed in this office.

ORP-1 (concl'd)
Serial No. 13402-02

Calendar Year 1956

Course for Teachers of Homebound Children - This activity of the District Teacher's College is in a planning stage. Active cooperation by the Rehabilitation Department of the Clinical Center in the teaching of medical aspects of handicapped children is a likely development.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

Part A. Project Description Sheet

1. 13412 - 12

SERIAL NUMBER

2. Clinical Center

INSTITUTE OR DIVISION

3. Employee Health Service Branch

LABORATORY, BRANCH, OR DEPARTMENT

4.

SECTION OR SERVICE

5.

LOCATION (IF OTHER THAN BETHESDA)6. Employee Health

PROJECT TITLE

7. John M. Lynch, M. D., Chief

PRINCIPAL INVESTIGATOR

8. Walter R. Thayer, M. D., Frances S. Wolford, R. N.

OTHER INVESTIGATORS

9. IF THIS PROJECT RESEMBLES, COMPLEMENTS, OR PARALLELS RESEARCH DONE ELSEWHERE IN THE PUBLIC HEALTH SERVICE (WITHOUT INTERCHANGE OR PERSONNEL, FACILITIES OR FUNDS), IDENTIFY SUCH RESEARCH: (BY SERIAL NO. (S) IF WITHIN NIH).

Plant Safety Branch, DBO
Sanitary Engineering Branch, DRS

10. PROJECT DESCRIPTION:

OBJECTIVES AND METHODS EMPLOYED

In summary, the Employee Health Service has a dual responsibility; first to management, in general to act as the focal point for all matters relating to the health of employees, to assist in the prevention and control of occupational injury and disease, and to reduce sickness absenteeism. Secondly there is a responsibility to the employees to assist them in maintaining their health at the highest possible level consistent with good preventive health practices by the provision of such services as immunizations, health advice and guidance, and periodic physical examinations.

NUMBERS AND KINDS OF MAJOR SERVICES RENDERED

	<u>1956</u>	<u>1955</u>
Total Visits	23,339	20,959
Visits for Occupational Injuries and Diseases	2,960	2,633
Immunizations	3,009	2,413
Preemployment Physical Examinations	1,915	1,351
Laboratory Examinations	5,945	6,475
Referrals to Personal Physicians	1,353	1,681

MAJOR PROBLEMS, PRESENT STATUS

1. Excessive workload, due both to the high number of new employees coming to NIH and the sudden loss of several staff nurses during the year, has been our most difficult problem. Fortunately our nursing staff is now up to its authorized level. Staff enlargement, including clerical, medical, and laboratory personnel, still is necessary however.

2. Space is currently barely adequate in the Building 10 Health Unit. In the future, this space will be entirely inadequate.

IMPORTANT PROGRESS OR IMPROVEMENT ACHIEVED

1. The trend in program emphasis continues in the proper direction in favor of preventive medicine over curative medicine. This trend should be strengthened in the future as a result of the new Commissioned Officers' Dependent Medical Care legislation which will make it more unlikely that we will be called upon to provide services for dependents. Highly successful preventive medical programs continuing from previous years include periodic vaginal cytology examinations, trichomonas control, beta hemolytic streptococci control, periodic chest X-rays, and the provision of influenza virus and tetanus toxoid immunizations. The continuing services of a Psychiatric Consultant, assigned to us by NIMH, has been of great value in assessing emotional and behavior problems, and in making referrals when necessary. Likewise the Weekly Skin Clinici, staffed by NCI Dermatologists, and the many other courtesy services extended by the other Institutes and CC Departments, have been very helpful.

2. Acquisition of a second medical officer has increased the quantity of services available to employees and has eliminated the necessity for calling upon Institute physicians to serve as relief-duty officers for the Employee Health Service. The addition of another Public Health nurse to the staff was of great assistance in our efforts to emphasize preventive medicine. Although covered completely in previous reports, we feel compelled to restate the tremendous contributions the medical students made to our program during the Summer.

3. Progress in Occupational Disease Control has been steady although much more remains to be done in this area. Results of the joint efforts of the various service groups which comprise the Environmental Health Advisory Group have been encouraging, particularly the Building 6 survey. Currently, Building 7 is under study, and because of the biological hazards associated with this building, we are hopeful that this particular study will achieve much in the prevention and control of Occupational Diseases. Notable efforts in Occupational Disease Control this year have included polio immunizations for all of DBS personnel, an expanded program of tuberculosis skin testing in addition to periodic chest X-rays, and a revised program of periodic blood chemistries for employees exposed to toxic chemicals. The Division of Biologic Standards has been particularly helpful during the year in our efforts to improve our Occupational Disease Control program and there is currently underway a project with DBS to evaluate thoroughly all of the various administrative and technical problems relating to such a program. It is hoped that the lessons learned can be applied to the other Institutes and service areas in the near future.

PROPOSED COURSE OF ACTIVITIES DURING THE NEXT CALENDAR YEAR

1. Emphasis will be placed on increased activities in the area of Occupational Disease Control. Greater efforts will be made to collaborate more actively in projects sponsored by the Environmental Health Advisory Group, particularly those pertaining to biological and toxic chemical hazards. Progress in alleviating the serious problems caused by allergies to laboratory animal dusts and danders can be expected during the coming year as a result of the establishment of an Allergy Clinic in cooperation with the National Cancer Institute. The Clinic to be staffed by a Cancer Institute physician will be held once weekly in the Employee Health Service. The Cancer Institute hopes to benefit from the project by obtaining a readily available group of subjects with allergic conditions some of which might hold the clue for the interesting interrelations between allergy and cancer.

2. In as much as several collaborative projects with Institute physicians over the past years have indicated the existance of valuable research material in an employee population, additional efforts will be made as time permits to discover and develop the vast potential for research material that exists in the NIH employee population. As our employee population stabilizes, it could become, in the hands of qualified investigators, a valuable tool in following the progress of the degenerative diseases. The Employee Health Service welcomes an opportunity, and feels it has a responsibility, to collaborate with any Institute physicians along these lines.

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PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- | | |
|---|---|
| 1. <u>A-100</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Anesthesiology</u>
SECTION OR SERVICE |
| 5. <u>Electrocardiographic and electroencephalographic changes in patients undergoing hypothermia and prolonged light general anesthesia</u>
PROJECT TITLE | |
| 6. <u>J. W. Severinghaus, M.D.</u>
PRINCIPAL INVESTIGATOR | 7. <u>C. L. Hebert, M.D., J. E. Merzig, M.D.</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

Certain technical difficulties arise in the monitoring of heart action and brain activities during the actual processes concerned with the lowering of body temperature for therapeutic purposes in conjunction with some types of surgery. Similar problems are encountered during the rewarming phase. The ordinary external electrical leads attached to the limbs of patients become disarranged during certain maneuvers thus interfering with electrical recordings. Studies were made to determine the advantages that accrue with the use of electrocardiographic leads attached to an internal probe inserted into the esophagus. A special device called the Telecor was designed and constructed by the principal investigator which will permit the recording of electrocardiographic readings from the esophageal probe and in addition will produce an audible signal with each beat of the heart, an additional safeguard in the management of patients in precarious circulatory conditions.

Electroencephalographic studies on patients under prolonged light general anesthesia were done to determine the value of this modality in the safe handling of patients where circumstances do not permit use of more potent but explosive anesthetic agents.

(For remaining data see Report Serial Number 13432-34.)

PART B.

No special budget for this project. See Anesthesiology Department Main Report, Serial No. 13432-34.

PART C.

See Anesthesiology Department, Serial No. 13432-34.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| <p>1. <u>A-101</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Anesthesiology</u>
SECTION OR SERVICE</p> |
| <p>5. <u>Effects of rapid administration of cold blood on body temperature during surgery requiring transfusion of large amounts of blood</u>
PROJECT TITLE</p> | |
| <p>6. <u>C. L. Hebert, M.D.</u>
PRINCIPAL INVESTIGATOR</p> | <p>7. <u>G. R. Christenson, M.D.</u>
OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

Special clinical observations were made to determine the influence of a rapid administration of large quantities of blood on the body temperature. Since clinical methods for determining blood pressure become less accurate with lowered body temperature, it was found to be very important to take body temperature into consideration when difficulty with blood pressure determinations was observed. These studies indicated that a definite fall in temperature occurred with the rapid administration of cold blood such as might be required during pelvic surgery. Accordingly blood pressure readings had to be interpreted with a view to body temperature in order to obtain a correct assessment of the current circulatory status of the patient. The value of monitoring body temperature in patients receiving large quantities of transfused blood was shown to have a definite advantage.

(For remaining data see Report Serial Number 13432-34.)

PART B.

No special budget for this project. See Anesthesiology Department Main Report, Serial No. 13432-34.

PART C.

See Anesthesiology Department, Serial No. 13432-34.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

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|--|---|
| 1. <u>A-102</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Anesthesiology</u>
SECTION OR SERVICE |
| 5. <u>Development of an inflatable plastic immersion tub for inducing hypothermia in the operating room</u>
PROJECT TITLE | |
| 6. <u>J. E. Merzig, M.D.</u>
PRINCIPAL INVESTIGATOR | 7. <u>C. L. Hebert, M.D.</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

Certain technical difficulties arise in the lowering of body temperature in anesthetized patients by immersion methods. Experience in removing patients from operating table into a tub for cooling or warming purposes and transferring them back to the operating table indicated that such movements were undesirable from the standpoint of producing undesirable circulatory reflexes and the dislodgement of leads, catheters, needles, etc. attached to the patient. A plastic inflatable tub was designed to fit on top of the operating table where it could be placed under the patient and inflated or deflated at will. Thus the patient could be immersed in water of any desired temperature. Studies are being continued to improve the design of this apparatus.

(For remaining data see Report Serial Number 13432-34.)

PART B.

No special budget for this project. See Anesthesiology Department Main Report, Serial No. 13432-34.

PART C.

See Anesthesiology Department, Serial No. 13432-34.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

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| 1. <u>A-103</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Anesthesiology</u>
SECTION OR SERVICE |
| 5. <u>Evaluation and modification of disposable plastic blood transfusion apparatus</u>
PROJECT TITLE | |
| 6. <u>C. L. Hebert, M.D.</u>
PRINCIPAL INVESTIGATOR | 7. _____
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

Laboratory and clinical tests were carried out on the new type of disposable plastic blood set designed for the administration of blood under pressure. The rapid and safe administration of blood under pressure and the elimination of the hazard of air embolism can be readily accomplished by this set which was developed by an independent manufacturer with certain suggestions from us. This device will be made commercially available in 1957.

(For remaining data see Report Serial Number 13432-34.)

PART B.

No special budget for this project. See Anesthesiology Department Main Report, Serial No. 13432-34.

PART C.

See Anesthesiology Department, Serial No. 13432-34.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

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| <p>1. <u>A-104</u>
 SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
 INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
 LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Anesthesiology</u>
 SECTION OR SERVICE</p> |
| <p>5. <u>Evaluation of devices producing artificial respiration in patients with respiratory depression</u>
 PROJECT TITLE</p> | |
| <p>6. <u>C. L. Hebert, M.D.</u>
 PRINCIPAL INVESTIGATOR</p> | <p>7. <u>J. E. Merzig, M.D.</u>
 OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

An experimental apparatus was supplied to us by the manufacturer for use in maintaining respiratory function over long periods of time. This improved device is an adjunct to the respiratory ventilator which we use in conjunction with anesthesia machines during prolonged surgery. Clinical tests were made to ascertain if the standard anesthesia ventilator modified by the addition of a no-rebreath head would have clinical application in the field of respiratory treatment. There seems to be a general trend for intermittent cycling devices which will deliver atmospheres under pressure into the respiratory tract of patients to accomplish artificial respiration rather than depending upon the iron lung type of equipment for this purpose. Therefore studies of respiratory ventilation equipment which may be used outside the operating room are definitely in order.

(For remaining data see Report Serial Number 13432-34.)

PART B.

No special budget for this project. See Anesthesiology Department Main Report, Serial No. 13432-34.

PART C.

See Anesthesiology Department, Serial No. 13432-34.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-01</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
| <p>5. <u>Early changes of protein characteristics in virus infected tissue culture cells detected by ultraviolet television microscopy.</u>
PROJECT TITLE</p> | |
| <p>6. <u>G. Z. Williams</u>
PRINCIPAL INVESTIGATORS</p> | <p>7. <u>C. H. Zierdt</u>
OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

Caspersson in the Karolinska Institute of Stockholm, Sweden, has indicated in a personal communication that tissue culture cells of various types, for instance, monkey kidney cells after infection by certain viruses show a marked increase in density and an altered distribution of the protein in the cytoplasm. This can be detected by ultraviolet absorption characteristics. Our instrumentation for direct visualization of ultraviolet absorption patterns in living cells by the television instrument makes it feasible for us to directly view large numbers of tissue culture cells which have been treated in various manners, particularly after injection with different viruses. In cooperation with Dr. Joel Warren of the Division of Biologics Standards, we are obtaining tissue cultures of various cells and infecting them with different viruses. The ultraviolet absorption pattern of these cells is being determined and recorded before and at varying periods after the virus infection in an attempt to learn the earliest possible period at which the virus infection will be manifested by an increased density or other alteration of the living cultured cell.

If very early significant characteristics and alterations are detected, this technic constitutes a rapid method for determining virus infection and will greatly aid in more rapid diagnostic and checking procedures.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-02 + 2. Clinical Center
 SERIAL NUMBER INSTITUTE OR DIVISION

3. Professional Services 4. Clinical Pathology
 LABORATORY, BRANCH, OR DEPARTMENT SECTION OR SERVICE

5. Cytochemical studies of marrow cells in patients with anemia, leukemia and infections by ultraviolet television microscopy and oscillography.
 PROJECT TITLE...

6. G. Z. Williams 7. T. F. Dutcher
 PRINCIPAL INVESTIGATORS OTHER INVESTIGATORS

8. PROJECT DESCRIPTION

It has been reported by one other investigator and has been confirmed in our studies that progenitor cells of the bone marrow when differentiated sufficiently will show the presence of small amounts of hemoglobin in the cytoplasm when the cells are differentiating to erythrocytes. In the differential diagnosis of leukemia, leukemoid reaction and certain unusual anemias, this property is very helpful in distinguishing between young cells which are of the red cell series and those which are of the leukemic types. Such information is valuable in combination with phage microscopy and the Giemsa stained preparations of the bone marrow in arriving at correct diagnosis of these blood disorders in patients in the Clinical Center.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department; Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-03</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
- Alterations of the ultraviolet absorption of cytoplasm and nucleus of
5. living cells (liver) produced by injury and cell deaths.
PROJECT TITLE
6. G. Z. Williams
PRINCIPAL INVESTIGATOR

7. PROJECT DESCRIPTION

Most of the cytological studies of injury have been done on killed and fixed and otherwise altered cell preparations, and there is little information comparing the changes seen in these preparations with the state of the same cellular structures in life. With the ultraviolet microscope, the cells may be observed in the living state without alteration and then photographed by motion picture or serial photographs as injury is occurring after the addition of agents such as distilled water, fixatives, etc. These changes can be followed as they occur in the nucleus and the cytoplasm because of the nature of ultraviolet absorption which simultaneously provides chemical information and morphological pattern. These studies are being done with mouse and rat liver preparations. One of the surprising results is that the appearance and the apparent nature of the chromatin material in the nucleus of cells is much different in the living cell from that in the cell which has been fixed by alcohol, formaldehyde, or which has been injured by distilled water, hypertonic salt solutions, and other agents. Even early autolysis produces marked changes in the shape and absorption characteristics of the nucleus.

(For remaining data see Report Serial No. 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-04 2. Clinical Center
 SERIAL NUMBER INSTITUTE OR DIVISION
2. Professional Services 4. Clinical Pathology
 LABORATORY, BRANCH, OR DEPARTMENT SECTION OR SERVICE
5. Studies in Supravital Enzyme Cytochemistry (investigation of metabolic enzyme reactions within living cells). I. Localization of esterases in liver cells. PROJECT TITLE II. Localization of phosphatases in liver cells. III. Localization of dehydrogenases in liver cells.
6. G. Z. Williams 7. T. F. Dutcher, A. Peacock, R. Reid
 PRINCIPAL INVESTIGATOR OTHER INVESTIGATORS

8. PROJECT DESCRIPTION

These projects all involve the observation of living cells while enzyme substrates are applied for the purpose of visualizing the location within the cells where the enzymes act to split the substrate from the side chain producing an ultraviolet absorbing chemical. By the Gomeri procedure applied to freshly prepared liver cells, we have demonstrated a diffuse and apparently uniform darkening of the cell cytoplasm due to release of the naphthol group which becomes insoluble as the enzyme enterase acts on the parent chemical to which the cell is exposed. Similarly with the new chemical compound, formazan phosphate, first successfully synthesized by Dr. Peacock, the soluble material is absorbed by the liver cell and the phosphatase present in the cytoplasm splits off the phosphate group leaving a relatively insoluble formazan which precipitates in very minute granules at the site of this action. Very recently this phenomenon has been demonstrated in living cells under the TV ultraviolet microscope with a uniform distribution of the apparent activity throughout the cytoplasm, but not in the nucleus of the cell. Similar technics are being utilized in an attempt to localize a number of different enzymes and their co-enzymes in the living cell by utilization of a battery of varying tetrazolium compounds and substrate. Following the modified technics of Farber and Glick and others a system of compounds and substrates which can be tolerated by the specially prepared living cells is being devised for visual localization of these enzyme activities within the intact cell.

(For remaining data see Report Serial No. 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. <u>CP 56-05</u> SERIAL NUMBER	2. <u>Clinical Center</u> INSTITUTE OR DIVISION
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3. <u>Professional Services</u> LABORATORY, BRANCH, OR DEPARTMENT	4. <u>Clinical Pathology</u> SECTION OR SERVICE
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5. Investigation of the multiple nature of serum acid phosphatases.
PROJECT TITLE

6. A. C. Peacock
PRINCIPAL INVESTIGATORS

7. PROJECT DESCRIPTION

It has been well-established that there are a number of acid phosphatases in human serum. An attempt is being made to characterize these and devise methods for their assay as separate enzymes. It is anticipated that some clinical utility may be achieved by thus increasing the specificity of the measurements.

(For remaining data see Report Serial No. 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.



PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-06</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
| <p>5. <u>Isolation of viruses from mouse ascites tumor cell cultures.</u>
PROJECT TITLE</p> | |
| <p>6. <u>G. Z. Williams</u>
PRINCIPAL INVESTIGATORS</p> | <p>7. <u>R. Reid, and C. H. Zierdt</u>
OTHER INVESTIGATORS</p> |

8. PROJECTION DESCRIPTION

Degenerative changes in ascites tumors, particularly HS-1 and K-2 have led to the belief that there may be virus contamination of these tumors. Macerated portions of animals host to these tumors and of the tumor ascites preparations themselves have been inoculated into mouse brains and into tissue cultures in an attempt to isolate and if successful in isolation, to identify any viruses which may be present in these tumors. To date no evidence of presence of such viruses has been obtained, but the project is being continued for further and more definitive information.

(For remaining data see Report Serial No. 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| 1. <u>CP 56-11</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
5. Identification and comparison of non-tuberculous chromogenic acid-fast organisms for pathogenicity.
 PROJECT TITLE
6. E. Singer
 PRINCIPAL INVESTIGATORS

7. PROJECT DESCRIPTION

One strain was isolated early in 1956, two more during the year. It was tried to develop methods which could:

- a) distinguish these strains from M. tuberculosis;
- b) from non-pathogenic acid-fast contaminants.

Standard tests as used for the determination of virulence, such as test for "cording" in Dubos medium, neutral red test, etc., failed completely. Some saprophytic strains gave positive tests and some virulent strains negative tests. Further trials were made with the testing of these strains against antibiotics. Pathogenic strains are all resistant to antibiotics, Para-amino-salicylic acid and iso-nicotinic-acid amide, but so are some of the saprophytic strains.

Morphologically, the strains resemble the saprophytic strains more closely than M. tuberculosis, but there is no sharp distinguishing mark. Attempts to differentiate the strains serologically have failed. Sera produced against virulent and avirulent strains give cross-reactions and can be cross-absorbed.

The only reliable test so far seems to develop from animal experimentation. The pathogenic strains seem to be able to infect guinea pigs, and, although they produce only a limited infection, sensitize the animal against tuberculin.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

CP 56-11 (Continued)

Some saprophytic strains produce local abscesses, and the organisms can be recovered from lymph glands and spleen; but the animals remain non-reactive to tuberculin.

(For remaining data see Report Serial No. 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| 1. <u>CP-56-12</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
- Study of phage types of staphylococci in the patient population of the
5. Clinical Center in relation to pathogenicity.
PROJECT TITLE
6. E. Singer
PRINCIPAL INVESTIGATOR

7. PROJECT DESCRIPTION

Strains of staphylococci which are isolated from wounds, throat-swabs, stools, etc., are tested with standard phages and at the same time for the production of diffusible antigens by an agar-diffusion technique.

The problems studied are:

- 1) Whether pathogenic strains can be distinguished from apathogenic strains by either technique.
- 2) Whether strains which produce enteric symptoms (e. g., in patients treated with antibiotics) are of a certain phage type or are characterized by certain precipitation bands.
- 3) Whether enteric strains are identical with strains carried by the patient himself or by nursing personnel.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department; Serial No. 13432-37

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| 1. <u>CP 56-13</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>Bactericidal properties of blood of leukemic and non-leukemic patients.</u>
PROJECT TITLE | |
| 6. <u>E. Singer</u>
PRINCIPAL INVESTIGATORS | |

7. PROJECT DESCRIPTION

Plans had been made to compare the bactericidal properties of blood from normal controls with the blood from patients who are notoriously sensitive to infections, such as patients suffering from leukemia, diabetes, etc.

A few tests have been made; but, since Dr. Kirschstein left, no further work could be done.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-14</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
5. A serological survey of agglutinins against listeria in the blood of Clinical Center patients.
PROJECT TITLE
6. E. Singer
PRINCIPAL INVESTIGATORS

7. PROJECT DESCRIPTION

Approximately 10% of the patients and a smaller percentage of employees and blood donors give a positive agglutination with one or more serotypes of *Listeria monocytogenes*.

(For remaining data see Report Serial Numer 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

1. CP 56-21
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. The measurement of the concentration and relative distribution of Human Serum Proteins by electrophoretic and chemical methods on normal subjects in active and resting states.
PROJECT TITLE
6. A. T. Ness
PRINCIPAL INVESTIGATORS
7. H. C. Dickerson
OTHER INVESTIGATORS

8. PROJECT DESCRIPTION

Diagnosis and treatment of some diseases are partly based on serum protein analyses referred to protein analyses on normal subjects in the active state. Since many patients are usually in an extended resting state, it is necessary to know normal values on subjects also in the extended resting state, if comparative data is to be properly assessed. It has been observed that out-patients show a significant marked difference in relative distribution and concentration of serum proteins compared to in-patients, and seemingly independent of the disease state.

It is proposed to obtain protein analyses on normal subjects in active and extended resting states.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-22</u>
 SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
 INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
 LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
 SECTION OR SERVICE</p> |
| <p>5. <u>A study of the factors which affect the electrophoretic mobility and dye absorption of proteins in paper electrophoresis.</u>
 PROJECT TITLE</p> | |
| <p>6. <u>A. T. Ness</u>
 PRINCIPAL INVESTIGATORS</p> | <p>7. <u>H. C. Dickerson</u>
 OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

Paper electrophoresis is rapidly establishing itself as a routine procedure for determining the distribution of serum proteins. It is important to evaluate critically the experimental factors involved in this technique, since the voluminous literature of recent years has reported confusing and conflicting results.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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|---|---|
| 1. <u>CP 56-23</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>A study of the protein-binding capacity of blood fatty acids using
 radio-active tagged compounds and paper electrophoresis.</u>
PROJECT TITLE | |
| 6. <u>A. T. Ness</u>
PRINCIPAL INVESTIGATORS | 7. <u>H. C. Dickerson and R. S. Gordon</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

This is a cooperative project in basic research on some aspects of fat metabolism. Studies are being made of the factors involved in the transport of fatty acids by the proteins of blood. The use of paper electrophoresis and radio-actively tagged fatty acids has indicated that these acids are bound to serum albumin rather than being transported as free fatty acids.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

- 1. CP 56-24
SERIAL NUMBER
- 2. Clinical Center
INSTITUTE OR DIVISION
- 3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
- 4. Clinical Pathology
SECTION OR SERVICE
- 5. An investigation of the various factors and conditions required for the specific determination of Blood Glucose.
PROJECT TITLE
- 6. A. T. Ness
PRINCIPAL INVESTIGATORS
- 7. H. C. Dickerson
OTHER INVESTIGATORS

8. PROJECT DESCRIPTION

Accurate blood glucose analyses are necessary for the diagnosis and treatment of certain metabolic diseases. Our recent comparative evaluation of various methods of determining blood glucose has revealed that the currently used methods too frequently yield erratic results. Our study has resulted in some degree of improvement, but further investigation is being continued.

(For remaining data see Report Serial No. 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| 1. <u>CP 56-25</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>A study of the factors which influence the binding of the dye of Hydroxy-</u>
<u>benzeneazobenzoic Acid with protein, with particular reference to Human</u>
PROJECT TITLE Serum Albumin. | |
| 6. <u>A. T. Ness</u>
PRINCIPAL INVESTIGATOR | 7. <u>H. C. Dickerson</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

This is the dye used for the determination of serum albumin by a procedure developed in this laboratory. Rarely, a serum is encountered in which the albumin does not quantitatively bind the dye. It seems that the albumin of these subjects is either qualitatively different from normal albumin or that some of the dye-binding sites are occupied by other molecules which cannot be displaced by the dye. The exact cause of this interference has not been ascertained, and the investigation is being continued.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-26</u>
 SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
 INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
 LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
 SECTION OR SERVICE</p> |
| <p>5. <u>The measurement of free beta-1-globulin (metal-binding protein) which is an important factor in diseases involving iron metabolism.</u>
 PROJECT TITLE</p> | |
| <p>6. <u>A. T. Ness</u>
 PRINCIPAL INVESTIGATORS</p> | <p>7. <u>H. C. Dickerson</u>
 OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

Certain hematological diseases require accurate data for serum iron and serum total iron-binding capacity. A new and simple method for determining serum iron has been developed in this laboratory and has been written up for publication. The available methods for measuring the serum iron-binding capacity are inadequate in precision and accuracy. Study is in progress to develop a method to obtain more reliable data from this determination.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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|-----------------------------------|------------------------------|
| 1. <u>CP 56-31</u> | 2. <u>Clinical Center</u> |
| SERIAL NUMBER | INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u> | 4. <u>Clinical Pathology</u> |
| LABORATORY, BRANCH, OR DEPARTMENT | SECTION OR SERVICE |

The effect of a high protein meal on the level of individual plasma amino acids in humans at various intervals after feeding.

PROJECT TITLE

6. E. Frame

PRINCIPAL INVESTIGATORS

7. PROJECT DESCRIPTION

Because of the lack until recently of suitable analytical techniques, little is known about the absorption from the intestine of the products of protein feeding. With the new technique of chromatography on columns of ion-exchange resins for the quantitative determination of all the common amino acids, a fresh approach is being made to this study. Normal persons are given a high-protein meal, and the plasma drawn at varying intervals after the meal is analyzed for its individual amino acid content. Changes from the fasting values are compared with the composition of the protein fed. Preliminary results indicate that the individual amino acids are absorbed into, or removed from, the plasma at different rates. In the present study, after the picture in normal persons has been established, it is proposed to extend the work into clinical fields.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

THE UNIVERSITY OF CHICAGO

DEPARTMENT OF CHEMISTRY

RESEARCH REPORT

NO. 10

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PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-32</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
| <p>5. <u>Quantitative analysis of the individual amino acids in normal and neoplastic tissues.</u>
PROJECT TITLE</p> | |
| <p>6. <u>K. M. Herrold</u>
PRINCIPAL INVESTIGATORS</p> | <p>7. <u>E. Frame</u>
OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

The free amino acid content of cells is considered to be a function of their metabolic activity. The method used in this experiment is chromatographic analysis of the protein free extracts on columns of sulfonated polystyrene resins. The comparison of the pattern of free and easily extractable amino acids in normal and neoplastic tissue may show some biochemical differences. Also, antimetabolites and chemicals when used in the treatment of cancer may reflect changes in these patterns. Better understanding of biochemical differences between normal and neoplastic tissue may further elucidate the potential roll and value of specific antagonists in the chemotherapeutic approach to cancer.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT SHEET

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|---|---|
| <p>1. <u>CP 56-33</u>
 SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
 INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
 LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
 SECTION OR SERVICE</p> |
| <p>5. <u>Evaluation of simplified technic for the determination of serum transaminase.</u>
 PROJECT TITLE</p> | |
| <p>6. <u>E. Frame</u>
 PRINCIPAL INVESTIGATOR</p> | <p>7. <u>K. B. Stokes</u>
 OTHER INVESTIGATOR</p> |

8. PROJECT DESCRIPTION

The clinical value of serum transaminase levels is well known, and a large number of such determinations are performed in this laboratory each week. The method now being used is quite time-consuming. If a simple technique which has recently been described is found to give reliable results, there will be a considerable saving in technician time. Preliminary results have been encouraging.

(For remaining data see Report Serial Number 13432-37)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| 1. <u>CP 56-34</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Service</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>The effect of the administration of Bromsulfalein on serum protein-bound iodine levels.</u>
PROJECT TITLE | |
| 6. <u>E. Frame</u>
PRINCIPAL INVESTIGATOR | 7. <u>J. V. Pastewka</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

It has been suggested that the administration of Bromsulfalein may cause falsely elevated values of serum protein-bound iodine. It is important to have definite information on this point for the interpretation of results in certain patients. Preliminary results indicate that Bromsulfalein administration is without significant effect on the level of serum protein-bound iodine.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

THE UNIVERSITY OF CHICAGO
DEPARTMENT OF CHEMISTRY

MEMORANDUM FOR THE RECORD
DATE: 1954

RE: [Illegible]

BY: [Illegible]

APPROVED: [Illegible]

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-35
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. A study of the electrolyte levels of serum from blood drawn under oil and
PROJECT TITLE without oil.
6. E. Frame
PRINCIPAL INVESTIGATOR
7. K. B. Stokes
OTHER INVESTIGATOR

8. PROJECT DESCRIPTION

It is known that when blood is exposed to air, carbon dioxide escapes from the plasma and there are exchanges of sodium, potassium and chloride between cells and plasma. In order to minimize such changes in the determinations of serum electrolytes, our present practice is to analyze serum from blood drawn under oil. Information is not available as to the magnitude or direction of changes which are encountered when this precaution is not taken. It is important to obtain this knowledge because an occasional specimen is received in our laboratory which has not been drawn under oil, and also for purposes of comparison of results with those from other laboratories where this precautionary measure is taken. Preliminary results indicate that there is a significant difference in electrolyte values between the two methods of handling the blood.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-41</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
| <p>5. <u>Study of possible seasonal changes in red cell size.</u>
PROJECT TITLE</p> | |
| <p>6. <u>G. Brecher</u>
PRINCIPAL INVESTIGATOR</p> | <p>7. <u>J. C. Peden and T. F. Dutcher</u>
OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

Recently, electronic devices have become available that permit counting of red blood cells with high accuracy. Since the volume of the red cell must be determined from the volume of packed cells divided by the number of cells, the better red cell counts have also improved measurement of red cell volume. During these studies a possible seasonal variation in red cell size was observed. If confirmed, these observations should further our understanding of forces which maintain red cell size in narrow limits in the body.

(For remaining data see Report Serial No. 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| 1. <u>CP 56-42</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>Investigation of disparity of red cell, hemoglobin and hematocrit values from finger puncture and venous blood.</u>
PROJECT TITLE | |
| 6. <u>G. Brecher</u>
PRINCIPAL INVESTIGATOR | 7. <u>J. C. Peden</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

The disparity between venous and peripheral red cell values is of practical interest. Significant differences have been observed occasionally which may conceivably be of clinical importance. Moreover, arterio-venous differences in red cell size, if confirmed, and exploration of causes of this difference should help our understanding of normal physiology of red cells.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-43
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. Histochemical procedures to aid in the differential diagnosis of leukemia.
PROJECT TITLE
6. T. F. Dutcher
PRINCIPAL INVESTIGATOR

7. PROJECT DESCRIPTION

Differential diagnosis of infectious and leukemic leukocytosis (chronic myelogenous leukemia) is one of the most difficult diagnostic problems in hematology. Measurements of WBC alkaline phosphatase by histochemical and test tube methods aid in distinguishing these two conditions (alkaline phosphatase being high in normal granulocytes, low in leukemic ones), although these cells may be indistinguishable by routine stains.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-44 SERIAL NUMBER 2. Clinical Center INSTITUTE OR DIVISION

3. Professional Services LABORATORY, BRANCH, OR DEPARTMENT 4. Clinical Pathology SECTION OR SERVICE

5. Differentiation of various white blood cells by new histochemical technics. PROJECT TITLE

6. T. F. Dutcher PRINCIPAL INVESTIGATOR

7. PROJECT DESCRIPTION

This success of histochemical method led us to explore histochemical means to distinguish different types of morphologically similar leukemias. If a subdivision of leukemias into biochemically different types and correlation with the effects of treatment could be established, this would be a major advance in present evaluation of chemotherapy.

(For remaining data see Report Serial No. 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

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PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
INDIVIDUAL PROJECT REPORT

- 1. CP 56-45
SERIAL NUMBER
- 2. Clinical Center
INSTITUTE OR DIVISION
- 3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
- 4. Clinical Pathology
SECTION OR SERVICE
- 5. Fractionation of serum from patients with lupus and study of the relation-
ship of so-called L.E. material to phagocytosis by white blood cells.
PROJECT TITLE
- 6. G. Brecher
PRINCIPAL INVESTIGATOR
- 7. T. F. Dutcher
OTHER INVESTIGATORS

8. PROJECT DESCRIPTION

The "L.E. phenomenon" see in the blood of patients with lupus erythematosus consists of alteration of the nucleoprotein of WBC and subsequent ingestion of this altered nucleoprotein by normal cells. We have been able to separate these two stages and to show that only the first stage depends on the presence of the serum factor in typical lupus erythematosus. However in atypical cases, the altered nucleoprotein is not ingested by normal cells. This part of the question presents a serious diagnostic problem because the significance of these atypical L.E. tests is unknown. It is now being investigated by fractionation of L.E. serum and search for inhibitors of phagocytosis in these atypical cases.

(For remaining data see Report Serial No. 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-46
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. The role of cephalin and normal plasma lipids in blood coagulation, tested with the aid of Russel's viper venom.
PROJECT TITLE
6. G. Brecher
PRINCIPAL INVESTIGATOR
7. J. C. Peden and A. C. Peacock
OTHER INVESTIGATORS

8. PROJECT DESCRIPTION

Russel's viper venom is a "partial thromboplastin" which requires cephalin for optimal clotting activity. However, excess of cephalin inhibits the reaction. The probable explanation is the presence of both an activator and inhibitor in the crude cephalin. This appears borne out by preliminary experiments in which a purified fraction was still serving as an activator but was not inhibitory in excess concentration. The problem is of practical importance for the performance of clotting tests and of possible physiological importance for the role of normal and abnormal serum lipids in blood clotting.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH
 INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-47</u>
 SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
 INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
 LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
 SECTION OR SERVICE</p> |
| <p>5. <u>The normal turnover of leukocytes as determined by experimental transfusion</u>
 PROJECT TITLE of white cells.</p> | |
| <p>6. <u>G. Brecher</u>
 PRINCIPAL INVESTIGATOR</p> | <p>7. <u>J. C. Peden</u>
 OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

The rapid disappearance from the circulation of transfused leukocytes and the rapid fall in leukocyte values in certain shock stages led us to investigate the fate of these leukocytes. Preliminary findings suggest that the transfused cell may be removed by lymphnodes, as well as the spleen. There is some doubt as to the long-claimed role of lungs in leukocyte removal. Techniques for WBC transfusion developed at NIH have promise of solving this problem.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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| <p>1. <u>CP 56-48</u>
SERIAL NUMBER</p> | <p>2. <u>Clinical Center</u>
INSTITUTE OR DIVISION</p> |
| <p>3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT</p> | <p>4. <u>Clinical Pathology</u>
SECTION OR SERVICE</p> |
| <p>5. <u>Influence of minor daily bleedings of 30-50 cc. on reticulocyte levels and other blood cell indices, and concepts of regulation of red cell production.</u>
PROJECT TITLE</p> | |
| <p>6. <u>G. Brecher</u>
PRINCIPAL INVESTIGATOR</p> | <p>7. <u>J. C. Peden</u>
OTHER INVESTIGATORS</p> |

8. PROJECT DESCRIPTION

Regulation and maintenance of a steady RBC level has been ascribed to stimulation of RBC production by anoxia. Present experiments indicate that red cell production can be doubled and normal values maintained by daily bleedings of 30 - 50 cc. which represent 1% or less of blood volume and are too small to cause anoxia. These experiments have a bearing on the fundamental question of regulation of erythropoiesis.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

THE UNIVERSITY OF CHICAGO

PHYSICS DEPARTMENT

REPORT ON THE PROGRESS OF WORK

FOR THE YEAR 1912

BY

ROBERT A. MILLIKAN

AND

WALTER D. HULL

CHICAGO, ILL., 1913

THE UNIVERSITY OF CHICAGO PRESS

104 EAST HAWTHORNE AVENUE

CHICAGO, ILL.

1913

PRINTED IN THE U.S.A.

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1913

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- | | |
|--|--|
| 1. <u>CP 56-49</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>Speed of replacement of iron deficient (hypochronic) cells by normal ones</u>
PROJECT TITLE under iron therapy. | |
| 6. <u>G. Brecher</u>
PRINCIPAL INVESTIGATOR | 7. <u>J. C. Peden and T. F. Dutcher</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

DISCONTINUED.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

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|--|--|
| 1. <u>CP 56-50</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>Menstrual changes in serum iron content, possible attributable to hemolysis and resorption.</u>
PROJECT TITLE | |
| 6. <u>G. Brecher</u>
PRINCIPAL INVESTIGATOR | 7. <u>J. C. Pedan</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

Normally, only about one-third to one-half of the specific iron-binding protein in serum ("siderophyllin") is saturated with iron. Full saturation was noted in a few women during menstruation. This appears worthwhile establishing although the significance of these findings is unknown. The project is dormant for lack of volunteers and time in doing the large number of iron determinations.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

- | | |
|---|--|
| 1. <u>CP 56-51</u>
SERIAL NUMBER | 2. <u>Clinical Center</u>
INSTITUTE OR DIVISION |
| 3. <u>Professional Services</u>
LABORATORY, BRANCH, OR DEPARTMENT | 4. <u>Clinical Pathology</u>
SECTION OR SERVICE |
| 5. <u>The effect of serotonin (in vivo and in vitro) on blood clottings.</u>
PROJECT TITLE | |
| 6. <u>T. F. Dutcher</u>
PRINCIPAL INVESTIGATOR | 7. <u>B. J. Haverback</u>
OTHER INVESTIGATORS |

8. PROJECT DESCRIPTION

Several publications have appeared stating that the serotonin carried in the platelets of the blood is an important factor in the cessation of bleeding. Upon depleting platelets of their serotonin by administering reserpine to patients, we have determined that serotonin is not essential for the normal coagulation of blood as measured in the laboratory. We also demonstrated that the bleeding time of these patients was not prolonged following the serotonin depletion of their platelets. This work was published in the New England Journal of Medicine.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-52
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. Effect of Hydrocortisone in vitro on various types of white blood cells,
PROJECT TITLE
6. T. F. Dutcher
PRINCIPLE INVESTIGATOR

7. PROJECT DESCRIPTION

It is well known that the adrenal steroids, particularly hydrocortisone, will cause the lymphocytes to fall off in numbers in the circulating blood of normal persons but will not affect other circulating white cells, the neutrophils. It is sometimes impossible, by currently known methods, to differentiate between acute lymphocytic leukemia and acute myelocytic leukemia because the cells seen in the blood and bone marrow are extremely immature and all such immature cells resemble one another morphologically. If hydrocortisone would have the same effect on the immature lymphocytes seen in leukemia as it does in the normal lymphocytes and similarly have no effect on the immature neutrophils, it might then be possible to correctly diagnose these leukemias early. Studies are being done along this line by incubating the white cells of lymphocytic and myelocytic leukemias with a recently available water soluble hydrocortisone.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

To the Hon. Secy of the Interior

Washington, D.C.

Dear Sir:

I have the honor to acknowledge the receipt of your letter of the 10th inst.

and in reply to inform you that the same has been forwarded to the proper authorities.

I am, Sir, very respectfully,
Your obedient servant,

J. M. [Name]

Special Agent in Charge

Department of the Interior

Washington, D.C.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-53
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Services
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. Studies on the nature of the azutophil granules in lymphocytes.
PROJECT TITLE
6. T. F. Dutcher
PRINCIPAL INVESTIGATOR

7. PROJECT DESCRIPTION

Since the introduction of the Giemsa stain for blood smears over fifty years ago, observers have described the presence of red-purple staining granules in the cytoplasm of lymphocytes; but no one has ever described the chemical composition of such granules. Studies are being carried out in an attempt to discover the chemical nature of these granules.

(For remaining data see Report Serial Number 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

INDIVIDUAL PROJECT REPORT

1. CP 56-54
SERIAL NUMBER
2. Clinical Center
INSTITUTE OR DIVISION
3. Professional Service
LABORATORY, BRANCH, OR DEPARTMENT
4. Clinical Pathology
SECTION OR SERVICE
5. Clinical correlation of elevated serum phosphodiesterase.
PROJECT TITLE
6. A. C. Peacock
PRINCIPAL INVESTIGATOR
7. T. F. Dutcher
OTHER INVESTIGATOR

8. PROJECT DESCRIPTION

Dr. Peacock has recently devised a method for the assay of the enzyme phosphodiesterase in the blood and has done a large number of such assays on random blood samples both from the patient population of the hospital and from the professional and technical staff of the laboratories. He then noted several patients in whom this enzyme was elevated above the range of values obtained in the blood of the normal persons of the laboratory staff, and of most of the hospital patients. We are now in the process of carefully reviewing the case histories of those patients with elevated blood levels of this enzyme in an attempt to find a common denominator with which to explain the elevation. If such a correlation can be found, we may be able to utilize this test as a diagnostic aid in disease.

(For remaining data see Report Serial No. 13432-37.)

PART B.

No special budget for this project. See Clinical Pathology Department Main Report, Serial No. 13432-37.

PART C.

See Clinical Pathology Department, Serial No. 13432-37.

21. [Faint text]

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$$= -\frac{2}{x^3}$$

$$= -\frac{2}{x^3}$$

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